Mentalni poremećaji u djece i adolescenata s prekomjernom tjelesnom masom i debljinom: sustavni pregled i meta-analiza

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MENTAL DISORDERS AMONG CHILDREN AND ADOLESCENTS WITH OVERWEIGHT AND OBESITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Foreword

I want to thank my mentor, Professor Josip Milas, co-mentor, Assistant Professor Ivan Miškulin, Professor Maja Miškulin, Professor Marija Heffer, Professor Livija Puljak, and Professor Sanja Musić Milanović, who are all responsible for my professional and personal development.

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LIST OF ABBREVIATIONS

BMI	body mass index
CAPI	Computer Assisted Personal Interview
CBCL	Child Behavior Checklist
C-C	case-control
CDC	Centers for Disease Control and Prevention
COSI	Childhood Obesity Surveillance Initiative
CPMS	Childhood Psychopathology Measurement Schedule
C-S	cross-sectional
DIA-X	Diagnostic Interview
DPCL	Developmental Psychopathology Check List for Children
DSM	Diagnostic and Statistical Manual of Mental Disorders
F	female
GDP	Gross domestic product
GHQ-28	General Health Questionnaire
ICD	International Classification of Diseases
IOTF	International Obesity Task Force
KID-SCID	Structured Clinical Interview for DSM-IV Childhood Disorders
K-SADS-PL	Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version
M	male
M-CIDI	Munich Composite International Diagnostic Interview
MSQA	Multidimensional Sub-health Questionnaire of Adolescent
N	number
NA	not available
NR	not reported
OB	obesity
OR	odds ratio

OW	overweight
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSC-17	Pediatric Symptom Checklist
SCL-90R	Symptom Checklist-90-Revised instrument
SD	standard deviation
SDQ	Strengths and Difficulties Questionnaire
SSQ	Stem Item Screening Questionnaire
UW	underweight
WHO	World Health Organization
WMH-CIDI-A	World Mental Health Composite International Diagnostic Interview A
y	years

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1. Introduction

Childhood and adolescent overweight and obesity are currently among the most significant public health burdens worldwide. Prevalences exceeding even underweight arouse practitioners and scientists, thus implicating the need for strong and effective public health policies. In 2014 the worldwide age-standardized prevalence of obesity among children was around 5 %, while the global number of children and adolescents affected with obesity was estimated to be 110 million (1). The estimation in 2016 implicates that the prevalence of school-age children and adolescents affected with obesity in the last four decades had enlarged more than tenfold (2, 3). When taking overweight into account, numbers are even more alarming. Estimates in 2016 suggest that 40 million children younger than five years and more than 330 million children and adolescents aged 5–19 years had overweight or obesity (4). In 2010, The Childhood Obesity Surveillance Initiative (COSI) approximated that around 25 % of children living in Europe aged 6-9 years have overweight or obesity (5). In the United States, about one-third of children and adolescents are affected by overweight or obesity (6).

Although a plateau in the frequency of children and adolescents with overweight and obesity has recently appeared in some countries, especially the high-income ones, the prevalence remains very high in those countries (7). However, the rise in prevalence accelerated in parts of Asia and many low and middle-income countries, thus transitioning from the wealthy to the poor in low- and middle-income countries (5-9). In the last four to five decades, the obesity increase has been noticeable, especially in Pacific Island countries, some countries in Polynesia and Micronesia, the Middle East, North Africa, the Caribbean, and also in the United States (7, 10).

Over the past year, due to the COVID-19 pandemic and lockdowns, a significant rise in obesity prevalence appeared again, revoking the recent plateau in high-income countries. The global nutrition target of WHO of “no increase in childhood overweight by 2025” in the “Comprehensive Implementation Plan for Maternal, Infant and Young Child Nutrition” is seriously endangered (11). The UK records the most significant single-year increase in more than the last decade (12). In the course of the COVID-19 pandemic, the rate of BMI increase raised twofold among individuals aged 2-19 years in the USA compared to a prepandemic period (0.10 versus 0.05 kg/m2). The largest increase is present among younger school-aged children and persons previously affected with overweight or obesity (13). The long-term effect

of COVID-19 on worldwide trends of overweight and obesity among children is yet to be seen. However, currently, it seems that the consequences will be significant.

Positive trends and high prevalences of overweight and obesity indicate future major public health struggles since children and adolescents affected with obesity are most often individuals who will have excess weight as adults (6, 8). Around 50 % of children with high body mass index (BMI)-for-age become adolescents with high BMI, and approximately 80 % of them have high BMI in adulthood (14, 15).

The occurrence of many short-term and long-term consequences of obesity is especially alarming. The comorbidities of obesity start already in childhood and follow the individual into adulthood. Obesity affects almost every child's organ system (16). Children who have overweight or obesity are more likely to suffer from musculoskeletal pain and reduced physical function, which impacts their fitness, strength, and motor skills (4, 17). Overweight or obesity in childhood is a significant risk factor for asthma and wheeze (18), liver disease (19, 20), high blood pressure (21), diastolic dysfunction (22), type 2 diabetes, dyslipidemia, lower vitamin D level (23), dental problems (24, 25), and high intraocular pressure (21). Obesity causes low-grade systemic inflammation and impairs immunity (26, 27). It can decrease the immunogenicity of vaccines such as hepatitis B and increase the risk of infections by Mycobacterium tuberculosis, H1N1 influenza, and COVID-19 (26, 28). Overweight and obesity during childhood increase the risk of some cancers in adulthood (29).

Obesity also affects the psychosocial functioning of children and causes a great variety of psychological and psychiatric conditions. The root of the mental health disorders is stigmatization, discrimination, teasing, and sometimes even bullying of children affected with obesity, which adds to dissatisfaction and negative body image (30-32). The stigmatization of obesity may come from peers, parents, educators, or the media. It is manifested in negative stereotypes, victimization, and social marginalization, which can cause psychological problems in children even when being overweight (14, 33-36). As a result, extreme weight control behaviors and eating disorders can occur, as well as low self-esteem, depressive symptoms, anxiety, conduct disorder, and an overall decline in quality of life (31, 37-40). Likewise, clinically significant forms of depression, suicidality, and severe eating disorders may manifest in this population, although less frequently (41).

The burden of childhood and adolescent mental health disorders is significant as the burden of obesity. The worldwide prevalence of mental disorders among children and adolescents is

estimated to be 13.4 % (CI 95 % 11.3-15.9) (42). Although overdiagnosis and overtreatment are present to some extent, there is also evidence that mental health disorders are considerably underdiagnosed and undertreated (42-44). Mental disorders impair the quality of life and can cause crime, self-harming, problems in school, social functioning problems, suicide attempts, or realization of suicide (45, 46). Mental disorders damage individuals, but they also significantly contribute to the global burden of disease, increase disability-adjusted life years, and cause high costs to healthcare systems (47).

In the literature, estimates of the prevalence of mental disorders among children and adolescents with overweight and obesity vary between 10 % (48) and 50 % (49), even 60 % or 70 % (50) when specific subgroups are taken into account. There is no estimate of the worldwide prevalence of mental disorders among children and adolescents affected with overweight and obesity. However, understanding the magnitude is crucial to inform public health providers, for resource allocation, service, education, and research planning (42). The meta-analytic approach provides a more accurate estimate of disease frequency, as well as geographical coverage of the research and identification of sources of prevalence estimates variability. Understanding samples characteristics and studies' methodological characteristics contribute to the interpretation of etiology and planning the design of subsequent studies (51). It is essential to delineate the need for new studies and consider guidelines for their design to avoid unfruitful research and unnecessary expenses. Systematic reviews and meta-analyses are very valuable from this point of view, and they comprehensively analyze our current insights and reveal the gaps in the knowledge. The meta-analytic approach is also an effective and inexpensive method of analyzing cross-cultural variation and the cross-temporal stability of estimates. Estimating the prevalence would appraise underdiagnosis and underestimation of mental disorders as obesity comorbidity and assist endeavors focused on identifying subjects affected with them.

There are many narrative reviews summarizing the association between obesity and mental disorders. However, they have not used a systematic methodology nor performed a meta-analysis. The conclusions regarding the strength, direction and moderators in the association between obesity and mental disorders are very inconsistent, to the extent that some studies are even seriously questioning the established belief that obesity endangers mental well-being (52-54). However, this rather indicates high heterogeneity in the relationship between these illnesses (55, 56).

There are several causes of inconsistent research conclusions. Firstly, while studying population-based samples, some authors have not found an association between obesity and mental disorders (54, 57, 58). Many other authors focused on clinical samples of individuals with obesity and supported the idea that mental disorders are mainly comorbidity affecting individuals with severe obesity who require obesity treatment (34, 52, 59-61). Although existing studies enhance higher rates of mental disorders in clinical samples, community samples of children and adolescents also bear a considerable amount of psychosocial and psychiatric burden (62). Analysis of research conducted within community settings would provide knowledge about potential interventions at a community level, strengthen prevention, and inform clinical practice.

Gender seems to be a significant moderator, and various studies made different conclusions regarding its impact on psychopathology development. Gouveia et al. detected no difference between boys and girls affected with obesity regarding mental disorders while studying children and adolescents aged 8-18 years (63). However, many other studies detected gender, alongside age and ethnicity, as important moderators of the association between mental disorders and obesity (34, 64).

Some specific occurrences impact current conclusions. One of them is body image dissatisfaction, which is considered a significant moderator of the association between obesity and psychopathology partly due to its impact on self-esteem (34, 54, 65). However, body image dissatisfaction depends on other factors like age, gender, puberty, community setting, or body weight perception (63, 66-68), resulting in contradictory findings when diverse samples are analyzed, thus introducing undesirable incomprehension.

Inconsistent methodology of studies originates not only from diverse samples but also from various psychiatric tools and assessments. There are many screening tools used in this field that can collect information from different informants, i.e., children, adolescents, parents, or teachers. Considering the informant, reports of psychopathology among youth can vary (69).

Association between obesity and mental disorders is actually only partially analyzed. Various studies focused on different but only limited sets of disorders. Among them, depression has gained a disproportionate amount of attention, yielding few meta-analyses (31, 70-72). Anxiety and eating disorders are also comprehensively studied (73, 74), and as a result, reviews on this topic usually mention only these disorders. However, a recent meta-analysis of the association between obesity and conduct disorder shed light on other noteworthy but less studied disorders

(37). Studying individual disorders again introduces a large amount of inconsistency due to heterogeneity between subgroups (75). There are contradictory findings concerning every mental disorder and every subgroup analyzed in the context of obesity (76). This field would obviously benefit from an inductive approach that would at least partially resolve existing confusion and discrepancies before working out comprehensive research on the specific disorders to additionally explain such heterogeneous associations as the one between obesity and mental disorders is.

Evidence is scarce considering the direction of association between obesity and mental disorders. There are not many reviews that focus on this topic. Researchers state that there is evidence for mutual causality (77). However, Rankin et al. (33) consider the possibility that obesity and mental disorders are the repercussions of common risk factors existing among susceptible individuals. Carsley et al. (78) found an association between the weight status of preschool children and more frequent mental health service utilization in later childhood, which was strongest among girls. Small and Aplasca (64) reviewed the time interval which is different between specific age groups and wrote that increased body weight in early childhood affects mental well-being sometime later, after puberty onset. In contrast, increased weight among adolescents can affect mental health already after two years. However, it seems that this association is also strongly influenced by age, gender, and even cultural background, which is supported by recent longitudinal and cross-cultural studies from Germany and China (79). Many questions remain unanswered regarding mental disorders incidence among children and adolescents affected with excess weight, however, attempts to answer them are still too weak in the scientific community, although the obesity trend announces a substantial threat in terms of the comorbidities which arise from it. Analysis of the direction of association also provides knowledge about etiology. Precisely analyzing the burden of obesity consequences is one of the public health priorities.

Body image is one of the essential concerns in youth lives. As already mentioned, body dissatisfaction is one of the mediators between obesity and mental disorders. There is evidence that it concerns not only girls but also boys, and it can vary depending on society's culture. Also, there is a strong association between weight stigma and mental health (68, 80-82). Some critics weigh current public health interventions in terms of contribution to the stigmatization of obesity and body dissatisfaction enhancement due to their impact on weight preoccupation, focus on weight loss, and emphasis on individual responsibility (80, 83, 84). As such, public health programs themselves can act as risk factors for extreme dieting and mental disorders,

while in terms of increasing healthier behavior and reducing obesity, they seem to be relatively ineffective (83, 85). Since obesity trends are positive and associated with countries' economic development, public health programs also strengthen at a similar pace. Analysis of mental disorders dynamics in the population of children and adolescents affected with overweight and obesity and their association with economic development indicators can inform public health authorities about the potentially detrimental effects of antiobesity campaigns.

When associated with obesity, mental disorders can greatly affect a child's motivation and the ability for weight reduction due to weak treatment compliance and adherence (34, 86). The association between these conditions is also noteworthy since certain medications induce weight gain, like antipsychotics and antidepressants, which have been widely prescribed even in the pediatric population since the 1990s (87-89). A comprehensive analysis of the association between obesity and mental disorders would benefit clinical practice regarding the treatment of mental disorders.

2. Hypothesis

Children and adolescents with overweight and obesity have a higher risk of mental disorders than those with normal weight.

The positive time trend of prevalence and risk of mental disorders among children and adolescents with overweight and obesity exists.

There is a correlation between the prevalence and risk of mental disorders among children and adolescents with overweight and obesity and economic indicators of the countries from which they originate.

3. Study aims

The study aims were:

1. To calculate the worldwide prevalence of mental disorders among children and adolescents affected with overweight and obesity
2. To evaluate the cross-sectional and longitudinal association between mental disorders and overweight and obesity among children and adolescents
3. To assess differences between children and adolescents, boys and girls, and overweight and obesity
4. To evaluate the time trend of mental disorders among children and adolescents having overweight and obesity
5. To evaluate the association between mental disorders risk and economic indicators of countries from which study participants originate
6. To quantitatively and qualitatively evaluate studies about the prevalence and association between mental disorders and overweight and obesity among children and adolescents
7. To estimate heterogeneity and sources of heterogeneity among studies
8. To identify the need for new studies and their characteristics.

4. Materials and methods

4.1. Study design

The study design is a systematic literature review. It is designed and reported according to the guidelines for reporting the meta-analyses of observational studies in epidemiology (90) and according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (91). The study was registered in the PROSPERO database (No. CRD42020216523), and the project titled “Mental disorders among children and adolescents with overweight/obesity: a systematic review and meta-analysis” was established on Open Science Framework, where all materials will be publicly available after study publishment to achieve complete transparency and public availability,

4.2. Material

The study material is published research and unpublished ("grey") literature. The material was collected through a systematic literature review of several online databases in February 2019. Also, the data from the World Bank database was used. Information about the Gross domestic product (GDP) of countries from which participants of included studies originate is collected. GDP for a particular country is extrapolated for the year the study was conducted.

4.3. Methods

4.3.1. Data sources and study selection

The research was conducted in MEDLINE via OVID, PsycINFO, PsycARTICLES, and CINAHL with Full Text via EBSCOhost, Web of Science databases (Science Citation Index Expanded, Social Sciences Citation Index, Arts & Humanities Citation Index, Book Citation Index– Science, Book Citation Index– Social Sciences & Humanities, Emerging Sources Citation Index, Current Contents Connect, Data Citation Index, KCI-Korean Journal Database, Russian Science Citation Index, SciELO Citation Index) via Web of Science interface, Google Scholar (first 1000 results), and ProQuest Dissertations & Theses Global without language and

time limits. The authors developed the search strategy, and the librarian was asked to review it. The articles published from 1935 to January 7, 2019, were eligible for search.

Two authors independently searched databases according to a priorly defined strategy. The search results were exported to EndNote software (EndNote, Clarivate Analytics, Philadelphia, PA, USA) and deduplicated. Two authors independently screened bibliographic records retrieved by search (titles, abstracts) and then screened potentially eligible full-text manuscripts. The reference lists of eligible manuscripts and identified reviews related to the topic were also screened to detect additional relevant studies (92). Finally, recognized major cohort studies concerning the issue from several countries were additionally manually searched. Discrepancies were resolved via discussion or consultation with a third author.

4.3.2. Search strategy

The search strategy for MEDLINE was designed as follows:

1 exp Pediatric Obesity/

2 (p?ediatric or youth$ or child$ or adolescen$ or student? or pupil? or kid? or juvenile? or teen$).tw.

3 (obes$ or overweight$ or BMI or body mass index or fat or excess weight or adipos$).tw.

4 2 and 3

5 1 or 4

6 exp Mental Disorders/

7 (mental$2 or psychiatri$ or psycholog$ or psychopatholog$).tw.

8 6 or 7

9 5 and 8.

The search strategy for EBSCOhost was designed as follows:

p?ediatric or youth? or child* or adolescen* or student? or pupil? or kid? or juvenile? or teen*

AND

obes* or overweight* or BMI or "body mass index" or fat or "excess weight" or adipos*

AND

mental* or psychiatri* or psycholog* or psychopatholog*

AND

(MH "Pediatric Obesity")

AND

(MH "Mental Disorder").

The search strategy for Web of Science was designed as follows:

TS=(p$ediatric or youth* or child* or adolescen* or student* or pupil* or kid$ or juvenile* or teen*)

AND

TS=(obes* or overweight or BMI or "body mass index" or fat or "excess weight" or adipos*)

AND

TS=(mental* or psychiatri* or psycholog* or psychopatholog*).

4.3.3. Review inclusion criteria

Cross-sectional, case-control or longitudinal studies providing data on prevalence or risk of mental disorders among children and adolescents with overweight or obesity from any country were eligible for inclusion. Studies from which prevalence or risk could be calculated were also eligible for inclusion, as well as randomized clinical trials if they provided data on prevalence or risk before trial commencement.

The criterion for inclusion was that participants were aged 2 to 25 years (93), that nutritional status was indicated as a BMI-for-age, whether it was obtained from measured or reported body weight and height and categorized according to any growth reference. Regarding mental disorders, the criterion for inclusion was the use of validated questionnaires for mental disorders screening or diagnosis obtained through standardized diagnostic procedures, clinically or using validated tests and according to the International Statistical Classification of Diseases and Related Health Problems (ICD-8, ICD-9, ICD-10) or Diagnostic and Statistical Manual of Mental Disorders (DSM-III, DSM-III-R, DSM-IV, or DSM-V) diagnostic criteria.

Studies conducted only on participants with morbid obesity were not included to avoid bias. The meta-analyses aimed to obtain results representative of all degrees of excess weight. Studies conducted on clinical samples, college students, or some specific groups such as specific ethnic samples, athletes, or dancers were also excluded. The exclusion criterion was data obtained from healthcare insurers or physician´s databases to avoid bias (94).

Studies using anthropometric indicators other than BMI-for-age, such as the waist or hip circumference, waist-to-height ratio, waist-to-hip ratio, or skinfold thickness, were not eligible for inclusion. If duplicate studies were detected, the one that contained more data or longer follow-up was included. Studies assessing only one gender were included only in the subgroup analysis. Case reports, editorials, comments, letters, conference abstracts, conference proceedings, and other irrelevant studies were excluded.

4.3.4. Data extraction and coding decisions

Data extractions were performed in duplicate using a predesigned form for data extraction, and disagreements were resolved by discussion or another author. The authors of eligible studies were contacted in cases of missing information. The data controlled for confounders was prioritized and extracted from studies and included in the meta-analyses in the cases where it was available. Studies in languages other than English and German were translated using Google Translate, as it proved to be an accurate tool for data extraction from non-English articles (95). Any uncertainties were planned to be resolved through contact with native speakers of languages other than English; however, there were no uncertainties.

When studies provided multiple models representing different obesity trajectories, only models representing constant obesity (or obesity at both time points of evaluation) were included and compared to constant normal weight. When longitudinal studies provided multiple models for children affected and non-affected with mental disorders in the first time point of evaluation, then only the model representing children without mental disorders at the beginning of the study was included.

The data about the first author, study year, country, area, methodological design, sample size and characteristics, subgroups characteristics and sizes, data obtainment methods, questionnaires and their characteristics, informant, and effect sizes were extracted.

The age range was coded in two levels: childhood=2-9 and adolescence=10-24. The study area and sample representativeness were coded as follows: small-medium area – probably representative/not representative<500 000 inhabitants, large area – probably representative/not representative>500 000 inhabitants. The study location was coded in seven levels: Europe, Asia, Africa, North America, South America and Caribbean, Middle East, and Oceania.

4.3.5. Assessment of the quality and publication bias

Two authors independently performed the quality assessment according to the Joanna Briggs Institute tools (96) for critical appraisal of analytical cross-sectional, case-control, prevalence, and cohort studies without blinding. Studies were assessed using the checklist for the data that was extracted, and consequently, if the study is longitudinal but provides cross-sectional data that is eligible for inclusion in the meta-analysis, then the study was appraised as a cross-sectional study. Disagreements were resolved by discussion or by the involvement of the third author.

As a quality indicator of the study, an average quality was calculated for each study. It represents a proportion of positive answers of the total items in the critical appraisal tool used. This was performed since different types of studies were included in the meta-analysis, and they require the use of various tools for critical appraisal with a differing number of items. So to represent a total quality of evidence in each meta-analysis, the relative indicators had to be used.

The funnel plot was visually inspected, and Orwin's Fail-safe N and Egger's test were calculated to evaluate the publication bias. Duvall and Tweedie trim-and-fill procedures were planned to be used if publication bias was found (97-102).

4.4. Data synthesis and statistical analysis

Meta-analysis was conducted using ORs as effect sizes. Since some studies provided regression coefficients, correlation coefficients had to be coded according to Peterson and Brown (103). The correlation coefficients were also calculated from the mean and standard deviation (SD) values of the study groups compared in some studies. ORs were further derived from correlation

coefficients using the Comprehensive Meta-analysis software package (Biostat; http://www.meta-analysis.com/index.php).

Data were analyzed using the Comprehensive Meta-analysis. A random-effects model was used to analyze the data since a common effect size among studies is not assumed (101). Studies were units of analysis in the main meta-analyses, contrastly, subgroups within studies were units of analysis in the subgroup analyses since we expect a correlation between subgroups due to the common control groups or estimates obtained from the same participants in the different time points (101). Independent studies conducted on the same datasets were combined in the main meta-analysis.

I^2 and Cochran's Q-statistic were used to evaluate the statistical heterogeneity among the studies. Cochran's Q-statistic was considered significant based on $p<0.10$ (104-106). The I^2 statistic was calculated and interpreted as follows to quantify heterogeneity: I^2=25 % - 50 % was considered modest heterogeneity, I^2>50 % was regarded as large heterogeneity, and I^2>75 % was considered considerable heterogeneity (97, 104, 107).

The moderating effects of gender, age category (childhood or adolescence), weight category (overweight, obesity), type of study sample, study location, study area and sample representativeness, method of weight and height obtainment (measured or reported), type of child growth chart, psychiatric instruments, study informants, transforming the effect sizes (transformed or untransformed), borderline or abnormal cut-offs for psychiatric tests, and inclusion of participants with underweight in the control group were assessed using the mixed-effects model (97). It was planned to analyze the moderating effect of the diagnostic procedure (clinical interview using a validated diagnostic assessment measure, self-report questionnaire, or symptomatology rating scale); however, there were not enough studies in each group to conduct this analysis.

The mediating effects of the number of controlled confounders in the studies, mean age of participants, and economic indicators were analyzed by meta-regression (108). It was planned to use meta-regression to examine the mediating effect of the estimated Cronbach´s α of psychiatric tools used in the studies; however, there were too few studies that calculated and reported Cronbach´s α of psychiatric tools used. A cumulative meta-analysis was used to assess the time trend of effect sizes (97). A sensitivity analysis was conducted to evaluate the outcome of effect size transformation. Studies in which there was evidence of multicollinearity in resulting regression coefficients were excluded from meta-analysis due to the inability to

convert such regression coefficients into OR. Studies comprising not normally distributed data were also excluded from the meta-analysis (97, 103, 108, 109).

In some studies, mean age and SD were presented separately for the two study groups. The mean and SD for the total sample was calculated according to formulae:

$$M=(N1M1+N2M2)/(N1 + N2)$$

$$SD=\{(N1-1)SD1^2+(N2–1)SD2^2\ [(N1N2/N1+N2)(M1^2+M2^2–2M1M2)]\}/(N1+N2–1)$$

Where M is the mean, SD is the standard deviation, and N is the number of participants.

Comprehensive Meta-Analysis software package version 3, R: A language and environment for statistical computing (R Core Team (2020), R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/) and Microsoft Office Excel 365 were used for statistical analysis. Statistical significance was defined at $p<0.05$.

5. Results

5.1. Systematic review results

The systematic review yielded 15 448 abstracts after deduplication of 26 968 search results, from which 117 studies were selected for full-text analysis. Additional three studies were identified by screening the review articles, searching notable cohort studies, and screening the reference lists of the included studies. Between authors, there was agreement considering the eligibility of 68/120 studies, 49 discrepancies were resolved by discussion, and the involvement of the third author resolved the remaining 3. Discrepancies majorly originated in the unclear statistical analysis of studies or unclear descriptions of the sample.

Forty-six studies met the inclusion criteria. The included studies were published from 1999 to 2019 and conducted between 1980 and 2018 in 26 countries. Some of the studies were conducted on the same samples; however, they were all included in analyses since they provided additional data which could be included in subgroup analyses (110, 111). 2 studies were written in the Portuguese language, 1 in Korean, 1 in German, 1 in Spanish, and the rest in the English language. Figure 5.1. presents the search results in the PRISMA flow diagram and the main reasons for exclusion after the full-text review. There was an attempt to reach 11 corresponding authors via e-mail or ResearchGate in the cases where the e-mail address was invalid, to obtain additional data which would make the study eligible for inclusion, however, not any of the attempts for contact was fruitful. Five studies were excluded during the data extraction when it was recognized that the outcomes were ineligible.

Throughout the data extraction, corresponding authors were again contacted regarding the missing data. Out of 5 attempts, one could not be performed due to an invalid e-mail address and authors not having ResearchGate, two did not answer, and two corresponding authors answered and provided the data.

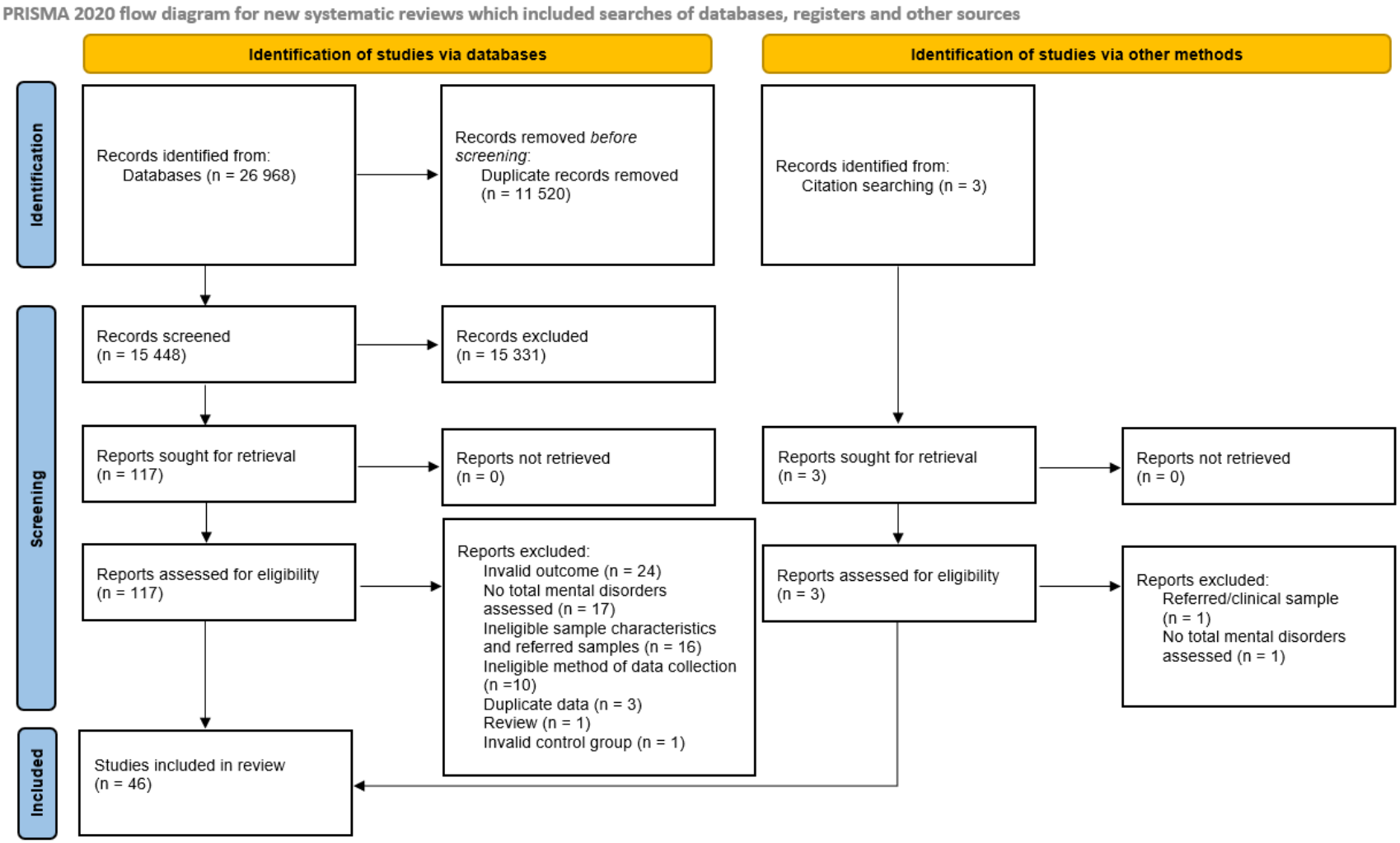

Figure 5.1. PRISMA 2020 flow diagram (91). n, number.

5.2. Worldwide prevalence of mental disorders among children and adolescents with overweight and obesity

A total of 17 studies (57, 112-128) were included in the meta-analyses to estimate the prevalence of mental disorders among children and adolescents with overweight and obesity. They were all conducted between 1995 and 2016 and originated from 12 different countries. The characteristics of the studies included in the analyses are presented in Table 5.1.

Ten studies (114, 115, 117, 120-126) comprising 18 separate effect sizes and 9 278 participants were included in the random-effects meta-analysis to obtain the prevalence of mental disorders among children and adolescents with overweight and obesity of 23.80 % (95 % CI, 17.10-32.10; z=-5.93, p<0.01) was obtained. A forest plot is shown in Figure 5.2. The meta-analysis results indicated a large degree of variance in the study effect sizes (Q=326.39; df=9; p<0.01; I^2=96.30). The distribution of the studies by country is shown in Figure 5.3.

A funnel plot representing the possibility of publication bias for the prevalence of mental disorders among children and adolescents with overweight and obesity is shown in Figure 5.4. The funnel plot seemed asymmetric by visual inspection. Duvall and Tweedie trim-and-fill procedure suggested inputting two studies on the right side of the mean to obtain an unbiased estimate of the prevalence of 27.47 % (95 % CI, 18.20-39.22). The Egger's linear regression method intercept of 4.20 (95 % CI, -2.53-10.92) with a non-significant one-tailed p-value of 0.09 indicated no evidence for publication bias.

A meta-regression was planned to explore the association between the prevalence estimates and the mean age of the study samples; however, there was an inadequate number of studies.

Table 5.1. Characteristics of the studies included in the prevalence analyses

First author	Study year	Study country	Study design	Sample (representa-tive)	Sample size	Subgroups according to weight	Age range (≥10 AD)	Mean age	Growth reference	BMI measured or reported	Psychiatric tool	Informant	Effect size groups
Aditya	2015	Indonesia	C-S	Community	103	OB	6 to 12	NA	CDC	Measured	PSC-17	Parent	Total
Buddeberg-Fischer	NA	Switzerland	C-S	Community	136	OW+OB	15 to 20	17,4	Must, Dallal, Dietz 1991	Measured	SSQ, DIA-X	Self-report	F
Canals-Sans	NA	Spain	C-S	Community	485	OW and OB	6,5 to 10	8,54	IOTF	Measured	CBCL/6-18	Parent	Total, OW, OB - borderline included; Total, OW, OB - only clinical
Cataneo	2002	Brazil	C-S	Covenient	53	OW+OB	10 to 12	NA	Must, Dallal, Dietz 1991	Not reported	Rutter scale	Parent or guardian	Total
Doaei	NA	Iran	C-C	Community	160	OW+OB	13 to 18	15	WHO	Measured	GHQ-28	Self-report	F
Hammar	2007 - 2008	Sweden	C-S	Community	573	OW+OB	12 y	NA	IOTF	School-reported	CBCL/4-18	Parent	Total CBCL, Total SDQ, F OW, F OB

NR, not reported; AD, adolescents; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Taskforce; WHO, World Health Organization; M-CIDI, Munich Composite International Diagnostic Interview; SDQ, Strengths and Difficulties Questionnaire; OR, odds ratio; SD, standard deviation; M, male; F, female; OW, overweight; OB, obese; y, years old; BMI, body mass index; NA, not available; CBCL, Child Behavior Checklist; MSQA, Multidimensional Sub-health Questionnaire of Adolescent; C-S, cross-sectional; C-C, case-control; PSC-17, Pediatric Symptom Checklist; SSQ, Stem Item Screening Questionnaire; DIA-X, Diagnostic Interview; GHQ-28, General Health Questionnaire; CPMS, Childhood Psychopathology Measurement Schedule; CAPI, Computer Assisted Personal Interview; SCL-90R, Symptom Checklist-90-Revised instrument; K-SADS-PL, Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version; KID-SCID, Structured Clinical Interview for DSM-IV Childhood Disorders; OW+OB, overweight and obesity are analysed together; OW and OB, overweight and obesity are examined as separate subgroups, results for both subgroups are provided;

Table 5.1. Characteristics of the studies included in the prevalence analyses continued

First author	Study year	Study country	Study design	Sample (representa-tive)	Sample size	Subgroups according to weight	Age range (≥10 AD)	Mean age	Growth reference	BMI measured or reported	Psychiatric tool	Informant	Effect size groups
Hestetun	2010	Norway	C-S	Community	744	OW+OB	12 to 13	NA	IOTF	Measured	SDQ	Parent	Total
Kumar Shenoy	NA	India	C-S	Community	1263	OB	NR	11,6	CDC	Measured	CPMS	Parent	Total, M, F
Lamertz	1995	Germany	C-S	Community	174	OB	14 to 24	NA	IOTF	Self-reported	CAPI, M-CIDI, SCL-90R	Self-report	M 14-17 y, F 14-17 y, M 18-24 y, F 18-24 y
Rodríguez-Hernández	2006	Spain	C-S	Nationally	5271	OW and OB	4 to 15	NA	IOTF	Parent-reported	SDQ	Parent	OW, OB
Sepulveda	2012-2016	Spain	C-S	Community	170	OW+OB	8 to 12	10,03	National Spanish	Measured	K-SADS-PL	Self-report, parent checked	M, F
Sepulveda	2012-2016	Spain	C-C	Community	100	OB	8 to 12	10	IOTF	Measured	K-SADS-PL	Self-report	Total

NR, not reported; AD, adolescents; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Taskforce; WHO, World Health Organization; M-CIDI, Munich Composite International Diagnostic Interview; SDQ, Strengths and Difficulties Questionnaire; OR, odds ratio; SD, standard deviation; M, male; F, female; OW, overweight; OB, obese; y, years old; BMI, body mass index; NA, not available; CBCL, Child Behavior Checklist; MSQA, Multidimensional Sub-health Questionnaire of Adolescent; C-S, cross-sectional; C-C, case-control; PSC-17, Pediatric Symptom Checklist; SSQ, Stem Item Screening Questionnaire; DIA-X, Diagnostic Interview; GHQ-28, General Health Questionnaire; CPMS, Childhood Psychopathology Measurement Schedule; CAPI, Computer Assisted Personal Interview; SCL-90R, Symptom Checklist-90-Revised instrument; K-SADS-PL, Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version; KID-SCID, Structured Clinical Interview for DSM-IV Childhood Disorders; OW+OB, overweight and obesity are analysed together; OW and OB, overweight and obesity are examined as separate subgroups, results for both subgroups are provided;

Table 5.1. Characteristics of the studies included in the prevalence analyses continued

First author	Study year	Study country	Study design	Sample (representa-tive)	Sample size	Subgroups according to weight	Age range (≥10 AD)	Mean age	Growth reference	BMI measured or reported	Psychiatric tool	Informant	Effect size groups
Seyedamini	2008	Iran	C-S	Community	300	OW and OB	7 to 12	9,01	CDC	Measured	CBCL	Parent	F OW, F OB
Turer	2005-2009	USA	C-S	Nationally	17224	OW and OB	10 to 17	13,57	CDC	Parent-reported	Columbia Impairment Scale	Parent	OW, OB
Vanvlierberghe	NA	Belgium	C-S	Convenient	73	OW+OB	8 to 18	13,74	CDC	Measured	KID-SCID	Self-report	Total
Wu	2015-2016	China	C-S	Community	8457	OW and OB	13 to 18	15,52	WHO	Measured	MSQA	Self-report	Total OW, Total OB, M OW, M OB, F OW, F OB
Harahap	2009	Indonesia	C-S	Convenient	94	OB	6 to 12	8,9	NR	NR	CBCL	Parent	Total CBCL, M CBCL, F CBCL, Total PSC, M PSC, F PSC
Krause	2003-2006	Germany	C-S	Nationally	216	OW and OB	11 to 17	NA	German national	Measured	SDQ	Self-report	11-13 y: Total OW, Total OB, M OW, M OB, F OW, F OB; 14-17 y: Total OW, Total OB, M OW, M OB, F OW, F OB;

NR, not reported; AD, adolescents; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Taskforce; WHO, World Health Organization; M-CIDI, Munich Composite International Diagnostic Interview; SDQ, Strengths and Difficulties Questionnaire; OR, odds ratio; SD, standard deviation; M, male; F, female; OW, overweight; OB, obese; y, years old; BMI, body mass index; NA, not available; CBCL, Child Behavior Checklist; MSQA, Multidimensional Sub-health Questionnaire of Adolescent; C-S, cross-sectional; C-C, case-control; PSC-17, Pediatric Symptom Checklist; SSQ, Stem Item Screening Questionnaire; DIA-X, Diagnostic Interview; GHQ-28, General Health Questionnaire; CPMS, Childhood Psychopathology Measurement Schedule; CAPI, Computer Assisted Personal Interview; SCL-90R, Symptom Checklist-90-Revised instrument; K-SADS-PL, Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version; KID-SCID, Structured Clinical Interview for DSM-IV Childhood Disorders; OW+OB, overweight and obesity are analysed together; OW and OB, overweight and obesity are examined as separate subgroups, results for both subgroups are provided;

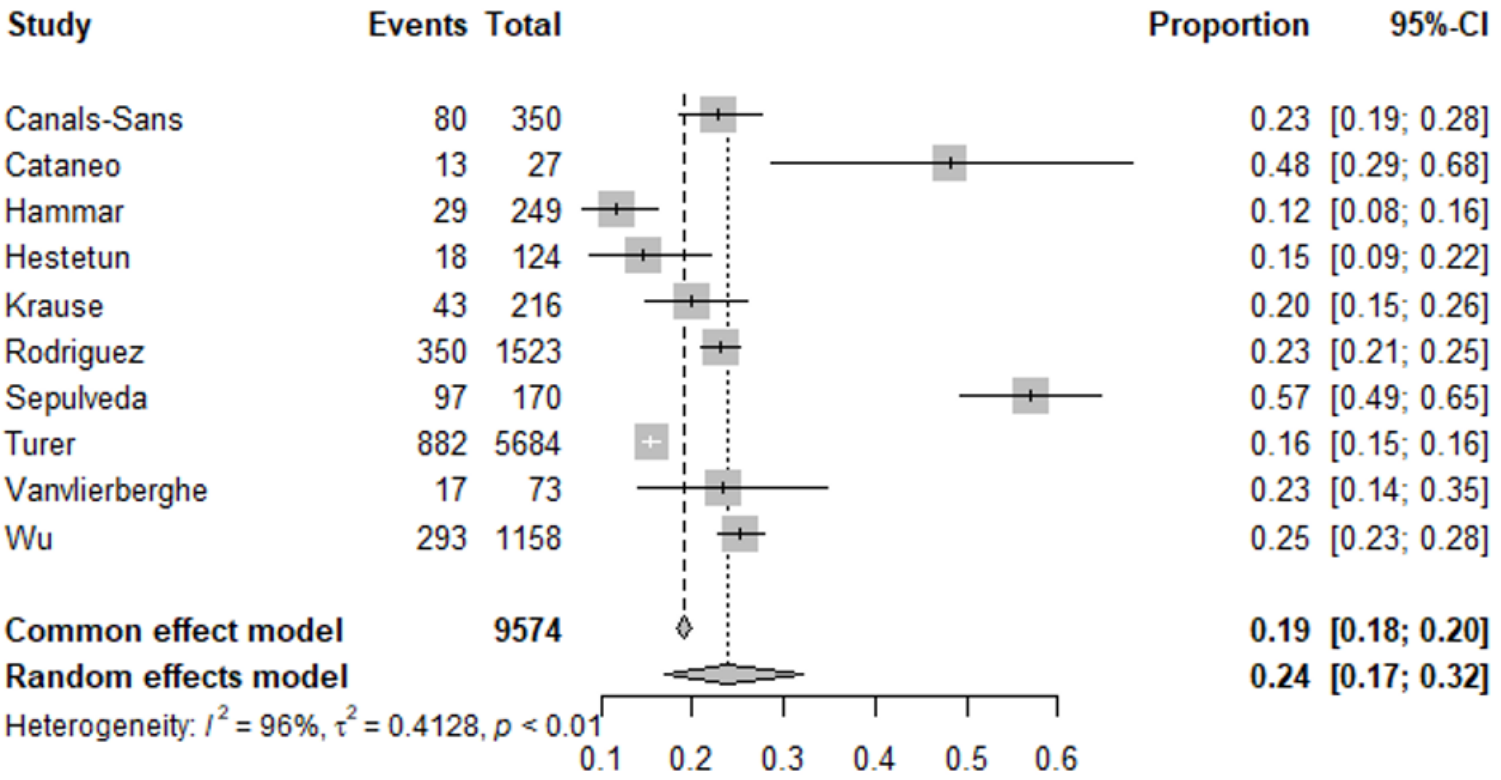

Figure 5.2. Forest plot for the prevalence of mental disorders among children and adolescents with overweight and obesity. CI, confidence interval.

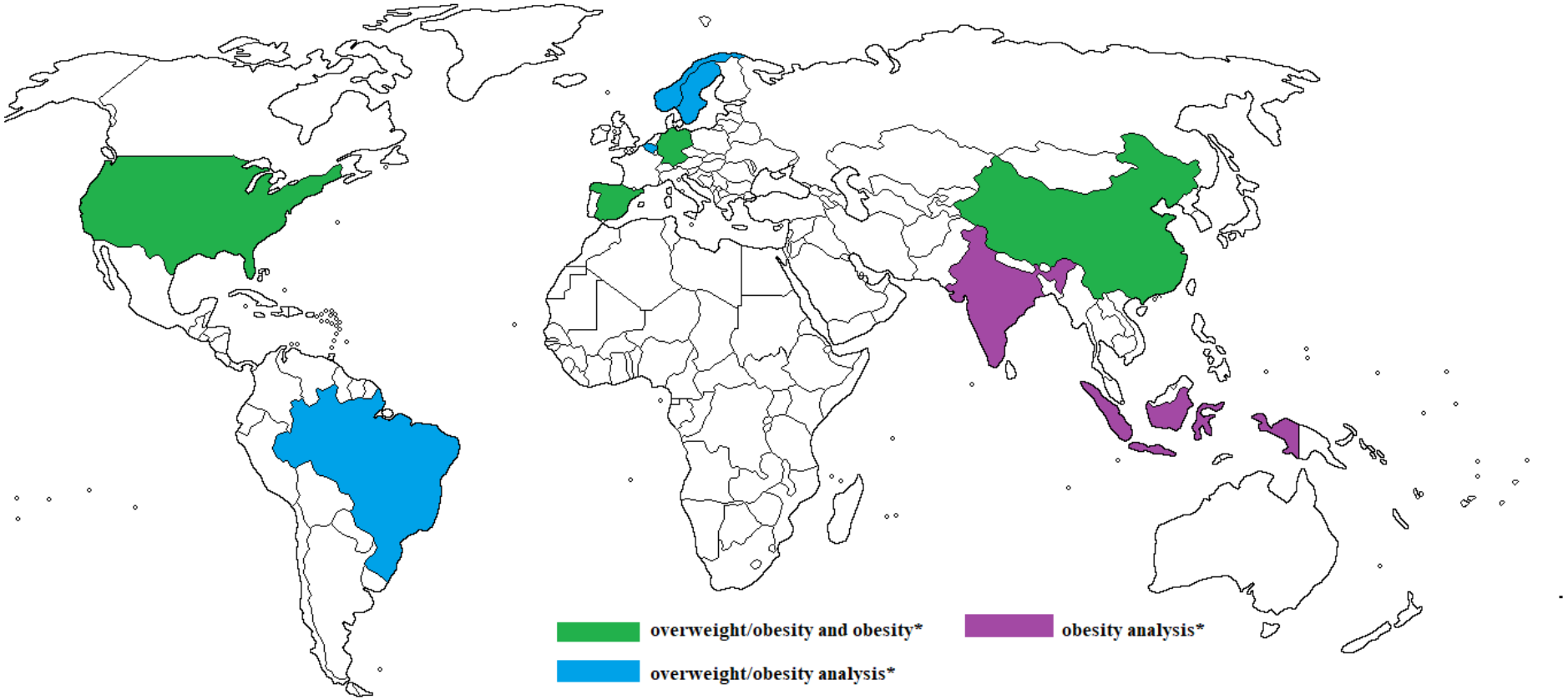

Figure 5.3. Distribution of the studies included in the prevalence analyses by country. *green countries are included in both analyses, overweight/obesity, and only obesity, blue and purple countries are included in a single analysis overweight/obesity or obesity. The territories on the map may not correspond to the actual borders of the countries. Downloaded with permission from: https://hr.wikipedia.org/wiki/Datoteka:Blank_map_political_world_territories.png. Author: Roy Nick Norse.

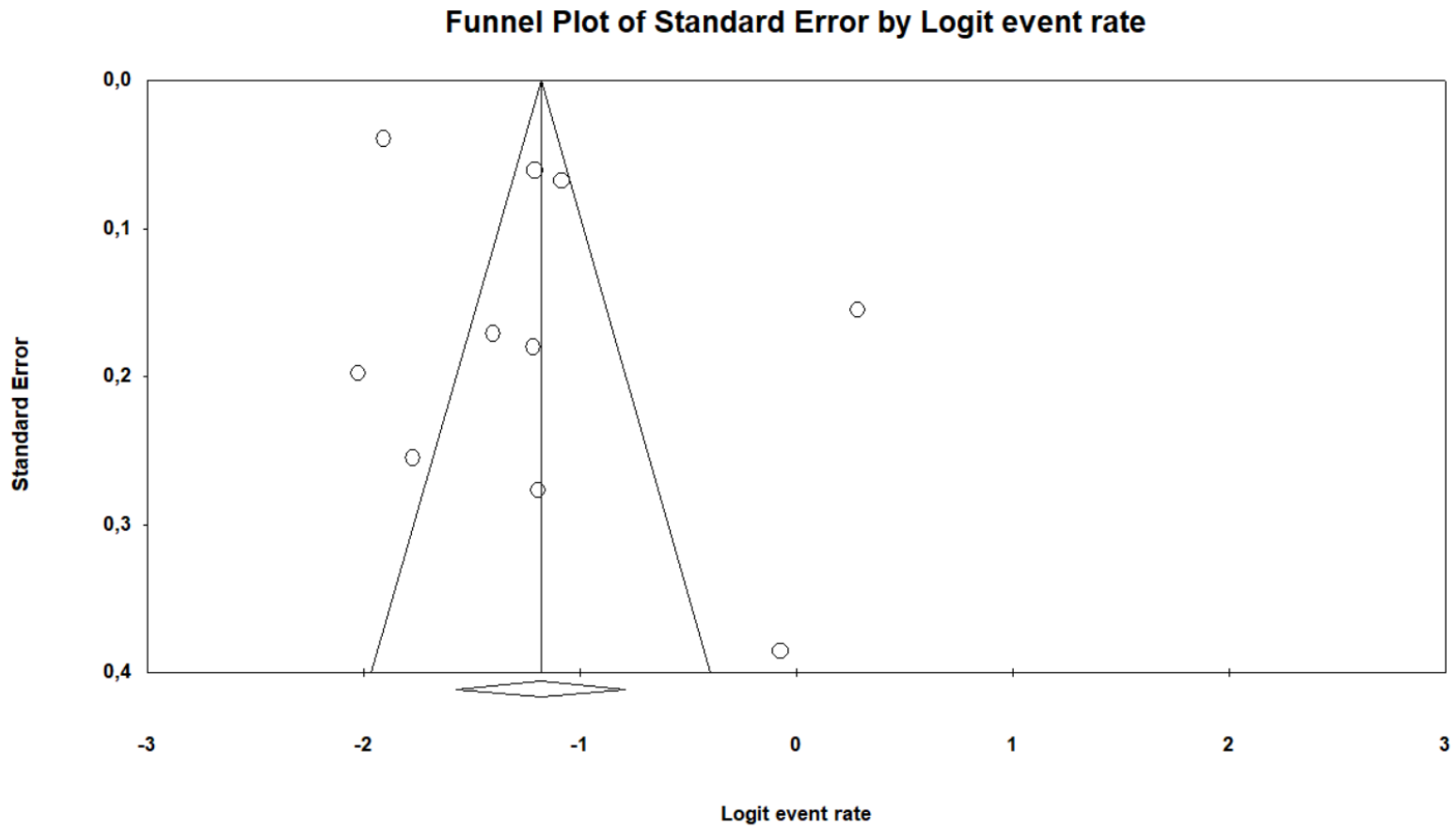

Figure 5.4. Funnel plot for the prevalence of mental disorders among children and adolescents with overweight and obesity

Additional studies were included in the moderator analysis, and those were studies that comprised only single-gender or only individuals with obesity. Overall and subgroup analyses of the prevalence are shown in Table 5.2.

Moderator analysis of 10 studies indicated a significant difference (Q=8.26; df=1; p<0.01) in the prevalence between the samples consisting of participants with overweight or obesity. There was also a significant difference (Q=6.07; df=1; p<0.05) in the prevalence between the children and adolescents samples.

There was no difference in the prevalence between the samples according to gender (Q=0.03; df=1; p=0.86). According to the sample coding, there was no significant difference in the prevalence between the studies (Q=4.00; df=2; p=0.14). There was no difference in the prevalence between the studies in which participants reported weight and height and those where participants were measured (Q=0; df=1; p=0.99), in the prevalence between the studies in which the informant was a parent and those where self-report of the psychiatric instrument was used (Q=3.16; df=1; p=0.08) or in the prevalence between the studies including only clinically significant psychiatric test results and those including borderline results (Q=2.59; df=1; p=0.11).

Table 5.2. Overall and subgroup analyses of the prevalence of mental disorders among children and adolescents with overweight and obesity

Type of analysis	N of studies (subgroups)	Prevalence	95 % CI	Heterogeneity
Prevalence among children and adolescents with overweight and obesity	10 (18)	23.80 %	17.10-32.10	Q=326.39; df=9; p<0.01; I^2=96.30
Prevalence among children and adolescents with overweight	5 (6)	17.00 %	11.40-24.70	Q=129.31; df=5; p<0.01; I^2=96.13
Prevalence among children and adolescents with obesity	10 (15)	33.40 %	25.30-42.60	Q=289.73; df=14; p<0.01; I^2=95.17
Prevalence among boys	3 (7)	26.20 %	17.60-370	Q=39.29; df=6; p<0.01; I^2=84.73

N, number; CI, confidence interval;

Table 5.2. Overall and subgroup analyses of the prevalence of mental disorders among children and adolescents with overweight and obesity continued

Type of analysis	N of studies (subgroups)	Prevalence	95 % CI	Heterogeneity
Prevalence among girls	7 (13)	27.30 %	19.60-36.70	Q=80.50; df=12; p<0.01; I^2=85.10
Prevalence in Europe	7 (13)	23.60 %	17.50-30.90	Q=144.54; df=12; p<0.01; I^2=91.70
Prevalence among large and probably representative samples	3 (8)	18.50 %	13.50-24.90	Q=170.36; df=7; p<0.01; I^2=95.89
Prevalence among large and probably unrepresentative samples	4 (7)	30.90 %	20.30-44.00	Q=140.11; df=6; p<0.01; I^2=94.24
Prevalence among small or medium and probably unrepresentative samples	3 (3)	20.10 %	15.00-26.50	Q=3.63; df=2; p=0.16; I^2=44.87
Prevalence among children and adolescents	3 (5)	35.80 %	22.70-51.50	Q=105.89; df=4; p<0.01; I^2=96.22
Prevalence among adolescents	6 (12)	18.50 %	14.20-23.70	Q=177.62; df=11; p<0.01; I^2=93.81
Prevalence among participants that reported weight and height	4 (8)	23.10 %	15.70-32.60	Q=321.78; df=7; p<0.01; I^2=97.83
Prevalence among measured participants	6 (10)	23.10 %	20.30-26.20	Q=14.47; df=9; p=0.11; I^2=37.79
Prevalence in studies in which the informant was a parent	6 (9)	18.30 %	13.60-24.10	Q=191.00; df=8; p<0.01; I^2=95.81
Prevalence in studies where self-report of the psychiatric instrument was used	3 (7)	24.20 %	21.20-27.40	Q=7.72; df=6; p=0.26; I^2=22.25
Prevalence in studies including borderline psychiatric test results	3 (6)	19.60 %	15.80-24.10	Q=6.57; df=5; p=0.26; I^2=23.88
Prevalence in studies including only clinically significant psychiatric test results	10 (40)	24.60 %	20.50-29.10	Q=738.51; df=39; p<0.01; I^2=94.72

N, number; CI, confidence interval;

Cumulative meta-analysis results are shown in Figure 5.5.

The average quality score of the ten studies included in the analysis of the prevalence of mental disorders among children and adolescents with overweight and obesity according to The Joanna Briggs Institute Critical Appraisal tools was 76.50 %, with no studies scoring less than 50 % of points. Four studies were of high quality, while the other six were of moderate quality, with no studies of low quality included (Table 5.3, Table 5.4., pages 33-36).

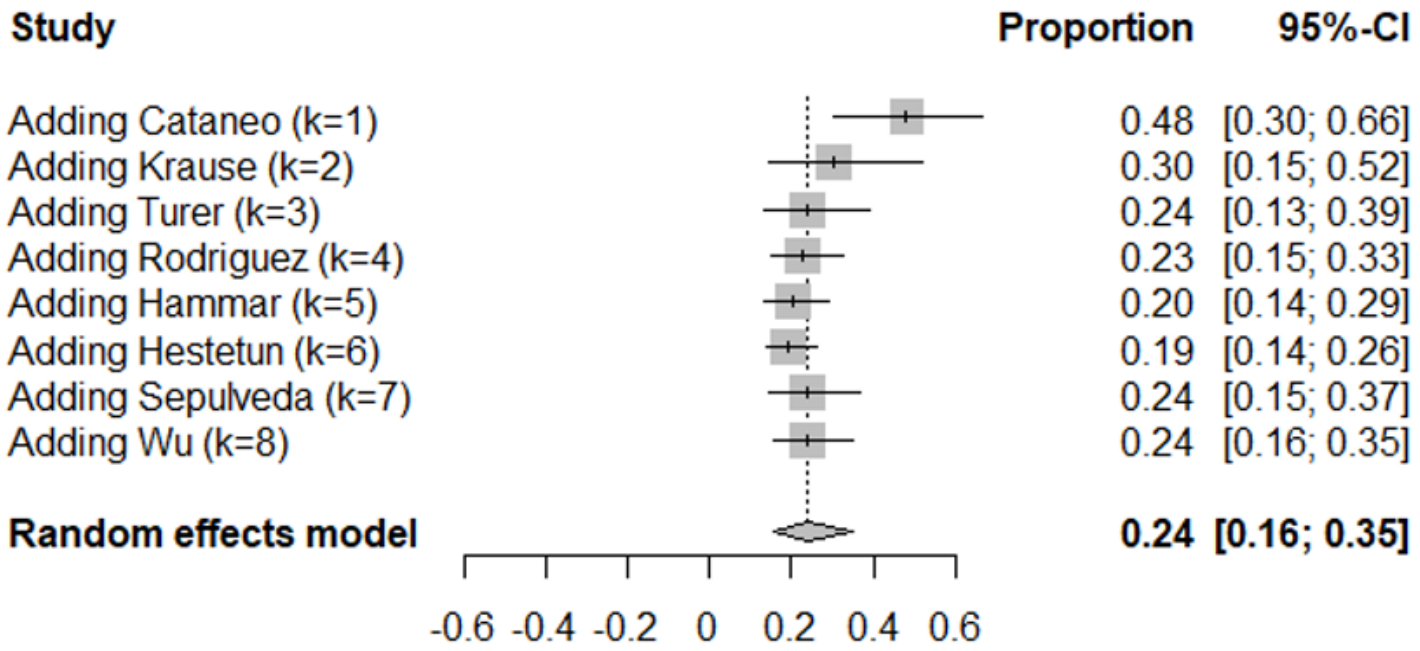

Figure 5.5. Cumulative meta-analysis of studies analyzing the prevalence of mental disorders among children and adolescents with overweight and obesity. CI, confidence interval.

5.3. Worldwide prevalence of mental disorders among children and adolescents with obesity

A total of 10 studies (57, 112, 114, 116, 118, 120, 122, 123, 126, 127) were included in the meta-analysis to assess the prevalence of mental disorders among children and adolescents with obesity which yielded a prevalence of 30.43 % (95 % CI, 23.20-38.77; z=-3.45, p<0.01). A forest plot is presented in Figure 5.6. The results of the meta-analysis indicated a large degree of variance in the study effect sizes (Q=280.57; df=9; p<0.01; I^2=96.80). Characteristics of the studies included in the analyses are presented in Table 1. The distribution of the included studies by country is shown in Figure 5.3.

The funnel plot seemed asymmetric by visual inspection (Figure 5.7). Duvall and Tweedie trim-and-fill procedure suggested inputting 1 study on the right side of the mean to obtain an unbiased estimate of the prevalence of 32.23 % (95 % CI, 23.13-42.92). The Egger's linear regression method intercept of 4.43 (95 % CI, -2.31-11.17) with a non-significant two-tailed p-value of 0.17 indicated no evidence for publication bias.

Two additional studies were included in the moderator analysis. There was no significant difference (Q=0.01; df=1; p=0.91) in the prevalence between subgroups consisting of boys (I^2=81.62) or girls (I^2=82.52).

A meta-regression was planned to explore the association between the prevalence estimates and the mean age of the study samples; however, there was an inadequate number of studies.

Cumulative meta-analysis results are shown in Figure 5.8.

The average quality score of the ten studies included in the analysis of the prevalence of mental disorders among children and adolescents with obesity was 68.70 %. Four studies were of high quality, five were of moderate quality, and 1 study was of low quality (Table 5.3, Table 5.4.).

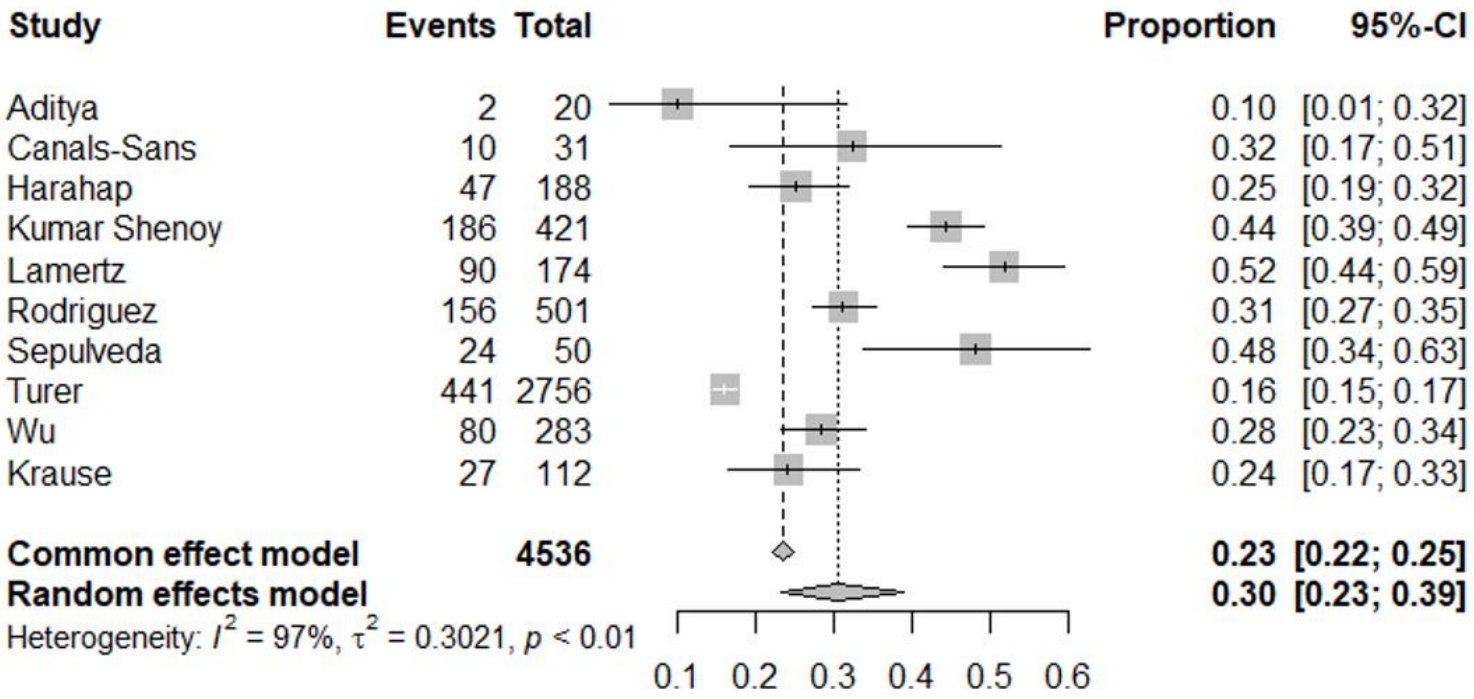

Figure 5.6. Forest plot for the prevalence of mental disorders among children and adolescents with obesity. CI, confidence interval.

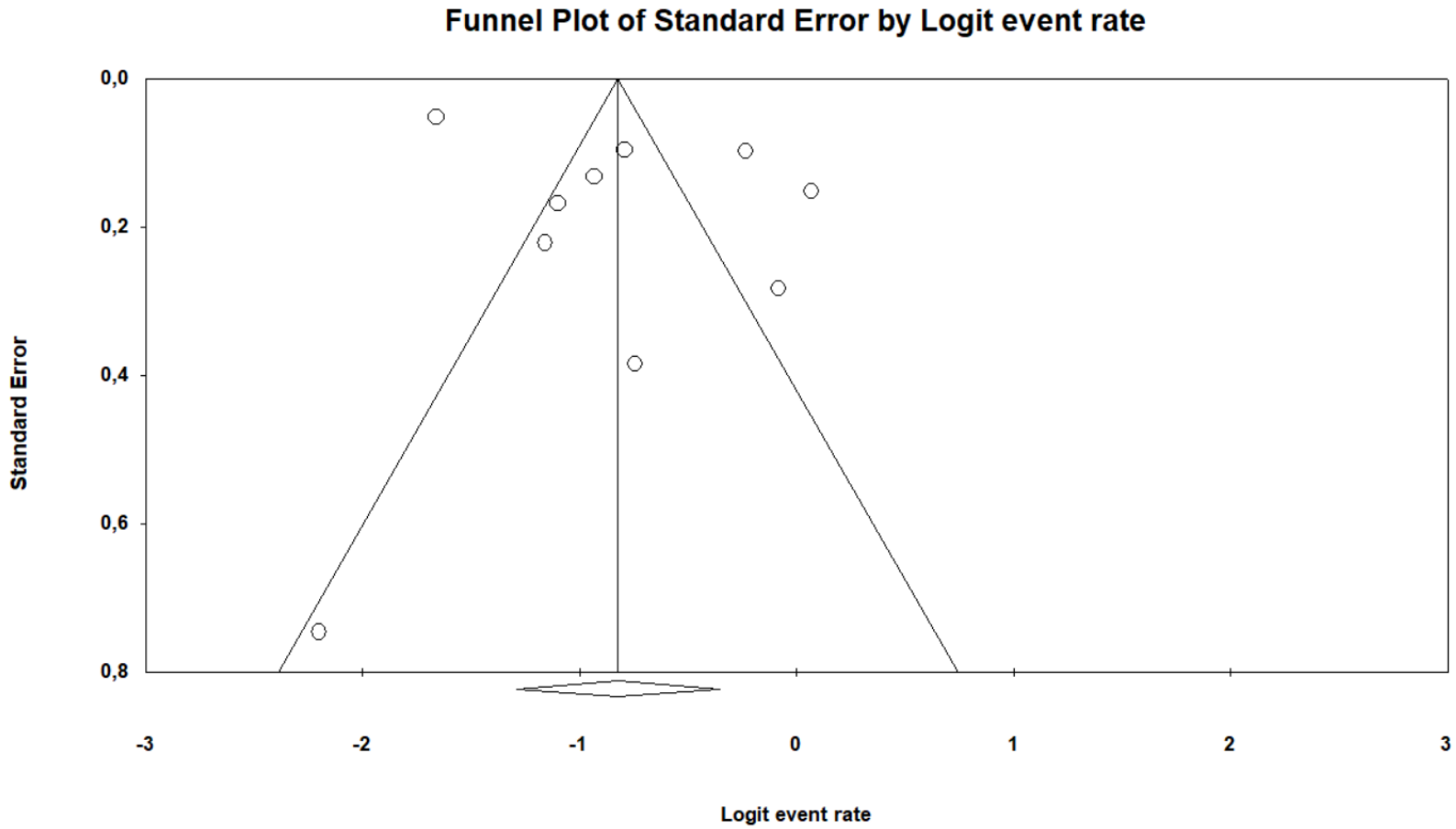

Figure 5.7. Funnel plot for the prevalence of mental disorders among children and adolescents with obesity

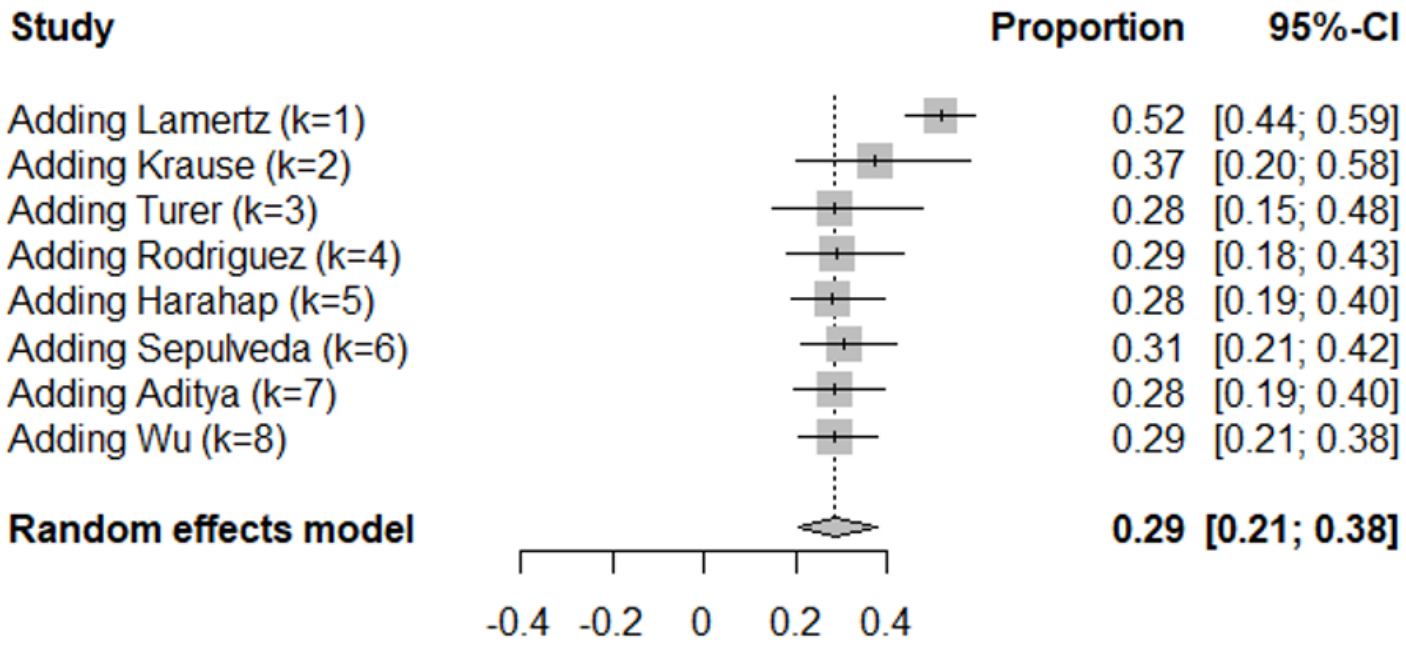

Figure 5.8. Cumulative meta-analysis of the studies analyzing the prevalence of mental disorders among children and adolescents with obesity

Table 5.3. The methodological quality of the cross-sectional studies included in meta-analyses of prevalence and OR of mental disorders among children and adolescents with overweight and obesity according to The Joanna Briggs Institute Critical Appraisal tool

Study first author	Study year	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?	Yes (n/8)
Aditya	2015	Yes	No	Yes	Yes	No	No	Yes	Yes	4/8
Borges	2005	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	6/8
Buddeberg-Fischer	NA	Yes	No	Yes	Yes	No	No	Yes	Yes	6/8
Canals-Sans	NA	Yes	No	Yes	Yes	No	Yes	Yes	Yes	6/8
Cataneo	2002	Yes	Yes	Unclear	Yes	No	No	Yes	Yes	4/8
Chan	2017-2018	Yes	Yes	Unclear	Yes	No	No	Yes	Yes	4/8
Drukker	2004-2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7/8
Erermis	NA	No	No	Yes	Yes	No	No	Yes	Yes	5/8
Freitas-Rosa	NA	Yes	No	Yes	Yes	No	No	Yes	Yes	5/8
Hammar	2007-2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	5/8
Hestetun	2010	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6/8
Huang	2007	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	4/8
Hwang	NA	Yes	No	Unclear	Yes	No	No	Yes	Yes	3/8

NA, not available; n, number;

Table 5.3. The methodological quality of the cross-sectional studies included in meta-analyses of prevalence and OR of mental disorders among children and adolescents with overweight and obesity according to The Joanna Briggs Institute Critical Appraisal tool continued

Study first author	Study year	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?	Yes (n/8)
Kagawa	2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/8
Kumar Shenoy	NA	Yes	No	Yes	Yes	No	No	Yes	Yes	4/8
Lamertz	1995	Yes	Yes	No	Yes	No	No	Yes	Yes	5/8
Pitrou	2004-2005	Yes	Yes	No	Yes	No	Yes	Yes	Yes	6/8
Ren	2014-2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7/8
Rodriguez	2006	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	7/8
Seyedamini	2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/8
Tanofsky-Kraff	NA	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	5/8
Terbogt	1997-1998	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	7/8
Tiffin	2007	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6/8
Turer	2005-2009	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	7/8

NA, not available; n, number;

Table 5.3. The methodological quality of the cross-sectional studies included in meta-analyses of prevalence and OR of mental disorders among children and adolescents with overweight and obesity according to The Joanna Briggs Institute Critical Appraisal tool continued

Study first author	Study year	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?	Yes (n/8)
Vuuren	2010-2015	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	6/8
Vanvlierberghe	NA	No	No	Yes	Yes	No	Yes	Yes	Yes	6/8
Wu	2015-2016	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6/8
Krause	2003-2006	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	7/8
Sawyer	2004	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	6/8
Jansen	2006-2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/8
Harahap	2009	No	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	6/8
Jauregui	NA	No	No	Yes	Yes	No	No	Yes	Yes	4/8

n, number;

Table 5.4. The methodological quality of the case-control studies included in meta-analyses of prevalence and OR of mental disorders among children and adolescents with overweight and obesity according to The Joanna Briggs Institute Critical Appraisal tool

Study first author	Study year	Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	Were cases and controls matched appropriately?	Were the same criteria used for identification of cases and controls?	Was exposure measured in a standard, valid and reliable way?	Was exposure measured in the same way for cases and controls?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were outcomes assessed in a standard, valid and reliable way for cases and controls?	Was the exposure period of interest long enough to be meaningful?	Was appropriate statistical analysis used?	Yes (n/10)
Annayagari	2011-2013	Yes	Yes	Yes	No	Yes	No	No	Yes	Unclear	Yes	6/10
Doaei	NA	Unclear	Unclear	Yes	Yes	Yes	No	No	Yes	Unclear	Yes	4/10
Sepulveda	2012-2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	9/10

NA, not available; n, number;

5.3. Cross-sectional association between overweight and obesity and mental disorders among children and adolescents

A total of 37 studies (57, 78, 112-116, 120, 122-125, 128-148) comprising 120 242 children and adolescents were included in the meta-analyses to estimate the OR of mental disorders among children and adolescents with overweight and obesity from cross-sectional studies. They were conducted between 1986 and 2018 and originated from 26 different countries. The general and methodological characteristics of the studies included in the analyses are presented in Table 5.5 and Table 5.6. The distribution of studies included in the analyses of OR by country is shown in Figure 5.9.

A statistically significant OR of 1.28 (95 % CI, 1.19-1.40; z=6.24, p<0.01) of mental disorders among children and adolescents affected with overweight and obesity was estimated by a random-effects meta-analysis of 26 studies (110, 111, 114, 115, 120, 122-126, 130, 131, 134-141, 143-148) comprising 60 separate effect sizes and 117 705 participants. A forest plot is presented in Figure 5.10. The meta-analysis results indicated a large degree of variance in the study effect sizes (Q=175.03; df=24; p<0.01; I^2=86.29).

Eleven studies were analyzed to assess the gender of the study participants as moderator. There was no significant difference in the OR between samples consisting of boys or girls (Q=2.85; df=1; p=0.09). Overall and subgroup cross-sectional analyses are shown in Table 5.7. Seven additional studies were included in the meta-analysis to analyze the weight category as a moderator. There was a significant difference in the OR between samples consisting of participants with overweight or obesity (Q=6.60; df=1; p<0.05). According to location, there was no significant difference (Q=67.34; df=4; p=0.45) in the OR between the samples. There was no significant difference in the OR between samples consisting of children and samples consisting of adolescents (Q=0; df=1; p=0.10). There was a significant difference in the OR between community or nationally representative samples and convenient study samples (Q=28.76; df=2; p<0.01). There was no significant difference in the OR between the probably not representative samples from a large area, probably representative samples from a large area, or probably not representative samples from a small area (Q=3.26; df=2; p=0.20). There was no significant difference between studies with transformed and those with untransformed effect sizes (Q=0.06; df=1; p=0.80). There was no significant difference between studies in which the informant was a parent, teacher, or participant themself (Q=0.07; df=2; p=0.96). There was no significant difference between studies using CDC, WHO, IOTF, or National growth reference

(Q=4.16; df=3; p=0.25). There was no significant difference between studies using SDQ, CBCL, or MSQA (Q=4.39; df=2; p=0.11).

There was no significant difference between studies in which participants were measured or studies in which participants reported height and weight (Q=0.38; df=1; p=0.54). There was no significant difference between studies in which the control group included underweight or studies in which did not (Q=3.32; df=1; p=0.07). There was no significant difference in the OR between studies including borderline psychiatric assessment results or only abnormal psychiatric assessment results (Q=0.08; df=1; p=0.78).

The effect sizes were additionally stratified according to gender and weight status category, and there was a significant difference in the OR between samples consisting of a female with overweight, a female with obesity, a male with overweight, or a male with obesity (Q=10.28; df=3; $p<0.05$).

A sensitivity analysis was conducted to test the effect of transformed effect sizes. The OR remained significant when only studies with untransformed effect sizes were included in the meta-analysis (OR 1.30 (95 % CI, 1.20-1.40; z=6.60, $p<0.01$); Q=180.94; df=25; $p<0.01$; I^2=86.18).

Table 5.5. Characteristics of the studies included in the analyses of the association between overweight, obesity, and mental disorders among children and adolescents

First author	Study year	Study country	Sample size	Age category	Age range	Study design	Sample (representative)
Aditya	2015	Indonesia	103	Children and adolescents	6 to 12	Cross-sectional	Community
Annayagari	2011-2013	India	64	Adolescents	11 to 16	Case-control	Convenient
Borges	2005	Mexico	3005	Adolescents	12 to 17	Cross-sectional	Community
Buddeberg-Fischer	NA	Switzerland	136	Adolescents	15 to 20	Cross-sectional	Community
Canals-Sans	NA	Spain	485	Children	6,5 to 10	Cross-sectional	Community
Cataneo	2002	Brazil	53	Adolescents	10 to 12	Cross-sectional	Covenient
Chan	2017-2018	Hong Kong	355	Children and adolescents	8 to 12	Cross-sectional	Covenient
Doaei	NA	Iran	160	Adolescents	13 to 18	Case-control	Community
Drukker	2004-2005	Netherlands	1221	Children	5 to 6, 13 to 14	Cross-sectional	Community
Erermis	NA	Turkey	60	Adolescents	12 to 16	Cross-sectional	Convenient
Freitas-Rosa	NA	Portugal	287	Adolescents	14 to 19	Cross-sectional	Community
Griffiths	2003, 2005	UK	22309	Children	3 y, 5 y	Cross-sectional	Nationally
Hammar	2007-2008	Sweden	573	Adolescents	12 y	Cross-sectional	Community
Hestetun	2010	Norway	744	Adolescents	12 to 13	Cross-sectional	Community
Huang	2007	China	10403	Adolescents	12 to 24	Cross-sectional	Community
Hunsberger	2007-2008, 2009-2010	Belgium, Cyprus, Estonia, Italy, Germany, Hungary, Spain, Sweden	7831	Children	2 to 9	Cohort	Community
Hwang	NA	South Korea	453	Adolescents	10 to 12	Cross-sectional	Community
Jauregui	NA	Spain	85	Adolescents	NR	Cross-sectional	Convenient

NA, not available;

Table 5.5. Characteristics of the studies included in the analyses of the association between overweight, obesity, and mental disorders among children and adolescents continued

First author	Study year	Study country	Sample size	Age category	Age range	Study design	Sample (representative)
Kagawa	2012	Chile	1481	Children	6	Cross-sectional	Nationally
Kumar Shenoy	NA	India	1263	Adolescents	NR	Cross-sectional	Community
Lamertz	1995	Germany	337	Adolescents	14 to 24	Cross-sectional	Community
Lawlor	1986-1991, 1995-1998	Australia	2875	Children and adolescents	5 y, 14 y	Cohort	Community
Perez-Bonaventura	2009	Spain	611	Children	3 y, 4 y, 5 y	Cross-sectional	Community
Pitrou	2004-2005	France	941	Children and adolescents	6 to 11	Cross-sectional	Community
Ren	2014-2015	China	3841	Adolescents	11 to 16	Cross-sectional	Community
Rodriguez	2006	Spain	5271	Children and adolescents	4 to 15	Cross-sectional	Nationally
Sawyer	2004	Australia	4934	Children	4 to 5	Cross-sectional	Nationally
Jansen	2004, 2006, 2008, 2010	Australia	5841	Children	4 to 11	Cross-sectional	Nationally
Sepulveda	2012-2016	Spain	100	Children and adolescents	8 to 12	Cross-sectional	Community
Seyedamini	2008	Iran	300	Children and adolescents	7 to 12	Cross-sectional	Community
Tanofsky-Kraff	NA	USA	162	Children and adolescents	6 to 13	Cross-sectional	Community
Terbogt	1997-1998	Netherlands	7556	Adolescents	11 to 16	Cross-sectional	Nationally
Tiffin	2007	UK	3769	Children and adolescents	5 to 16	Cross-sectional	Nationally
Turer	2005-2009	USA	17224	Adolescents	10 to 17	Cross-sectional	Nationally
Vuuren	2010-2015	Netherlands	17683	Adolescents	13 to 16	Cross-sectional	Community
Wu	2015-2016	China	8457	Adolescents	13 to 18	Cross-sectional	Community
Krause	2003-2006	Germany	6813	Adolescents	11 to 17	Cross-sectional	Nationally

NA, not available;

Table 5.6. Methodological characteristics of the studies included in the OR analyses

First author	UW in the control group	OW in the control group	Growth reference	BMI measured or reported	Psychiatric tool	Informant	Effect size measure	Effect size groups	Controlled confounders
Aditya	yes	yes	CDC	Measured	PSC-17	Parent	OR	Total	NA
Annayagari	no	no	WHO	School-reported	DPCL	Parent	Mean (SD)	Total	NA
Borges	no	no	CDC	Self-reported	WMH-CIDI-A, CAPI	Self-report	OR	Total, M, F	NA
Buddeberg-Fischer	no	no	Must, Dallal, Dietz 1991	Measured	SSQ, DIA-X	Self-report	OR	F	NA
Canals-Sans	no	no	IOTF	Measured	CBCL/6-18	Parent	OR	Total, OW, OB - borderline included; Total, OW, OB - only clinical	NA
Cataneo	no	no	Must, Dallal, Dietz 1991	NR	Rutter scale	Parent or guardian	OR	Total	NA
Chan	maybe	no	Hong Kong´s growth charts	Unclear	Brief Symptom Rating Scale-5	Self-report	Mean (SD)	Total	NA

UW, underweight; OW, overweight; OB, obesity; OR, odds ratio; SD, standard deviation; CAPI, Computer Assisted Personal Interview; DPCL, Developmental Psychopathology Check List for Children; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; CBCL, Child Behavior Checklist; M, male; F, female; PSC-17, Pediatric Symptom Checklist; SSQ, Stem Item Screening Questionnaire;

Table 5.6. Methodological characteristics of the studies included in the OR analyses continued

First author	UW in the control group	OW in the control group	Growth reference	BMI measured or reported	Psychiatric tool	Informant	Effect size measure	Effect size groups	Controlled confounders
Doaei	no	no	WHO	Measured	GHQ-28	Self-report	OR	F	NA
Drukker	no	no	IOTF	Measured	SDQ	Parent-reported	B coefficient	Children OW, Children OB, Adolescents OW, Adolescents OB	age, gender, SES
Erermis	no	no	National Iranian	Measured	CBCL	Parent-reported	Mean (SD)	OB	NA
Freitas-Rosa	no	no	CDC	Measured	Brief Symptom Inventory	Self-reported	Mean (SD)	Total	NA
Griffiths	maybe	no	IOTF	Measured	SDQ	Parent	OR	OW 3 y B, OB 3 y B, OW 3 y F, OB 3 y F, OW 5 y M, OB 5 y M, OW 5 y F, OB 5 y F	child's ethnicity, maternal SES, mother's highest academic qualification, maternal age at birth, household income, lone-motherhood status, N of children in the household, maternal treatment for depression or anxiety, maternal weight status
Hammar	maybe	no	IOTF	Measured	CBCL/4-18, SDQ	Parent, Self-report	OR	CBCL, SDQ, F OW, F OB	NA

UW, underweight; OW, overweight; OB, obesity; OR, odds ratio; SD, standard deviation; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; CBCL, Child Behavior Checklist; M, male; F, female; SDQ, Strengths and Difficulties Questionnaire; SES, socioeconomic status; y, years; N, number; GHQ, General Health Questionnaire;

Table 5.6. Methodological characteristics of the studies included in the OR analyses continued

First author	UW in the control group	OW in the control group	Growth reference	BMI measured or reported	Psychiatric tool	Informant	Effect size measure	Effect size groups	Controlled confounders
Hestetun	yes	no	IOTF	Measured	SDQ	Parent	OR	Total	maternal education, peer problems
Huang	maybe	no	Chinese national	Unclear	MSQA	Self-reported	OR	OW M, OB M, OW F, OB F	grade, SES, residential background, personality, N of friends
Hunsberger	yes	no	IOTF	Measured	SDQ	Parent	OR	Total	age, sex, parental education, intervention and country
Hwang	maybe	no	Korean national	Unclear	CBCL	Parent	Mean (SD)	OW, OB	NA
Jauregui	maybe	no	IOTF	Measured	GHQ	Self reported	Correlation coeficient	Total	NA
Kagawa	no	no	WHO	Measured	CBCL	Parent	B coefficient	Total	child's breastfeeding length, birth weight, sex, indigenous status; household wealth, primary caregiver's BMI, level of education
Kumar Shenoy	maybe	maybe	CDC	Measured	CPMS	Parent	OR	Total, M, F	NA

UW, underweight; OW, overweight; OB, obesity; OR, odds ratio; SD, standard deviation; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; CBCL, Child Behavior Checklist; M, male; F, female; SDQ, Strengths and Difficulties Questionnaire; SES, socioeconomic status; y, years; N, number; GHQ, General Health Questionnaire; CPMS, Childhood Psychopathology Measurement Schedule; MSQA, Multidimensional Sub-health Questionnaire of Adolescent;

Table 5.6. Methodological characteristics of the studies included in the OR analyses continued

First author	UW in the control group	OW in the control group	Growth reference	BMI measured or reported	Psychiatric tool	Informant	Effect size measure	Effect size groups	Controlled confounders
Lamertz	no	yes	IOTF	Self-reported	CAPI, M-CIDI, SCL-90R	Self-reported	OR	14 to 17 y: M, F; 18 to 24 y: M, F	eating disorders
Lawlor	maybe	no	IOTF	Measured	CBCL	Parent	OR	M 5 y, F 5 y, M 14 y, F 14 y	age, pubertal stage, maternal age at birth, ethnicity, parental education, family income, parental BMI
Perez-Bonaventura	maybe	yes	WHO	Measured	SDQ	Parent	B coefficient	3 y, 4 y, 5 y	SES
Pitrou	maybe	no	IOTF	Parent-reported	SDQ	Parent	OR	Borderline SDQ Abnormal SDQ	NA
Ren	no	no	Chinese national	Measured	SDQ	Self-reported	OR	M, F	age, parents' education level, household income level, pubertal development stage, parents smoking
Rodriguez	maybe	no	IOTF	Parent-reported	SDQ	Parent	OR	OW abnormal, OW borderline, OB abnormal, OB borderline	age, sex and social class

UW, underweight; OW, overweight; OB, obesity; OR, odds ratio; SD, standard deviation; WHO, World Health Organization; IOTF, International Obesity Task Force; CBCL, Child Behavior Checklist; M, male; F, female; SDQ, Strengths and Difficulties Questionnaire; SES, socioeconomic status; y, years; N, number; CAPI, Computer Assisted Personal Interview; M-CIDI, Munich Composite International Diagnostic Interview; SCL-90R, Symptom Checklist-90-Revised instrument;

Table 5.6. Methodological characteristics of the studies included in the OR analyses continued

First author	UW in the control group	OW in the control group	Growth reference	BMI measured or reported	Psychiatric tool	Informant	Effect size measure	Effect size groups	Controlled confounders
Sawyer	yes	no	IOTF	Measured	SDQ	Parent	Mean (SD)	Parent-reported OW Parent-reported OB	children's Indigenous status, whether children speak a language other than English, family occupation, family income, and neighborhood disadvantage, mother's education level, whether mother speaks a language other than English
Jansen	yes	no	IOTF	Measured	SDQ	Parent	B coefficient	Parent-reported 6-7 y, 8-9 y, 10-11 y, Teacher-reported 4-5 y, 6-7 y, 8-9 y, 10-11 y	child sex, child age, indigenous status, whether a primary language other than English is spoken at home, SES, maternal psychological distress
Sepulveda	no	no	IOTF	Measured	K-SADS-PL	Self-reported	OR	Total	sex, age, BMI z-score, Tanner stage, SES
Seyedamini	no	no	CDC	Measured	CBCL	Parent	OR, Mean (SD)	F OW, F OB, F OW+OB	TV watch duration, crisis experience during last six months, maternal educational level, previous disease history, birth order, birth weight
Tanofsky-Kraff	maybe	no	Must Dallal Dietz 1991	Measured	CBCL 4/18	Parent	Mean (SD)	Total	age, race, SES, gender, pubertal stage

UW, underweight; OW, overweight; OB, obesity; OR, odds ratio; SD, standard deviation; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; CBCL, Child Behavior Checklist; M, male; F, female; SDQ, Strengths and Difficulties Questionnaire; SES, socioeconomic status; y, years; N, number; K-SADS-PL; Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version;

Table 5.6. Methodological characteristics of the studies included in the OR analyses continued

First author	UW in the control group	OW in the control group	Growth reference	BMI measured or reported	Psychiatric tool	Informant	Effect size measure	Effect size groups	Controlled confounders
Terbogt	no	no	Dutch Quotelet standards	Self-reported	YSR	Self-reported	B coefficient	Total	age, gender, FAS, living with both parents, quality relationship with parents and peers
Tiffin	no	no	IOTF	Measured	SDQ	Parent	Mean (SD)	OW, OB	NA
Turer	no	no	CDC	Parent-reported	Columbia Impairment Scale	Parent	OR	OW, OB	gender, age, race/ethnicity, poverty status, residence in MSA, health insurance, survey y
Vuuren	no	no	IOTF	Measured	SDQ	Self-reported	OR	OW+OB, OB	sex and ethnicity
Wu	no	no	WHO	Measured	MSQA	Self-report	OR	OW, OB, M OW, M OB, F OW, F OB	NA
Krause	no	no	German national	Measured	SDQ	Self-report	OR	11-13 y: Total OW, Total OB, M OW, M OB, F OW, F OB; 14-17 y: Total OW, Total OB, M OW, M OB, F OW, F OB;	age

UW, underweight; OW, overweight; OB, obesity; OR, odds ratio; SD, standard deviation; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; YSR, Youth Self Report; M, male; F, female; SDQ, Strengths and Difficulties Questionnaire; SES, socioeconomic status; y, years; NA, not available; N, number; MSQA, Multidimensional Sub-health Questionnaire of Adolescent; FAS, family affluence status; MSA, metropolitan statistical area;

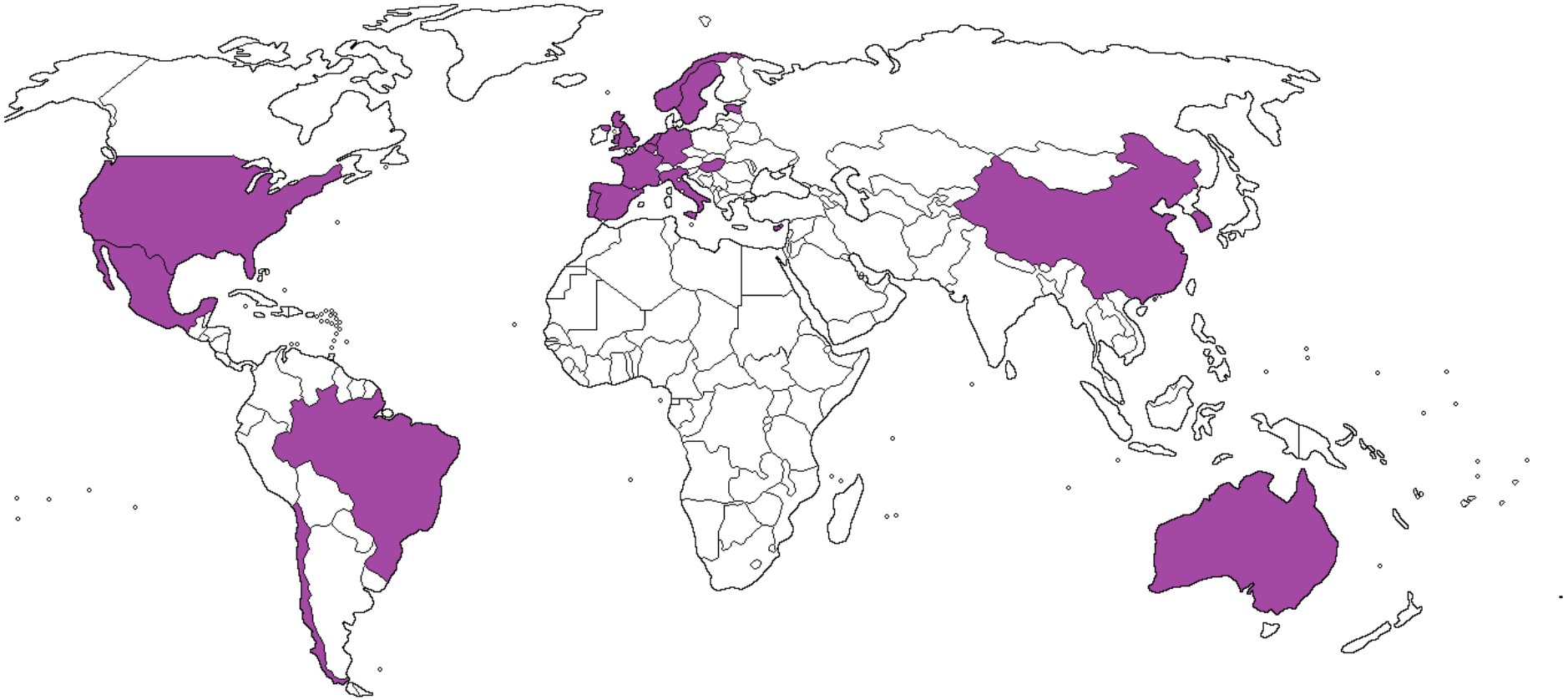

Figure 5.9. Distribution of the studies included in the analysis of mental disorders odds ratio among children and adolescents with overweight and obesity by country. The territories on the map may not correspond to the actual borders of the countries. Downloaded with permission from: https://hr.wikipedia.org/wiki/Datoteka:Blank_map_political_world_territories.png. Author: Roy Nick Norse.

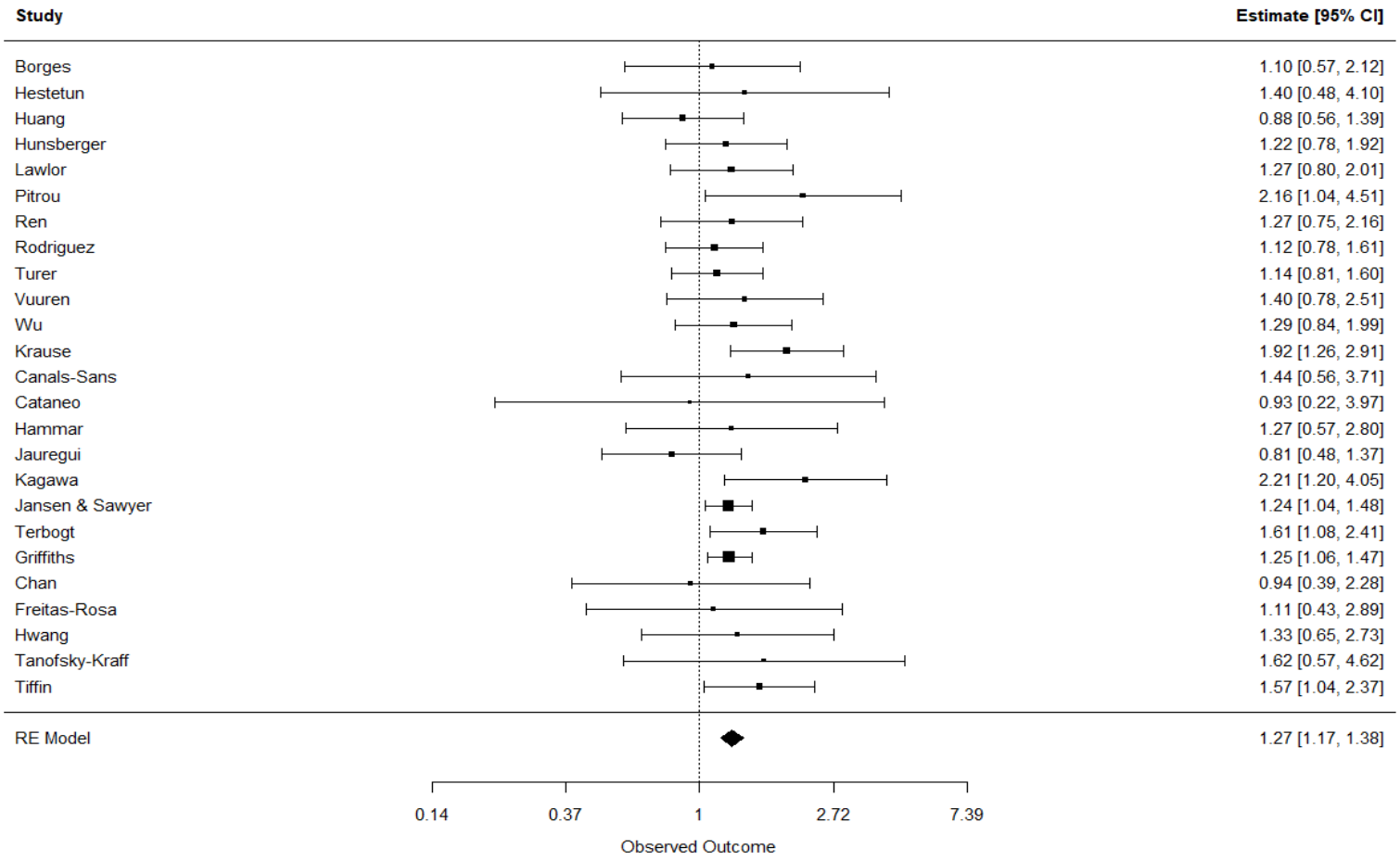

Figure 5.10. Forest plot for the cross-sectional association between overweight/obesity and mental disorders among children and adolescents. RE, random effects; CI, confidence interval.

Table 5.7. Overall and subgroup cross-sectional analyses of overweight/obesity with the risk of having a mental disorder

Type of analysis	N of studies (subgroups)	Odds ratio	95 % CI	p-value	Heterogeneity
OR among children and adolescents with overweight/obesity	25	1.28	1.19-1.4	p<0.01	Q=175.03; df=24; p<0.01; I^2=86.29
Limited to overweight	11 (18)	0.95	0.66-1.35	p=0.76	Q=1280.95; df=17; p<0.01; I^2=98.67
Limited to obesity	18 (29)	1.80	1.28-2.52	p<0.01	Q=1520.92; df=28; p<0.01; I^2=98.16
Limited to Asia	5 (11)	1.12	0.96-1.31	p=0.14	Q=22.28; df=10; p<0.05; I^2=55.11
Limited to Europe	13 (30)	1.41	1.04-1.90	p<0.05	Q=2707.38; df=29; p<0.01; I^2=98.93
Limited to North America	3 (4)	1.15	1.03-1.28	p<0.05	Q=4.24; df=3; p=0.24; I^2=29.18
Limited to Oceania	2 (13)	1.25	1.11-1.41	p<0.01	Q=71.87; df=12; p<0.01; I^2=83.30
Limited to South America and Caribbean	2 (2)	1.70	0.78-3.70	p=0.19	Q=2.40; df=1; p=0.12; I^2=58.36
Limited to adolescents	16 (30)	1.29	1.17-1.43	p<0.01	Q=153.58; df=29; p<0.01; I^2=81.12
Limited to children	6 (20)	1.29	0.89-1.85	p=0.18	Q=2609.27; df=19; p<0.01; I^2=99.27
Limited to male	7 (16)	1.71	1.17-2.48	p<0.01	Q=671.80; df=15; p<0.01; I^2=97.77
Limited to female	11 (21)	1.17	0.92-1.47	p=0.20	Q=771.26; df=20; p<0.01; I^2=97.41
Limited to community representative samples	14 (26)	1.24	1.14-1.36	p<0.01	Q=42.08; df=25; p<0.05; I^2=40.60

OR, odds ratio; N, number; CI, confidence interval; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; SDQ, Strengths and Difficulties Questionnaire; MSQA, Multidimensional Sub-health Questionnaire of Adolescent; CBCL, Child Behavior Checklist;

Table 5.7. Overall and subgroup cross-sectional analyses of overweight/obesity with the risk of having a mental disorder continued

Type of analysis	N of studies (subgroups)	Odds ratio	95 % CI	p-value	Heterogeneity
Limited to nationally representative samples	8 (31)	1.38	1.08-1.75	p<0.05	Q=2765.62; df=30; p<0.01; I^2=98.92
Limited to convenient sample	3 (3)	0.83	0.73-0.94	p<0.01	Q=0.47; df=2; p=0.79; I^2=0
Limited to large area – probably not representative sample	11 (18)	1.13	1.01-1.27	p<0.05	Q=46.75; df=17; p<0.01; I^2=63.63
Limited to large area – probably representative sample	10 (34)	1.40	1.11-1.76	p<0.01	Q=2775.57; df=33; p<0.01; I^2=98.81
Limited to small area – probably not representative sample	4 (8)	1.31	1.05-1.62	p<0.05	Q=11.54; df=7; p=0.12; I^2=39.35
Limited to studies with untransformed effect sizes	12 (30)	1.27	1.16-1.40	p<0.01	Q=100.15; df=29; p<0.01; I^2=71.04
Limited to studies with transformed effect sizes	13 (31)	1.32	1.02-1.71	p<0.05	Q=2747.43; df=30; p<0.01; I^2=98.91
Limited to studies using SDQ	10 (37)	1.38	1.09-1.76	p<0.01	Q=2702.29; df=36; p<0.01; I^2=98.67
Limited to studies using CBCL	5 (10)	1.44	1.13-1.84	p<0.01	Q=29.42; df=9; p<0.01; I^2=69.41
Limited to studies using MSQA	2 (6)	1.06	0.87-1.30	p=0.56	Q=12.37; df=5; p<0.05; I^2=59.56
Limited to studies in which the informant was parent	15 (37)	1.34	1.05-1.72	p<0.05	Q=2681.82; df=36; p<0.01; I^2=98.66

OR, odds ratio; N, number; CI, confidence interval; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; SDQ, Strengths and Difficulties Questionnaire; MSQA, Multidimensional Sub-health Questionnaire of Adolescent; CBCL, Child Behavior Checklist;

Table 5.7. Overall and subgroup cross-sectional analyses of overweight/obesity with the risk of having a mental disorder continued

Type of analysis	N of studies (subgroups)	Odds ratio	95 % CI	p-value	Heterogeneity
Limited to studies in which the informant was participant himself	10 (19)	1.30	1.15-1.48	p<0.01	Q=75.40; df=18; p<0.01; I^2=76.13
Limited to studies in which the informant was teacher	1 (4)	1.28	1.03-1.60	p<0.05	Q=30.80; df=3; p<0.01; I^2=90.26
Limited to studies using CDC growth reference	3 (4)	1.16	1.08-1.25	p<0.01	Q=2.95; df=3; p=0.40; I^2=0
Limited to studies using WHO growth reference	2 (3)	1.57	1.05-2.36	p<0.05	Q=26.04; df=2; p<0.01; I^2=92.32
Limited to studies using IOTF growth reference	12 (38)	1.31	1.04-1.66	p<0.05	Q=2700.00; df=37; p<0.01; I^2=98.63
Limited to studies using National growth reference	8 (16)	1.32	1.10-1.58	p<0.01	Q=68.48; df=15; p<0.01; I^2=78.09
Limited to studies in which participants were measured	15 (40)	1.37	1.10-1.71	p<0.01	Q=2749.68; df=39; p<0.01; I^2=98.58
Limited to studies in which participants reported weight and height	6 (12)	1.26	1.07-1.48	p<0.01	Q=72.23; df=11; p<0.01; I^2=84.77
Limited to studies including underweight in the control group	3 (12)	1.25	1.11-1.40	p<0.01	Q=67.04; df=11; p<0.01; I^2=83.59

OR, odds ratio; N, number; CI, confidence interval; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; SDQ, Strengths and Difficulties Questionnaire; MSQA, Multidimensional Sub-health Questionnaire of Adolescent; CBCL, Child Behavior Checklist;

Table 5.7. Overall and subgroup cross-sectional analyses of overweight/obesity with the risk of having a mental disorder continued

Type of analysis	N of studies (subgroups)	Odds ratio	95 % CI	p-value	Heterogeneity
Limited to studies not including underweight in the control group	12 (20)	1.46	1.29-1.64	p<0.01	Q=125.10; df=19; p<0.01; I^2=84.81
Limited to studies including borderline psychiatric test results	7 (18)	1.34	1.18-1.51	p<0.01	Q=107.40; df=17; p<0.01; I^2=84.17
Limited to studies including only abnormal psychiatric test results	22 (44)	1.29	1.03-1.61	p<0.05	Q=2740.77; df=43; p<0.01; I^2=98.43
Limited to female with obesity	7 (10)	1.66	1.03-2.67	p<0.05	Q=240.88; df=9; p<0.01; I^2=96.26
Limited to female with overweight	5 (7)	0.86	0.59-1.27	p=0.45	Q=126.95; df=6; p<0.01; I^2=95.27
Limited to male with obesity	6 (9)	2.67	1.31-5.45	p<0.01	Q=319.14; df=8; p<0.01; I^2=97.50
Limited to male with overweight	4 (6)	1.60	1.14-2.24	p<0.01	Q=88.19; df=5; p<0.01; I^2=94.33

OR, odds ratio; N, number; CI, confidence interval; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; SDQ, Strengths and Difficulties Questionnaire; MSQA, Multidimensional Sub-health Questionnaire of Adolescent; CBCL, Child Behavior Checklist;

A meta-regression was conducted to explore the association between effect sizes and GDP of the countries from which participants originate, the mean age of the studies samples, and the number of confounders controlled in the analyses. Bubble plots are shown in Figures 5.11., 5.12., and 5.13. The meta-regression showed that there was no association between effect sizes and GDP, mean age, and the number of controlled confounders.

A cumulative meta-analysis of the association between overweight, obesity, and mental disorders among children and adolescents is shown in Figure 5.14.

The funnel plot for the association between overweight/obesity and mental disorders among children and adolescents seemed asymmetric by visual inspection (Figure 5.15.). The Egger`s test indicated no publication bias with ist two-tailed p of 0.09. Orwin's Fail-safe N suggested

the imputation of 51 studies with an OR of 1.05 to bring the estimated OR under a trivial value of 1.10. Duvall and Tweedie trim-and-fill procedure suggested inputting 0 studies to obtain the unbiased effect size. The Egger`s test, Orwin's Fail-safe N, and Duval and Tweedie trim-and-fill procedure all suggested the absence of publication bias.

The average quality score of the 26 studies included in the analysis of the odds ratio for mental disorders among children and adolescents with overweight and obesity was 82.40 %. Eight studies were of high quality, 17 were of moderate quality, and 1 study was of low quality (Table 5.3., Table 5.4.).

The age ranges of studies participants are shown in Figure 5.16.

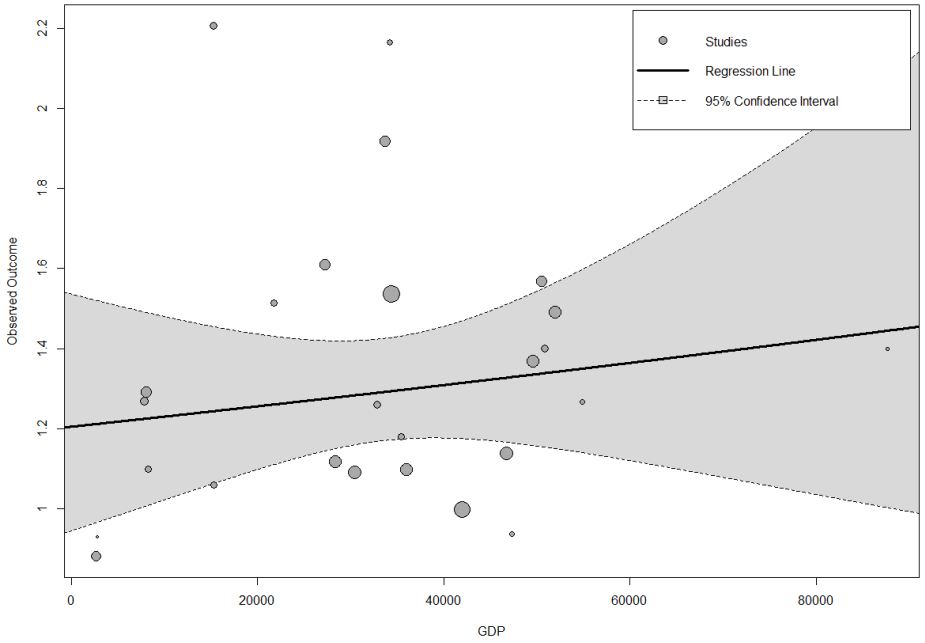

Figure 5.11. Bubble plot for the association between OR of mental disorders among children and adolescents with overweight and obesity and GDP of the country from which examinees originate. OR, odds ratio; GDP, Gross domestic product.

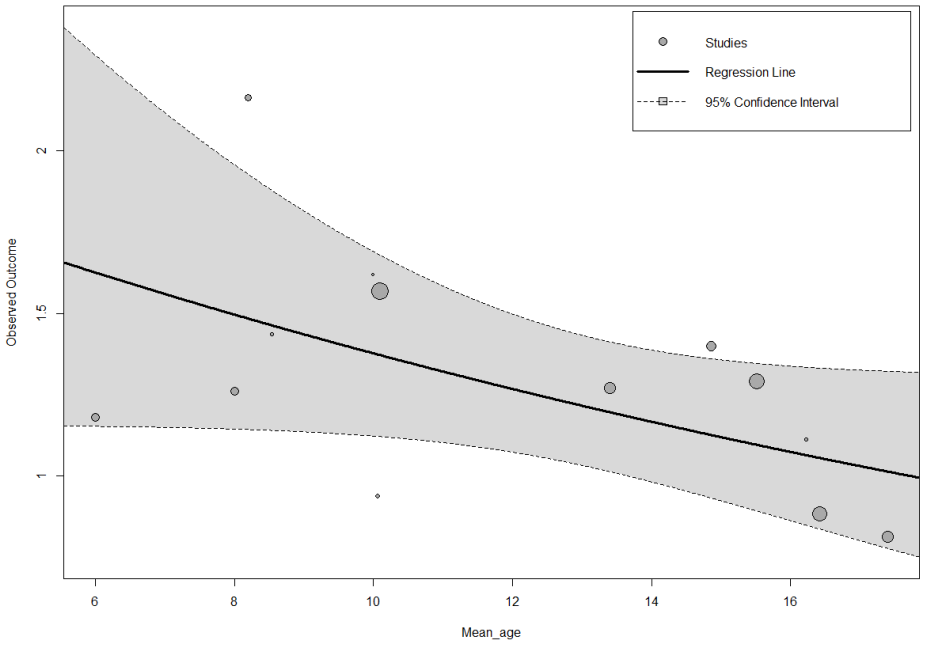

Figure 5.12. Bubble plot for the association between OR of mental disorders among children and adolescents with overweight and obesity and mean age of study samples. OR, odds ratio;

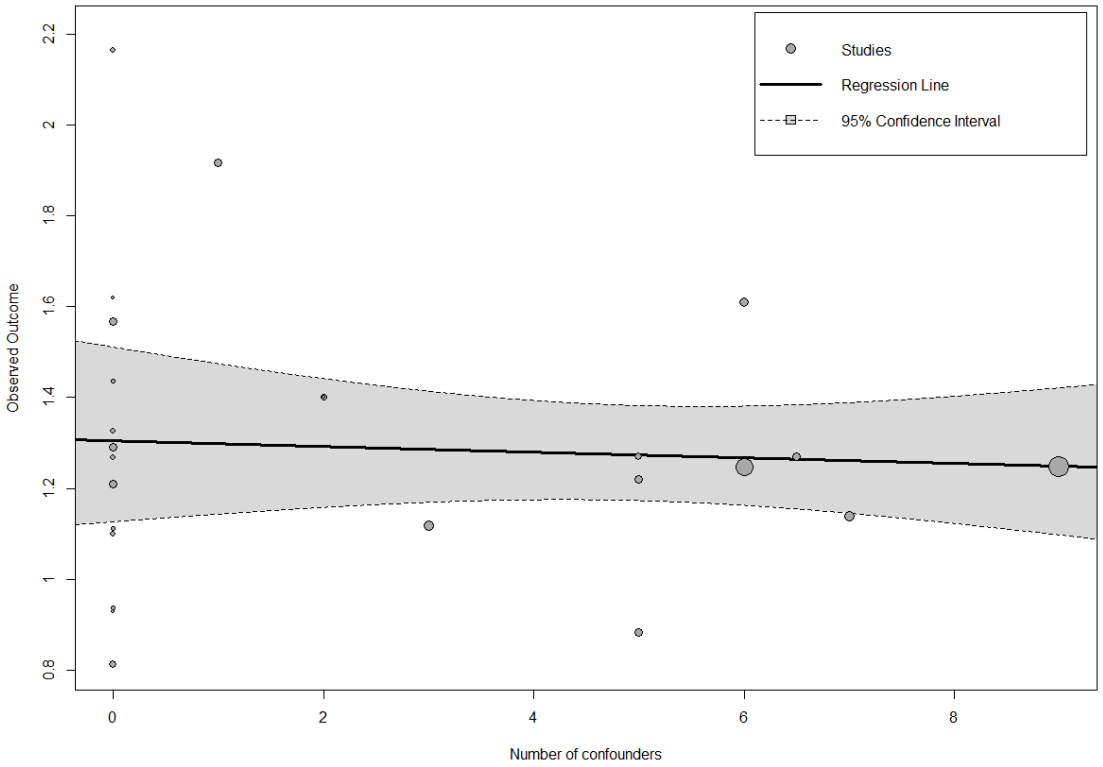

Figure 5.13. Bubble plot for the association between OR of mental disorders among children and adolescents with overweight and obesity and number of the confounders controlled for in the analyses. OR, odds ratio;

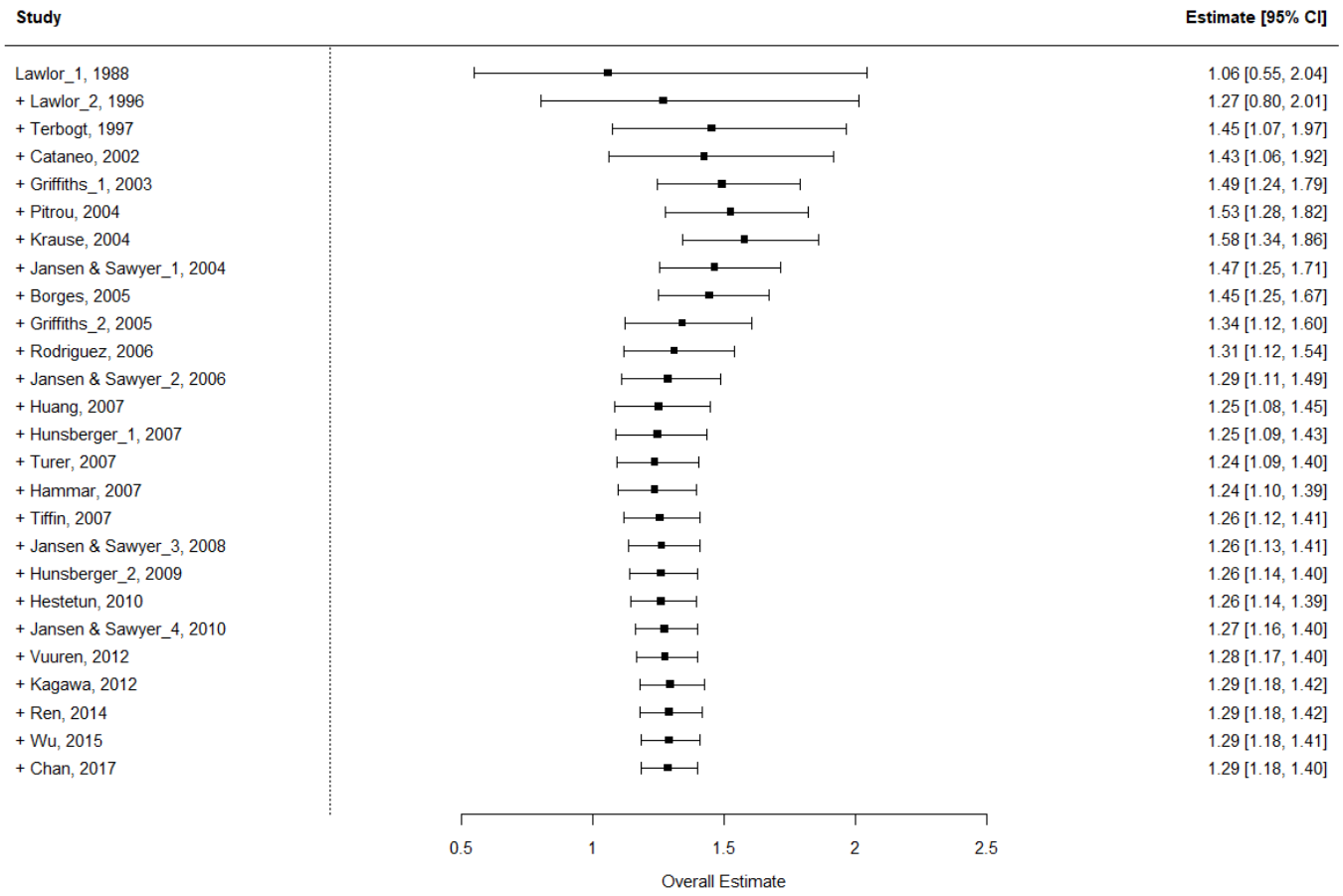

Figure 5.14. Cumulative meta-analysis for the association between overweight/obesity and mental disorders among children and adolescents. CI, confidence interval.

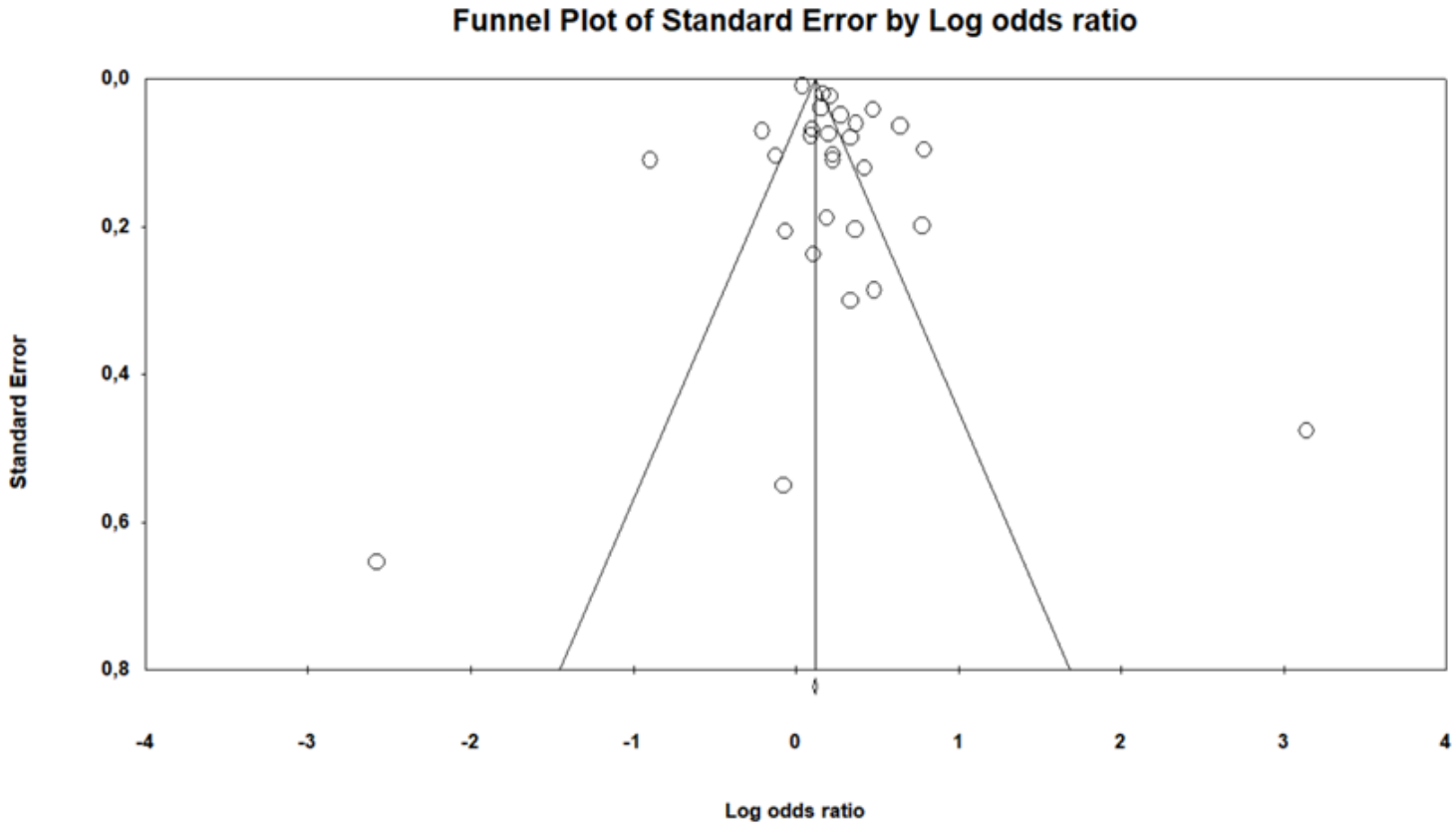

Figure 5.15. Funnel plot for the association between overweight/obesity and mental disorders among children and adolescents

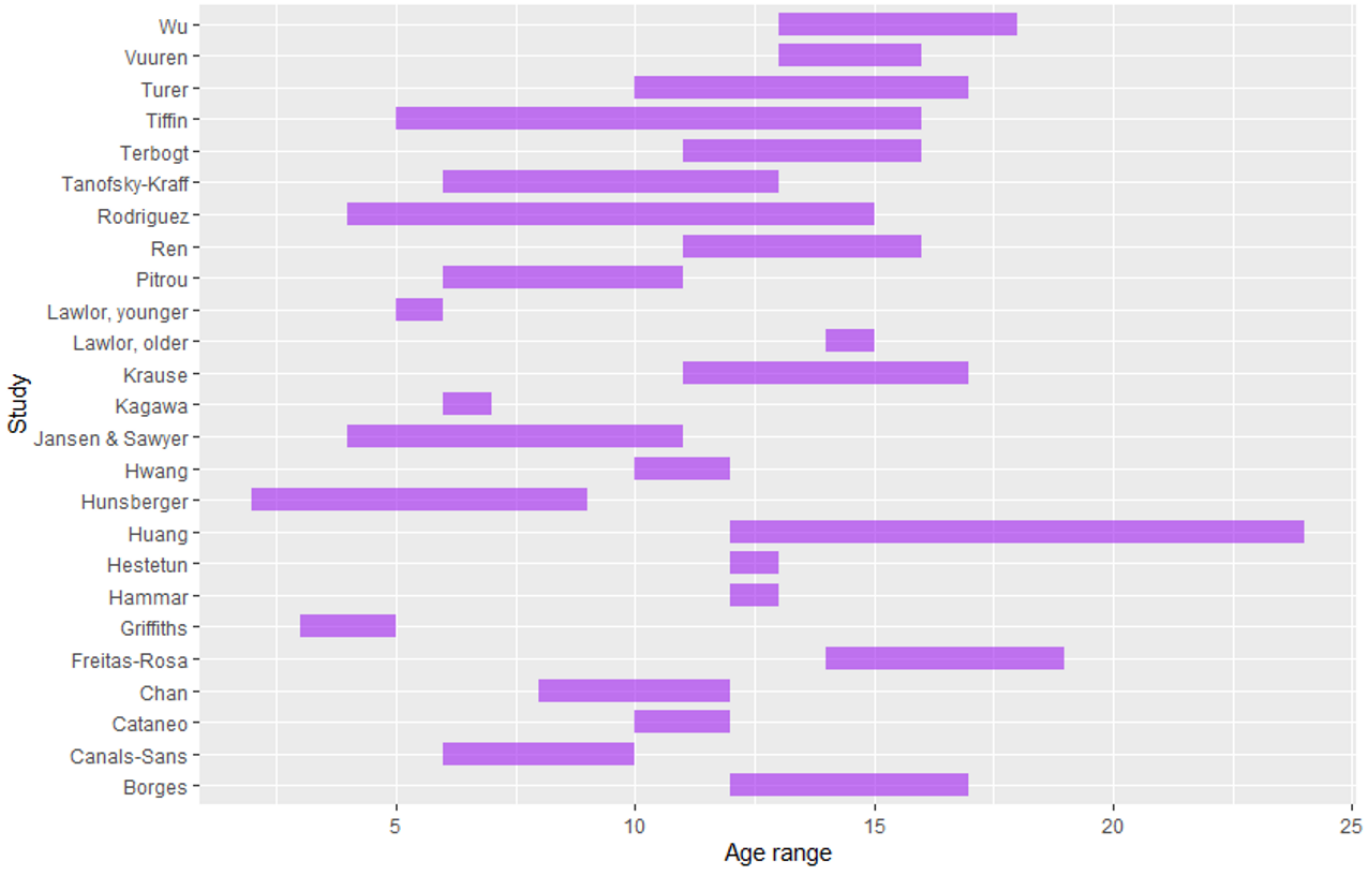

Figure 5.16. Age ranges of the participants across the included studies analyzing the association between overweight, obesity, and mental disorders among children and adolescents

5.4. Cross-sectional association between obesity and mental disorders among children and adolescents

Studies comprising only of participants with obesity were additionally analyzed. A total of 18 studies (57, 110, 112, 114, 116, 118, 120, 122, 123, 126, 129, 133, 135, 136, 138, 142, 145, 148) comprising 35 separate effect sizes were included in the meta-analysis to estimate the prevalence of mental disorders among children and adolescents with obesity. They were all conducted between 1995 and 2016 and originated from 11 different countries (Turkey, South Korea, India, Indonesia, China, Spain, Netherlands, USA, Germany, Australia, UK). Characteristics of the studies included in the analyses are presented in Table 5.5 and Table 5.6. The distribution of studies included in the analyses of OR by country is shown in Figure 5.17.

A statistically significant OR of 1.80 (95 % CI, 1.45-2.24; z=6.32, p<0.01) of mental disorders among children and adolescents affected with obesity was estimated by random-effects meta-analysis of 18 studies. A forest plot is shown in Figure 5.18. The meta-analysis results indicated a large degree of variance in the study effect sizes (Q=217.95; df=17; p<0.01; I^2=92.20).

The publication bias was illustrated by the funnel plot for the association between obesity and mental disorders among children and adolescents (Figure 5.19). The funnel plot visually seemed symmetric, and Egger`s test indicated no publication bias (p=0.11). Orwin's Fail-safe N indicated that 129 studies with an OR of 1.05 are needed to bring the OR under a trivial value of 1.10. The funnel plot, Egger`s test, and Orwin's Fail-safe N suggested no publication bias.

The average quality score of the 18 studies included in the analysis of the prevalence of mental disorders among children and adolescents with obesity was 72.67 %. Seven studies were of high quality, ten were of moderate quality, and 1 study was of low quality (Tables 5.3. and 5.4.).

A cumulative meta-analysis of the association between obesity and mental disorders among children and adolescents is shown in Figure 5.20.

The age ranges of study samples are shown in Figure 5.21.

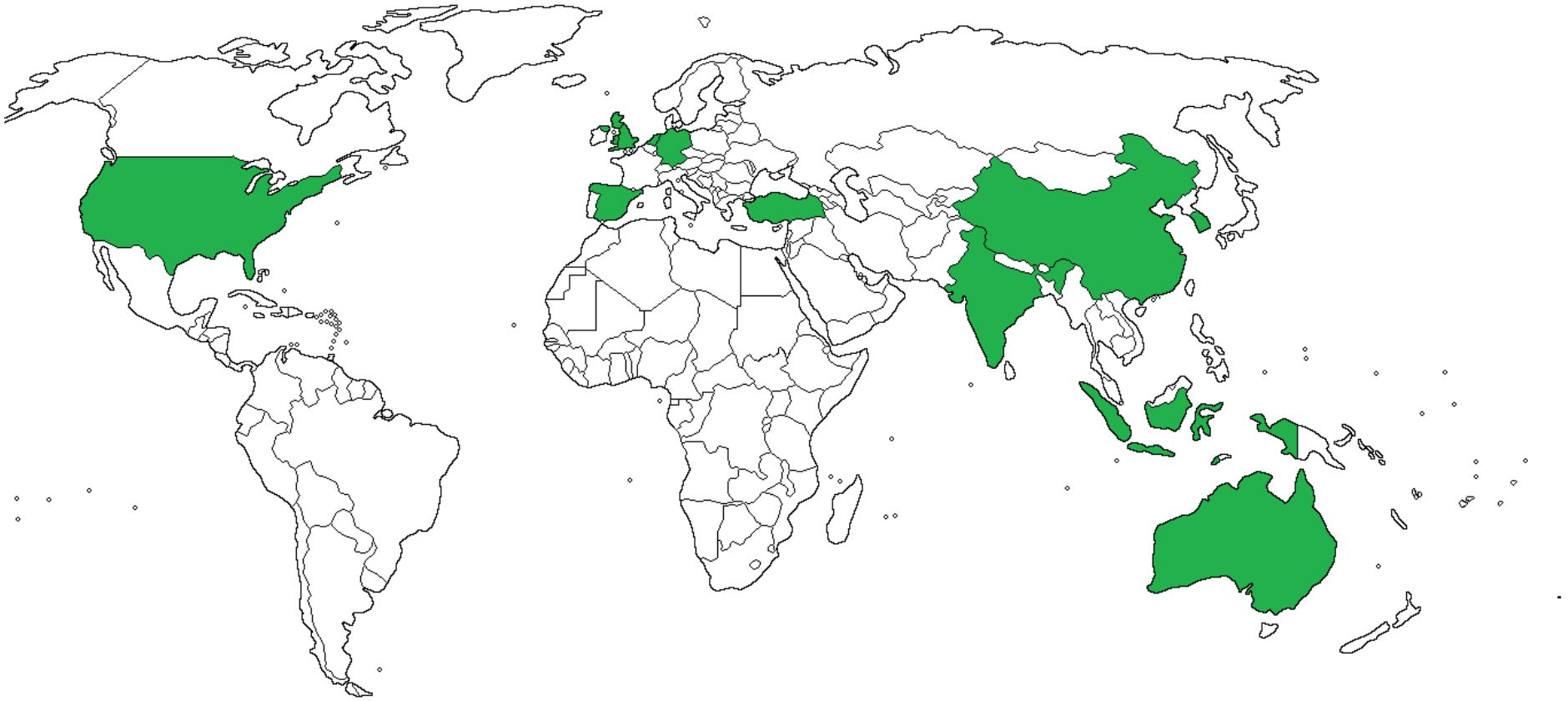

Figure 5.17. Distribution of the studies included in the analysis of mental disorders odds ratio among children and adolescents with obesity by country. The territories on the map may not correspond to the actual borders of the countries. Downloaded with permission from: https://hr.wikipedia.org/wiki/Datoteka:Blank_map_political_world_territories.png. Author: Roy Nick Norse.

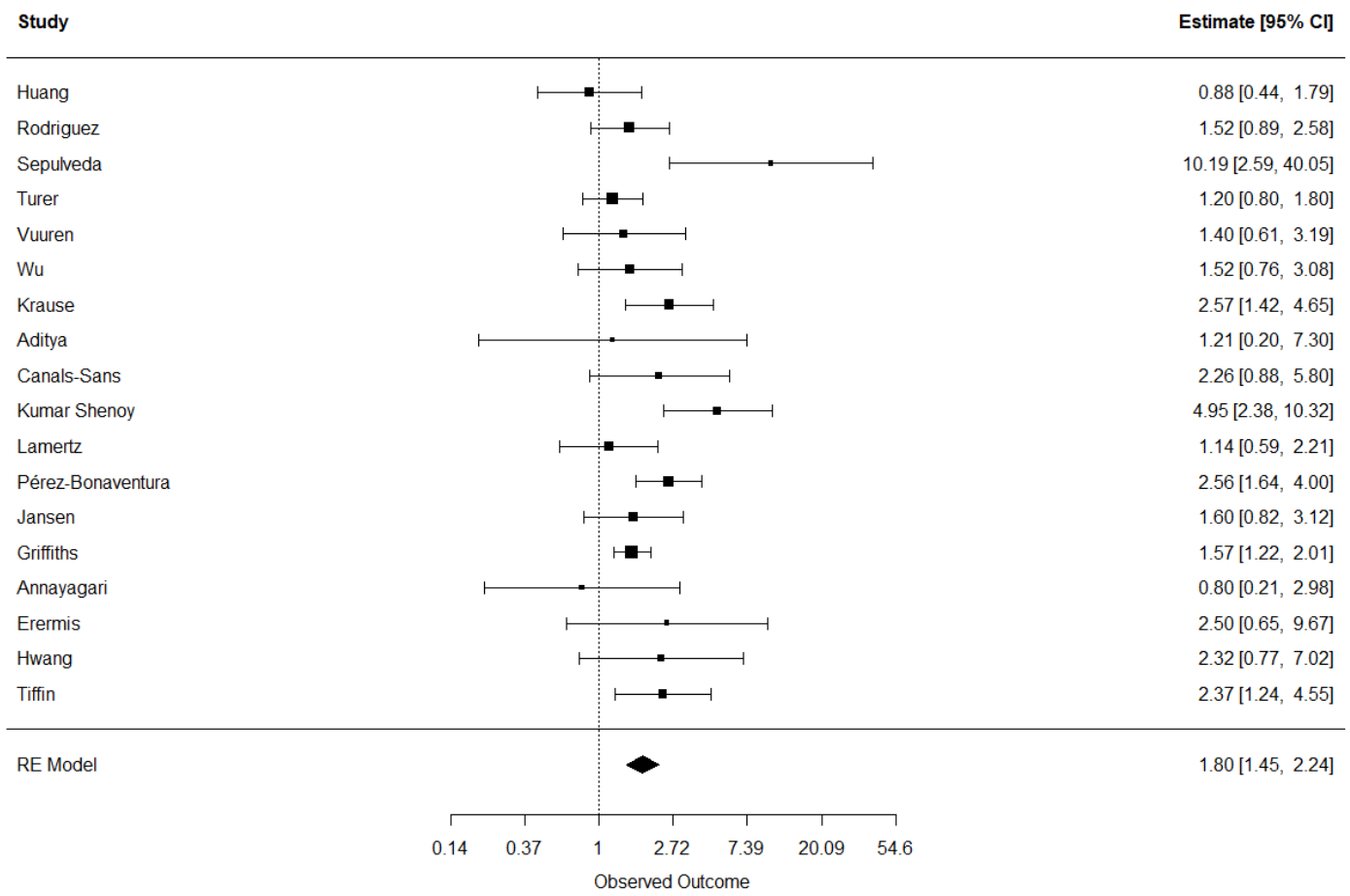

Figure 5.18. Forest plot for the association between obesity and mental disorders among children and adolescents. RE, random effects; CI, confidence interval.

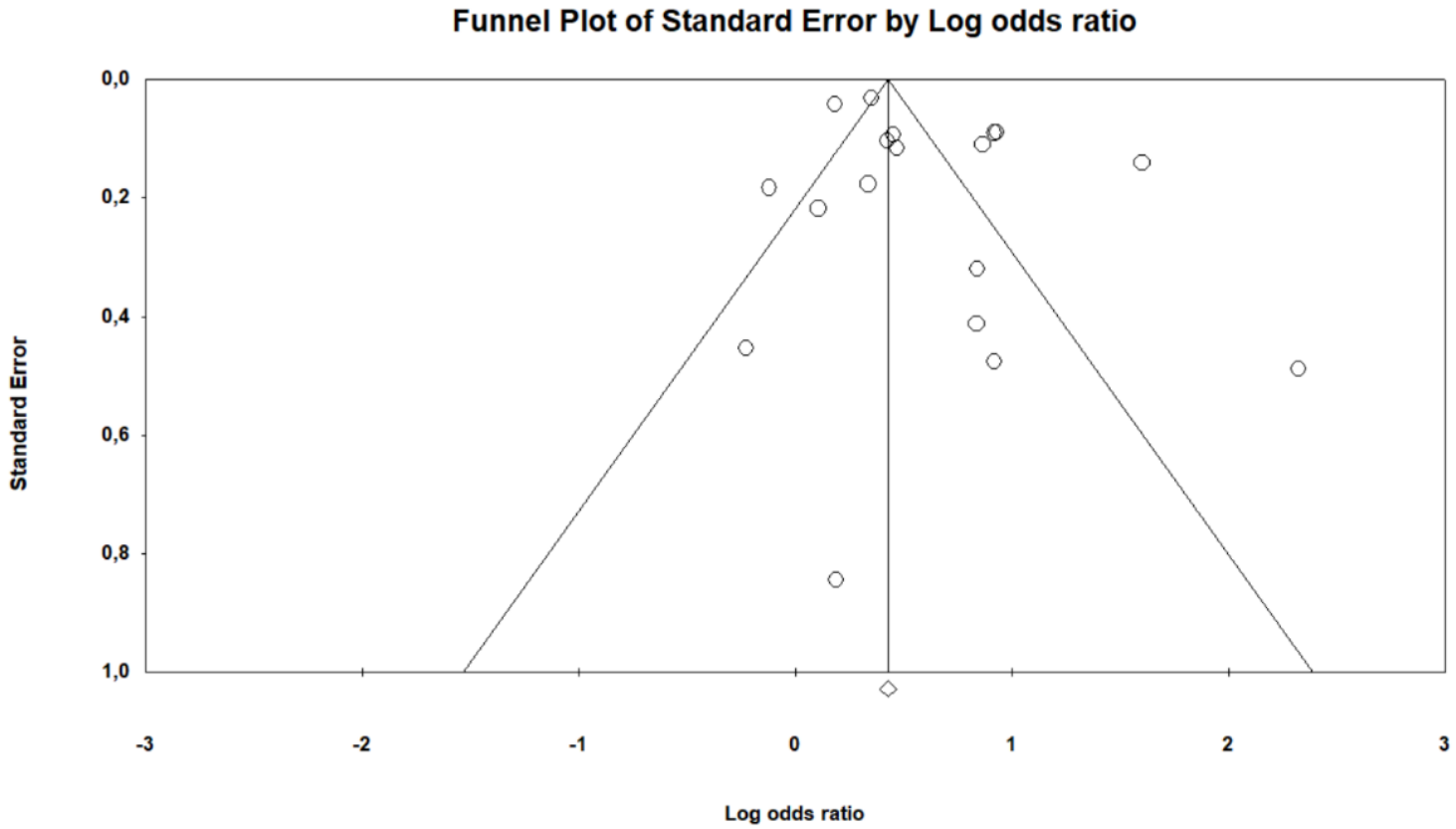

Figure 5.19. Funnel plot for the association between obesity and mental disorders among children and adolescents

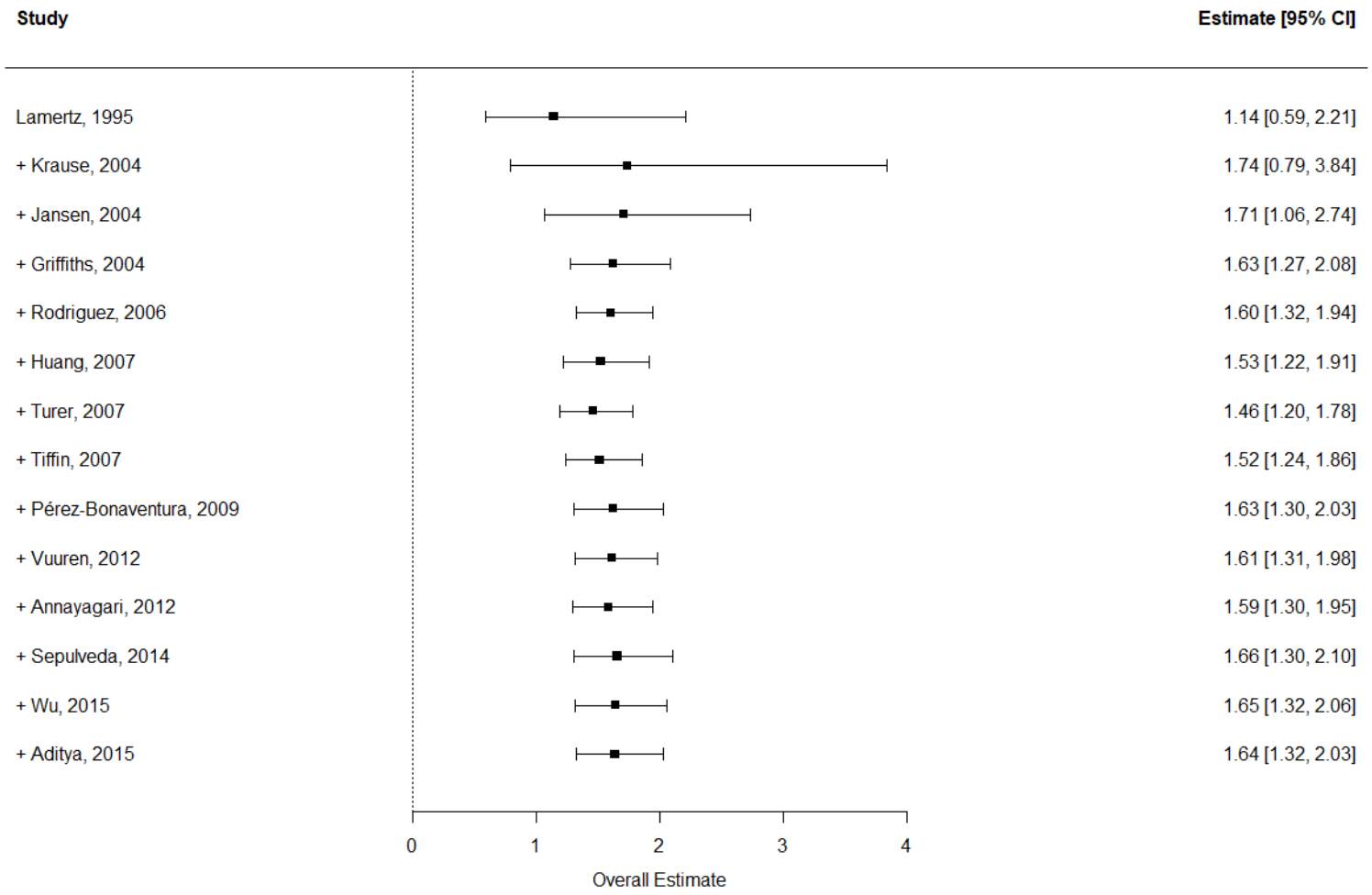

Figure 5.20. Cumulative meta-analysis for the association between obesity and mental disorders among children and adolescents. CI, confidence interval.

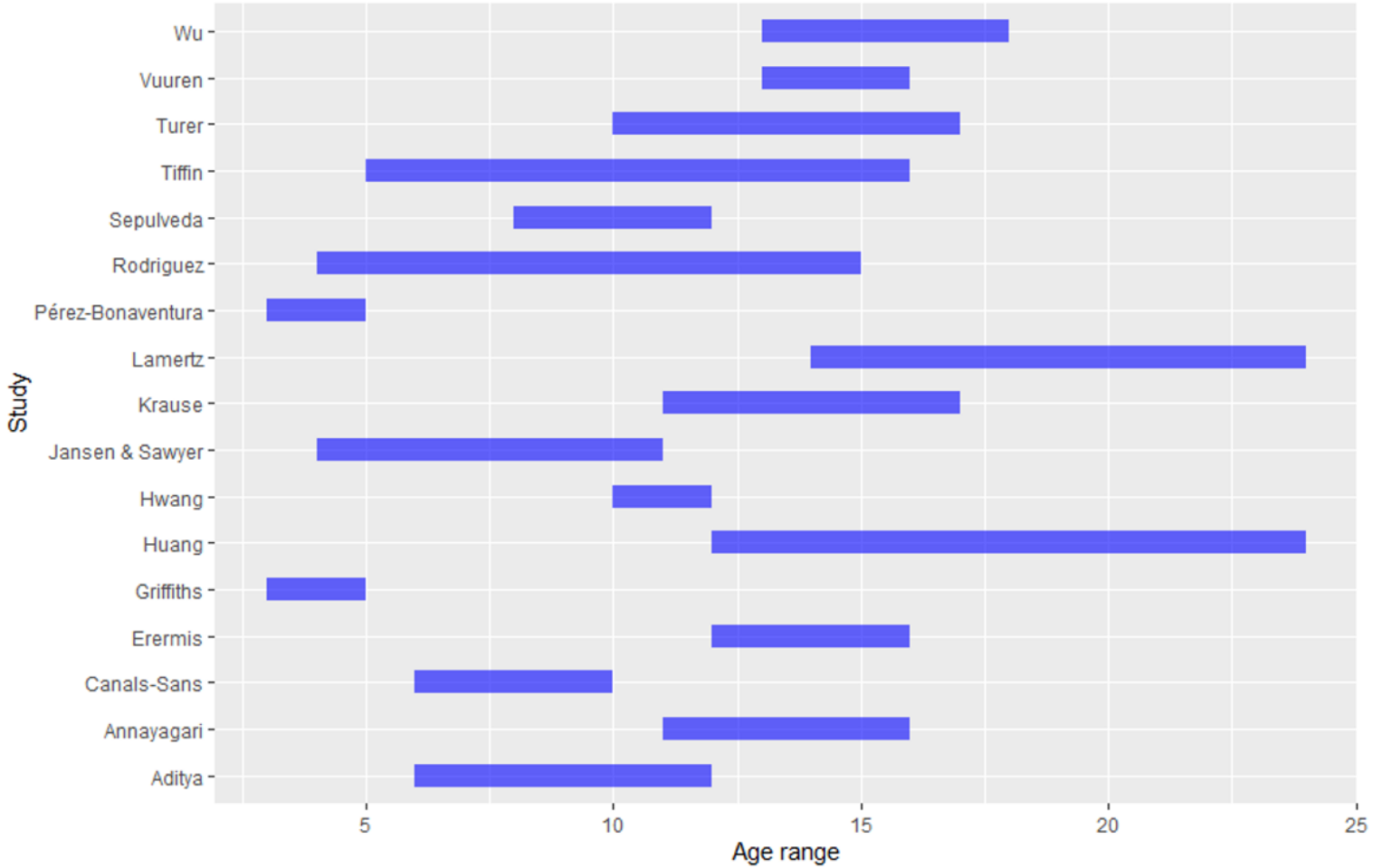

Figure 5.21. Age ranges of the participants across the included studies analyzing the association between obesity and mental disorders among children and adolescents

To explore the association between effect sizes and GDP of the countries from which examinees originate and a number of the confounders controlled for in the analyses, meta-regression was conducted. There was no association between effect sizes and GDP (z=1.02, p=0.31). There was no association between effect sizes and the number of confounders (z=-1.66, p=0.10). Bubble plots are shown in Figure 5.22. and 5.23.

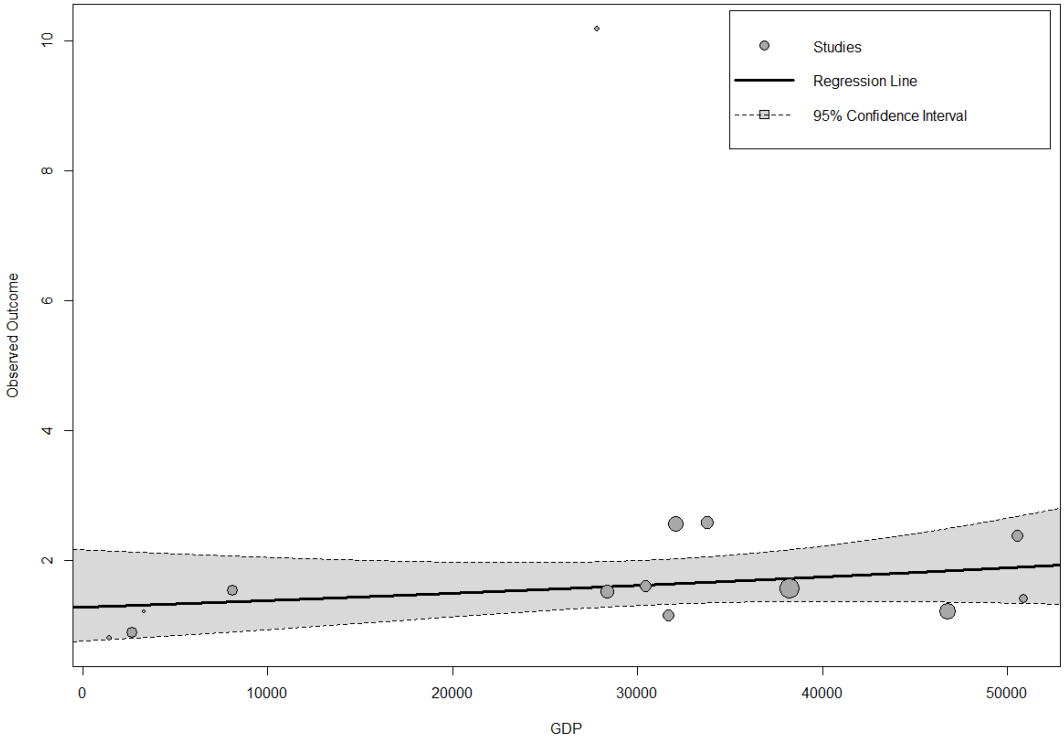

Figure 5.22. Bubble plot for the association between odds ratio for mental disorders among children and adolescents with obesity and GDP of the countries from which examinees originate. GDP, Gross domestic product.

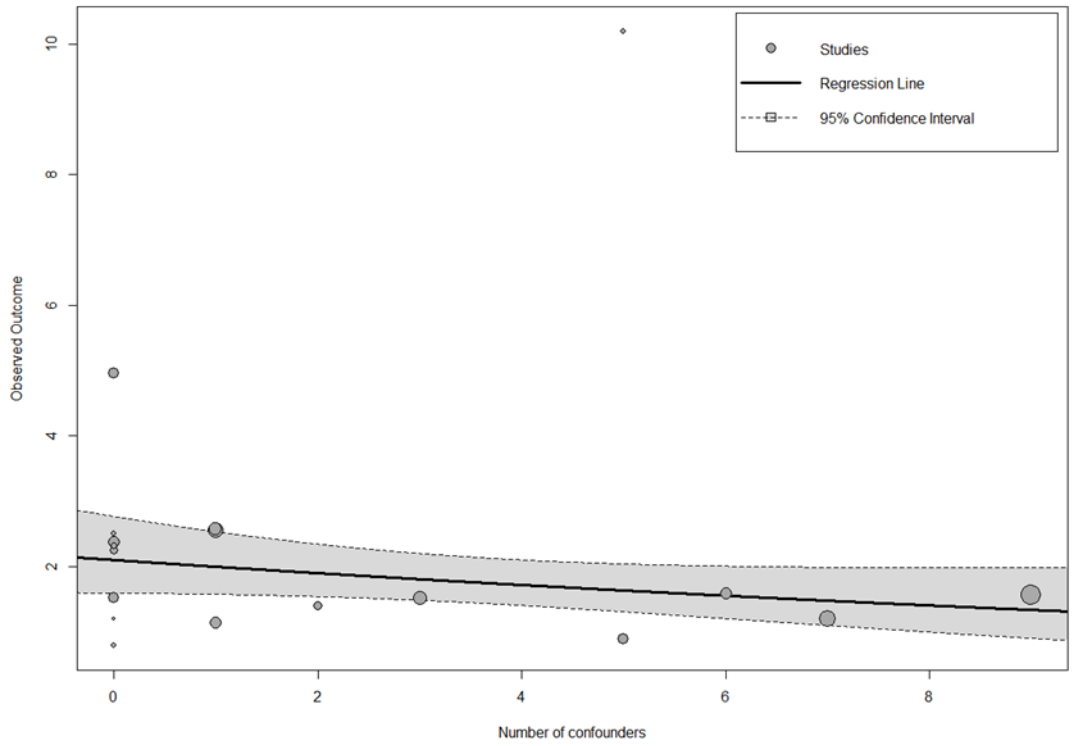

Figure 5.23. Bubble plot for the association between odds ratio for mental disorders among children and adolescents with obesity and number of confounders controlled for in the analyses

Overall and subgroup analyses are shown in Table 5.8. There was no significant difference (Q=0.41; df=1; p=0.52) in the OR between the samples from Europe or Asia. There was no significant difference in the OR between samples consisting of children and samples consisting of adolescents (Q=0.26; df=1; p=0.61). There was no significant difference in the OR between community, nationally representative samples, or convenient study samples (Q=0.26; df=2; p=0.88). There was no significant difference in the OR between the probably not representative samples and probably representative samples from a large area (Q=0.39; df=1; p=0.54). There was no significant difference between studies in which the informant was a parent or participant themself (Q=0.39; df=1; p=0.53). There was no significant difference between studies using CDC, WHO, IOTF, or National growth reference (Q=0.27; df=3; p=0.97). There was no significant difference between studies using SDQ, CBCL, or MSQA (Q=5.34; df=2; p=0.07). There was a significant difference between studies in which participants were measured or studies in which participants reported height and weight (Q=4.33; df=1; p<0.05). There was no significant difference between studies in which the control group included overweight or studies in which did not (Q=0.01; df=1; p=0.93). There was no significant difference in the OR

between studies including borderline psychiatric assessment results or studies including only abnormal psychiatric assessment results (Q=0.62; df=1; p=0.43).

A sensitivity analysis was conducted to test the effect of transformed effect sizes. The OR remained significant when only 7 studies with untransformed effect sizes were included in the meta-analysis (OR 1.62 (95 % CI, 1.23-2.15; z=3.38, p<0.01); Q=56.25; df=6; p<0.01; I^2=89.33).

Table 5.8. Overall and subgroup cross-sectional analyses of obesity with the risk of having a mental disorder

Type of analysis	N of studies (subgroups)	Odds ratio	95 % CI	p-value	Heterogeneity
OR among children and adolescents with obesity	18	1.83	1.52-2.21	p<0.01	Q=217.95; df=17; p<0.01; I^2=92.20
Limited to Asia	6 (7)	1.51	0.81-2.80	p=0.20	Q=71.84; df=6; p<0.01; I^2=91.65
Limited to Europe	7 (17)	1.97	1.15-3.36	p<0.05	Q=1399.90; df=16; p<0.01; I^2=98.86
Limited to adolescents	10 (15)	1.58	1.16-2.14	p<0.01	Q=134.85; df=14; p<0.01; I^2=89.62
Limited to children	3 (8)	1.99	0.87-4.58	p=0.11	Q=1347.65; df=7; p<0.01; I^2=99.48
Limited to community representative samples	8 (14)	1.90	1.32-2.72	p<0.01	Q=107.48; df=13; p<0.01; I^2=87.90
Limited to nationally representative samples	6 (11)	1.79	1.02-3.14	p<0.05	Q=1357.07; df=10; p<0.01; I^2=99.26
Limited to convenient sample	2 (2)	1.40	0.46-4.30	p=0.56	Q=3.04; df=1; p=0.08; I^2=67.09

OR, odds ratio; N, number; CI, confidence interval; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; SDQ, Strengths and Difficulties Questionnaire; MSQA, Multidimensional Sub-health Questionnaire of Adolescent; CBCL, Child Behavior Checklist;

Table 5.8. Overall and subgroup cross-sectional analyses of obesity with the risk of having a mental disorder continued

Type of analysis	N of studies (subgroups)	Odds ratio	95 % CI	p-value	Heterogeneity
Limited to large area – probably not representative sample	8 (14)	1.64	1.15-2.35	p<0.01	Q=102.46; df=13; p<0.01; I^2=87.31
Limited to large area – probably representative sample	7 (12)	2.02	1.17-3.47	p<0.05	Q=1373.37; df=11; p<0.01; I^2=99.20
Limited to studies with untransformed effect sizes	7 (10)	1.61	1.26-2.06	p<0.01	Q=61.55; df=9; p<0.01; I^2=85.38
Limited to studies with transformed effect sizes	10 (18)	1.81	1.05-3.09	p<0.05	Q=1437.54; df=17; p<0.01; I^2=98.82
Limited to studies using SDQ	7 (14)	1.96	1.13-3.41	p<0.05	Q=1381.49; df=13; p<0.05; I^2=99.06
Limited to studies using CBCL	2 (2)	2.37	1.41-3.99	p<0.01	Q=0.02; df=1; p=0.89; I^2=0
Limited to studies using MSQA	2 (3)	1.11	0.71-1.73	p=0.66	Q=6.90; df=2; p<0.05; I^2=71.01
Limited to studies in which the informant was parent	11 (17)	1.91	1.20-3.01	p<0.01	Q=1471.81; df=16; p<0.01; I^2=98.91
Limited to studies in which the informant was participant himself	6 (11)	1.59	1.14-2.21	p<0.01	Q=46.65; df=10; p<0.01; I^2=78.57
Limited to studies using CDC growth reference	3 (3)	2.07	0.62-6.88	p=0.24	Q=93.75; df=2; p<0.01; I^2=97.87
Limited to studies using WHO growth reference	3 (5)	1.99	1.30-3.06	p<0.01	Q=31.82; df=4; p<0.01; I^2=87.43
Limited to studies using IOTF growth reference	7 (14)	1.71	0.93-3.12	p=0.08	Q=1335.00; df=13; p<0.01; I^2=99.03

OR, odds ratio; N, number; CI, confidence interval; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; SDQ, Strengths and Difficulties Questionnaire; MSQA, Multidimensional Sub-health Questionnaire of Adolescent; CBCL, Child Behavior Checklist;

Table 5.8. Overall and subgroup cross-sectional analyses of obesity with the risk of having a mental disorder continued

Type of analysis	N of studies (subgroups)	Odds ratio	95 % CI	p-value	Heterogeneity
Limited to studies using National growth reference	4 (6)	1.75	1.09-2.81	p<0.05	Q=27.00; df=5; p<0.01; I^2=81.48
Limited to studies in which participants were measured	10 (16)	2.36	1.37-4.06	p<0.01	Q=1457.33; df=15; p<0.01; I^2=98.97
Limited to studies in which participants reported weight and height	4 (8)	1.29	1.10-1.51	p<0.01	Q=9.45; df=7; p=0.22; I^2=25.99
Limited to studies including borderline psychiatric test results	2 (3)	2.06	1.24-3.40	p<0.01	Q=13.07; df=2; p<0.01; I^2=84.69
Limited to studies including only abnormal psychiatric test results	9 (13)	1.54	0.93-2.57	p=0.10	Q=1343.28; df=12; p<0.01; I^2=99.11
Limited to studies including overweight in the control group	3 (8)	1.79	1.19-2.68	p<0.01	Q=30.07; df=7; p<0.01; I^2=76.72
Limited to studies not including overweight in the control group	3 (19)	1.74	1.15-2.64	p<0.01	Q=1386.77; df=18; p<0.01; I^2=98.70

OR, odds ratio; N, number; CI, confidence interval; WHO, World Health Organization; CDC, Centers for Disease Control and Prevention; IOTF, International Obesity Task Force; SDQ, Strengths and Difficulties Questionnaire; MSQA, Multidimensional Sub-health Questionnaire of Adolescent; CBCL, Child Behavior Checklist;

The total number of the included cross-sectional and case-control studies about mental disorders associated with overweight and obesity published by year is presented in Figure 5.24.

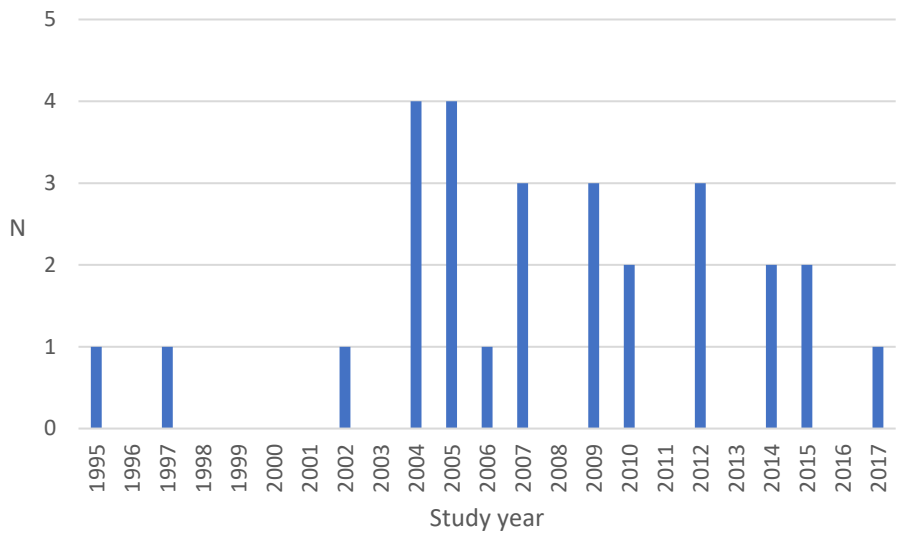

Figure 5.24. The number of cross-sectional and case-control studies about mental disorders associated with overweight and obesity published by year. N, number of studies.

5.5. Longitudinal association between overweight/obesity and mental disorders among children and adolescents

A total of 9 studies (135, 137, 141, 142, 149-153) were included in the meta-analyses to estimate the prospective association between mental disorders and overweight and obesity among children and adolescents. They were all conducted between 1980 and 2011 and originated from 11 different countries. Characteristics of the studies included in the analyses are presented in Table 5.9. and Table 5.10.

Six studies (135, 137, 141, 150, 152, 153) comprising 12 separate effect sizes and 24 338 participants were included in the random-effects meta-analysis to obtain the longitudinal association between overweight/obesity and mental disorders among children and adolescents. When analyzing longitudinal studies, there was no statistically significant OR for mental disorders among children and adolescents with overweight and obesity (OR 1.02 (95 % CI, 0.87-1.21; z=0.25, p=0.81)). A forest plot is shown in Figure 5.25. There was no observed heterogeneity (Q=4.41; df=6; p=0.49; I^2=0).

A meta-regression of 6 studies indicated no significant relationship between the effect sizes of the studies and the duration of follow-up (z=0.08, p=0.93). The bubble plot is shown in Figure 5.26.

Table 5.9. Characteristics of the included longitudinal studies

First author	Study years	Study country	Sample size	Growth reference	Age category	Age range at the beginning	Age range at the follow-up	Follow up after N years	Sample (representative)	Subgroups according to weight
Assuncao	2004-2008	Brazil	4325	WHO	Adolescents	11 to 12	14 to 15	3,5	Community	OB
Clark	2001-2003	UK	1461	UK 1990 growth reference	Adolescents	11 to 14	13 to 16	2	Community	OW+OB
Griffiths	2003-2007	UK	11202	IOTF	Children	3	5	2	Nationally	OW and OB
Hunsberger	2007-2010	Belgium, Cyprus, Estonia, Germany, Hungary, Italy, Spain, Sweden	7213	IOTF	Children	2 to 9	NR	2	Community	OW+OB
Lawlor	1986-1998	Australia	2430	IOTF	Adolescents	5	14	9	Community	OW+OB
Pérez-Bonaventura	2009-2011	Spain	1119	WHO	Children	3	4	2	Community	OB
Viner	1980-2000	Great Britain	8490	UK 1990 growth reference	Adolescents	10	29 to 30	20	Nationally	OB
Wang	2000-2008	Hong Kong	4976	WHO	Children	2 to 3	10 to 11	8	Community	NR
Sawyer	2004-2008	Australia	3363	Made for this sample	Children	4 to 5	8 to 9	4	Nationally	OW and OB

WHO, World Health Organization; IOTF, International Obesity Task Force; NR, not reported; N, number; OW, overweight; OB, obesity; OW+OB, overweight and obesity are analyzed together; OW and OB, overweight and obesity are analyzed as separate subgroups, results for both subgroups are provided;

Table 5.10. Methodological characteristics of the included longitudinal studies

First author	UW in the control group	OW in the control group	Growth reference	BMI measured or reported	Psychiatric tool	Informant	Effect size measure	Subgroups in study	Controlled confounders
Assuncao	maybe	maybe	WHO	Measured	SDQ	Parent	B coefficient	Total, M, F	skin color, SES, maternal education, regime in the last y, use of weight loss medication in the last y, self-perception of body image, maternal SRQ score, SDQ score at 11 y
Clark	maybe	no	UK 1990 growth reference	Measured	SDQ	Self-report	OR	Total, OB	age, gender, gender x age, ethnicity, eligibility for free school meals, general health status, long-standing illness, smoking, alcohol use, drug use
Griffiths	maybe	no	IOTF	Measured	SDQ	Parent	OR	M OW, M OB, F OW, F OB	child's ethnicity, maternal SES, mother's highest academic qualification, maternal age at birth, household income, lone-motherhood status, N of children in the household, maternal treatment for depression or anxiety, maternal weight status, prior problems at age 3, weight status at age 5
Hunsberger	yes	no	IOTF	Measured	SDQ	Parent	OR	Total	age, sex, parental education, intervention, country
Lawlor	maybe	no	IOTF	Measured	CBCL	Parent	OR	M, F	age (in days) of the children at 14 y follow up, mother's age at childbirth, maternal and paternal education, ethnicity, Tanner's score of pubertal development, maternal and paternal BMI, family income
Pérez-Bonaventura	maybe	yes	WHO	Measured	SDQ	Parent	B coefficient	4 y, 5 y	SES, SDQ scores at baseline
Viner	maybe	maybe	UK 1990 growth reference	Measured	Rutter Scale	Self-report	OR	M, F	maternal education, social class in childhood and adulthood, maternal and paternal BMI, height at 10 and 30 y
Wang	maybe	no	WHO	Healthcare-reported	Rutter Scale	Parent	B coefficient	Total	sex, age at Rutter Scales measurement, highest parental education, household income per head at birth, mother's place of birth
Sawyer	maybe	no	Made for this sample	Measured	SDQ	Parent	OR	Parent-reported, Teacher reported	mother's education level, mother's Kessler K6 scale score, whether the mother spoke a language other than English at home, child's indigenous status, mother's occupation, neighborhood disadvantage, SDQ or PedsQL scale score at age 4 to 5 y

UW, underweight; OW, overweight; OB, obesity; OR, odds ratio; SD, standard deviation; WHO, World Health Organization; IOTF, International Obesity Task Force; M, male; F, female; SDQ, Strengths and Difficulties Questionnaire; SES, socioeconomic status; y, years; N, number; SES, socioeconomic status; CBCL, Child Behavior Checklist; BMI, body mass index; PedsQL, Pediatric Quality of Life Inventory;

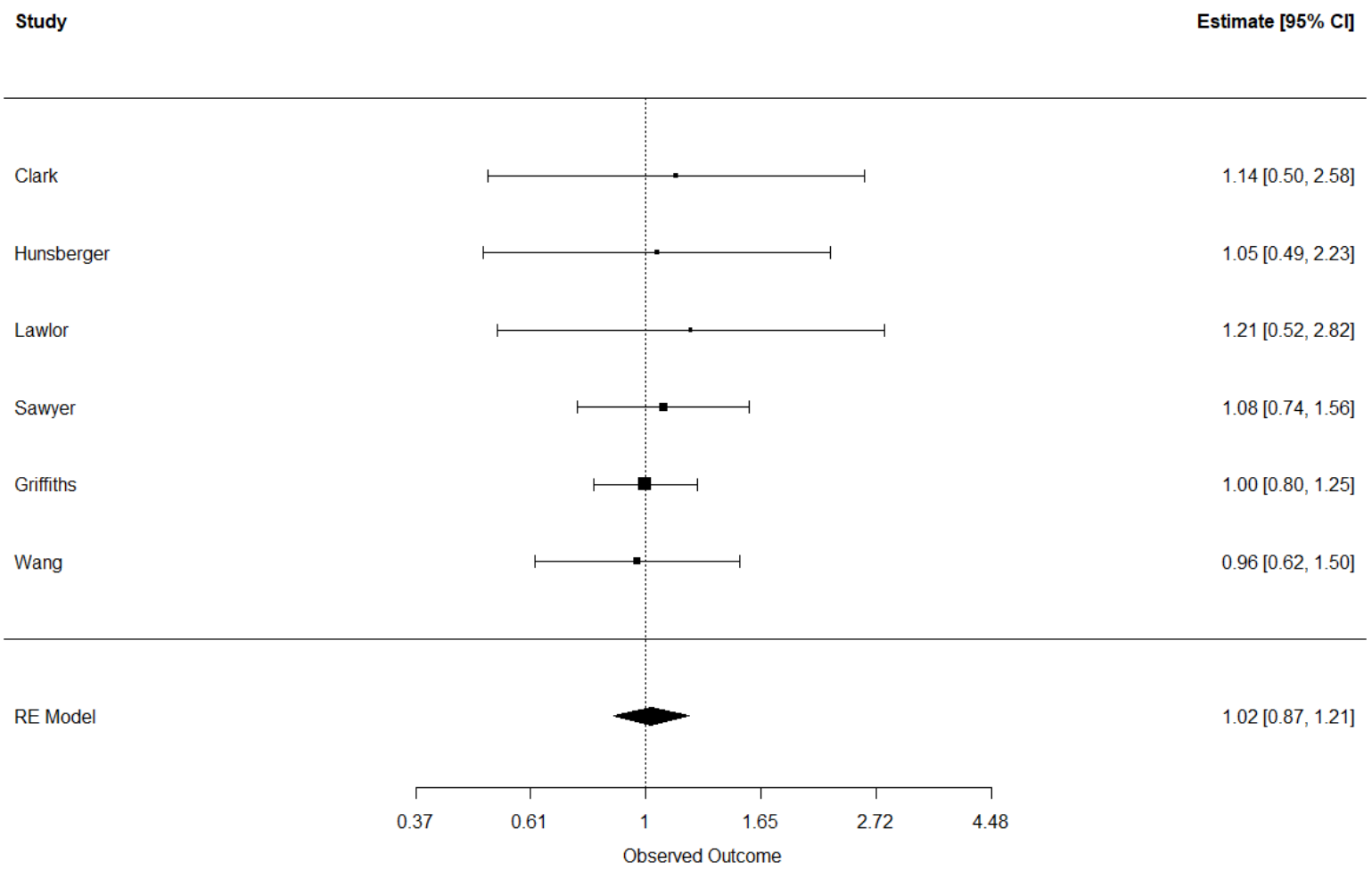

Figure 5.25. Forest plot for the longitudinal association between overweight/obesity and mental disorders among children and adolescents

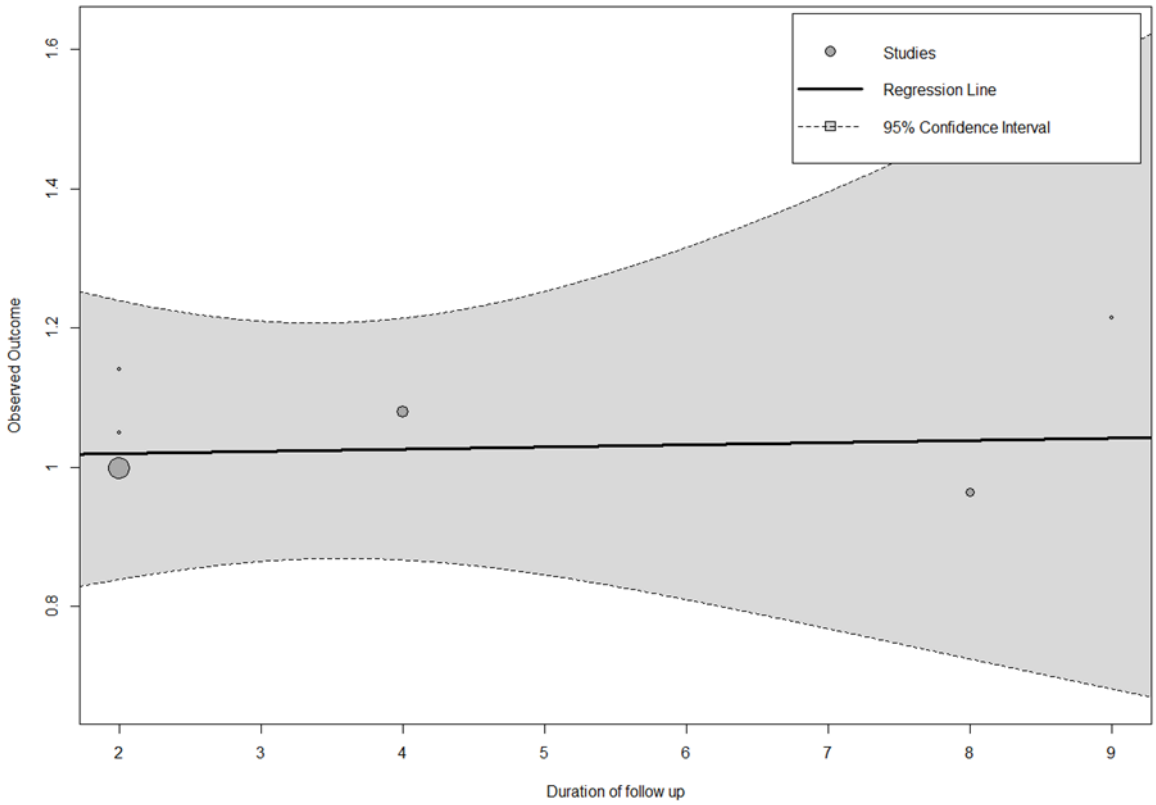

Figure 5.26. Bubble plot for the association between longitudinal odds ratio for mental disorders among children and adolescents with overweight and obesity and duration of follow up in studies

Two studies were analyzed to assess the gender of the study participants as moderator. There was no significant difference in the OR between samples consisting of boys or girls (Q=0.56; df=1; p=0.46). Additional three studies were included to assess the weight status category as a moderator. The analysis suggested no significant difference (Q=0.38; df=1; p=0.54) in the OR between the samples consisting of children and adolescents with overweight and obesity or obesity only. There were no significant differences (Q=0.04; df=1; p=0.85) in the OR between the samples from Europe or Oceania. There was no significant difference in the OR between samples consisting of children and samples consisting of adolescents (Q=0.12; df=1; p=0.73). There was no difference in the OR between community or nationally representative samples (Q=0.02; df=1; p=0.88). There was no significant difference between studies in which the informant was a parent or participant themself (Q=1.38; df=1; p=0.24). There was no significant difference between the studies using the SDQ, CBCL, or Rutter scale (Q=0.85; df=2; p=0.66).

There was no significant difference between studies regarding sample coding (Q=0.28; df=2; p=0.87). Overall and subgroup analyses are shown in Table 5.11.

A sensitivity analysis revealed that OR remained insignificant when the meta-analysis was limited to studies with untransformed effect sizes (Table 5.11.).

Table 5.11. Overall and subgroup longitudinal analyses of overweight/obesity with the risk of having a mental disorder

Type of analysis	N of studies (subgroups)	Odds ratio	95 % CI	p-value	Heterogeneity
All longitudinal studies	6	1.01	0.97-1.05	p=0.81	Q=4.41; df=5; p=0.49; I^2=0
Limited to female	2 (3)	0.86	0.34-2.13	p=0.74	Q=225.74; df=2; p<0.01; I^2=99.11
Limited to male	2 (3)	1.33	0.66-2.68	p=0.43	Q=137.54; df=2; p<0.01; I^2=98.55
Limited to obesity	5 (8)	1.29	0.64-2.60	p=0.48	Q=823.50; df=7; p<0.01; I^2=99.15
Limited to Oceania	2 (4)	1.09	0.99-1.20	p=0.09	Q=2.17; df=3; p=0.54; I^2=0
Limited to Europe	3 (6)	1.03	0.61-1.77	p=0.9	Q=533.72; df=5; p<0.01; I^2=99.06
Limited to adolescents	1 (1)	1.14	0.81-1.60	p=0.45	Q=0; df=0; p=1; I^2=0
Limited to children	5 (10)	1.05	0.75-1.47	p=0.78	Q=538.81; df=9; p<0.01; I^2=98.33
Limited to community representative samples	4 (5)	0.99	0.91-1.09	p=0.84	Q=1.83; df=4; p=0.77; I^2=0
Limited to nationally representative samples	2 (6)	1.03	0.64-1.65	p=0.91	Q=537.39; df=5; p<0.01; I^2=99.07

N, number; CI, confidence interval; SDQ, Strengths and Difficulties Questionnaire; CBCL, Child Behavior Checklist;

Table 5.11. Overall and subgroup longitudinal analyses of overweight/obesity with the risk of having a mental disorder continued

Type of analysis	N of studies (subgroups)	Odds ratio	95 % CI	p-value	Heterogeneity
Limited to studies with untransformed effect sizes	4 (6)	1.09	0.99-1.19	p=0.06	Q=2.30; df=5; p=0.81; I^2=0
Limited to studies using SDQ	4 (8)	1.04	0.70-1.56	p=0.84	Q=537.94; df=7; p<0.01; I^2=98.70
Limited to studies using CBCL	1 (2)	1.21	0.73-2.02	p=0.46	Q=0.15; df=1; p=0.70; I^2=0
Limited to studies in which the informant was parent	5 (9)	1.04	0.71-1.51	p=0.85	Q=534.11; df=8; p<0.01; I^2=98.50

N, number; CI, confidence interval; SDQ, Strengths and Difficulties Questionnaire; CBCL, Child Behavior Checklist;

Publication bias could not be assessed for longitudinal studies analyzing the association between overweight, obesity, and mental disorders, since less than ten studies were included in the analysis.

The average quality score of the nine studies included in the analysis of the prospective association between overweight and obesity and mental disorders among children and adolescents was 73.74 %. Five studies were of high quality, three were of moderate quality, and one study was of low quality (Table 5.12).

The summary of all analyses conducted in this study and their findings are presented in Table 5.13.

Table 5.12. The methodological quality of the included longitudinal studies according to The Joanna Briggs Institute Critical Appraisal tool

Study first author	Were the two groups similar and recruited from the same population?	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Was the exposure measured in a valid and reliable way?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the groups/ participants free of the outcome at the start of the study (or at the moment of exposure)?	Were the outcomes measured in a valid and reliable way?	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	Were strategies to address incomplete follow up utilized?	Was appropriate statistical analysis used?	Yes (n/11)
Assuncao	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Not applicable	Yes	9/11
Clark	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	9/11
Griffiths	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	10/11
Hunsberger	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	No	No	Yes	8/11
Lawlor	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	9/11
Perez-Bonaventura	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Not applicable	Yes	9/11
Viner	No	Yes	No	Yes	Yes	Unclear	Yes	Unclear	No	No	Yes	5/11
Wang	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	6/11
Sawyer	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	8/11

n, number;

Table 5.13. Summary of all conducted analyses and their main characteristics and findings

Meta-analysis	N of included studies	N of participants	Outcome and heterogeneity	Average quality of studies	Moderators	Conclusion
Prevalence of mental disorders among children and adolescents with OW and OB	17	9 278	Prevalence 23.80 % (95 % CI, 17.10-32.10) I^2=96.30	76.50 %	Weight category, age	Around 24 % of children and adolescents with overweight and obesity have a mental disorder
Prevalence of mental disorders among children and adolescents with OB	10	4 442	Prevalence 30.43 % (95 % CI, 23.20-38.77) I^2=96.80	68.70 %	None	Around 30 % of children and adolescents with obesity have a mental disorder
OR for mental disorders among children and adolescents with OW and OB	25	117 705	OR 1.28 (95 % CI, 1.19-1.40) I^2=86.29	82.40 %	Weight category, sample design	Children and adolescents with overweight and obesity have 30 % higher odds of mental disorders than their peers with normal weight
OR for mental disorders among children and adolescents with OB	18	37 204	OR 1.83 (95 % CI, 1.52-2.21) I^2=92.20	72.67 %	Gender, measurement of height and weight	Children and adolescents with obesity have 80 % higher odds of mental disorders than their peers with normal weight
Longitudinal OR for mental disorders among children and adolescents with OW and OB	6	24 338	OR 1.02 (95 % CI, 0.87-1.21) I^2=0	73.74 %	None	Overweight and obesity do not lead to mental disorders among children and adolescents

N, number; OW, overweight; OB, obesity; OR, odds ratio; CI, confidence interval;

6. Discussion

This is, to the author's knowledge, the first systematic review of the prevalence of total psychopathology among the worldwide population of children and adolescents with overweight and obesity, about the association between these illnesses, and the first aim to quantitatively and qualitatively analyze the existing studies on this topic. This study revealed that almost every fourth child and adolescent affected with overweight or obesity has a mental disorder. Children and adolescents affected with overweight and obesity have more than 30 % higher odds of any mental disorder compared to their peers with normal weight. However, according to analyzed studies, this meta-analysis shows that overweight or obesity do not increase the odds of mental disorders in the future.

The systematic review yielded around 15 500 bibliographic records, which is far more than existing systematic reviews focused on specific mental disorders did (31, 154); however, this is not surprising considering that the search strategy needed to be very sensitive and reach all the studies analyzing psychopathology in total. Out of 120 full texts analyzed, less than half were included, although the criteria for inclusion were very wide. As can be seen from Figure 1, the reason for exclusion originated majorly from the way of reporting results, i.e., invalid outcomes. Many authors reported screening results for separate subscales; however, they failed to report total screening results. Since separate subscales could not be combined, while a single participant could have had more than one mental disorder, this data could not be utilized. Also, many authors analyzed only certain disorders or groups of disorders, not total psychopathology, which was the aim of this study. It is already recognized that mismatching outcomes are very frequent reasons for excluding articles retrieved by systematic literature search (155). When considering the association between obesity and psychopathology, research outcomes are very heterogeneous; thus, there are not many studies that can be combined. Finally, a total of 46 studies were included, out of which 18 provided information about the prevalence of mental disorders, while OR was obtained from 37 cross-sectional or case-control studies and 9 longitudinal studies.

There were attempts to obtain additional data which would make studies eligible for inclusion, as well as throughout data extraction to enable more comprehensive analyses. However, out of 16 attempts for contact, only two were successful, which is 12.50 %, and is way too inconsiderable. Contacting authors can modify crucial outcomes of systematic reviews;

however, the prevalence of replies seems to be very low. Earlier studies reported replying prevalence of 43 % from the Cochrane systematic reviews on randomized clinical trials (156). The reason for such a low replying prevalence in this study could be a smaller sample, but it also could emanate from the fact that clinical trials authors are used to more rigorous methods of reporting, greater transparency, and data sharing, while authors of observational studies are not. However, data sharing would benefit not only clinical trials and as such should be strongly promoted.

The earliest studies analyzing mental disorders and obesity emerged in the 1980s and continued in the 1990s. This is the period when community surveys providing credible estimates of mental disorders and employing solid epidemiological methods and standardized diagnostic criteria were conducted (42). The great majority of studies included in these meta-analyses were conducted in the last two decades, specifically, between 2002 and 2012 (Figure 5.24.) Longitudinal studies were majorly conducted between 2000 and 2010. There is an obvious upsurge of interest in this topic starting in 2000; however, it is evident that interest diminishes after 2012. Since the search for this systematic review was conducted in early 2019, it is possible that some recent studies are not included; however, a negative trend in the number of studies starting in the 2010s is evident. This is not the case when considering some other childhood obesity comorbidities, like asthma, hypertension, or cardiovascular disease, for which research interest remained steady or even expanded in the last decade (157-159). It is unknown why mental disorders do not experience such attentiveness as obesity comorbidity; however, this trend is not desirable nor encouraging since there are still many uncertainties regarding how obesity affects youth mental health. Furthermore, the onset of mental disorders occurs mainly before age 25, so it is of particular importance to assess their etiology in young individuals (160). Research in this field should be enormously boosted and encouraged to resolve many remaining questions.

A random-effects meta-analysis including more than 9 000 participants estimated the prevalence of mental disorders among children and adolescents with overweight and obesity at 23.50 % (95 % CI, 17.20-31.20). This estimate is based on moderate-quality studies and, as can be seen from Figure 5.3., includes participants from several continents, except Africa and Australia. There was a very high degree of variance in the study effect sizes (I^2=97.24). The asymmetric funnel plot for the prevalence of mental disorders among children and adolescents with overweight and obesity (Figure 5.4.) suggested possible publication bias. It indicated a tendency for the scarce publication of high estimates, and the Duvall and Tweedie trim-and-fill

procedure supported it by suggesting the imputation of 2 studies on the right side of the mean to obtain the unbiased estimate. However, this is rather a consequence of a lack of studies than a scarce publication since the result of scarce publication would probably be a lack of studies with low estimates and overrepresentation of mental disorders in the affected population. Given that a funnel plot must be carefully interpreted, the reasonable conclusion would be that there is no publication bias, and that was supported by Egger's linear regression method intercept (p=0.09).

The cumulative meta-analysis (Figure 5.5.) showed the time-tendency of the prevalence from 2002 towards lower estimates in 2016, suggesting that the prevalence of mental disorders among children and adolescents with overweight and obesity moves towards lower estimates as time passes. This has to be interpreted with caution since not many studies were included in this analysis, and the first study in this analysis had a very low sample size (n=27).

Throughout moderator analysis, weight category was detected as a significant moderator of the prevalence estimate ($p<0.01$). Prevalence of mental disorders among children and adolescents with overweight, although it remained significant, was lower (17.00 % (95 % CI, 11.40-24.70). However, the prevalence among individuals with obesity was significantly higher (33.40 % (95 % CI, 25.30-42.60). Heterogeneity remained very large, and additional studies analyzing obesity added to the subgroup analysis probably further contributed to it.

Since studies were very heterogenous in the means of weight categories assessed, not all of the studies were included in the main analysis. That was supported by the finding that weight category is a significant moderator of the prevalence estimate. Consequently, studies analyzing only participants with obesity, who were compared to the participants with normal weight, were added to the moderator analysis in order to gain more comprehensive insight and utilize all the available data. However, they have not been included in the main meta-analysis since they would bias the results. Cochrane handbook states that the most important finding is the outcome of the main meta-analysis, and subgroup analyses should be reduced to the lowest required level. Also, experts usually recommend that all of the studies included in the meta-analysis need to be combined into a single meta-analysis, and the impact of certain moderators should be analyzed by subgroup analysis (97). However, it seems that this approach is very hard to achieve when researching excess weight because of specific characteristics of certain degrees of overweight.

This systematic review revealed how studies and reporting of mental disorders among individuals with excess weight are inconsistent. Some studies focus only on obesity, while others assess overweight as well. This is especially important to consider when planning the research since previous findings suggest that different comorbidities, including mental disorders, can affect individuals with overweight without the difference (37, 161). Consequently, omission of the analysis of overweight represents an important gap limiting our insights into the distribution and associations of comorbidities. However, inconsistency arises also from the way of reporting results. Some studies report results for both excess weight categories combined, while others report overweight and obesity separately or report only obesity, which remarkably limits the meta-analytic approach. Combining those subgroups into a single meta-analysis would produce erroneous conclusions since this meta-analysis shows that there are significant differences between these subgroups. Subgroups comprising only obesity would introduce bias into the results.

In the subgroup analysis of studies on prevalence, age also emerged as a significant moderator. Since the number of studies was low, only a subgroup comprised of adolescents in opposition to a subgroup comprised of children and adolescents combined was possible. This resulted in unexpected findings. There was a significant difference between these subgroups, according to which children and adolescents, when combined, had a significantly higher prevalence of mental disorders (35.80 %) than adolescents (18.50 %). This would implicate that children considerably contribute to the prevalence estimate. This is opposed to previous findings which state that age does not moderate the relationship between obesity and mental disorders (76). However, these results have to be cautiously interpreted since there is a low number of studies assessed. They were comprised of small samples. 2 of 3 studies in the subgroup of children and adolescents were comprised of less than 100 participants.

A notable finding is also that there was no difference between boys and girls in subgroup analysis. When analyzing separate disorders, authors report gender differences, and some are in favor of girls (37), while others are in favor of boys (72). However, when analyzing total psychopathology, those differences did not emerge. The reason could lie in the markedly heterogenous nature of obesity; thus, when analyzing total psychopathology, distinct disorders, some of which are more strongly associated to the female gender, while others to male gender, contribute to the final pool in the way that they annul gender differences.

When analyzing subgroups according to the weight and height obtainment, there was no difference, which implies that lower-quality procedures of BMI obtainment did not bias the results of the meta-analysis. Also, there was no difference between studies, according to the informant. This contradicts the previous findings of low-to-moderate correspondence between informants (162). However, previous findings were based on clinical assessment. In this subgroup analysis, only studies using screening tools were tested. Since screening tools are not so precise as clinical assessment, they may not result in different estimates depending on the informant.

Also, there were no differences when taking only clinically significant psychiatric test results or borderline results into account. It would be expected that including borderline results would enlarge prevalence estimates, which are usually lower when we consider only clinically significant results. However, this analysis does not support this notion. This probably results from borderline phenotypes not contributing much to the burden of psychopathology among individuals with excess weight.

Subgroup analysis according to the continent was not possible due to the small number of studies, and it was possible only to pool results for Europe. Prevalence did not differ from the outcome of the main meta-analysis (23.60 %, CI 95 %, 17.50-30.90). Also, this analysis did not reduce heterogeneity. There were no differences according to the size and representativeness of the samples; however, this analysis reduced heterogeneity to some extent. Heterogeneity was still significant in most subgroup analyses, except among subgroups in which participants were measured, in which self-report of the psychiatric instrument was used, and in which borderline psychiatric test results were included. However, the important finding is that studies using different methodology did not introduce bias, which is supported by moderator analyses; they rather only increased heterogeneity of the results.

Since the weight category emerged as a significant moderator, the worldwide prevalence of mental disorders among children and adolescents affected only with obesity was separately analyzed. Since the main meta-analysis uses study as a unit of analysis, while moderator analysis uses subgroups as the units of analysis, the prevalence result from this analysis (30.4 %) is slightly different than the one in which overweight was included. Then, obesity was analyzed as a subgroup. Since statisticians recommend using the study as a unit of analysis when conducting a meta-analysis, this result should be used when discussing the prevalence of mental disorders among individuals with obesity.

There were ten studies in this analysis, originating from every part of the world except Africa (Figure 5.3.). There was a large degree of variance in the study effect sizes (I^2=96.79). Although the funnel plot seemed asymmetric, and Duvall and Tweedie trim-and-fill procedure suggested inputting 1 study on the right side of the mean, it is not expected to result from publication bias. Egger's linear regression method also supports this (p=0.08). The finding of the prevalence of 30.40 % of mental disorders among children and adolescents with obesity is based on moderate-quality studies.

When analyzing only obesity, a cumulative meta-analysis revealed no time trend in the prevalence of mental disorders among children and adolescents with obesity in the time period between 1995 and 2015. However, this cumulative meta-analysis has to be interpreted with caution since the low number of studies is included.

Previous research indicated that between 30-60 % of children with overweight and obesity aged 5 to 18 years show at least one internalizing or externalizing mental disorder (54). However, these estimates are based on the population of children referred for overweight treatment; thus, a strong comparison with the results of this meta-analysis can not be drawn. On the other hand, a meta-analytic study estimated the worldwide prevalence of mental disorders among the general population of children and adolescents at 13.40 % (CI 95 % 11.30-15.90) (42). Results from this meta-analysis point out significantly higher prevalences of mental disorders among children and adolescents with excess weight (23.40 % for overweight and obesity and 30.50 % for obesity). These results show the importance of routine screening for mental disorders and further assessment of the individuals at high risk. Those estimates are considerable. When considering the high worldwide prevalence of overweight and obesity among children and adolescents, the prevalence of mental disorders among them indicates the major extent of the problem, which requires further attention. Every country dealing with obesity incidence positive trend among children and adolescents can predict future demands and burden on mental health resources. However, if there are no increased demands, it could suggest underdiagnosis and undertreatment of the mental health problems.

The meta-analysis conducted on the cross-sectional studies analyzing the association between mental disorders and excess weight revealed increased odds for mental disorders of almost 30 % among children and adolescents affected with overweight or obesity in comparison to their peers with normal weight. This finding is based on high-quality studies comprising almost 120

000 participants from every part of the world except Africa (Figure 5.9.). There was no publication bias.

Same as for the prevalence estimate, there was not a single study originating from Africa included in this meta-analysis. That is not surprising since less than 1 % of the world˙s research is produced in Africa (163). Also, there are still many children affected with underweight in Africa, so excess weight and its comorbidities have not reached such research attention yet. However, a recent meta-analysis conducted on studies originating from 15 African countries (164) reveals that overweight and obesity have a prevalence of around 15 %. There is a positive trend in incidence of overweight and obesity in low and middle-income countries where rates exceed the underweight (8). Consequently, there is a need for research on this topic in Africa.

Weight category again emerged as a significant moderator after subgroup analysis. There was a difference between overweight and obesity; after subgroup analysis, only OR in the obesity subgroup remained significant, and it was considerably higher (1.80, CI 95 % 1.28-2.52). This is in line with the results from meta-analyses evaluating only depression (31, 72); however, it is opposed to the findings considering conduct disorder (37). Those findings suggested no difference between overweight and obesity. More precisely, the association between excess weight and conduct disorder was positive when considering overweight same as when considering only obesity. Although it is not known to what extent distinct mental disorders contribute to the total psychopathology among children and adolescents with excess weight, if their distribution complies with the distribution among the general population, then the explanation could be that there is a higher proportion of depression in the total psychopathology (42). In that case, less prevalent conduct disorder does not contribute to the extent that its impact is visible in the analysis of total psychopathology, and when total psychopathology is analyzed, there is a significantly higher OR for obesity compared to overweight. On the other hand, many studies are included in this meta-analysis and those evaluating the association between obesity and depression. When considering the association between obesity and conduct disorder, there is very limited research. A possible explanation could also arise from the inability of these studies to reveal the real differences between overweight and obesity. However, there is a high number of studies included in this meta-analysis, comprising of a high number of participants suggesting higher credibility of analyses and resulting in the positive association between mental disorders and obesity, while there is no association with overweight.

Another subgroup meta-analysis revealed that OR did not differ according to the study locations. This is an unexpected finding due to the great variability of sociocultural factors across the globe. The significance of cultural influence on psychopathology development and manifestations implicates that the origin of study participants is an important factor (165). Conceptualizations of normality and deviations, coping schemas, help-seeking behaviors, as well as the course and expression of mental disorders are all dependent on sociocultural determinants (165). Furthermore, attitudes regarding obesity can also vary markedly depending on the cultural background with regard to body size perception, thin-ideal internalization, and appearance standards which depend on the cultural norms (166, 167). Irrespective of all this, this meta-analysis supports no cultural divergency in the association between obesity and mental disorders. However, results need to be interpreted with caution since some subgroups are comprised only of 2 or 3 studies. Furthermore, sociocultural factors also vary across distinct populations, consequently, the continent from which study participants originate can not define cultural factor per se (167). Thus, it is hard to draw plausible conclusions without detailed descriptions and credible comparisons of observed samples. Subgroup analysis according to the location reduced heterogeneity to some extent.

Socioeconomic aspects were further analyzed by meta-regression in which effect sizes were correlated with economic indicators of countries from which study samples originate. There was no significant relationship between effect sizes and the GDP of the countries from which participants originate. Also, a cumulative meta-analysis of the studies analyzing OR for mental disorders among children and adolescents with overweight and obesity represented stability of the estimates through the period between 1986 and 2017 and suggested temporal stability of the association between mental disorders and overweight and obesity. These findings are unexpected considering changes in populations in the time period of 30 years and also differences between countries depending on the economic development.

Gender did not emerge as a significant moderator throughout the subgroup analysis, and that is consistent with the prevalence estimates analysis. This meta-analysis shows that boys affected with excess weight have the same odds of mental disorders as girls. As opposed to the prevalence estimates analysis, OR did not differ between subgroups consisting of children or adolescents. This analysis is probably more credible than the one comprised of prevalence estimates since it included larger samples of studies in both subgroups. Analyses regarding age and gender did not reduce heterogeneity.

When analyzing study representativeness as a moderator, it was observed that only from community and nationally representative samples emerged significant ORs (1.24 and 1.38, respectively). Although, when analyzing convenient samples, OR was significant, its value was less than 1 (0.83, CI 95 % 0.73-0.94), implicating that overweight and obesity are protective factors of mental health. This represents the evidence of erroneous conclusions which can arise from improper sampling techniques. This analysis also reduced heterogeneity to some extent. When further analyzing sampling and representativeness of samples, it appears that there was no difference in study effect sizes depending on the size of the area where participants live and the type of sample representativeness.

The other determinants of lower quality studies did not bias the meta-analysis results since the means of BMI obtainment and the structure of the control groups did not impact the final estimates. Regarding the structure of the control groups, including underweight in the control groups is especially questionable. The non-linear association between mental disorders and BMI exists since being underweight is associated with mental disorders the same as obesity; thus, researchers always have to account for possible bias introduction when they include participants with underweight in the analyses, especially when they are a part of the control group (168). In the majority of the studies, authors do not state how they treated participants with underweight or did they excluded them from the analyses. The criterium for the inclusion of participants in the control group was majorly BMI under a certain cut-off, which implicates that underweight is probably included in the analyses.

OR remained significant when analyzing only studies with untransformed effect sizes, implicating that statistical manipulation of the data did not bias results. Although, transformation introduced high heterogeneity. This is also evident from previous research on this topic. When analyzing the association between conduct disorder and obesity, conversion of study effect sizes also introduced heterogeneity largely (37). As shown in Table 5.6, 40 % of studies required effect size transformation to be included in the meta-analysis. It implicates a very heterogenous way of reporting the outcomes in the studies analyzing the association between mental disorders and obesity. Effect sizes conversion can always introduce errors; however, omission of these studies in the analysis would seriously diminish the comprehensiveness of this systematic review and meta-analyses. However, by conducting sensitivity analysis, erroneous conclusions are avoided (169).

There was a wide range of screening tools used in the included studies (Table 5.6.). Consequently, it was very hard to perform a comprehensive subgroup analysis. For the majority of screening tools, there was only 1 study in the meta-analysis; thus, it was impossible to include them in the subgroup analysis. All tools are validated and useful for the analysis of mental disorders in the assessed population. Finally, SDQ, CBCL, and MSQA are analyzed as moderators, and there was no significant difference between them. This analysis reduced heterogeneity to some extent. However, another important finding is that only three studies (57, 113, 130) obtained diagnosis through standardized diagnostic procedures. Although it was preplanned to conduct a subgroup analysis comparing screening tools and validated diagnostic procedures, it was not possible. This also implicates how deficient existing knowledge about associations between total mental disorders and obesity is. Psychiatric screening tools are very useful, inexpensive, and important first steps in detecting mental health problems that can be easily and efficiently incorporated into primary health care. Also, they can be easily administered to the populations at high risk and can detect individuals who require further assessment and thus overcome our inability to perform complex diagnostic procedures on every individual at risk. However, screening tools can not provide a definitive diagnosis, and further evaluation of examinees is needed (170). Consequently, we do not have an accurate picture of the occurrence of mental disorders among children and adolescents with overweight and obesity, and values obtained by meta-analyses are probably overestimated to some extent. However, considering the high prevalence of mental disorders among children and adolescents with excess weight and the strong relationship between these disorders obtained by screening tools, it is necessary and of great public health importance to conduct research using validated diagnostic procedures among the affected population. This would provide us with better insight into the disease burden and also depict the importance and need of further interventions considering mental disorders and obesity.

Regarding the screening tool informant, growth reference, and borderline or abnormal psychiatric assessment results, there were no significant differences between subgroups. These analyses reduced heterogeneity to some extent. Results need to be interpreted with some caution due to several subgroups comprising only a few studies.

There was a possibility to additionally stratify the results according to the gender and weight category since authors most usually report separate results for these subgroups. It emerged that male participants affected with obesity had the most significant OR for mental disorders. This estimate significantly differed when compared with the males with overweight, females with

overweight, and females with obesity. An especially alarming finding is that this subgroup analysis not only revealed males with obesity to have differing OR, but this estimate was strikingly high (2.67, CI 95 % 1.31-5.45). Mental disorders among individuals with obesity frequently arise from body image disturbances. The previous viewpoint was that body image disturbances affect females more often, so the research focused on them (171, 172). Causes of depression, which is probably, in the context of obesity, the most profoundly analyzed mental disorder, were found in body image disturbance. That also explains the stronger association for a female to some extent (31). However, results from this meta-analysis implicate a broad set of new unknowns. Which disorders affect boys, and what drives them? Previous research implicates a stronger relationship between conduct disorder and obesity among boys than girls (37); however, conduct disorder is not so prevalent as depression or anxiety. The reason for such high OR among males with obesity should be further comprehensively analyzed.

Since there were some studies analyzing only obesity, and weight category emerged as a significant moderator of the association between excess weight, and mental disorders, additional analysis covering only obesity was conducted. A random-effects meta-analysis comprised of 18 studies, 35 separate effect sizes, and around 120 000 participants yielded an OR of 1.83 (95 % CI, 1.52-2.21) for mental disorders among children and adolescents with obesity. Heterogeneity was considerable (I^2=92.20). The results are based on moderate-quality studies, from every continent, except South America and Africa. There was no publication bias.

During the moderator analysis, not any of the analyzed moderators emerged as significant, except for the way of BMI obtainment. This subgroup analysis yielded significantly higher OR for studies where participants were measured (2.36, 95 % CI, 1.37-4.06). Previous research indicates the importance of self-report bias among adults with overweight and obesity (173). When considering children and adolescents, there are various recommendations. Some authors state that self-reported measurements are reliable proxy measures among adolescents (174); however, others warn that underreporting of weight is common among adolescents (175). Furthermore, self-report bias is also unpredictable to some extent since some factors like gender, age, or weight category can increase bias (176). This is in line with results from this study, according to which reported measurements emerged as a significant moderator only when analyzing obesity; however, when analyzing overweight and obesity, there were no differences in the estimates. Furthermore, several studies used parent-reported measures, which are also recognized as inaccurate and dependent on certain factors (177). According to this meta-analysis and previous findings, it is recommended to conduct measurements whenever

possible and avoid reported measurements when performing research on overweight and obesity among children and adolescents.

When analyzing only obesity, gender was not analyzed as a moderator again since this analysis was conducted in the previous meta-analysis and gender emerged as a significant moderator. Boys affected with obesity had significantly higher OR for mental disorders than girls ($p<0.01$).

When analyzing the methodology of the included studies, the composition of the control groups emerged as noteworthy. Many studies assessed obesity in comparison to all weight categories, which are under certain cut-offs; thus, control groups incorporated the overweight category as well. Subgroup analysis on studies including or not including overweight in the control group was performed. Although there were no differences between these subgroups, and OR remained similar for both groups, showing that result of this meta-analysis is not biased, including overweight in control groups is not recommendable when considering previous subgroup analyses which showed differences between overweight and obesity.

Only a few subgroup analyses reduced heterogeneity (psychiatric tool, BMI obtainment); however, heterogeneity still remained considerable. Although many studies were included in meta-analyses, it was difficult to obtain credible conclusions by subgroup analyses due to markedly heterogenous studies and unavailable information. From missing data, cumulative meta-analysis especially suffered. Many authors did not report the year of study commencement, thus enabling these studies to be included in the cumulative meta-analysis. The included studies showed that there was no time trend in the OR from 1995 to 2015.

When considering analyses comprised of cross-sectional and case-control studies, regardless of prevalence or OR as the outcome, it seems that the difference between overweight and obesity is a very robust finding resulting in strong conclusions. Also, that is one of the few subgroup analyses which were conducted majorly using studies that provide prevalence or OR for both groups, i.e., overweight and obesity; thus, those subgroups were compared. Such analyses are highly credible since the moderator can be tested while all other unmeasured factors within studies remain stable. This approach is more advantageous than the one in which studies are grouped according to some characteristic. Unlike the weight category, other subgroup differences emerged inconsistently. For example, gender emerged as a significant moderator only when analyzing OR among individuals with obesity, all other analyses resulted in the same estimates for boys and girls. Furthermore, analyses implicate that certain methodological procedures can result in differing outcomes in certain conditions; however, in others, they seem

to have no effect on the final estimates. Consequently, when analyzing OR among children and adolescents with overweight and obesity, convenience sampling appeared to produce unexpected and implausible OR suggesting a protective effect of excess weight. There were no differences between convenience sampling and other more acceptable sampling techniques in other analyses. The method of BMI obtainment was also a significant moderator in only one analysis. Weight self-reporting emerged as a cause of underestimation of mental disorders among studies analyzing OR among children and adolescents with obesity. Due to inconsistent findings, strong conclusions can not be drawn; however, these findings need further consideration.

Longitudinal studies analyzing the association between overweight and obesity and mental disorders were systematically reviewed, and a meta-analysis was performed to assess the directionality of the association. There was no significant OR when pooling six longitudinal studies comprising almost 25 000 participants (1.01, 95 % CI, 0.97-1.05). There was no observed heterogeneity (I^2=0 %). After sensitivity analysis, OR remained insignificant. Furthermore, not any of the subgroup analyses resulted in significantly different OR; thus, the findings are robust.

These results are unexpected considering the established notion that obesity endangers mental health. Previous research also showed a prospective association between obesity and depression stronger for females (70, 154) and a prospective association between obesity and conduct disorder among males (37). However, according to this meta-analysis, there is no prospective association between overweight and obesity and total mental disorders among boys or girls. These results have to be interpreted with caution. There are less than ten studies included in this analysis, so the publication bias could not be assessed. Three of the six included studies were high quality, while the other three were moderate quality.

Additional studies were included in the longitudinal analysis of mental disorders among individuals with obesity; however, OR remained insignificant (1.29, CI 95 %, 0.64-2.60).

Subgroup analyses were hard to perform since there was a low number of studies, and they were very heterogeneous. During the subgroup analyses, heterogeneity increased, and the most important source of that increase was again effect size conversion. Longitudinal studies were also very heterogenous in the weight categories structure. Many of them obviously included overweight and underweight in the control groups (Table 5.10.), some studies did not conclusively report the exclusion of participants with underweight and overweight from the

control groups, so there is a possibility that control groups are comprised of them. It was planned to conduct a sensitivity analysis regarding the structure of the control group; however, there were not enough studies to perform that.

Prevalence of mental disorders among individuals with excess weight is high, and there is a strong association obtained from cross-sectional and case-control studies; however, the result from the meta-analysis of longitudinal studies does not support the association in the direction from obesity to mental disorders. This is in contrast to the previous notion that causality is possible in both ways (77) and represents an important finding. The longitudinal association may persist only for distinct disorders but not for total psychopathology. Although there are not many studies in this meta-analysis, findings seem robust and stable since none of the subgroup or sensitivity analyses revealed significant OR. Thus it is very important to analyze further and explain which disorders occur among individuals with obesity and who are the individuals at risk. It would further contribute to our understanding of etiology and aid the prevention, identification of the affected individuals, and treatment. Also, considering the stigmatization of obesity, it is especially important to clarify such claims as "obesity leads to mental disorders". This statement obviously still has no foundation in evidence-based medicine, it is imprecise, inaccurate, and it certainly does not benefit the individuals with obesity, nor physicians or scientists. The scientific community should strive to comprehensively explain the association between obesity and mental disorders and its directionality. A strong association between cross-sectional and case-control studies and the lack of association from longitudinal studies implicates many unknowns, and further research is needed.

The results of meta-analyses in this study are majorly based on moderate-quality studies. The average quality of the studies included in the analyses of prevalence was 76.50 % and 68.70 %. The average quality of the cross-sectional and case-control studies included in the analyses of OR was 82.40 % and 72.70 %, while the average quality of longitudinal studies analyzing prospective association was 73.70 %. As can be seen, only OR obtained from cross-sectional and case-control studies is based on high average quality (>80 %), while other analyses are based on moderate average quality. Lower appraisal scores are majorly due to the non-identification of confounding factors (Tables 5.3. and 5.4.). In this study, the criterium was minimally three confounding factors assessed to gain a positive score on this item. That is also the reason why some studies were rated positively on the item "Were strategies to deal with confounding factors stated?". In contrast, they were rated negatively on the item about the

identification of the confounding factors. Those studies assessed less than three confounding factors.

Although the cut-off regarding confounding factors was set, there are still many open questions considering confounders that the authors assessed. When the lists of confounding factors are analyzed, it is evident that there is no consensus in this field. Among the studies, the number of analyzed confounders varies from 1 to 11, and they are very heterogeneous. Assessment of SES, which is a very important factor associated with obesity, as well as with mental disorders, is absent in many studies. Further, only a few studies analyze characteristics of family environment, previous diseases, stressful life events, and parental mental health, which are all possible confounders (178, 179). Confounding factors may disguise present association or indicate an association when there is no one, so it is important to assess them in all types of studies to avoid erroneous conclusions (180). Obesity and mental disorders can be the result of common risk factors; however, other causal links in both ways are possible (77). To precisely explain the associations, a broad set of confounders need to be taken into consideration when analyzing these illnesses.

When considering the longitudinal studies' quality, the item “Was the follow-up time reported and sufficient to be long enough for outcomes to occur?” could not be assessed for any of the included studies since, in the literature, there are no assessments of the duration of exposure to excess weight which would result in the occurrence of mental disorders. Specifically, there are no existing aims for analyzing that time period. So all of the studies were unclear according to that item. However, this did not significantly decrease appraisal of the quality since the cut-off for high study quality was set at 9 out of 11 points. Follow-up in the longitudinal studies varied from 2 to 20 years; the median is 3.5 years. Meta-regression was conducted to assess the association between follow-up and effect sizes; however, no association was detected

When considering time ranges and critical time points in the association between obesity and mental disorders, there is one more signal from the characteristics of the included studies, which signifies a notable lack of knowledge, and that is marked heterogeneity of age ranges of examinees among the included studies. Studies vary considerably regarding the age ranges (Figures 5.16. and 5.21.), to the extent that there are no major overlaps between studied age ranges. Children and adolescents go through significant physical and mental changes in their development from early childhood to late adolescence, which is gender-dependent. Specific important moderators of the association between obesity and mental disorders, like self-esteem

and body image, also change through that development. A longitudinal study conducted in the USA analyzed weight concerns and cigarette use in adolescence. Authors found that early- to mid-adolescence is the most sensitive period in which risk for cigarette use rises among the girls with weight concerns, however, not among the boys. The association was significant from 11 to 16 years for girls, and the peak was at 12.7 years (181). Another study from Canada showed an increase in depressive symptoms from ages 14 through 17, which started to decrease at age 21 and was positively correlated with BMI. The pattern was similar for both genders (182). However, mental disorders are found among children with obesity as well. On the other hand, a previous study concluded that the association between obesity and mental disorders does not depend on the age of the affected individuals (76). Comprehensive longitudinal studies analyzing developmental trajectories of the mental disorders among children and adolescents with obesity are needed to reveal the critical periods, the possibilities for prevention and aid in identifying individuals at highest risk.

Subgroup analyses according to the location, cumulative meta-analyses, and meta-regressions on the economic indicators of studied populations yielded no significant results and thus led to the rejection of the hypotheses about positive time trends and correlations between prevalence and risk and economic indicators. This was unexpected considering marked differences in economic development, culture, religion, language, and health systems. However, these findings are important pieces of evidence about the temporal and cross-cultural stability of the results. This is similar to findings of mental disorders among the general population of children and adolescents (42). This diminishes the importance of sociocultural determinants of distinct populations in the etiology of mental disorders among individuals with obesity and emphasizes the other factors, like genetic, biological, and the general socioeconomic, sociocultural, and psychological factors present at the individual level, which are common to the different cultural milieus.

Several possible mechanisms are included in the association between obesity and mental disorders. The possible links can be psychosocial, biological, genetic, or related to daily habits. There is already mentioned stigmatization and teasing of individuals affected with obesity, which cause body dissatisfaction and further lead to eating disorders, depression, or anxiety. It seems that an unhealthy diet is associated both with obesity and mental disorders, same as sleep patterns and sedentary behavior (183). However, there are also pathological mechanisms revealed in biological pathways. Obesity and psychiatric disorders are both characterized by low-level chronic systemic inflammation and oxidative stress (154, 183). Proinflammatory

cytokines released from adipose tissue, as well as leptin, can affect the mental and cognitive status of individuals affected with obesity (184). There is evidence that low serum levels of vitamin D, which are widely distributed among individuals with obesity, are associated with mood disorders (185). Other pathways include the abnormal activity of the hypothalamic-pituitary-adrenal axis, abnormal cortisol secretion, and disturbance in the dopaminergic reward system (154). Mentioned mechanisms can work in both directions regarding causality.

This systematic review and meta-analyses provided a holistic picture of research and knowledge about total mental disorders among children and adolescents with obesity. Findings contribute to the design of future surveys. Regarding the characteristics of future studies, this study provided several guidelines. Sampling techniques must be credible, measuring height and weight is strongly recommended, a multi-informant approach should be considered, there is a broad spectrum of useful psychiatric tools which can be used; however, standardized diagnostic procedures should be conducted among individuals with indicative screening results to precisely estimate the burden and explain which disorders and in what extent contribute to the total psychopathology. There are confounding factors that should be assessed, such as SES, previous diseases, stressful life events, family environment, and family disease history. It is important to analyze and report results separately for overweight and obesity when assessing excess weight. Participants of all ages through childhood and adolescence should be included and stratified according to age to reveal key points in the developmental pathways. Researchers should strongly consider these guidelines when conducting research on obesity and mental disorders since different approaches can result in different findings. Carefully designed longitudinal studies are also recommended.

This systematic review yielded worldwide pooled estimates of prevalence and ORs of mental disorders among children and adolescents with overweight and obesity and also assessed the direction of the association from excess weight to mental disorders. Those estimates can be generalized to almost all parts of the world, not only high-income or western countries. The meta-analyses revealed stable estimates across time and space, as well as across different cultures and economies of countries, thus enabling public health authorities to predict the future burden of mental disorders.

This study reveals the burden of mental disorders in the community since only studies analyzing community samples are included, as opposed to previous studies focusing on clinical samples; thus, it clearly signifies the scope of the problem. It emphasizes the importance of obesity

prevention and depicts the importance of further mental health screening and assessment of mental disorders among young individuals affected with obesity. Association between obesity and mental disorders is independent of the communities cultural or socioeconomic aspects. Also, the association is not prone to changes through time, implicating that there are strong and stable links between these illnesses and also revealing the communities' vulnerability to the difficulties and the absence of detailed comprehension and solutions. Considering positive time trends of the obesity prevalence and incidence globally, especially triggered by the COVID-19 pandemic, healthcare systems need to be prepared and well organized to maintain the future accompanying pandemic of psychiatric and psychological difficulties.

7. Conclusions

This systematic review and meta-analyses lead to several conclusions:

-A quarter of children and adolescents with overweight and obesity worldwide are affected by a mental disorder, and every third child and adolescent with obesity is affected by a mental disorder.

-Based on the high-quality studies and more than 120 000 children and adolescents, the odds of mental disorder are increased by almost 30 % among children and adolescents with overweight and obesity compared to their peers with normal weight. When analyzing only participants with obesity, the odds are even higher, climbing up to 80 %. Boys with obesity have higher odds than girls, and their odds are increased by almost 170 %. However, there are no differences between children and adolescents.

-There is no longitudinal association between overweight, obesity, and mental disorders in the direction of excess weight to mental disorders for children and adolescents or any of the analyzed subgroups.

-Robust temporal stability of the estimates is observed, thus enabling solid predictions of future mental disorders burden. Correlation of the effect sizes and economic indicators of countries is not observed, and there was no publication bias.

-There were not many studies analyzing mental disorders and excess weight despite no time limits set in the search strategy. The number of longitudinal studies analyzing mental disorders as a consequence of overweight and obesity was especially low. Regarding the quality of studies, only the ones analyzing OR were of high quality, while all other estimates (prevalences and longitudinal association) were based on moderate-quality studies.

-Marked heterogeneity of the methodological characteristics of the studies is observed. High statistical heterogeneity was also observed, and conversion of effect sizes was detected as a major source of heterogeneity.

-During the moderator analyses, sampling techniques, informants, and methods of BMI obtainment emerged as significant. Credible sampling, a multi-informant approach, and measuring of height and weight should be implemented in future studies. Also, assessing a broad set of confounding factors is necessary to obtain credible estimates.

-Findings are generalizable to the whole world except Africa; however, they emerge from screening assessments. In future studies, standardized diagnostic procedures are recommended to reveal precise estimates because screening tools obtain high estimates.

8. Summary

Objectives: This study aimed to qualitatively and quantitatively appraise studies on the association of overweight, obesity and mental disorders among children and adolescents and estimate the prevalence and odds ratio of mental disorders among youth with excess weight. The aim was also to analyze gender and age differences and differences regarding the time and location of the study and the development of the country from which participants originate.

Study design: The study was designed as a systematic review and meta-analysis of all published studies about mental disorders among children and adolescents with overweight and obesity obtained through database search without time and language limits set.

Results: Analysis of the 17 moderate quality studies estimated the prevalence of mental disorders among children and adolescents with overweight and obesity of 23.50 % (95 % CI, 17.20-31.20, I^2=97.24) and of 30.50 % (95 % CI, 21.60-41.20, I^2=96.79) among children and adolescents with obesity. Analysis of 37 high-quality studies comprising more than 120 000 participants indicated a significant association between overweight, obesity, and mental disorders among children and adolescents (OR 1.28 [95 % CI, 1.19 - 1.40], I^2=86.29). OR among individuals with obesity was estimated to be (OR 1.83 [95 % CI, 1.52 – 2.21], I^2=92.20). Analysis of 6 moderate quality longitudinal studies showed no prospective association between overweight, obesity, and mental disorders (OR 1.01 [95 % CI, 0.97-1.05], I^2=0). There is no significant time trend in the prevalence and OR estimates nor association between estimates and economic development of the countries from which participants originate. There was no publication bias.

Conclusion: There is a high prevalence of mental disorders among children and adolescents with overweight and obesity, and positive association between these illnesses based on the high number of participants from almost all parts of the world. The burden of mental disorders especially affects boys with obesity. However, there is no prospective association obtained from longitudinal studies. Estimates are cross-culturally and cross-temporally stable, and they are not correlated with economic development.

Keywords: adolescents; children; mental disorders; meta-analysis; obesity; overweight; systematic review;

9. Sažetak

Mentalni poremećaji u djece i adolescenata s prekomjernom tjelesnom masom i debljinom: sustavni pregled i meta-analiza

Cilj istraživanja: Cilj istraživanja bio je kvalitativno i kvantitativno procijeniti istraživanja o povezanosti prekomjerne tjelesne mase, debljine i mentalnih poremećaja u djece i adolescenata i procijeniti prevalenciju i omjer šansi mentalnih poremećaja u mlađih s povećanom tjelesnom masom. Cilj je bio istražiti spolne i dobne razlike te razlike s obzirom na vrijeme i mjesto provođenja studije kao i razlike s obzirom na ekonomsku razvijenost zemlje iz koje potječu ispitanici.

Nacrt studije: Studija je sustavni pregled i meta-analiza svih objavljenih istraživanja o mentalnim poremećajima u djece i adolescenata s prekomjernom tjelesnom masom i debljinom prikupljenih kroz pretragu baza podataka bez vremenskih i jezičnih ograničenja.

Rezultati: Analiza 17 studija srednje kvalitete polučila je prevalenciju mentalnih poremećaja u djece i adolescenata s prekomjernom tjelesnom masom i debljinom od 23.50% (95 % CI, 17.20-31.20, I^2=97.24) i 30.50 % (95 % CI, 21.60-41.20, I^2=96.79) u djece i adolescenata s debljinom. Analiza 37 studija visoke kvalitete koje su uključivale više od 120 000 ispitanika ukazuje na značajnu povezanost između prekomjerne tjelesne mase, debljine i mentalnih poremećaja u djece i adolescenata (OR 1.28 [95 % CI, 1.19 - 1.40], I^2=86.29). Omjer šansi među ispitanicima s debljinom je procijenjen na 1.83 (95 % CI, 1.52 – 2.21, I^2=92.20). Analiza 6 longitudinalnih studija srednje kvalitete nije ukazala na značajnu povezanost između između prekomjerne tjelesne mase, debljine i mentalnih poremećaja (OR 1.01 [95 % CI, 0.97-1.05], I^2=0). Nema značajnog trenda u procjenama prevalencija i omjera šansi kao niti povezanosti s ekonomskim razvojem zemalja iz kojih potječu ispitanici. Nije bilo sustavne greške publiciranja.

Zaključak: Visoka je prevalencija mentalnih poremećaja u djece i adolescenata s prekomjernom tjelesnom masom i debljinom i značajna povezanost među ovim bolestima. Procjene se temelje na visokom broju ispitanika iz gotovo svih dijelova svijeta. No, nema značajne povezanosti iz združenih procjena longitudinalnih studija. Procjene su stabilne među kulturama kroz vrijeme i nisu povezane s ekonomskim razvojem.

Ključne riječi: adolescenti; debljina; djeca; mentalni poremećaji; meta-analiza; prekomjerna tjelesna masa; sustavni pregled;

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11. Curriculum vitae

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List of References and Congress Attendance:

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- 12th Symposium "Štamparovi dani", online, 4.-6.12.2020. Holik D, Kribl M, Nujić D. Epidemiološka obilježja mentalnih poremećaja mladih s područja Osijeka. Abstract

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