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#### REVIEW

Pediatric Obesity



# Weight-loss interventions for adolescents with Down syndrome: a systematic review

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# **Abstract**

Objective: Youth with Down syndrome (DS) experience high rates of overweight and obesity; therefore, weight-loss interventions are warranted. We aimed to systematically review weight-loss interventions for adolescents with DS to better understand the most effective strategies and identify the current gaps in the literature.

Methods: This systematic review followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (International Prospective Register of Systematic Reviews [PROSPERO] #CRD42022303781). Databases were searched through July 28, 2023, and screening, evaluation, and data extraction were performed by two independent reviewers. Change scores for weight or BMI were presented by study design and intervention components.

**Results:** The 26 included papers describing 24 unique studies included a total of n = 1171participants, of whom n = 393 were participants with DS. Eleven studies focused on physical activity, one on diet, and two on physical activity and diet; seven studies used multicomponent interventions; and three studies investigated laparoscopic sleeve gastrectomy. Thirteen studies using either a multicomponent intervention, a physical activity intervention, or surgery resulted in weight loss or a decrease in BMI in adolescents with DS.

Conclusions: Weight-loss interventions can be effective for adolescents with DS and could benefit from increasing duration/intensity to meet the existing weight-loss intervention recommendations. More research on surgery and weight-loss medications is needed.

# INTRODUCTION

Down syndrome (DS) or trisomy 21 is the most common chromosomal abnormality associated with an intellectual disability

[Correction added on 20 March 2025, after first online pulication: Thessa I.M. Hilgenkamp's and Keith M. Diaz's names have been updated in the author byline.l

(ID) caused by extra chromosome 21 material in all or some cells of the body [1]. The prevalence of DS among children aged 0 to 4 years in the United States is about 12.7 per 10,000 [2]. Obesity (body mass index [BMI]-for-age ≥ 95th percentile) and overweight (BMI-for-age 85th-94.9th percentile) are more prevalent among youth with DS compared with both the general youth population [3-7] and youth with other IDs [6, 8-12]. For example, data from

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electronic medical record review of youth with IDs found that the prevalence of overweight and obesity, combined, was 49% and 34% in those with and without DS, respectively [6]. Obesity in adolescents with DS has been associated with several negative health outcomes, including obstructive sleep apnea, insulin resistance, dyslipidemia, and gait disorders [8, 13–15]. Therefore, effective weight-management interventions for adolescents with DS are warranted.

Obesity in adolescents with DS is likely due to both behavioral patterns (e.g., high energy intake/poor diet quality and physical inactivity) [6, 8, 16, 17] and genetic/physiological factors (e.g., decreased energy expenditure, increased leptin, and hypotonia) [4, 7, 18, 19]. Additionally, adolescents with DS have limitations with reasoning, money management, memory, and decision-making, which require increased assistance from parents/guardians for the completion of daily activities and can impact choices around diet and physical activity. Therefore, existing weight-management interventions developed and tested in typically developing adolescents cannot be applied directly to adolescents with DS.

Multicomponent interventions that include diet, physical activity, and behavioral guidance and support have consistently demonstrated improvements in weight status for up to 12 months in typically developing children and adolescents with obesity [20, 21]. The quality and quantity of data to base recommendations for effective weight management specifically for adolescents with DS is almost nonexistent. The most recent systematic review in youth/ adolescents with DS, published in 2016 [8], identified only five trials with weight-loss interventions that included adolescents with DS, most of which recommended increasing physical activity without a dietary component and were conducted over short durations in small samples with inadequate statistical power. Additionally, a 2020 systematic review examining interventions that targeted changes in body composition in individuals exclusively with DS identified only three trials in adolescents [22], all of which were short-term (i.e., 12-week) physical activity programs. An unpublished scoping review by our team identified several weightmanagement interventions conducted since 2016 that included adolescents with DS and included a nutrition and/or behavior change component, as well as surgical interventions. Including these newer interventions in an updated systematic review would benefit health care professionals and researchers alike by offering evidence-based practices for weight management and advancing the development of effective lifestyle interventions targeting longterm changes in body weight.

Therefore, to better understand the most effective strategies (e.g., physical activity, nutrition, multicomponent, pharmacological, surgical) for weight loss in adolescents with DS and to identify the current gaps in the literature, we conducted an updated systematic review on weight-loss interventions for adolescents with DS, including both interventions that were developed exclusively for adolescents with DS and those that included adolescents with DS.

# **Study Importance**

#### What is already known?

- Reviews have shown that multicomponent interventions are effective for weight loss for adolescents in the general population.
- Two previous reviews in adolescents with Down syndrome (DS) have included interventions focused mostly on physical activity alone, with short durations and small sample sizes.

#### What does this review add?

- This review included 26 studies in adolescents with DS and included multicomponent interventions with behavioral strategies, as well as laparoscopic sleeve gastrectomies for the first time
- This review, for the first time, to our knowledge, showed that population-specific weight-loss interventions can be effective for adolescents with DS to lose weight.

# How might these results change the direction of research or the focus of clinical practice?

- Clinical practitioners and researchers can use this review to recommend or design weight-loss interventions that are likely to be effective for adolescents with DS.
- Further research is needed on weight-loss medications and interventions that adhere to recommended multicomponent weight-loss intervention guidelines.

# **METHODS**

This study was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) [23] and was registered with International Prospective Register of Systematic Reviews (PROSPERO; #CRD42022303781).

## Information sources and search strategy

The following databases were included in our systematic search strategy: Pubmed (NCBI); Embase (Elsevier); CINAHL (EBSCO); American Psychological Association (APA) PsycINFO (EBSCO); Web of Science (all databases, all collections; Clarivate); and Cochrane Central Register of Controlled Trials (Wiley). The complete search strategy is included in online Supporting Information. The database specialist (John Usseglio) performed the initial search on March 22, 2022, and then updated the database search on July 28, 2023. The reference list of each review paper found through this search on this topic was independently screened by two members of the research team to identify

any further relevant papers. These manually added papers were listed separately in the flow diagram (Figure 1).

# Eligibility criteria

The study selections for this review were assessed as eligible by the following inclusion criteria:

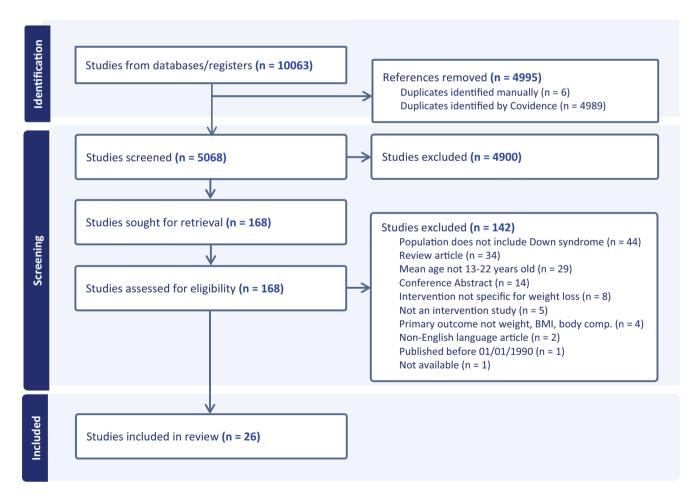
- 1. The study population comprised individuals with IDs, and the study sample had to include individuals with DS of any gender;
- The mean age of the study sample had to be between 13 and 22 years:
- The study investigated an intervention that was specifically aimed at weight loss;
- 4. Primary outcome measures included weight, BMI, or body composition (e.g., body fat percentage, waist circumference, waist-hip ratio, fat mass);
- Only intervention studies with at least five participants were included:
- 6. The paper was published in the English language; and
- 7. The paper was published after January 1, 1990.

Studies were excluded if they did not comply with these inclusion criteria. Studies were grouped for synthesis by study design (randomized-controlled trials [RCTs], non-RCTs, pre-post studies, or other designs) and by type of intervention (physical activity or diet only, diet and physical activity combined, diet and physical activity combined with other components, and other [surgical]).

#### Selection process

After importing all of the eligible records in Covidence review management software, all members of the research team independently screened the titles and abstracts of identified papers, with all records being reviewed by two different researchers. Results were collated automatically, and any disagreements were resolved through a consensus discussion with a third member of the research team.

Next, all papers selected in the title-abstract screening were moved to full-text screening, and portable document formats (PDFs) were retrieved and added to the records in Covidence. These full texts were then reviewed for inclusion and exclusion criteria independently by two members of the research team (all members involved). Results were collated automatically, and any disagreement was resolved



**FIGURE 1** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram. [Color figure can be viewed at wileyonlinelibrary.com]



through a consensus discussion with a third member of the research team.

# Data extraction process

In Covidence, a data extraction form was developed based on variables listed in the protocol to extract relevant information from included studies. The extraction form was piloted and adapted to best fit the different study designs. Data were extracted from all included studies by two members of the research team independent of each other. Extracted data were compared in group meetings, and discrepancies were resolved through consensus discussion.

#### **Data items**

Data extracted included general characteristics (i.e., study design, study aim, country, sampling period, sample size, target population, comparison group, inclusion and exclusion criteria for the study, sampling method, level of ID, etiology of ID, weight status, living circumstances, age, sex, ethnicity, presence of known cardiovascular disease risk factors, medication use, and physical activity level), intervention characteristics (i.e., setting, duration, intensity, data collection time points, modality description of the intervention components, involved health care professionals and other supports, and description of control group), and intervention outcomes for weight, BMI, BMI *z* scores (BMIz), or body composition (i.e., body fat percentage, waist circumference, waist-hip ratio, and fat mass). When change scores were not provided, authors were contacted to provide those.

# Rating of methodological quality

We used the Standard Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields [24] to evaluate the risk of bias of the studies. This standard tool consists of 14 questions, answered with "Yes" (2 points), "Partial" (1 point), or "No" (0 points); not every question was applicable for each study, as indicated by "N/A" (not factored into calculations). Congruent with recommendations from Kmet et al. [24], we calculated the total possible sum, total sum, and the summary score. The total possible sum was the highest possible score if all of the items that were applicable to a specific study scored 2 points. The actual score on those selected items (total sum) was divided by the total possible sum for those items, arriving at a ratio that was comparable across the different studies. This ratio was called the summary score and yielded a value between 0 and 1. A higher score indicates a higher quality study. The summary score can be used to determine which studies should be included in a systematic review by virtue of establishing specific cut points determined by the authors. However, rather than using the summary score to decide which studies to exclude from this review, we decided to include all studies that met inclusion criteria for our search and provide summary scores for each study as a descriptive metric. The risk of bias of all studies was independently evaluated by two members of the research team, and data were collected in Covidence. Results were automatically collated and discussed with a third reviewer to reach consensus.

#### Data synthesis and analysis

Intervention outcomes (both immediate and for follow-up data points if available) were expressed in absolute values or change scores for weight, BMI, BMIz, or body composition (i.e., body fat percentage, waist circumference, waist-hip ratio, and fat mass). Author-provided outcomes of statistical tests for differences within groups (pre-post) or between groups (intervention-control) were included in the tables. Study and sample characteristics of all included studies were provided in a table organized by study design, as well as the description of the interventions of all included studies. Study outcomes in absolute values and change scores for weight and BMI were summarized in separate tables only including the studies that reported weight and/or BMI, organized by study design. If change scores were not provided, the authors were contacted to provide this information. Mean change was calculated if only absolute values were available. Study outcomes were further synthesized by type of intervention, i.e., physical activity only, diet only, physical activity and diet, multiple components, and other, such as surgeries. Because not all studies reported both weight and BMI as outcome measures, reporting bias could influence the results. Studies that are not included in the tables for lack of that specific outcome measure are explicitly mentioned in the Results section for transparency regarding any reporting bias.

# **RESULTS**

## Study selection

Initially, we found 4678 records in database searching and manually added 5 records after screening of the reference lists of review papers. After removal of 326 duplicates, we screened 4351 records for title and abstract, after which we screened the full text of 155 papers. Out of those, 20 papers were included in our systematic review. The updated search resulted in an additional 719 new records to screen, of which 6 records were included in this review and of which 2 were additional papers of a study that was already included [25, 26], resulting in 4 added studies [27–30].

The main reasons for being excluded were sample related (e.g., sample did not include participants with DS, mean age was not between 13 and 22 years) or the paper was not a peer-reviewed publication investigating an intervention (Figure 1).

#### Risk of bias in studies

Figure 2 presents the risk of bias of the included studies (full details in Table 1). The mean quality assessment score for the 24 studies was 0.75, indicating low-to-moderate bias. A score over 0.75 was achieved by 11 (45.9%) of the included studies. A large percentage of the studies sufficiently described the study objective and statistical analysis plan, provided an estimate of variance in the main results, and sufficiently reported their results and conclusion. Reductions in quality assessment scores were commonly related to lack of intervention blinding or use of a control group.

#### **Description of individual studies**

Of the 26 included papers describing 24 unique studies, 11 studies were RCTs [27–29, 31–38], 2 were non-RCTs [39, 40], 8 employed a pre-post study design without a control group [30, 41–47], and the remaining 3 were laparoscopic sleeve gastrectomy studies that only reported a 1-year follow-up [48–50]. Details are provided in Table 2.

## Study and sample characteristics

Sample characteristics are presented in Table 2. Six RCTs and two pre-post studies were conducted with participants with DS only; and five RCTs, six pre-post studies, and all studies with other designs

included a sample of participants with intellectual and developmental disabilities (IDDs) with different etiologies, including DS, as well as autism, cerebral palsy, seizure disorder/epilepsy, and/or spastic quadriplegia. Sample sizes ranged from 5 to 297; 5 studies had a total sample between 0 and 20 participants, 12 studies had a total sample between 21 and 50 participants, 5 studies had a total sample between 51 and 100 participants, and 2 studies had >100 participants. The mean age of the groups within the studies ranged from 13.4 to 21.9 years. Only one study included only male individuals [46], and all other studies included male and female individuals, with most studies having a fairly balanced distribution. Ethnicity was reported in 9 of the total 24 studies (4 of 11 RCTs, none of the non-RCTs, 3 of 8 prepost studies, and 2 of the 3 surgical studies). Out of the nine studies that reported ethnicity, four studies had a majority of participants who identified as White [31, 32, 35, 36], four studies had a majority of participants who identified as Hispanic [42, 45, 47, 50], and one study had a majority of participants who identified as Black [49].

#### Intervention characteristics

The intervention characteristics are described in detail in Table 3. Out of the 24 unique studies, 11 focused on physical activity only [27–29, 33, 34, 37–40, 45, 46], 1 study focused on diet only [44], 2 studies focused on a combination of physical activity and diet [41, 47], 7 studies were multicomponent interventions [30–32, 35, 36, 42, 43], and 3 studies investigated the effects of a surgical intervention, i.e., a

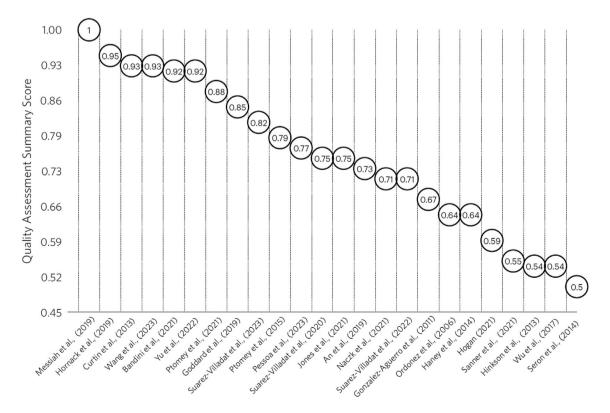


FIGURE 2 Overview of quality assessment scores per included paper.



**TABLE 1** Quality assessment scores.

	Qu	ality a	assessme	ent qu	estion n	umbers									Summary
Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	score (range 0-1)
Bandini et al., 2021	2	2	2	2	2	0	N/A	2	2	2	2	2	2	2	0.92
Curtin et al., 2013	2	2	2	2	2	0	2	2	2	2	2	2	2	2	0.93
Gonzalez-Aguero et al., 2011	2	2	1	1	1	N/A	N/A	2	1	2	1	0	2	1	0.67
Naczk et al., 2021	2	2	1	1	2	0	0	1	1	2	2	2	2	2	0.71
Ptomey et al., 2015	2	2	2	2	1	0	0	2	1	2	2	2	2	2	0.79
Ptomey et al., 2021	2	2	2	2	2	0	N/A	2	2	2	2	1	2	2	0.88
Suarez-Villadat et al., 2020	2	2	1	2	1	0	0	2	2	2	1	2	2	2	0.75
Suarez-Villadat et al., 2023 <sup>a</sup>	2	1	1	2	1	0	0	2	1	2	2	2	2	2	0.71
Suarez-Villadat et al., 2023 <sup>b</sup>	2	2	1	2	1	2	0	2	1	2	2	2	2	2	0.82
Wang et al., 2023	2	2	2	2	1	2	1	2	2	2	2	2	2	2	0.93
Yu et al., 2022	2	2	1	2	2	2	N/A	2	2	2	2	1	2	2	0.92
Seron et al., 2014	1	1	1	1	N/A	0	0	2	1	2	1	0	2	1	0.50
Wu et al., 2017	1	1	1	1	0	0	N/A	2	1	1	2	0	2	2	0.54
An et al., 2019	2	2	1	1	N/A	N/A	N/A	1	0	2	2	1	2	2	0.73
Haney et al., 2014	1	1	1	1	N/A	N/A	N/A	2	1	2	2	0	1	2	0.64
Hinkson et al., 2013	2	1	1	2	N/A	N/A	1	2	0	0	2	0	0	2	0.54
Hogan 2001	1	1	1	0	N/A	N/A	N/A	1	2	1	2	0	2	2	0.59
Ordonez et al., 2006	1	1	1	1	N/A	N/A	N/A	2	1	2	2	0	1	2	0.64
Pessoa et al., 2023	2	1	1	1	N/A	N/A	N/A	2	1	2	2	1	2	2	0.77
Sanner et al., 2021	2	2	2	2	N/A	N/A	N/A	1	0	0	2	N/A	0	0	0.55
Goddard et al., 2019	2	2	2	1	N/A	N/A	N/A	2	2	2	1	N/A	1	2	0.85
Hornack et al., 2019	2	2	2	2	N/A	N/A	N/A	2	1	2	2	2	2	2	0.95
Jones et al., 2021	2	2	N/A	2	N/A	N/A	N/A	N/A	0	2	0	N/A	2	2	0.75
Messiah et al., 2019	2	2	N/A	2	N/A	N/A	N/A	2	2	2	2	2	2	2	1.00

Note: Scores are calculated based on guidelines from Kmet et al. [24]. Scores correlate with the degree to which a criterion posed in each question is met. A score of 0 = "no"; a score of 1 = "partial"; and a score of 2 = "yes." "N/A" for "not available" indicates that the criterion does not apply to the study. Summary score = sum of all scores divided by total possible score (i.e., 28). A higher summary score indicates a higher quality study. Quality assessment score questions reprinted from Kmet et al. [24]: 1) Question/objective sufficiently described?; 2) Study design evident and appropriate?; 3) Method of subject/comparison group selection or source of information/input variables described and appropriate?; 4) Subject (and comparison group, if applicable) characteristics sufficiently described?; 5) If interventional and random allocation was possible, was it described?; 6) If interventional and blinding of investigators was possible, was it reported?; 7) If interventional and blinding of subjects was possible, was it reported?; 8) Outcome and (if applicable) exposure measure(s) well defined and robust to measurement/misclassification bias? Means of assessment reported?; 9) Sample size appropriate?; 10) Analytic methods described/justified and appropriate?; 11) Some estimate of variance is reported for the main results?; 12) Controlled for confounding?; 13) Results reported in sufficient detail?; and 14) Conclusions supported by the results?

laparoscopic sleeve gastrectomy [48–50]. Excluding the 1-day surgical interventions, the intervention length ranged widely from 4 days (health camp) [47] to 9 or 10 months (school-based or after-school program) [38, 42], with the exception of one study performing a longer intervention, which was an after-school-based intervention of 1 to 2 years [45]. The interventions that were not (after-) school-based took 8 weeks [35], 10 weeks [43], 12 weeks [29, 39, 40, 46], 14 weeks [41], 16 weeks [27], 20 weeks [28], 21 weeks [33], 24 weeks [30–32, 36, 44], 33 weeks [34], or 36 weeks [37]. Most studies reported other outcomes measures in addition to weight and BMI (Table 3). In addition to the three surgical studies that reported long-term follow-up outcomes, only five other studies included a

follow-up measurement beyond the postintervention measurements [25, 26, 29, 31, 32, 43].

# Results of individual studies

# Weight

Weight was reported as an outcome measure in 16 unique studies (including 11 RCTs; Table 4), but not in the remaining 8 studies [30, 41–43, 47, 49, 50].

<sup>&</sup>lt;sup>a</sup>Suarez-Villadat, 2023, strength vs. aerobic exercise.

<sup>&</sup>lt;sup>b</sup>Suarez-Villadat, 2023, effectiveness of exergames.

**TABLE 2** Descriptive information for included studies.

Author, year, country	Sample size	Etiology of ID	Age, mean (SD),	Gender n (%), M, F	Race and ethnicity, n (%)
RCT		<u> </u>		,	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
Bandini et al., 2021, United States	Total <i>n</i> = 31 1: FBBI directly, 14 2: Wait list, 13	30 DS 1: DS, 8 2: DS, 7		1: M, 4 (28.6), F, 10 (71.4) 2: M, 5, F, 8	1: White, 14 (100) 2: White, 13 (93), Hispanic, 1 (7)
Curtin et al., 2013, United States	Total <i>n</i> = 21 1: NAE, 10 2: NAE + BI, 11	DS, 21 1: DS, 10 2: DS, 11	1: 20.5 (4.1) 2: 20.5 (2.4)	1: M, 1 (10), F, 9 (90) 2: M, 3 (27.3), F, 8 (72.7)	1: White, 10 (100) 2: White, 10 (91), Hispanic, 1 (9)
Gonzalez-Aguero et al., 2011,	Total $n=25$	DS, 25		, , , , ,	
Spain	1: Intervention, 12 (48) 2: Control, 13 (52)	1: DS, 12 2: DS, 13	1: 13.7 (2.6) 2: 15.4 (2.5)	1: M, 5 (41.7), F, 7 (58.3) 2: M, 8 (61.5), F, 5 (38.5)	Not reported
Naczk et al., 2021, Poland	Total $n=22$	DS, 22			
	1: Intervention, 11 2: Control, 11	1: DS, 11 2: DS, 11	1: 14.9 (2.35) 1: 14.4 (1.97)	1: M, 7 (64), F, 4 (36) 2: M, 7 (64), F, 4 (36)	Not reported
Ptomey et al., 2015, United	Total $n=21$				
States	1: eSLD, 10 2: CD, 10	1: DS, 5 (50) Autism, 4 (40) Other, 1 (10) 2: DS, 3 (30) Autism, 5 (50) Other, 2 (20)	1: 15.9 (1.8) 2: 13.9 (2.2)	1: M, 5 (50), F, 5 (50) 2: M, 4 (40), F, 6 (60)	1: White, 6 (60), Black, 4 (40) 2: White, 8 (80), Asian, 1 (10), >1 race, 1 (10)
Ptomey et al., 2021, 2022,	Total $n = 110$				
2023, United States	1: FTF/CD, 36 2: RD/CD, 39 3: RD/eSLD, 35	1: DS, 17 (47) Autism, 15 (42) Other, 4 (11) 2: DS, 21 (54), Autism, 14 (36), Other, 4 (10) 3: DS, 15 (43), Other, 13 (37), Unknown, 7 (20)	1: 16.3 (2.7) 2: 15.6 (1.7) 3: 16.7 (2.5)	1: M, 20 (56), F, 16 (44) 2: M, 15 (39), F, 24 (61) 3: M, 17 (49), F, 18 (51)	1: White, 30 (83), Black, 3 (8), Hispanic, 2 (6), >1 race, 3 (8) 2: White, 0 (0), Black, 0 (0), Hispanic, 2 (5), >1 race, 1 (3) 3: White, 29 (83), Black, 4 (11), Hispanic, 4 (11), >1 race, 2 (6)
Suarez-Villadat et al., 2020,	Total $n = 45$				
Spain	1. Intervention, 15 2. Control, 30	1: DS, 15 (100) 2: DS, 30 (100)	1: 13.93 (1.23) 2: 13.71 (1.24)	1: M, 8 (53), F, 7 (47) 2: M, 17 (57), F, 13 (43)	Not reported
Suarez-Villadat et al., 2023, <sup>a</sup>	Total <i>n</i> = 50				
Spain	Aerobic     Strength	1: DS, 25 (100) 2: DS, 25 (100)	1: 18.37 (1.51) 2: 18.30 (1.33)	1: M, 17 (68), F, 8 (32) 2: M, 14 (56), F, 11 (44)	Not reported
Suarez-Villadat et al., 2023, <sup>b</sup>	Total <i>n</i> = 49				
Spain	1. Intervention, 24 2. Control, 25	1: DS, 24 (100) 2: DS, 25 (100)	1: 14.06 (1.16) 2: 14.32 (0.99)		Not reported



TABLE 2 (Continued)

			1: M, 14 (58), F, 10 (42) 2: M, 16 (64), F, 9 (36)	
Total <i>n</i> = 30  1. Intervention, 15  2: Control, 15	1: DS, 3 (20), ASD, 2 (13), Unknown, 10 (67) 2: DS, 1 (7), ASD, 2 (13), Unknown, 12 (80)	1: 14.60 (2.20), range 12–18 2: 13.73 (1.44), range 12–18	1: M, 9 (60), F, 6 (40) 2: M, 13 (87), F, 2 (13)	Not reported
Total <i>n</i> = 61  1: Intervention, 39  2: Control, 11	1: DS, 3 (5.1), Other, 36 (89.7) 2: DS, 2 (13.6), Other, 20 (90.9)	1: 14.95 (1.52) 2: 15.05 (1.84)	1: M, 31 (79.5), F, 8 (20.5) 2: M, 14 (63.6), F, 8 (36.4)	Not reported
Total <i>n</i> = 41  1: Control, 16  2: Aerobic, 15  3: Resistance, 10	1: DS, 16 (100) 2: DS, 15 (100) 3: DS, 10 (100)	1: 14.4 (2.5) 2: 15.7 (2.7) 3: 16 (2.8)	1: M, 4 (40), F, 6 (60) 2: M, 11 (69), F, 5 (31) 3: M, 10 (67), F, 5 (33)	Not reported
Total <i>n</i> = 43  1: Normal weight, 15 2: Obesity exercise, 14 3: Obesity control, 14	1: DS, 3 (20), Autism, 1 (6.5), Other, 11 (73.5) 2: DS, 4 (29), Autism, 1 (7), Other, 9 (64) 3: Autism, 1 (7), Other, 13 (64)	1: 16.94 (1.46) 2: 16.22 (1.47) 3: 17.79 (0.37)	1: M, 8 (53), F, 7 (47) 2: M, 6 (43), F, 8 (57) 3: M, 5 (36), F, 9 (64)	Not reported
14	DS, 2 Other, 14	13.36 (0.93), 12-15	M, 9 (64), F, 5 (36)	Not reported
52	DS, 3 (5.8), Autism, 19 (36.5), CP, 1 (1.9), Other, 32 (61.5)	13.7 (4.7), 6.5- 22.4	M, 39 (75), F, 13 (25)	White, 6 (12), Black, 12 (23), Hispanic, 34 (65)
17	DS, 2 (11.8) Other, 15 (88.2)	14 (4), 7-20	M, 10 (58.8), F, 7 (41.2)	Not reported
Total $n = 66$	Total		, ,,	
1: More weight gain, 34 2: Maintain rate of weight gain, 21 3: Slowed rate of weight gain, 11	1: CP, 16, SQ, 13, Other, 5 2: CP, 12, SQ, 3, Other, 6 3: CP, 4, SQ, 5, Other, 2	1: 21.9 (6.2) 2: 20.1 (8.8) 3: 19.6 (7.6)	1: M, 19 (55.9), F, 15 (44.1) 2: M, 10 (47.6), F, 11 (52.4) 3: M, 11 (52.4), F, 7 (63.6)	Not reported
	2: Control, 15  Total <i>n</i> = 61  1: Intervention, 39  2: Control, 11  Total <i>n</i> = 41  1: Control, 16  2: Aerobic, 15  3: Resistance, 10  Total <i>n</i> = 43  1: Normal weight, 15  2: Obesity exercise, 14  3: Obesity control, 14  14  52  17  Total <i>n</i> = 66  1: More weight gain, 34  2: Maintain rate of weight gain, 21  3: Slowed rate of	1. Intervention, 15 2: Control, 16 1: Intervention, 39 2: Control, 11 2: DS, 3 (20), ASD, 2 (13), Unknown, 10 (67) 2: DS, 1 (7), ASD, 2 (13), Unknown, 12 (80)  Total n = 61 1: Intervention, 39 2: Control, 11 1: DS, 3 (5.1), Other, 36 (89.7) 2: DS, 2 (13.6), Other, 20 (90.9)  Total n = 41 1: Control, 16 2: Aerobic, 15 3: Resistance, 10 2: DS, 16 (100) 3: DS, 10 (100)  Total n = 43 1: Normal weight, 15 2: Obesity exercise, 14 3: Obesity control, 14 3: Obesity control, 14 3: Obesity control, 14 4 DS, 2 Other, 11 (73.5) 2: DS, 4 (29), Autism, 1 (7), Other, 9 (64) 3: Autism, 1 (7), Other, 13 (64)  14 DS, 2 Other, 14 52 DS, 3 (5.8), Autism, 19 (36.5), CP, 1 (1.9), Other, 32 (61.5) 17 DS, 2 (11.8) Other, 15 (88.2)  Total n = 66 Total 1: More weight gain, 21 3: Slowed rate of weight gain, 21 3: Slowed rate of weight gain, 11 3: CP, 16, SQ, 13, Other, 5 2: CP, 12, 3: CP, 4, SQ, 5, Other, 6 3: CP, 4, SQ, 5,	1. Intervention, 15 2: Control, 15 2: DS, 1 (7), ASD, 2 (13), Unknown, 10 (67) 2: DS, 1 (7), ASD, 2 (13), Unknown, 12 (80)  Total n = 61 1: Intervention, 39 2: Control, 11 2: DS, 3 (5.1), Other, 36 (89.7) 2: DS, 2 (13.6), Other, 20 (90.9)  Total n = 41 1: Control, 16 2: Aerobic, 15 2: DS, 15 (100) 3: Resistance, 10  Total n = 43 1: Normal weight, 15 2: Obesity exercise, 14 3: Obesity control, 14 3: Obesity control, 14  Total n = 43 1: Normal weight, 15 2: DS, 4 (29), Autism, 1 (6.5), Other, 11 (73.5) 2: DS, 4 (29), Autism, 1 (7), Other, 9 (64) 3: Autism, 1 (7), Other, 13 (64)  14  DS, 2 Other, 14 (0.93), 12-15 52 DS, 3 (5.8), Autism, 1 (36.5), CP, 1 (1.9), Other, 32 (61.5) 17 DS, 2 (11.8) Other, 14 (0.93), 12-15 52 DS, 3 (5.8), Autism, 1 (936.5), CP, 1 (1.9), Other, 32 (61.5) 17 DS, 2 (11.8) Other, 14 (4), 7-20 15 (88.2)  Total n = 66 Total 1: More weight gain, 34 2: Maintain rate of weight gain, 21 3: Slowed rate of weight gain, 21 3: Slowed rate of weight gain, 11  Control, 10 1: 14.40 (2.20), range 12-18 2: 13.73 (1.44), range 12-18 2: 15.05 (1.60) 2: 15.05 (1.80) 3: 16 (2.8) 3: 17.79 (0.37) 3: 16 (2.8) 3: 17.79 (0.37) 3: 16 (2.8) 3: 17.79 (0.37) 3: 16 (2.9) 3: 17.79 (0.37) 3: 16 (2.9) 3: 17.79 (0.37) 3: 16 (2.9) 3: 17.49 (0.9) 3: 17.40 (0.9) 3: 17.40 (0.9) 3: 17.40 (0.9) 3: 17.4	Total $n=30$ 1. Intervention, 15 2: Control, 15 2: Control, 15 2: Control, 15 3: DS, 3 (20), ASD, 1: 14.60 (2.20), range 12-18 Unknown, 10 (67) 2: DS, 1 (7), ASD, 2 (13), range 12-18 Unknown, 12 (80)  Total $n=61$ 1: Intervention, 39 2: Control, 11 2: Control, 11 3: DS, 3 (5.1), 0ther, 36 (89.7) 2: DS, 2 (13.6), Other, 20 (90.9) 3: Control, 11 3: Control, 16 2: Associated as a control of the property of the p

TABLE 2 (Continued)

Author, year, country	Sample size	Etiology of ID	Age, mean (SD), range	Gender n (%), M, F	Race and ethnicity, n (%)
Messiah et al., 2019, United States	297	DS, 8 (2.7), Autism, 106 (35.7), Other, 183 (61.6)	14.1 (4.4), 6-22	M, 214 (72), F, 83 (28.0)	White, 29 (10), Black, 59 (20), Hispanic, 203 (70)
Ordonez et al., 2006, Spain	22	DS, 22	16.2 (1.0)	M, 22 (100)	Not reported
Pessoa et al., 2023, Brazil	16	DS, 16 (100)	15.2 (2.44)	M, 9 (56), F, 7 (44)	Not reported
Sanner et al., 2020, United States	16	DS, 4 (25.1), Autism, 8 (50), ID, 3 (18.8), Other, 1 (6.25)	13.5 (1.62)	M, 11 (68.8), F, 5 (31.2)	Parent ethnicity defined as Hispanic, 9 (56)
Other designs (surgeries)					
Goddard et al., 2019, United States	Total <i>n</i> = 54 1: DD, 10 2: Non-DD, 44	1: DS, 2 (20), Autism, 4 (40), CP, 1 (10), Sz, 1 (10) Other, 2 (20) 2: 44 neurotypical	1: 19.3 (4.6) 2: 17.0 (1.7)	1: M, 3 (30), F, 7 (70) 2: M, 7 (16) F, 37 (84)	Not reported
Hornack et al., 2019, United States	Total <i>n</i> = 63  1: ID, 17  2: Control, 46	1: DS, 3 (17.6), Other, 14 (82.3) 2: 45 neurotypical	1: 17.7 (2.7) 2: 17.6 (1.7)	1: M, 6 (35.3), F, 11 (64.7) 2: M, 16 (34.8), F, 30 (65.2)	1: White, 4 (24), Black, 11 (65), Hispanic, 1 (6), Other, 1 (6) 2: White, 12 (26), Black, 27 (59), Hispanic, 7 (15), Other, 0
Jones et al., 2021, United States	5	DS, 1 (20), Autism, 2 (40), Other, 2 (40)	15.6 (4.54), 11-23	M, 4 (80), F, 1 (20)	White, 2 (40), Black, 1 (20), Hispanic, 2 (40)

Abbreviations: ASD, autism spectrum disorder; BI, behavioral intervention; CD, conventional diet; CP, cerebral palsy; DD, developmental disabilities; DS, Down syndrome; eSLD, enhanced stop light diet; F, female; FBBI, family-based behavioral intervention; FTF, delivered face-to-face; ID, intellectual disability; M, male; NAE, nutrition and activity education; RCT, randomized-controlled trial; RD, remotely delivered; SQ, spastic quadriplegia; Sz, seizure disorder.

Six RCTs provided change values, and those studies reported statistically significant (either within-group or between-group) weight loss in the intervention groups (change scores ranged from -0.2 to -5.0 kg). With the exception of Ptomey et al. [35], which compared two different weight-loss interventions, all six RCTs that included between-group analyses reported a significant weight loss from the intervention compared with the nonintervention control group (change scores for the control groups ranged from +0.5 to +2.8 kg). The remaining five RCTs did not provide change values and/or did not test the outcomes for statistical significance.

The two non-RCTs (both physical activity-only interventions) reported weight loss for the aerobic, but not the resistance, exercise group [39] and a significant weight loss for the exercise group [40]. Between-group differences were either not reported or were not significant (Table 4). For the pre-post studies, only Hogan [44] provided

change values for each one of the weight-gain conditions, and only the group that aimed to gain more weight was able to significantly gain weight; however, a significant weight loss was reported by Ordonez et al. [46]. Only one surgical study provided weight data and reported a weight loss of 36.5 kg 1 year after surgery [48].

Three RCTs provided follow-up data [25, 26, 31, 32]. In the Bandini et al. study [31], weight loss at 12 months was significantly different in the group assigned to the 6-month primary intervention followed by a 6-month weight-maintenance intervention, compared with the group assigned to the primary intervention followed by no further intervention (-7.6 and - 3.2 kg, respectively). Weight differences assessed at 18 months (follow-up) for these same two groups were also significant (-6.1 and - 2.6 kg, respectively). Curtin et al. reported weight differences at 12 months (follow-up) between a group assigned to a 6-month education-only intervention and a group

<sup>&</sup>lt;sup>a</sup>Suarez-Villadat, 2023, strength vs. aerobic exercise.

<sup>&</sup>lt;sup>b</sup>Suarez-Villadat, 2023, effectiveness of exergames.



**TABLE 3** Descriptive summary of intervention protocols.

Year	Author	Intervention modality	Intervention length	Intervention description	Counseling contact hours	Outcomes	Measurement time points
2021	Bandini et al.	Diet, physical activity, other components	6-mo active intervention, 6-mo maintenance intervention	FBBI delivered by dietitians, lifestyle coaches, and researchers. Active intervention comprised 18 group nutrition and physical activity education sessions, 18 parent-only trainings in behavioral strategies, 6 individual family counseling sessions, and weekly phone calls. Maintenance intervention comprised 12 biweekly group education and individual family counseling sessions that focused on relapse prevention and refresher training.	Total 30 h (18 90-min group sessions plus 6 30-min individual sessions)	BMI, weight	Baseline, 6 mo, 12 mo, 18 mo
2013	Curtin et al.	Diet, physical activity, other components	6 mo	Family-based intervention delivered by dietitians, physical therapists, and behavioral specialists (only for 1 arm). All participants prescribed a diet with a 250-kcal/d deficit and an exercise program that included aerobic activity 5 d/wk, strength training 2 d/wk, and flexibility exercises. Participants and parents attended 16 40-min nutrition and physical activity education sessions delivered weekly/biweekly. The nutrition and activity education group completed 16 40-min sessions that included practice and taste tests for participants and informal support/discussion for parents. The nutrition and activity education plus behavioral intervention group completed 16 40-min sessions of parent training in behavioral intervention conducted by behavioral specialist.	Total 24 h (16 90-min group sessions)	Body fat percentage, weight	Baseline, 10 wk, 6 mo, 12 mo for all outcomes; additional measures of weight and body fat at 2, 4, 6, 8, 11, 13 wk
2011	Gonzalez- Aguero et al.	Physical activity	21 wk	Researcher-led group exercise sessions twice a week, 25 min per session that comprised circuit-based training, which included plyometric jumps, body weight exercises, and resistance band or ball exercises.	N/A	BMI, body fat percentage, fat mass, lean mass, weight	Baseline, 21 wk
2021	Naczk et al.	Physical activity	33 wk	Water-based group exercise and swimming program, 3 d/wk, 70–90 min per session.	N/A	BMI, body fat percentage, fat mass, weight	Baseline, 33 wk
2015	Ptomey et al.	Diet, physical activity, other components	8 wk	2 weight-loss diets plus prescribed physical activity and education sessions, supplemented with tablet computers as a diet and physical activity-tracking tool. Prescribed diets comprised either the eSLD	Total 4 h (8 30-min sessions)	BMI, waist circumference, weight	Baseline, 1 mo, 2 mo



TABLE 3 (Continued)

TABLE 3	(Continue	d) 					
Year	Author	Intervention modality	Intervention length	Intervention description	Counseling contact hours	Outcomes	Measurement time points
				with fruit and vegetables (≥5 servings/d) and high-volume, low-energy, portion-controlled meals (2 entrees/d and 2 shakes/d) or a reduced-energy diet that entailed a caloric deficit of 500-700 kcal/d, along with nutritionally balanced, high-volume, lower-fat (20%-30% energy) diet. Prescribed physical activity comprised 60 min/d of moderate-intensity activity at least 5 d/wk. Weekly at-home education sessions were conducted with participant and parent and delivered by dietitian and health educator.			
2021, 2022, 2023	Ptomey et al.	Diet, physical activity, other components	6 mo	Intervention entailed 3 arms: 1) remote delivery of the eSLD with fruit and vegetables (≥5 servings/d) and high-volume, low-energy, portion-controlled meals (2 entrees/d and 2 shakes/d); 2) remote delivery of a reducedenergy diet that entailed a caloric deficit of 500−700 kcal/d, along with nutritionally balanced diet that included ≥5 servings/d of fruit and vegetables; and 3) faceto-face delivery of the reducedenergy diet. All arms were prescribed physical activity that comprised 60 min/d of moderate-intensity activity at least 5 d/wk and 10,000 steps per day. Biweekly education sessions were conducted with participants and parents and were delivered by a health educator.	Total 6-9 h (12 sessions of 30-45 min)	BMI, waist circumference, weight	Baseline, 6 mo
2020	Suarez- Villadat et al.	Physical activity	36 wk	Swimming exercise 3 times/wk in small groups, each session 50 min: 10-min warm-up (front crawl and breaststroke), 35 min of exercises with technical support elements (higher intensity), then 5-min cooldown. Recreational swimming control group met 2 times/wk.	N/A	BMI, weight, body fat percentage, waist circumference	Baseline, 36 wk
2023ª	Suarez- Villadat et al.	Physical activity	16 wk	Aerobic group: 3 times/wk, 1-h sessions with treadmill walking and, adapted or modified collective games and sports. Strength exercise group: 3 times/wk, 1-h sessions with individualized curriculum aimed at improving physical fitness, aligned with physical education curriculum.	N/A	BMI, weight, waist circumference, waist-hip ratio	Baseline, 16 wk



TABLE 3 (Continued)

TABLE 3	(Continue	ea)					
Year	Author	Intervention modality	Intervention length	Intervention description	Counseling contact hours	Outcomes	Measurement time points
2023 <sup>b</sup>	Suarez- Villadat et al.	Physical activity	20 wk	Wii-based exercise program, 3 times/wk, 1-h sessions consisting of warm-up, training, and cooldown. Main focus was aerobic endurance in sportsrelated games. Control group received 3 times/wk, 1-h sessions of physical activity focused on motor skills and exploration and coordination.	N/A	BMI, weight, body fat percentage, waist circumference	Baseline, 20 wk
2023	Wang et al.	Physical activity	12 wk	School-based exercise 2 times/ wk, 1-h sessions, that consisted of 10-min warm-up, 45-min main exercise (including 2 15-min aerobic games and 15-min resistance training), and a 5-min cooldown. Each level lasted 4 wk: level 1 at 40% of heart rate reserve, level 3 at 70% of heart rate reserve. Wait-list control group did not receive any program and was asked to continue physical activity and eating habits.	N/A	BMI, weight, body fat percentage, waist circumference	Baseline, 12 wk, 24 wk
2022	Yu et al.	Physical activity	9 mo	School-based exercise sessions delivered by research team (with assistance from teachers) on the school playground during non-PE class time: 2 45-min sessions/wk, target HR of 30%-40% of HRR for first 3 mo, 40%-50% of HRR for months 3-6, and 50%-60% of HRR for months 6-9.	N/A	BMI, BMI z score, body fat percentage, waist circumference, waist to height ratio, weight	Baseline, 4 mo, 9 mo
Non-RCT							
2014	Seron et al.	Physical activity	12 wk	Group exercise classes that entailed 2 intervention arms: 1) aerobic training group, which comprised treadmill or cycling (3 d/wk, 50-min sessions, 50%-70% of HRmax); 2) resistance training group, which comprised 2 d/wk, 9 exercises with 3 sets of 12 reps.	N/A	BMI, body fat percentage, waist circumference, weight	Baseline, 12 wk
2017	Wu et al.	Physical activity	12 wk	School-based group circuit exercise sessions, 5 d/wk, 50 min/session (15 trips ascending/descending stairs, single aerobic device for 15–20 min, 50 sit-ups, 3 consecutive jumps over high barrier 15 times).	N/A	BMI, body fat percentage, fat mass, fat-free mass, skeletal muscle mass, weight	Baseline, 12 wk
Pre-post s							_
2019	An et al.	Diet, physical activity	14 wk	School-based mentoring program using the I Can Do It, You Can Do It model that comprised weekly 60– to 70-min mentoring session during lunch. Mentors comprised college students who were	N/A	BMI, BMI z score, waist circumference	Baseline, 14 wk
				<u>-</u>			(C t:



TABLE 3 (Continued)

Year	Author	Intervention modality	Intervention length	Intervention description	Counseling contact hours	Outcomes	Measurement time points
				supported by classroom teachers and paraprofessionals.  Mentorship involved tracking and ensuring the choice of food and beverage and tracking and participating in physical activity.			
2014	Haney et al.	Diet, physical activity, other components	10 mo	After-school park-based program based on <i>Sports, Play and Active Recreation for Kids</i> ( <i>SPARK</i> ), an active recreation curriculum, and <i>EmpowerMe4Life</i> , a health and wellness education curriculum. Program comprised 60 min of physical activity 5 d/wk that incorporated multiple sports and activities with a focus on developing and improving motor skills, movement knowledge, and social and personal skills, as well as nutrition education lessons 1–2 times/wk for 20–30 min each session.	Total ~43 h (weekly 60-min sessions)	BMI z score, hip circumference, mid- arm circumference, waist circumference, waist-hip ratio	Baseline, 10 mo
2013	Hinckson et al.	Diet, physical activity, other components	10 wk	Modified "Mind, Exercise, Nutrition. Do It!" (MEND) program, a school-based weightmanagement program that included exercise sessions, parent nutrition education, and parent behavior change counseling delivered by physiotherapist and dietitian with support from teachers, teacher aids, management, and social workers. Exercise sessions were 2 times/wk, 2 h/session: 1 h of family-based exercise and 1 h of students only that included exercise-based games. Parents attended 10 nutrition education sessions and 8 behavior change sessions.	Total 18 h (18 60-min sessions for parents)	BMI, waist circumference, weight	Baseline, 12 wk, 24 wk
2001	Hogan et al.	Diet	6 mo	Nutritional rehabilitation program delivered in chronic-care facility tailored to 3 different nutritional goals: group 1 (goal of weight gain): increase in energy density of usual foods by serving high-energy desserts, adding cream to milk, serving additional margarine with vegetables, adding polycose powder to items, and serving high-energy nutritional supplements; group 2 (goal of maintaining present weight): maintenance of energy density by continuing usual diet and portion sizes and monthly body weight monitoring; group 3 (goal	N/A	Weight-for-age z score, weight-for- height z score	Baseline, 6 mo



TABLE 3 (Continued)

Year	Author	Intervention modality	Intervention length	Intervention description	Counseling contact hours	Outcomes	Measurement time points
				of slowing down rate of weight gain): decrease in energy density of usual foods by serving lowenergy desserts, unsweetened fruits and fruit juices, low-fat/low-calorie items, and decreasing portion sizes. Program was supplemented with care and consultation from a multidisciplinary team of dietitians, doctors, nurses, occupational therapists, physical therapists, orthodontists, psychologist, social workers, and pharmacists.			
2019	Messiah et al.	Physical activity	1-2 school years	After-school park-based program based on <i>Sports, Play and Active Recreation for Kids (SPARK)</i> , an active recreation curriculum, and <i>EmpowerMe4Life</i> , a health and wellness education curriculum. Program comprised 60 min of physical activity 5 d/wk that incorporated multiple sports and activities with a focus on developing and improving motor skills, movement knowledge, and social and personal skills, as well as nutrition education lessons 1–2 times/wk for 20–30 min each session.	N/A	BMI, body fat percentage, weight	Baseline, end of first school year, end of second school year
2006	Ordonez et al.	Physical activity	12 wk	Physician supervised water- and land-based exercise program, 3 d/wk, 30–60 min/session, intensity level prescribed.	N/A	BMI, body fat percentage	Baseline, 12 wk
2023	Pessoa et al.	Diet, physical activity, other components	6 mo	Physical exercise 2 times/wk for 90 min, ensuring 60 min of exercise time. Nutritional education provided once per month with establishing goals and dietary advising for parents. Parental support was through involvement in exercise and nutritional education sessions.	Total 6 h (6 monthly 60-min sessions)	BMI, fat mass	Baseline, 6 mo
2020	Sanner et al.	Diet, physical activity	4 d	Community-based health camp delivered by licensed psychologists/psychologists in training over the course of 4 d in 1 wk. Each day included 9 h of educational nutrition activities and physical activity for children and 2 h of health education for parents that focused on nutrition and physical activity education.	N/A	BMI, BMI percentile, BMI z score, weight	Baseline, 4 mo

TABLE 3 (Continued)

Year	Author	Intervention modality	Intervention length	Intervention description	Counseling contact hours	Outcomes	Measurement time points
Other des	signs						
2019	Goddard et al.	Surgery	1 d (surgical); 1-y follow- up	Laparoscopic sleeve gastrectomy	N/A	BMI, weight	Baseline, 12 mo
2019	Hornack et al.	Surgery	1 d (surgical); 2-y follow- up	Laparoscopic sleeve gastrectomy	N/A	BMI, excessive BMI loss, percent total weight loss	Baseline, 6 mo, 12 mo, 24 mo
2021	Jones et al.	Surgery	1 d (surgical); 1-y follow- up	Laparoscopic sleeve gastrectomy supplemented with patient/ parent education, child life specialist counseling, caregiver support from social services, psychology assessment, dietician consultation	N/A	BMI, excessive BMI loss, weight	Baseline, 3 mo, 6 mo, 12 mo

Abbreviations: eSLD, enhanced stop light diet; FBBI, family-based behavioral intervention; HR, heart rate; HRR, heart rate reserve; N/A, not available; PE, physical education; RCT, randomized-controlled trial.

assigned to a 6-month education plus parent behavioral training/support (1.7 vs. -1.9 kg) [32]. Ptomey et al. [25, 26] reported that participants randomized to the enhanced stop light diet (eSLD) group continued to lose weight at 12 months (mean [SD] loss from baseline, -5.3 [6.3] kg), whereas those who were randomized to a conventional diet regained some weight loss. However, by 18 months, those in the eSLD group had regained some weight (mean [SD] loss from baseline, -2.2 [7.4] kg).

## BMI

BMI as an outcome measure was available for 19 studies, including 10 RCTs (Table 5). BMI was not reported in three studies [32, 44, 46], and an additional four studies only reported BMIz (standardized by age) [38, 42, 47] or BMI percentiles [45]. Average BMI values at the start of the studies ranged between 22.4 (healthy weight) and 34.2 kg/m<sup>2</sup> (obesity), with an exception for the surgical studies, for which the BMI values for the groups with IDs ranged from 47.8 to 51.5 kg/m<sup>2</sup> (severe obesity) [48-50]. Change values were provided for seven RCTs (BMI change for intervention groups ranged from -0.4 to  $-2.2 \text{ kg/m}^2$ ), but only five RCTs reported within-group analyses, of which three demonstrated significant decreases in BMI [29, 31, 38], whereas no significant difference was reported by Ptomey, who compared two different weight-loss interventions [35], and Suarez-Villadat, who evaluated exergames [28]. The between-group comparisons were reported for six RCTs, of which five demonstrated a significant BMI decrease from the intervention compared with the nonintervention control group (change scores for the control groups ranged from 0.04-0.68 kg/m<sup>2</sup>) [31, 34, 36-38].

The two non-RCTs showed a significant decrease in BMI for the aerobic, but not the resistance, exercise group [39] and a significant

decrease for the exercise group with obesity (mean [SD], -0.9 [0.6] kg/m²) [40]. For the pre-post studies, change scores were provided for two studies and indicated a significant decrease in BMI in one study (-0.3 kg/m², 95% confidence interval [CI]: -1.8 to 0.7) [41] and no significant decrease in BMI for the second study [43]. The surgical studies reported decreases in BMI, i.e., between 14.2 and 14.4 kg/m² 1 year after surgery [48–50], and, after 24 months, the decrease in BMI from baseline was still 13.8 kg/m² [49]; however, only Goddard et al. included statistical analyses for the within-group differences, which were significant (p < 0.001) [48].

# **RESULTS OF SYNTHESES**

Table 6 provides a visual summary of the data on significant weight loss or BMI decrease either between groups or within groups. Significant weight loss or decrease in BMI was shown for interventions focusing on physical activity only; for multicomponent interventions combining physical activity, diet, and other components (behavioral strategies, social support, etc.); and for laparoscopic sleeve gastrectomy.

Eight out of the eleven (73%) studies that focused on physical activity demonstrated statistically significant weight loss and/or decrease in BMI. Of the remaining three studies, two did not provide clear statistical outcomes on weight loss/decrease in BMI, and one did not find significant effects.

With respect to the multicomponent interventions combining physical activity, diet, and other components, four out of the seven (57%) studies demonstrated statistically significant weight loss and/or significant BMI decrease. The remaining three studies did not provide the statistical outcomes necessary to evaluate the significance of the outcomes.

Very few interventions that focused on diet only or on diet plus physical activity were included in this review, and the three that were

<sup>&</sup>lt;sup>a</sup>Suarez-Villadat, 2023, strength vs. aerobic exercise.

<sup>&</sup>lt;sup>b</sup>Suarez-Villadat, 2023, effectiveness of exergames.



**TABLE 4** Study results for weight.

TABLE 4	Study results for weight.		Weight at		Change values
Study	Intervention duration	Groups	baseline, mean ± (SD)	Change values at postintervention	at follow-up (duration)
RCT					
Bandini, 2021	6-mo weight-loss intervention, 6-mo maintenance intervention, 6-mo no-contact follow-up	<ol> <li>Weight-loss intervention:</li> <li>FBBI: delivered by dietitians, lifestyle coaches, and researchers</li> <li>Wait list + FBBI: no intervention for 6 mo followed by the FBBI intervention</li> <li>Follow-up weight maintenance:</li> <li>FBBI-M: 12 biweekly sessions of a comprehensive maintenance program</li> <li>FBBI-C: No contact for the 6-mo follow-up period after completing the FBBI intervention</li> </ol>	1: FBBI directly (n = 14), 81.0 ± 4.1 kg 2. Wait-list group (n = 13), 80.1 ± 4.2 kg	1: $-3.5 \pm 5.7$ kg ( $n = 14$ ), 2: $1.2 \pm 5.9$ kg ( $n = 13$ ) 1: Within-group, p = 0.021 2: Within-group, p = 0.45 Between-group, p = 0.034	3: $-7.6 \pm 1.2 \text{ kg}$ (12 mo) 4: $-3.2 \pm 1.2 \text{ kg}$ (12 mo) 3: $-6.1 \pm 1.2 \text{ kg}$ (18 mo) 4: $-2.6 \pm 1.2 \text{ kg}$ (18 mo) 12 mo: Between-group, p = 0.008 18 mo: Between-group, p = 0.039
Curtin, 2013	6 mo; 6-mo no- contact follow-up	<ol> <li>NAE: comprehensive program for children and parents</li> <li>NAE + BI: NAE intervention plus a parent behavioral intervention</li> </ol>	1: 77.3 ± 16.5 kg 2: 79.2 ± 14.9 kg	1: $0.5 \pm 0.8$ kg 2: $-2.7 \pm 0.8$ kg Within-group, not provided Between-group, p = 0.005	1: $1.7 \pm 0.8$ kg (12 mo) 2: $-1.9 \pm 0.8$ kg (12 mo) Within-group, not provided Between-group, $p = 0.002$
Gonzalez- Aguero, 2011	21 wk	<ol> <li>Exercise: 2 group exercise sessions/wk</li> <li>Control: no intervention</li> </ol>	1: 40.1 ± 9.6 kg 2: 48.7 ± 10.7 kg	1: -0.8 kg (calculated) 2: -0.8 kg (calculated)	No follow-up
Naczk, 2021	33 wk	1: Intervention 2: Control	1: 56.8 ± 7.8 kg 2: 57.3 ± 8.4 kg	No absolute change values provided. 1: $-3.03\%$ (SD: $1.60\%$ , 95% CI: $-3.98\%$ to $-2.08\%$ ) 2: $4.39\%$ (SD: $2.79\%$ , 95% CI: $2.74\%$ to $6.04\%$ ) Within-group, not provided Between-group, $p \le 0.05$	No follow-up
Ptomey, 2015	8 wk	<ol> <li>eSLD: eSLD with portion- controlled meals</li> <li>CD: CD using Dietary Guidelines for Americans</li> </ol>	1: 82.3 ± 29.8 kg 2: 65.1 ± 25.3 kg	1: $-3.9 \pm 2.7$ kg 2: $-2.2 \pm 1.4$ kg 1: Within-group, p = 0.001 2: Within-group, p = 0.001 Between-group, p = 0.094	No follow-up
Ptomey, 2021, 2022, 2023	6 mo	<ol> <li>FTF/CD</li> <li>RD/CD</li> <li>RD/eSLD</li> </ol>	1: 88.4 ± 29.5 kg 2: 74.9 ± 16.5 kg 3: 83.6 ± 26.4 kg	1: $-0.3 \pm 5.0$ kg 2: $-1.8 \pm 4.0$ kg 3: $-5.0 \pm 5.9$ kg Within-group, not provided Between-group, 1 vs. 2: $p = 0.16$ , 2 vs. 3: $p = 0.02$	12 mo 1: $+1.3 \pm 8.2$ kg 2: $-0.7 \pm 4.6$ kg 3: $-5.3 \pm 6.3$ kg Between-group, 1 vs. 2: p = 0.21, 2 vs. 3: p = 0.002



TABLE 4 (Continued)

Study	Intervention duration	Groups	Weight at baseline, mean ± (SD)	Change values at postintervention	Change values at follow-up (duration)
					18 mo 1: $+1.4 \pm 8.2 \text{ kg}$ 2: $-0.2 \pm 6.6 \text{ kg}$ 3: $-2.2 \pm 7.4 \text{ kg}$ Between-group, 1 vs. 2: p = 0.47, 2 vs. 3: $p = 0.28$
Suarez- Villadat, 2020	36 wk	<ol> <li>Intervention: swimming exercise</li> <li>Control: recreational swimming</li> </ol>	1: 50.86 ± 8.51 kg 2: 49.51 ± 12.78 kg	1: -1.46 kg (calculated) 2: +1.79 kg (calculated) Within-group, not provided Between-group, p = 0.613	·
Suarez- Villadat, 2023 <sup>a</sup>	16 wk	Aerobic     Strength	1: 58.77 ± 10.37 kg 2: 55.44 ± 6.36 kg	1: +1.51 kg (calculated) 2: +0.25 kg (calculated) Within-group, not provided Between-group, not provided	
Suarez- Villadat, 2023 <sup>b</sup>	20 wk	Intervention     Control	1: 51.76 ± 8.05 kg 2: 59.09 ± 7.34 kg	1: -2.47 kg (calculated) 2: +2.06 kg (calculated) Within-group, not provided Between-group, not provided	
Wang, 2023	12 wk	Intervention     Control	1: 67.45 ± 11.12 kg 2: 66.38 ± 14.03 kg	1: $-1.10$ (95% CI: $-1.77$ to 0.43) kg 2: 0.06 (95% CI: $-0.22$ to 0.34) kg Within-group, 1: $p = 0.003$ 2: $p = 0.652$ Between-group, not provided	1: $-1.00$ (95% CI: $-1.74$ to 0.26) kg (12 wk) 2: 0.13 (95% CI: $-0.31$ to 0.56) kg (12 wk) Within-group, 1: $p = 0.003$ 2: $p = 0.542$ Between-group, not provided
Yu, 2022	9 mo	Intervention     Control	1: 75.5 ± 15.2 kg 2: 71.2 ± 13.4 kg	1: -0.2 (95% CI: -1.1 to 0.8 kg) 2: 2.8 (95% CI: 1.5 to 4.1 kg) 1: Within-group, p = 0.737 2: Within-group, p < 0.001 Between-group, p < 0.001	
Non-RCT Seron, 2014	12 wk	<ol> <li>Control</li> <li>Aerobic</li> </ol>	1: 54.7 ± 11.8 kg	1: +0.5 kg (calculated)	



TABLE 4 (Continued)

Study	Intervention duration	Groups	Weight at baseline, mean ± (SD)	Change values at postintervention	Change values at follow-up (duration)
		3. Resistance	2: 61.5 ± 10.8 kg 3: 52.7 ± 10.0 kg	2: -0.7 kg (calculated) 3: 0.1 kg (calculated) 1: Within-group, p = 0.19 2: Within-group, p = 0.06 3: Within-group, p = 0.75	
Wu, 2017	12 wk	<ol> <li>Normal weight (no intervention)</li> <li>Obesity exercise</li> <li>Obesity control</li> </ol>	1: 52.7 ± 6.4 kg 2: 75.0 ± 11.3 kg 3: 73.1 ± 12.7 kg	1: N/A 2: -2.2 ± 1.5 kg 3: -0.2 ± 3.3 kg 2: Within-group, p < 0.01 3: Within-group, p = 0.80 Between-group, p = 0.06	
Pre-post stud	y				
Hogan, 2001	6 mo	More weight gain     Maintain rate of weight gain     Slow weight gain	1: 28.7 ± 9.9 kg 2: 34.9 ± 13.7 kg 3: 38.3 ± 10.3 kg	1: 1.2 kg 2: 1.1 kg 3: 1.3 kg 1: Within-group, p = <0.01 2: Within-group, p > 0.5 3: Within-group, p > 0.5	
Ordonez, 2006	12 wk	1. Intervention	1. 78.7 ± 4.8 kg	1: -3.6 kg (calculated) 1: Within-group, p < 0.05	
Other designs	S				
Goddard, 2019	1 d (surgical); 1-y follow-up	1. DD 2. Non-DD	1: 129.2 ± 33.4 kg 2: 137.9 ± 18.0 kg	N/A	1: -36.5 kg (1 y) 2: -34.9 kg (1 y) 1: Within-group, p < 0.001 2: Within-group, p < 0.001

Abbreviations: BI, behavioral intervention; CD, conventional diet; DD, developmental disabilities; eSLD, enhanced stop light diet; FBBI, family-based behavioral intervention; FTF, delivered face-to-face; N/A, not available; NAE, nutrition and activity education; RCT, randomized-controlled trial; RD, remotely delivered.

included did not report any significant weight-loss results or did not provide sufficient information to evaluate the outcomes.

Of the three studies that reported results of laparoscopic sleeve gastrectomy, only one reported the statistical outcomes, which showed a statistically significant decrease in BMI.

# **DISCUSSION**

This systematic review of weight-loss interventions for adolescents with DS was conducted to better understand the most effective

intervention strategies and to identify the current gaps in the literature, specifically for this important transitional age. The large number of recent studies from around the world confirmed the global urgency of this topic (18 conducted in the last 10 years). The need for more robust research designs has been identified in previous systematic reviews [51, 52], and the current review showed an increase of methodologically stronger studies on this topic. Of the 24 unique studies that were included in this review, 11 used RCT design methodology. Intervention components varied widely (physical activity and/or diet, multicomponent, surgical). Most studies demonstrated significant weight loss following a primary intervention, and the majority of

<sup>&</sup>lt;sup>a</sup>Suarez-Villadat, 2023, strength vs. aerobic exercise.

<sup>&</sup>lt;sup>b</sup>Suarez-Villadat, 2023, effectiveness of exergames.



**TABLE 5** Study results for BMI.

Study	Intervention duration	Groups	BMI at baseline, mean ± SD	Change values at postintervention	Change values at follow-up (duration)
RCT					
Bandini, 2021	6-mo weight- loss intervention, 6-mo maintenance intervention, 6-mo no- contact follow- up	<ol> <li>Weight-loss intervention:</li> <li>FBBI: FBBI by dietitians, lifestyle coaches, and researchers</li> <li>Waitlist + FBBI: no intervention for 6 mo followed by the FBBI intervention</li> <li>Follow-up weight maintenance:</li> <li>FBBI-M: 12 biweekly sessions of a comprehensive maintenance program</li> <li>FBBI-C: no contact for the 6-mo follow-up period after completing the FBBI intervention</li> </ol>	1: FBBI directly (n = 14), 33.6 ± 1.9 2: Wait list (n = 13), 32.9 ± 2.0	1: $-1.8 \pm 2.7$ 2: $0.6 \pm 2.8$ Within-group, 1: $p = 0.01$ 2: $p = 0.41$ Between-group, $p = 0.02$	3: $-3.3 \pm 0.5$ (12 mo) 4: $-1.5 \pm 0.6$ (12 mo) Between-group, $p = 0.020$ 3: $-2.8 \pm 0.5$ (18 mo) 4: $-1.3 \pm 0.5$ (18 mo) Between-group, $p = 0.043$
Gonzalez- Aguero, 2011	21 wk	<ol> <li>Exercise: 2 group exercise sessions per week</li> <li>Control: No intervention</li> </ol>	1: 24.3 ± 6.0 2: 22.4 ± 3.4	1: +0.6 (calculated) 2: -0.1 (calculated)	No follow-up
Naczk, 2021	33 wk	I. Intervention     Control	1: 25.1 ± 2.37 2: 25.4 ± 2.46	No absolute change values provided 1: $-4.63\%$ (SD: 1.80%, 95% CI: $-5.69\%$ to $-3.57\%$ ) 2: 2.38% (SD: 2.23%, 95% CI: 1.06% to 3.70%) Within-group, not provided Between-group, $p \le 0.05$	No follow-up
Ptomey, 2015	8 wk	<ol> <li>eSLD: eSLD with portion-controlled meals</li> <li>CD: CD using Dietary Guidelines for Americans</li> </ol>	1: 30.7 ± 7.3 2: 26.9 ± 5.3	1: $-1.6 \pm 0.9$ 2: $-1.0 \pm 0.4$ Within-group, not provided Between-group, $p = 0.078$	No follow-up
Ptomey, 2021	6 mo	<ol> <li>FTF/CD</li> <li>RD/CD</li> <li>RD/eSLD</li> </ol>	1: 34.1 ± 8.3 2: 31.3 ± 5.8 3: 32.7 ± 7.1	1: $-0.4 \pm 1.6$ 2: $-0.9 \pm 1.6$ 3: $-2.2 \pm 2.5$ Within-group, not provided Between-group, 1 vs. 2: $p = 0.24$ 2 vs. 3: $p = 0.02$	No follow-up
Suarez- Villadat, 2020	36 wk	<ol> <li>Intervention: swimming exercise</li> <li>Control: recreational swimming</li> </ol>	1. 34.18 ± 4.26 2. 24.77 ± 4.35	1: -1.17 (calculated) 2: +0.66 (calculated) Between-group, p < 0.001	No follow-up
Suarez- Villadat, 2023 <sup>a</sup>	16 wk	1: Aerobic 2: Strength	1: 25.26 ± 3.83 2: 24.11 ± 3.47	1: 0.51 ± 1.08 2: 0.10 ± 5.68 Within-group, not provided Between-group, not provided	No follow-up
Suarez- Villadat, 2023 <sup>b</sup>	20 wk	1. Intervention 2. Control	1: 28.34 ± 2.91 2: 27.59 ± 3.53	1: -1.51 ± 2.46 2: 0.27 ± 1.52 Within-group, 1: p = 0.651 2: p = 0.659	No follow-up



# TABLE 5 (Continued)

Study	Intervention duration	Groups	BMI at baseline, mean ± SD	Change values at postintervention	Change values at follow-up (duration)
				Between-group, not provided	
Wang, 2023	12 wk	Intervention     Control	1: 26.37 ± 2.74 2: 26.24 ± 2.95	1: -0.44 (95% CI: -0.68 to -0.20) 2: 0.04 (95% CI: -0.08 to 0.16) Within-group, 1: <i>p</i> = 0.002 2: <i>p</i> = 0.472 Between-group, not provided	1: $-0.43$ (95% CI: $-0.66$ to $-0.20$ ) (12 wk) 2: $0.04$ (95% CI: $-0.13$ to $0.21$ ) (12 wk) Within-group, 1: $p = 0.001$ 2: $p = 0.619$ Between-group, not provided
Yu, 2022	9 mo	1. Intervention 2. Control	BMI 1: 28.16 ± 3.69 2: 27.37 ± 3.99 BMIz 1: 2.13 ± 0.63 2: 1.89 ± 0.79	BMI  1: $-0.66$ (95% CI: $-1.06$ to $-0.25$ )  2: $0.68$ (95% CI: $0.16$ to $1.20$ )  BMIz  1: $-0.23$ (95% CI: $-0.32$ to $-0.14$ )  2: $0.10$ (95% CI: $-0.03$ to $0.22$ )  1: Within-group, $p = 0.002$ (BMI) and $p < 0.001$ (BMIz)  2: Within-group, $p = 0.13$ (BMI) and $p = 0.119$ (BMIz)  Between-group, $p < 0.001$ (BMIz)	
Non-RCT					
Seron, 2014	12 wk	<ol> <li>Control</li> <li>Aerobic</li> <li>Resistance</li> </ol>	1: 27.6 ± 3.8 2: 27.0 ± 4.4 3: 23.3 ± 4.3	1: 0 (calculated) 2: -0.5 (calculated) 3: -0.2 (calculated) 1: Within-group, <i>p</i> = 0.88 2: Within-group, <i>p</i> = 0.01 3: Within-group, <i>p</i> = 0.28	
Wu, 2017	12 wk	Normal weight (no intervention)     Obesity exercise     Obesity control	1: 22.0 ± 1.2 2: 30.9 ± 3.7 3: 28.6 ± 5.6	1: N/A 2: $-0.9 \pm 0.6$ 3: $-0.1 \pm 1.3$ 2: Within-group, $p < 0.01$ 3: Within-group, $p = 0.76$ Between-group, $p = 0.04$	
Pre-post stud	у				
An, 2019		1. Intervention	BMI, 1: 21.6 ± 4.5 BMIz, 1: 0.42 ± 1.19	BMI, 1: -0.3 (95% CI: -1.8 to 0.7) BMIz, 1: -0.07 (95% CI: -0.50 to 0.17) p = 0.27	
Haney, 2014	10 mo	Normal weight     Overweight and obesity	BMIz 1: -0.6 ± 0.2 2: 2.0 ± 0.2	BMIz 1: $0.2$ (95% CI: $-0.1$ to 0.6) 2: $-0.2$ (95% CI: $-0.5$ to 0.1) 1: Within-group, $p = 0.16$ 2: Within-group, $p = 0.27$	

TABLE 5 (Continued)

Study	Intervention duration	Groups	BMI at baseline, mean ± SD	Change values at postintervention	Change values at follow-up (duration)
Hinckson, 2013	10 wk	1. Intervention	1: 31 ± 8	1: 0.7 (±90% CI: ±0.4)	1: 0.3 (±90% CI: ±0.4) (34 wk)
Messiah, 2019	After 1 or 2 school years	1. Disabilities	1: BMI percentile 70.89 ± 32.06	1: BMI percentile Post-1 y: 70.7 ± 30.4 Post-2 y: 71.9 ± 32.8	
Pessoa, 2023	6 mo	1. Intervention	1: 28.43 ± 6.69	1: +0.1 (calculated)	
Sanner, 2021	4 d, follow-up at 4 mo	1. Intervention	BMIz 1: 2.1 ± 0.7	N/A	4-mo follow-up BMlz 1: -0.1 (calculated)
Other designs					
Goddard, 2019	1 d (surgical); 1-y follow-up	1. DD 2. Non-DD	1: 49.7 ± 7.3 2: 48.4 ± 5.4	N/A	1: -14.2 (1 y) 2: -12.4 (1 y) No SD available 1: Within-group, p < 0.001 2: Within-group, p < 0.001 Between-group, not provided
Hornack, 2019	1 d (surgical); 2-y follow-up	Cognitive impairment/DD     Non-cognitive impairment/DD	1: 51.5 ± 10.5 2: 51.1 ± 7.9	N/A	1: $-14.4 \pm 4.0$ (12 mo) 2: $-12.9 \pm 4.3$ (12 mo) 1: $-13.8 \pm 6.3$ (24 mo) 2: $-13.9 \pm 5.5$ (24 mo) Within-group, not provided Between-group, not provided
Jones, 2021	1 d (surgical); 1-y follow-up	1. ID	1: 47.8 ± 8.7	N/A	1: -14.2 ± 4.9

Abbreviations: BMIz, BMIz score; CD, conventional diet; DD, developmental disabilities; eSLD, enhanced stop light diet; FBBI, family-based behavioral intervention; FTF, delivered face-to-face; ID, intellectual disability; N/A, not available; RCT, randomized-controlled trial; RD, remotely delivered.

interventions were either multicomponent or physical activity only. Seven studies included a multicomponent intervention, of which four demonstrated significant results [25, 26, 31, 32, 35, 36], with a weight loss between -2.7 and -5.0 kg and a decrease in BMI between -1.6 and 2.2 kg/m². Eleven trials were physical activity only, and eight out of these studies [29, 33, 34, 37–40, 46] demonstrated significant results with slightly more modest results in weight loss ranging from -0.7 to -3.6 kg and BMI decreases ranging from -0.44 to -0.9 kg/m². The few studies that tested diet only or diet and physical activity interventions did not provide sufficient data to determine effectiveness. Ten studies included only individuals with DS [27, 28, 30–34, 37, 39, 46], but, in most of the remaining studies, individuals with DS comprised mostly a small portion of the total sample, making it difficult to draw specific conclusions for individuals with DS.

The focus on adolescents allows us to present outcomes specifically for this important transitional age (i.e., 13–22 years); however, it

also limits our ability to directly compare our outcomes to guidelines for weight management for the general population, as existing guidelines were developed specially for either children or adults. Additionally, there is some controversy regarding the best measure of adiposity change in adolescents (i.e., change in BMI, change in percent of the 95th percentile, change in percent of the 50th percentile, or change in BMIz) [53-56], and that change in BMI may not be an appropriate metric in growing children. However, only four studies in our systematic review reported change in BMIz, and no studies reported change in percent of the 95th percentile or change in percent of the 50th percentile, which limits our findings and prevents us from being able to determine the clinical relevance of the interventions. The two guidelines for adults (i.e., the 2013 Guidelines of the American College of Cardiology [ACC], the American Heart Association [AHA], and the Obesity Society [TOS] and the 2016 Guidelines of the American Association of Clinical Endocrinologists [AACE] and



**TABLE 6** Visual summary of syntheses.

	Design	Intervention duration	Statistically significant weight loss		Statistically significant BMI decrease	
			Between-group	Within-group	Between-group	Within-group
Physical activity only	•					
Gonzàlez-Agüero [33]	RCT	21 wk	N/A	Yes	N/A	N/A
Naczk [34]	RCT	33 wk	Yes	N/A	Yes	N/A
Suarez-Villadat [37]	RCT	36 wk	No	N/A	Yes	N/A
Suarez-Villadat [27]	RCT	16 wk	N/A	N/A	N/A	N/A
Suarez-Villadat [28]	RCT	20 wk	N/A	N/A	N/A	No
Wang [29]	RCT	12 wk	N/A	Yes	N/A	Yes
Yu [38]	RCT	9 mo	Yes	N/A	Yes	Yes
Seron [39]	Non-RCT	12 wk	N/A	Yes (aerobic only)	N/A	Yes (aerobic only)
Wu [40]	Non-RCT	12 wk	No	Yes	Yes	Yes
Ordonez [46]	Pre-post	12 wk	N/A	Yes	N/A	N/A
Messiah [45]	Pre-post	1-2 y	N/A	N/A	N/A (only BMI percentile)	N/A (only BMI percentile)
Diet only						
Hogan [44]	Pre-post	6 mo	N/A	Yes (weight gain)	N/A	N/A
Physical activity and	diet					
An [41]	Pre-post	14 wk	N/A	N/A	N/A	N/A
Sanner [47]	Pre-post	4 d	N/A	N/A	N/A	N/A
Physical activity, diet	plus other comp	oonents				
Bandini [31]	RCT	6 mo	Yes	Yes	Yes	Yes
Curtin [32]	RCT	6 mo	Yes	N/A	N/A	N/A
Ptomey [35]	RCT	8 wk	No (both intervention)	Yes in both diet groups	No (both intervention)	N/A
Ptomey [25, 26, 36]	RCT	6 mo	Yes (CD vs. eSLD)	N/A	Yes (CD vs. eSLD)	N/A
Haney [42]	Pre-post	10 mo	N/A	N/A	N/A	No
Hinckson [43]	Pre-post	10 wk	N/A	N/A	N/A	N/A
Pessoa [30]	Pre-post	6 mo	N/A	N/A	N/A	N/A
Surgeries						
Goddard [48]	Follow-up only	1-y follow- up	N/A	Yes	N/A	Yes
Hornack [49]	Follow-up only	2-y follow- up	N/A	N/A	N/A	N/A
Jones [50]	Follow-up only	1-y follow- up	N/A	N/A	N/A	N/A

*Note*: The gray-shaded cells indicate that this information (either on the outcome measure or the statistical test result) was not available from the original paper. Abbreviations: CD, conventional diet; eSLD, enhanced stop light diet; N/A, not available; RCT, randomized-controlled trial.

American College of Endocrinology [ACE]) [57, 58] provide a definition for clinically relevant weight loss (i.e., 5%–10% of initial body weight, which is  $\sim\!\!5$ –10 kg, in 6 months). In youth and adolescents, the American Academy of Pediatrics (AAP) 2023 guidelines do not provide a definition for clinically relevant weight loss, and neither does the US Preventive Services Task Force in its 2024 updated

guidelines for interventions for high BMI in children and adolescents [59]. When using the 5% to 10% weight-loss definition, only four studies in this systematic review were able to achieve clinically relevant weight loss, i.e., the three studies on laparoscopic sleeve gastrectomy and one multicomponent intervention (i.e., eSLD delivered remotely) [36]. Only four studies provided a change in BMIz, of which

two showed decreases in BMIz of 0.2 [42] and 0.23 [38]. None of the other intervention studies included in this review was able to show clinically relevant weight loss, even though 12 studies showed statistically significant weight loss. However, the intervention duration of four of those studies was only 8 to 12 weeks, with the possibility of further weight loss if the duration had been longer [35, 40, 46, 60].

A contributing factor to this limited success may, in part, be due to limitations in the design of the interventions, as most studies were not conducted in accordance with current adult or pediatric weightmanagement guidelines. For example, the current adult guidelines [57] recommend a comprehensive lifestyle program that assists participants in adhering to a lower-calorie diet and in increasing physical activity through the use of behavioral strategies, as is delivered in person for at least 6 months (>14 sessions) [61]. For children and adolescents, the AAP 2023 guidelines recommend intensive health behavior and lifestyle treatment. with an even higher number of contact hours, as they state that "Although weight management interventions above a threshold of 26 counseling contact hours are generally effective in reducing excess weight, higherdose interventions with contact time ≥52 h demonstrate a stronger and more consistent BMI reduction effect" [62]. Although three out of the four multicomponent interventions that found statistically significant results met the 14 sessions in 6 months recommendation for adults, only one of them met the existing guidelines for the >26 contact hours for youth [31]. Adult weight-management guidelines recommend increasing physical activity to at least 150 min of moderate-intensity physical activity per week and adhering to a diet with a calorie deficit of 500 kcal to achieve that weight loss over 6 months, whereas the AAP guidelines for children and adolescents require at least 60 min per day, with no guidance for a calorie deficit [62]. However, only two of the multicomponent interventions included in this review adhered to both the youth and adult physical activity and calorie-restriction guidelines [35, 36].

A systematic review of weight-loss interventions for youth/ adolescents (aged 2–19 years) in the general population showed that interventions with an estimated 26 contact hours or more consistently demonstrated reductions in excess weight, with more hours appearing to result in more weight loss [21]. In this review, less than clinically significant levels of weight loss were still reviewed as successes, and other cardiometabolic outcomes in addition to weight/ BMI were reviewed as important [21].

Our findings highlight that, although the quantity and methodological quality of the weight-loss intervention studies for adolescents with IDs and DS have increased in the past decade, the intervention programs are not yet adhering to the guidelines to effectively support clinically significant weight loss of 5% to 10% of initial body weight. Thus, the relatively minor decreases in weight or BMI in the included studies must be considered in light of potentially inadequate targeted health behavior interventions. Subclinical levels of weight loss may, however, be related to other positive outcomes such as the experience of gaining knowledge and pursuing potentially lifelong habits associated with dietary choice and physical activity that might prove useful across the life-span.

All guidelines recommend including a weight-maintenance program to be employed after weight loss, but few studies in our

systematic review included follow-up. Only two multicomponent trials included weight-maintenance education and support following 6-month weight-loss interventions [26, 31]. Bandini et al. [31] found that mean weight loss following completion of both the weight maintenance (intervention = -7.6 kg, control = -3.2 kg; p = 0.008) and 6-month no-contact follow-up (intervention = -6.1 kg, the control = -2.6 kg; p = 0.039) was significantly greater in the maintenance arm versus the control arm. The 18-month trial by Ptomey et al. [26] observed that participants randomized to the eSLD group continued to lose weight at 12 months (mean [SD] loss from baseline. -5.3 [6.3] kg), whereas those who were randomized to a conventional diet regained some weight loss. However, by 18 months, those in the eSLD group had regained some weight (mean [SD] loss from baseline, -2.2 [7.4] kg), suggesting that the eSLD may not be effective for long-term weight loss. Additional long-term weight-loss studies and studies focused on weight-loss maintenance in adolescents with DS following current weight-management guidelines are warranted.

This is the first systematic review, to our knowledge, that also included studies on laparoscopic sleeve gastrectomy in individuals with DS. The 2023 AAP guidelines for children and adolescents states that "Pediatricians and other [primary health care providers] should offer referral for adolescents 13 years and older with severe obesity (Class 2 obesity, BMI ≥35 kg/m<sup>2</sup> or BMI≥120% of the 95th percentile for age and sex whichever is lower with comorbid conditions, or Class 3 obesity, BMI ≥40 kg/m<sup>2</sup> or 140% of the 95th percentile for age and sex, whichever is lower) for evaluation for metabolic and bariatric surgery to local or regional comprehensive multidisciplinary pediatric metabolic and bariatric surgery centers" [62]. The current adult guidelines recommend considering bariatric surgery for patients with a BMI of at least 40 kg/m<sup>2</sup> and for those with at least one severe weightrelated condition and a BMI of at least 35 kg/m<sup>2</sup> when therapeutic goals cannot be attained using structured lifestyle change and pharmacotherapy alone [58]. However, the American Society for Metabolic and Bariatric Surgery, together with the International Federation for the Surgery of Obesity and Metabolic Disorders, recommended in 2022 that providers consider bariatric procedures for a larger patient population, including all patients with a BMI of 30 kg/m<sup>2</sup> who do not attain and sustain desired weight loss or improvement in weightrelated conditions [63]. Although samples were small, and statistical analyses were not consistently provided, the three surgical studies [48-50] were promising, demonstrating dramatic weight loss after 1 year in individuals with IDDs (including some individuals with DS) of 36.5 kg [48] or a BMI decrease between 14.2 kg/m<sup>2</sup> and 14.4 kg/m<sup>2</sup> [48–50]. Although healthy diet and regular physical activity are always recommended before and after other interventions, including pharmacologic agents and surgical interventions, the included studies show that bariatric surgery is accessible and effective in adolescents with IDs or DS, with one study explicitly showing that having IDs or DS does not alter or impact the effectiveness of the surgery [49]. As this is an area with rapid developments and great societal interest, it is of the utmost importance that individuals with DS are included in future research on bariatric surgery and that this procedure is considered in clinical practice.

Of note, the 2013 and 2016 adult guidelines include pharmacotherapy as the second treatment option for individuals with a BMI of 27 kg/m<sup>2</sup> or more when lifestyle interventions fail to result in weight loss or stop weight gain [57]. The 2023 AAP guidelines for children and adolescents states that "Pediatricians and other [primary health care providers] should offer adolescents 12 years and older with obesity (BMI ≥95th percentile) weight loss pharmacotherapy, according to medication indications, risks, and benefits, as an adjunct to health behavior and lifestyle treatment" [62]. The field of antiobesity medications (AOMs) is rapidly evolving and followed by families in the DS community with great interest, as a combination of lifestyle modifications with AOMs can produce greater and more sustained weight loss. Since these guidelines, several new medications have been approved or taken off the market. However, our systematic review did not identify any studies that have examined the effectiveness of AOMs in individuals with DS. Research evaluating the effectiveness of AOMs is needed in individuals with DS.

It is important to consider that weight and BMI are not the only important outcome measures for weight-loss studies. Benefits of losing weight and of improving nutrition and physical activity habits span a wide range of outcome measures such as cardiometabolic health, fitness, ability to participate in daily activities, mental health, and improved sleep patterns and quality of life. The studies included in this review varied regarding whether and which other outcome measures were reported, and future research would benefit from including these outcome measures to further advance our knowledge on the broader benefits of these interventions.

This review identified a wide range of behavioral strategies used to facilitate or motivate participants to adhere to the dietary and physical activity guidelines. Results suggest that interventions with preplanned exercise may promote increased participation as it contributes to ease of scheduling and a consistent routine for adolescents with DS. Among identified studies, intervention/weight-loss programs leveraged additional supports from the family setting [31, 32, 35, 36], school setting [29, 38, 40, 41, 43], and community setting [42, 45, 47], as well as incorporating peer-based support [42]. Results suggest that inclusion of additional parent support may promote lifestyle adherence and motivation, but further studies are needed to evaluate the feasibility, types, and delivery of other outside support to promote weight loss in adolescents with DS.

Although this systematic review followed a rigorous methodology, and the results are based on a large number of included studies, the evidence included in this review is limited by the broad range of differences in study design, intervention components, intervention duration, reporting of outcomes, and sample characteristics, making it challenging to determine the most effective strategies for weight loss and preventing any meta-analyses. Change scores are most informative for a comparison of intervention effects across studies but were not provided/available for many studies, even after contacting the authors. Additionally, most weight-management interventions were developed for adolescents with all IDs and included those with DS. However, individuals with DS have some specific genetic/physiological challenges regarding body proportions and weight loss, the effectiveness of interventions may be different in individuals with

IDDs compared with individuals with DS, and the current literature is too scarce on this topic to inform clinical practice. Future research should include DS-specific interventions or report weight loss by type of ID. Next, as part of the review process, we included only studies that reported that weight loss was the primary aim of their study. This necessarily excluded many intervention studies that aimed to improve health or fitness more generally and that included weight or BMI as outcomes. Those studies made decisions on intervention intensity, components, and duration based on different intervention goals and cannot be compared with interventions aiming at weight loss regarding effectiveness. Additionally, the use of BMI in individuals with DS is controversial due to their different body proportions, but, for lack of a better alternative, BMI is still widely used. The last limitation is the lack of follow-up data; although most interventions seem to be effective in achieving weight loss immediately post intervention, very few studies reported follow-up data, and the few that did show some amount of weight regain, suggesting that additional trials examining strategies for weight-loss maintenance are warranted.

Implications of these results for clinical practice are that weight-loss interventions based on physical activity only or on multicomponent interventions can be effective in achieving weight loss, although a lack of adherence to the guidelines regarding intervention intensity and duration may have prevented many interventions from supporting clinically significant weight loss of 5% to 10% of initial body weight. Future research is recommended to design adequately powered trials and, although challenging, to follow guidelines for the prescription of, and adherence to, physical activity and caloric deficits, combined with behavioral strategies, to produce clinically significant results. Furthermore, information is limited regarding long-term effects or follow-ups. Surgical interventions, although performed in small samples and in individuals with much higher BMI values than in the other included studies, seem effective in adolescents with IDDs of various etiology, including DS.

Future research is strongly encouraged to include control groups and change scores to facilitate comparison of effects across studies. A better evaluation of participant demographic characteristics such as race, household income, and socioeconomic status and how these relate to intervention outcomes is necessary, as resources available to access healthy foods and quality exercise areas can differ based on socioeconomic status and rurality. Including other health outcomes such as other cardiometabolic outcomes (e.g., blood pressure, lipid levels, glucose levels), as well as positive lifestyle behavior changes, can provide a more comprehensive answer to whether an intervention is clinically effective. Future research is still needed to determine which methods work best within a family dynamic to improve changes in weight and healthy lifestyle habits. Finally, research is urgently needed on safety, dosage, and effectiveness of pharmacological interventions with AOMs in adolescents and adults with DS to support clinical decision-making.

## CONCLUSION

Thirteen out of the twenty-four included studies resulted in significant weight loss or a decrease in BMI in adolescents with IDDs, including DS, and those studies used either a multicomponent intervention, a physical activity intervention, or bariatric surgery. Diet-only interventions and diet and physical activity interventions were included but did not provide sufficient data to evaluate effectiveness. Outside of the major effects of bariatric surgery, clinically relevant weight loss was only achieved in one study, and this could, in part, be due to not following general guidelines for weight-loss interventions regarding duration and intensity of physical activity, caloric restriction, and behavioral support. Although subclinical weight loss may still produce other positive health outcomes, such as improved cardiometabolic outcomes or positive lifestyle behavior changes, future research is recommended to follow guidelines for weight-loss interventions to produce clinically relevant weight-loss outcomes in adolescents with IDDs, including DS. More research on bariatric surgery and weightloss medications is urgently needed for this population. Overall, weight-loss interventions can be effective for adolescents with IDDs, including DS, and will likely be more effective with an increase in duration and intensity to meet the existing recommendations for weight-loss interventions.O

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#### **CONFLICT OF INTEREST STATEMENT**

The authors declared no conflicts of interest.

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#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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