Pediatric Obesity/Comorbidity

Are bidirectional associations of obesity and depression already apparent in childhood and adolescence as based on high-quality studies? A systematic review

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Summary

Our aim was to evaluate bidirectional associations of obesity and depression in cross-sectional and longitudinal studies with initial assessments in childhood or adolescence. The clarification of these relationships may support the development of innovative interventions, e.g. based on nutrition and mental health. A systematic literature search was conducted in MEDLINE. Main inclusion criteria were (i) assessment of subjects <18 years at baseline, (ii) use of validated psychometric instruments and (iii) elicitation of objectively measured anthropometric data at least at one time point. Twenty-four studies met our inclusion criteria. Out of 19, 14 cross-sectional studies confirmed a significant association of obesity and depression. Three out of eight longitudinal studies reported associations between obesity and subsequent depression in female children and adolescents only, and three out of nine studies obtained evidence in favour of the other direction with two studies revealing significant results only for female and one only for male children and adolescents. Evidence is mixed, and secure conclusions are hampered by the methodological variance of the included studies. Relationships are seemingly more readily detectable in female children adolescents and in the cross-sectional compared with the longitudinal analyses. Possibly, the joint development of obesity and depression in predisposed subjects accounts for the latter discrepancy.

Keywords: Bidirectional, cross-sectional, longitudinal, population-based.

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Introduction

Obesity is frequently accompanied by mental disorders (1). The significant association of obesity and depression represents a major example for such a comorbidity (1,2). In the past decades, psychiatric comorbidity of obesity was mainly assessed in clinical and population-based adult samples (1,2). More recently, single systematic reviews focused on prospective or retrospective longitudinal studies that assessed weight status and psychiatric symptoms/disorders in children or adolescents with particular emphasis on depression (3–5). Two of these reviews (4,5) only considered unidirectional associations between obesity and psychiatric symptoms/disorders. In their recent review of 16 prospective longitudinal studies based on clinical and population-based samples of children and/or adolescents, Korczak et al. (3) found female adolescents with obesity to have a higher risk of depressive symptoms in adulthood than normal-weight adolescents. Vice versa, mainly in female adolescents, depressive symptoms were associated with a higher risk of overweight in adulthood. Incledon et al. (4) performed a similar review of 15 longitudinal population-based studies (overlap of three studies with Korczak et al. (3)) and assessed the influence of several psychological...
predictors in childhood and adolescence for the development of obesity. Low global self-esteem was shown to be associated with the onset of obesity. Furthermore, depressive symptoms in obese male and female adolescents and a lack of physical appearance self-esteem in obese female adolescents entailed greater than average weight gain. Vámosi et al. (5) reviewed the relationship between psychological variables present during childhood and the development of adult obesity based on eight prospective or retrospective studies of clinical and population-based samples (overlap with Korczak et al. (3); three studies; no overlap with Incledon et al. (4)). A lack of childhood care, abuse, childhood anxiety disorders, learning difficulties and scholastic proficiencies were associated with adult obesity. Adolescent depression to a rather small extent was associated with adult obesity in female adolescents. Altogether, the evidence of these reviews (3–5) is mixed and not sufficiently consistent to allow any secure conclusions concerning the bidirectional influences of obesity and depression or reported depressive symptoms.

For the evaluation of the current evidence, some methodological aspects appear crucial. None of the cited reviews (3–5) included cross-sectional studies. Although longitudinal studies possess higher validity, cross-sectional studies of high methodological quality could additionally contribute to the sparse and partially inconsistent body of evidence in this field. Furthermore, the authors (3–5) pointed to several methodological limitations in many of the included studies such as small sample sizes and insufficient consideration of potential confounders. None of these reviews set limitations concerning the sample size of included studies or excluded studies based on self-reported anthropometric data. Self-reported weight is known to be highly biased, especially in samples of children and adolescents, who tend to underreport their weight (6). Overall, depression is associated with multiple cognitive impairments, including dysfunctions of perception and attention (7). Thus, depressed subjects may also suffer from misperceptions of their own body image resulting in an elevated reporting bias for anthropometric data, which could lead to erroneous results. On the other hand, a more realistic self-perception among depressed individuals has been discussed previously, potentially entailing a less pronounced weight-reporting bias compared with non-depressed subjects (8,9). Because a difference in the weight-reporting bias between depressed and non-depressed children and adolescents appears possible, the use of objective measures of weight status has been recommended repeatedly for the assessment of relationships between depression and weight status (8,9). In conclusion, these methodological aspects warrant consideration in future reviews.

With this review, we aimed to provide an update of the current evidence as based on those studies, which a priori fulfilled detailed several methodological criteria. To evaluate both unidirectional and bidirectional influences of obesity, we focused only on population-based samples of subjects aged <18 years at baseline to avoid the bias of overgeneralizing results that only pertain to treatment-seeking individuals from clinical samples (e.g. weight-loss or psychiatric treatments). As a further inclusion criterion, we required a sample size of at least 1,000 subjects to generate more representative results. Finally, the criterion of at least one instead of exclusively objective anthropometric measurements was chosen in order not to a priori exclude too many – in other aspects – potentially valuable studies. In fact, in the preceding reviews (3–5), the majority of included studies were based on exclusively self-reported anthropometric data. In sum, we attempt to re-address the association between obesity and depression in childhood and adolescence by focusing on studies fulfilling these stringent methodological criteria.

Methods

This review was prepared in six phases: (i) definition of the objectives; (ii) set of inclusion criteria; (iii) systematic literature research; (iv) selection of eligible studies; (v) data extraction; and (vi) evaluation of results. Figure 1 shows the flow diagram of the process of this systematic review according to the PRISMA guidelines (10).

Inclusion criteria

Studies with the following features were included in the review: population-based sample, sample size n ≥ 1,000, age of participants <18 years at baseline, anthropometric data measured objectively at least once during the study, and use of validated instruments of psychometric outcome related to depressive symptoms. We did not set any limitations concerning the study design (longitudinal vs. cross-sectional analysis).

Systematic literature research, study selection and data extraction

We conducted a systematic literature research in MEDLINE via PubMed. The search was conducted on 27 August 2014 without any time limit set. We used the following search terms for depression: (mood OR depress* OR affective disord*) AND obesity AND (child* OR adolesc* OR youth*) AND (longitudinal OR prospective OR epidemiological OR population). The titles and abstracts of all references were checked for relevance and according to the defined inclusion and exclusion criteria. For all remaining references not already excluded in this step, the full text was obtained and evaluated.

A summary of the eligible studies was extracted providing information on sample size, study design, population and study characteristics, type of anthropometric measures and
psychometric instruments and the main results (Tables 1 and 2). The studies were assigned to one of three categories (purely cross-sectional studies, longitudinal studies with cross-sectional analysis and purely longitudinal studies). We built subdivisions for the cross-sectional studies (correlation design, regression analysis: weight status as a predictor (statistical term used within regression analyses) for depression and vice versa; Table 1). Within the two categories of longitudinal studies, three subdivisions of analyses were defined (bidirectional influence, unidirectional influence of dimensionally or categorically assessed depression on weight status and vice versa; Table 2).

Results

The final selection consisted of 24 eligible studies, which fulfilled the predefined inclusion criteria. Sample sizes varied from 1,465 to 13,454 study participants. Seven studies were conducted in the USA, five in the UK, three in China, two in Iran and one each in Australia, The Netherlands, Norway and Turkey. A summary of the results is provided separately for cross-sectional and longitudinal analyses. We focus on the results concerning overweight and obesity, although some studies also provide results for the status of underweight (e.g. 15,18,26).

Results of cross-sectional analyses

Of 19 available studies (for country of origin, sample size and an overview of the results, see Table 1) including a cross-sectional design (including nine studies that additionally pursued a longitudinal approach), eight studies were based on a correlation analysis (8,11–17) and 11 on a regression analysis. Of the latter studies, 10 assessed weight status as a predictor of depression (18–27) and only two studies depression as a predictor of weight status (20,28).

Correlational analyses

Of the eight studies with correlational analysis, five found evidence for a relationship of obesity and depression. Marmorstein et al. (12) found a significant correlation \( r \) of the occurrence of obesity and major depressive disorder until the age of 24 years \( r = 0.14 \). Obesity and major depressive disorder were correlated when both began in early adolescence (11–14 years) \( r = 0.20 \), whereas no significant relationship was detected when major depressive disorder and obesity first occurred in late adolescence (14–20 years) or early adulthood (20–24 years). In the study of Larsen et al. (8), small significant positive correlations were found between depression and body mass index (BMI) in female adolescents at the age of ~14 years \( r = 0.12 \) and 1 year later \( r = 0.08 \). Similarly, Kubzansky et al. (14) stated that the
<table>
<thead>
<tr>
<th>Study, country of origin, sample size (%♀), and age</th>
<th>Measurements and definition</th>
<th>Depression</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geoffroy et al. (2014) UK; N=9,240 (%♀nr)</td>
<td>BMI (m): 7, 11, 16, 33, and 45 y; BMI (s): 23, 42 and 50 y; childhood: use of international age and sex-specific cut-offs (Cole et al., 2000); adulthood: underweight BMI &lt; 18.5, overweight ≥ 25, obesity ≥ 30</td>
<td>Bristol Social Adjustment Guide (teacher-rated questionnaire; assessment of internalizing symptoms): 7 and 11 y; Rutter Behaviour Scale (teacher-rated questionnaire; internalizing score): 16 y; Malaise Inventory (self-rated questionnaire, items for somatic symptoms excluded): 23, 33, 42 y; Malaise Inventory (short form with 8 items): 50 y; CIS: core depressive symptoms: 45 y; elevated symptom level: score ≥ 90th percentile at each age</td>
<td>na + na</td>
</tr>
<tr>
<td>Jari et al. (2014) Iran; N=5,528 (49.7%♀); mean age: 14.7 y</td>
<td>Calculation of BMI (m) and use of BMI categories according to the WHO reference curves (WHO, 2006)</td>
<td>WHO-GSHS questionnaire</td>
<td>+ na na</td>
</tr>
<tr>
<td>Larsen et al. (2014) The Netherlands; N=2,051 (49.4%♀); mean age (baseline): 13.8 y</td>
<td>BMI (m): baseline, 12 and 24 months; calculation of BMI z-scores with use of data from the 2000 CDC growth charts</td>
<td>Dutch version of the 20-item self-reported CES-D inventory</td>
<td>♂ + na na</td>
</tr>
<tr>
<td>Marmorstein et al. (2014) USA; N=1,512 (50.3%♀); mean age (baseline): 11.7 y</td>
<td>BMI (m): 11, 14, 17, 21, 24 y; 20–24 y: use of the standard body mass index cut-off of 30 to define obesity; &lt;20 y: use of CDC 2000 growth curves to determine obesity cut-offs (95th percentile) for each age and sex based on the average participant ages at each assessment</td>
<td>&lt;17 y: Diagnostic Interview Schedule for Children and Adolescents (MDD); ≥ 17 y: Structured Clinical Interview for DSM-III R (MDD)</td>
<td>+ na na</td>
</tr>
<tr>
<td>Wang et al. (2014) China; N=3,096 (49.0%♀); age range: 11–13 y</td>
<td>Calculation of BMI (m) and classification of overweight and obesity according to the reference norm for screening overweight and obesity in Chinese children and adolescents set up by the WGOC</td>
<td>CDI: 27 items (self-report)</td>
<td>na + na</td>
</tr>
<tr>
<td>Roberts et al. (2013) USA; N=4,175 (48.9%♀); age range: 11–17 y</td>
<td>BMI (m): baseline and 12 months; calculation of BMI percentiles; healthy weight: BMI &lt; 85th percentile, overweight: BMI 85th percentile ≤ BMI &lt; 95th percentile, obese: BMI ≥ 95th percentile; BMI percentiles based on CDC (2006)</td>
<td>DISC-IV: (a) any mood disorder (mania, hypomania, major depression and dysthymia), (b) major depression, and (c) disturbed mood in the past 12 months (depressed mood, irritable mood or anhedonia)</td>
<td>na + +</td>
</tr>
<tr>
<td>Kubzansky et al. (2012) USA; N=1,528 (51.2%♀); mean age: 14.4 y</td>
<td>BMI (m): baseline, 12, 24, 36, 48 months; calculation of BMI (no reference stated)</td>
<td>20-items CES-D</td>
<td>+ na na</td>
</tr>
<tr>
<td>Merikangas et al. (2012) USA; N=4,150 (48.3%♀); age range: 12–19 y</td>
<td>BMI (m): obesity defined as BMI ≥ 95th percentile using age-specific and sex-specific CDC 2000 growth charts</td>
<td>NIMH Computerized Diagnostic Interview Schedule for Children, a structured diagnostic interview; 16–19 y: child report only, 12–15 y: parent and child report</td>
<td>na na ♂ +</td>
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</tbody>
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Table 1. (Continued)

<table>
<thead>
<tr>
<th>Study, country of origin, sample size (% ♀), and age</th>
<th>Measurements and definition</th>
<th>Results</th>
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<tbody>
<tr>
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<tr>
<td>Study 1: Weight status (m) was defined using IOTF (Continues)</td>
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<td>(O → D)</td>
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<tr>
<td>Study 2: Calculation of BMI (m), use of IOTF criteria for weight status (normal weight, overweight and obesity)</td>
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<td>(D → O)</td>
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<td>Study 2: Emotional symptom scale of the Strengths and Difficulties Questionnaire (SDQ-ES)</td>
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<td>Study 2: CES-D, shortened version with 14 items</td>
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Table 1. (Continued)

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<tr>
<td></td>
<td>BMI (m/s)</td>
<td>Depression</td>
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<tr>
<td></td>
<td>(3) at risk for overweight (85th–95th percentile), (4) overweight (95th–97th percentiles plus 2 BMI units), (5) obese (≥97th percentile plus 2 BMI units)</td>
<td>19 items of the CES-D</td>
</tr>
<tr>
<td>Sweeting et al. (2005) UK; N = 2,127 (49.0%♀); age: 11 y (baseline)</td>
<td>BMI (m): 11 and 15 y; calculation of BMI, conversion into standard deviation scores based on the UK 1990 growth reference, obesity ≥95th percentile</td>
<td>11 and 15 y: Brief Depression Scale (Kandel &amp; Davies, 1982) with 6 items 15 y: Voice-DISC: present state (past 4 weeks) diagnoses via computer algorithms defined in accordance with DSM-IV criteria, including major depressive disorder and dysthymia</td>
</tr>
<tr>
<td>Xie et al. (2005) China; N = 2,179 (46.9%♀); mean age: 12.9 y</td>
<td>Calculation of BMI (m) and use of IOTF (Cole et al. 2000) age and sex-specific 85th percentile as cut-off for obesity</td>
<td>4-item short form of the CES-D</td>
</tr>
</tbody>
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### Table 2. Main results of the longitudinal analyses

<table>
<thead>
<tr>
<th>Study, country of origin and sample size (%♀)</th>
<th>Age from baseline to follow-up</th>
<th>Age from baseline to follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity → Depression Geoffroy et al. (2014) UK</td>
<td>N = 11,024 (%♀nr)</td>
<td>0–9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>♂ OR 1.34 (over all time points)</td>
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<tr>
<td></td>
<td></td>
<td>BMI: 7, 11, 16, 33, and 45 years (m), 23, 42 and 50 y (s); childhood: use of international age-specific and sex-specific cut-offs (Cole et al., 2000); adulthood (BMI): underweight &lt; 18.5, overweight ≥ 25, obesity ≥ 30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Depression: Bristol Social Adjustment Guide (teacher-rated questionnaire; assessment of internalizing symptoms): 7 and 11 y; Rutter Behaviour Scale (teacher-rated questionnaire; internalizing score): 16 y; Malaise Inventory (self-rated questionnaire, items for somatic symptoms excluded): 23, 33, 42 y; Malaise Inventory (short form with 8 items): 50 y; CIS: core depressive symptoms: 45 y; elevated symptom level: score ≥ 90th percentile at each age</td>
</tr>
<tr>
<td>Marmorstein et al. (2014) USA</td>
<td>N = 1,512 (50.3% ♀)</td>
<td>11–14</td>
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<td></td>
<td></td>
<td>♂♀ not differentiated</td>
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<td></td>
<td></td>
<td>♂ OR 5.89</td>
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<td></td>
<td></td>
<td>♂ OR 0.52 (ns)</td>
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<td></td>
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<td>♂+♀ OR 2.53</td>
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<tr>
<td></td>
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<td>BMI (m): 11, 14, 17, 21, 24 y; 20–24 y: use of the standard body mass index cut-off of 30 to define obesity; &lt;20 y: use of CDC 2000 growth curves to determine obesity cut-offs (95th percentile) for each age and sex based on the average participant ages at each assessment</td>
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<td>Depression: &lt; 17 y: Diagnostic Interview Schedule for Children and Adolescents (MDD); ≥17 y: Structured Clinical Interview for DSM-III R (MDD)</td>
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<tr>
<td>Frisco et al. (2013) USA</td>
<td>N = 5,243 (100% ♀)</td>
<td>13–18</td>
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<td></td>
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<td>♂ ns (data not presented), ♂+♀ data not presented</td>
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<tr>
<td></td>
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<td>BMI (m): baseline and follow-up; calculation of age-specific and sex-specific BMI percentiles according to guidelines of the US CDC; follow-up: calculation of BMI (not overweight BMI &lt;25, overweight 25 ≥ BMI &lt;30, obese BMI ≥ 30)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Depression: modified versions of the CES-D; 9-item version (cut-off-score: ≥11)</td>
</tr>
<tr>
<td>Roberts et al. (2013) USA</td>
<td>N = 3,134 (48.9% ♀)</td>
<td>13–17</td>
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<td></td>
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<td>♂ ns (data not presented), ♂♀ ns (data not presented)</td>
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<tr>
<td></td>
<td></td>
<td>BMI (m): baseline and follow-up; calculation of BMI percentiles based on CDC (2006)</td>
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<td>Depression: DISC-IV: (a) any mood disorder (mania, hypomania, major depression and dysthymia), (b) major depression and (c) disturbed mood in the past 12 months (depressed mood, irritable mood or anhedonia)</td>
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<table>
<thead>
<tr>
<th>Study, country of origin and sample size (% ♀)</th>
<th>Age from baseline to follow-up</th>
<th>0-9</th>
<th>10-19</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
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<tbody>
<tr>
<td><strong>Obesity → Depression</strong></td>
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<tr>
<td>Al Mamun et al. (2007) Australia N = 2,017 (50.6% ♀)</td>
<td>14–21</td>
<td>♂♀ not differentiated</td>
<td>BMI (m): baseline and follow-up; overweight was defined according to standard definitions derived from international surveys (Cole et al., 2000)</td>
<td>Depression: 14 y: CES-D; 21 y: YASR version of the CBCL, depression/anxiety score</td>
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<tr>
<td>Clark et al. (2006) UK UK N = 1,513 (♀ nr)</td>
<td>10–14 → 12–16</td>
<td>♂♀ not differentiated</td>
<td>BMI (m): baseline; use of the 1990 growth reference definition for determination of overweight (&gt;85th percentile) and obesity (&gt;95th percentile)</td>
<td>Depression: SMFQ; high score defined as ≥8 symptoms</td>
<td></td>
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</tr>
<tr>
<td>Swallen et al. (2005) USA N = 4,743 (51.8% ♀)</td>
<td>12–20 → 13–21</td>
<td>♂♀ not differentiated</td>
<td>BMI (m): baseline and follow-up; use of growth charts provided by the CDC to determine BMI percentiles for boys and girls of each age; definition of 5 categories: (1) underweight (≤5th percentile), (2) normal BMI (5th–85th percentile), (3) at risk for overweight (85th–95th percentile), (4) overweight (95th–97th percentiles plus 2 BMI units, and (5) obese (≥97th percentile plus 2 BMI units)</td>
<td>Depression: 19 items of the CES-D</td>
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<td>Sweeting et al. (2005) UK N = 2,127 (49.0% ♀)</td>
<td>11–15</td>
<td>♂♀ not differentiated</td>
<td>BMI (m): baseline and follow-up; calculation of BMI, conversion into standard deviation scores based on the UK 1990 growth reference, obesity ≥95th percentile</td>
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<td></td>
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<tr>
<td>Geoffroy et al. (2014) UK N = 11,024 (♀ nr)</td>
<td>7</td>
<td>♂♀ not differentiated</td>
<td>BMI and depression: see above (Obesity → Depression)</td>
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<td>Marmorstein et al. (2014) USA N = 1,512 (50.3% ♀)</td>
<td>11–14 y → 17–21 y</td>
</tr>
<tr>
<td>♀ OR 3.76 (11–14 y → 17–21 y)</td>
<td>♀ OR 0.33 (11–14 y → 17–21 y)</td>
</tr>
<tr>
<td>♀ + ♀ OR (11–14 y → 17–21 y) 1.42 (ns)</td>
<td>BMI and depression: see above ( Obesity → Depression)</td>
</tr>
<tr>
<td>**Larsen et al. (2014) Netherlands N = 1,465 (49.4% ♀)</td>
<td>11–16 y → 14–19</td>
</tr>
<tr>
<td>♀ ns (data not presented), ♀ ns (data not presented)</td>
<td>BMI and depression: see above ( Obesity → Depression)</td>
</tr>
<tr>
<td>BMI (m): baseline, 12 and 24 months; calculation of BMI z-scores with use of data from the 2000 CDC growth charts</td>
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</tr>
<tr>
<td>Depression: Dutch version of the 20-item self-reported CES-D inventory</td>
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<tr>
<td>**Frisco et al. (2013) USA N = 5,243 (100% ♀)</td>
<td>13–18 y → 19–25</td>
</tr>
<tr>
<td>♀ ♀ not differentiated</td>
<td>BMI and depression: see above ( Obesity → Depression)</td>
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<tr>
<td>**Roberts et al. (2013) USA N = 3,134 (48.9% ♀)</td>
<td>11–17 y → 12–18</td>
</tr>
<tr>
<td>♀ ♀ OR 2.87, ♀ ns (data not presented)</td>
<td>BMI and depression: see above ( Obesity → Depression)</td>
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<td>♀ ♀ not differentiated</td>
<td>BMI and depression: see above ( Obesity → Depression)</td>
</tr>
<tr>
<td>BMI (m): all time points (12, 24, 36 and 48 months); calculation of BMI (no reference stated)</td>
<td></td>
</tr>
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<td>Depression: 20-items CES-D</td>
<td></td>
</tr>
<tr>
<td>**Bjornelv et al. (2011) Norway N = 1,619 (53.9% ♀)</td>
<td>13–19 y → 15–21</td>
</tr>
<tr>
<td>♀ ♀ data not presented</td>
<td>BMI (m): baseline and 24 months; calculation of BMI using adult cut-offs for definition of weight categories</td>
</tr>
<tr>
<td>Depression: 20-items CES-D</td>
<td></td>
</tr>
<tr>
<td>**Gaysina et al. (2011) UK N = 4,559 (48.0% ♀ at 7 y)</td>
<td>7–15 y → 53</td>
</tr>
<tr>
<td>♀ ♀ data not presented</td>
<td>BMI + 0.63 kg/m²</td>
</tr>
<tr>
<td>BMI: 7, 11, 15, 36, 46, 53 y (m), 20, 26 y (s); calculation of BMI (no reference stated)</td>
<td></td>
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<tr>
<td>Depression: Rutter’s Teacher Questionnaire (teacher-rated): 13 and 15 y; Present State Examination: 36 y; Psychiatric Symptom Frequency scale: 43 y; 28-item General Health Questionnaire: 53 y</td>
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(Continues)
children and adolescents. In the study of Swallen et al. (26), obesity also did not predict depression in 12- to 20-year-old adolescents. Finally, in the study of Chaiton et al. (23), no significant effect of obesity on depression was found in 13- and 16-year-old adolescents.

### Depression as predictor for weight status

Both available studies yielded evidence for depression predicting obesity. In the study of Roberts et al. (20), any mood disorder (OR 2.2) and major depressive disorder (OR 2.7) predicted obesity but not overweight in 11- to 17-year-old adolescents. An increased risk of obesity in male adolescents at the age of 12–19 years with major depressive disorder (OR 2.7) was detected by Merikangas et al. (28).

### Results of longitudinal analyses

Four studies examined bidirectional influences of weight status and depression in longitudinal analyses (12,18,20,29). In addition, four studies with longitudinal design assessed the unidirectional influence of weight status on depression (17,26,30,31) and five studies the unidirectional influence of depression on weight status (8,14,15,32,33). For country of origin, sample size, duration of follow-up and an overview of the results, see Table 2.

### Influence of weight status on depression

The influence of obesity in childhood or adolescence on later depressive symptoms was assessed in eight studies with a longitudinal study design, of which three found evidence for such an influence. Geoffroy et al. (18) showed that only female subjects with obesity had an increased risk for depression over all ages from 7 to 50 years (OR 1.34). The study of Marmorstein (12) revealed that an obesity onset in late adolescence predicted the onset of major depression in early adulthood also only among female adolescents (OR 5.9). In the study of Frisco et al. (29), again only female adolescents at the age of 13 to 18 years had an increased risk of depression at follow-up 6 years later when they were obese at baseline (OR 2.0) or changed from normal weight (OR 2.1) or overweight (OR 1.9) to obesity compared with those who were never overweight.

In the remaining five studies, no corresponding evidence was obtained. In the study of Roberts et al. (20), weight status at the age of 11–17 years did not significantly predict a higher risk of depression (OR 1.9) at follow-up 12 months later. Al Mamun et al. (30) assessed adolescents at the age of 14 and 21 years and found that perceived overweight but not actual BMI in adolescence was related to depressive symptoms in early adulthood. Clark et al. (31) examined students at the age of 10–14 years and 2 years later. They did not find an increased risk of depression at follow-up by being overweight or obese at baseline (OR 1.04).
Consistently, in the study of Swallen et al. (26), no influence of BMI at the ages of 12–20 years on depressive symptoms (OR 0.99) by the time of the follow-up 12 months later was detected. Sweeting et al. (17) examined pupils at the ages 11 (baseline) and 15 years (follow-up). They did not observe any significant relationship between weight change and depressive symptoms at follow-up with the exception that becoming obese during adolescence was associated with a smaller increase of ‘low mood’ between 11 and 15 years (OR 0.69). In addition, adolescents changing from obesity to overweight or normal weight during adolescence experienced smaller increases of low mood from 11 to 15 years compared with those continuously non-obese (OR 0.91).

Influence of depression on weight status

Of nine available studies, three found that depression predicted obesity at different time points of follow-up. Marmorstein et al. (12) showed that an onset of major depression in early adolescence predicted an onset of obesity in late adolescence, but only in female adolescents (OR = 3.8). In the study of Roberts et al. (20), depression increased the risk of obesity in 11- to 17-year-old adolescents after 12 months more than twofold (any mood disorder: OR 2.1; major depression: OR 2.9). However, in an additional gender-specific analysis, this effect remained significant only for male adolescents with a sixfold increased risk for becoming obese when major depression was present at baseline. Gaysina et al. (32) assessed adolescents at the age of 15 years and followed them up to the age of 53 years. Women with adolescent-onset depressive symptoms, either with ‘repeated symptoms’ (depression in adulthood) or ‘good adult outcome’ (no depression in adulthood), had significantly higher rates of BMI increase during adulthood than women without depressive symptoms in adolescence. At the age of 53 years, BMI of women was 0.63 kg/m² higher, when they had adolescent depressive symptoms with ‘good adult outcome’ compared with those without depressive symptoms in adolescence.

In the remaining six studies, no evidence for a significant influence of depression on later obesity was obtained (Table 2). Geoffroy et al. (18) followed a birth cohort from the ages of 7 to 15 years at seven time points of follow-up. Larsen et al. (8) assessed students at the age of ~14 years over the course of 3 years. Frisco et al. (29) examined 13- to 18-year-old adolescents with a follow-up after 6 years. The study of Kubzansky et al. (14) included a baseline examination at the age of 14 years and four yearly follow-up assessments. In the study of Bjornelv et al. (15), 13- to 18-year-old adolescents were followed up after ~2.5 years. Finally, Viner et al. (33) assessed adolescents at the age of 16 years and re-examined them at the age of 30 years.

Discussion

The evidence for an association of obesity and depression in childhood and adolescence was substantiated in our analysis based on studies that fulfilled priorly defined stringent inclusion criteria. Thus, more than one-half of the cross-sectional studies (five out of eight: (8,12–14,17)) with correlational design revealed significant associations between overweight or obesity and depression. In the regression analyses, childhood or adolescent obesity was identified as a statistical predictor for depression in seven (18–21,24,25,27) out of 10 available studies with odds ratios ranging from 1.3 to 2.9. Potentially, the relationship is age-dependent. Thus, Geoffroy et al. (18) found a reduced risk of depression for obese children aged 7 years (OR 0.7). In contrast, obesity proved to be a risk factor for subsequent development of depression in older children and adolescents in all seven studies including Geoffroy et al. (18).

Concerning the risk of obesity by depression, the two available studies with regression analysis (20,28) both confirmed this direction with odds ratios of 2.2–2.7. Somewhat in discrepancy to the cross-sectional analyses, only three (12,18,29) out of eight available longitudinal studies yielded evidence for a significant association between childhood or adolescent obesity and the subsequent risk of depression. Significant results were exclusively obtained for female subjects with odds ratios ranging from 1.3 to 5.9. The differences in odds ratios potentially depend on the different time points of follow-up (12,18,29). Similarly, the majority of the included longitudinal studies (six out of nine) did not yield evidence for a significant relationship between depressive symptoms in childhood or adolescence and the risk of obesity in later life. Interestingly, in two studies, an effect of adolescent depression on future development of an elevated body weight applied to female adolescents only with an odds ratio of 3.8 for the onset of obesity in late adolescence by the onset of depression in early adolescence (12) or a mean increase of 0.63 kg/m² from early adolescence to the age of 53 years (32). In contrast, the third study observed an odds ratio of 6.0 for male adolescents with major depression to become obese 1 year later (20). Overall, we found stronger evidence for an association of obesity and depression in childhood and adolescence in the cross-sectional compared with the longitudinal analyses.

Potential mechanisms

Discussing mechanisms for the association of obesity and depression, potential mediators for the relationships should be taken into account. It is unclear if a high BMI entails an elevated depression score as a result of perceived stigmatization, bullying and victimization, reduced self-esteem or any other psychological mediator. Alternatively (or additionally), an elevated BMI and in particular an elevated visceral...
Based on the limited number and high heterogeneity of the included studies, no secure conclusion can be drawn. Methodological differences of the included studies must be taken into account in an attempt to explain the inconsistent results. These studies primarily varied in their method of statistical analysis, thus hampering a solid comparison. Due to this aspect but also because of methodological limitations or between study differences such as short and varying lengths of follow-up periods, variance in sample sizes, insufficient inclusion of children at younger ages and multiple testing without appropriate adjustment, solid conclusions cannot be reached. In some studies, odds ratios were merely presented for significant findings. Obviously, both the direction of an effect and its magnitude (even if non-significant) should be reported to allow for a thorough evaluation/assessment/understanding. Not all of the included studies considered several potentially confounding variables (e.g., gender, age, socio-economic status and perceived weight). For instance, adjustment for socio-economic status was considered several potentially confounding variables (e.g., gender, age, socio-economic status and perceived weight). For instance, adjustment for socio-economic status was considered several potentially confounding variables (e.g., gender, age, socio-economic status and perceived weight).
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internationally accepted guidelines (10), a limitation is given
logical prerequisites for the inclusion of studies forms an im-

ties. More ways both categorically (e.g. (20,32)) and dimensionally
(e.g. (8,13)) precluding direct comparison of the results
obtained in different studies. Only three studies used struc-
tured clinical interviews for the categorical assessment of
depression (12,20,28). The Center for Epidemiological
Studies Depression Scale (CES-D) has been used most
formed frequently; however, some studies (e.g. (27)) used only the
short form, again hampering comparisons with those studies
based on the complete CES-D.

Strengths and limitations of this review

The strengths of this review include a systematic research
strategy and a structure corresponding to the PRISMA
guidelines (10). We provide an update and extension of
the existing evidence based on stringent predefined inclusion
criteria, thus substantially adding to the recently published
reviews on this topic. Although the definition of methodo-
logical prerequisites for the inclusion of studies forms an im-
portant issue for systematic reviews and is recommended by
internationally accepted guidelines (10), a limitation is given
by the choice of the inclusion criteria, which to a certain de-
gree are arbitrary (e.g. sample size). Thereby, other studies
of good methodological quality have possibly been ex-
cluded a priori, which could have contributed to clarifying the
relationships of obesity and depression in childhood
and adolescence.

Conclusion

The results of the included studies still provide a mixed
body of evidence. Our results indicate that cross-sectional
studies have identified associations more frequently than
longitudinal studies, possibly suggesting a joint develop-
ment of both depression and overweight/obesity in those
presupposed subjects. Altogether, in line with recently pub-
lished reviews (3–5) there is consistent evidence for a gender
effect in bidirectional associations of obesity and depression
with a stronger relationship in female subjects. In contrast
to these reviews (no overlap with Korczak et al. (3) and
Vámosi et al. (5); one overlap with Incledon et al. (4,17)),
we found weaker evidence for bidirectional longitudinal as-
ociations in the studies that met our inclusion criteria.
While the majority of cross-sectional studies suggest that a
clear relationship between obesity and depression exists,
longitudinal studies are still too few to allow for an estima-
tion of the effect sizes of the bidirectional influences. More
longitudinal studies, especially focusing on the influence of
childhood and adolescent depression on the course of
weight and considering the subtype of depression (46), are
urgently needed to complement and clarify the currently in-
consistent results. To date, evidence for a significant bidir-
ctional association of obesity and depression in adulthood
(47) seems more substantiated than for childhood and adol-
scence. Given that meaningful associations of obesity and
depression in childhood and adolescence are further con-

c rare

Conflict of interest statement

Y. M. and J. H. report grants received by their institution from
the German Federal Ministry of Education and Research
(BMBF, project no. 01GI1120A/B) during the conduction of
this study. J. H. reports German grants (non-industrial) and
personal honoraria outside the submitted work. J. A. and
M. F. have nothing to disclose.

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