Evaluation of Obesity Treatments in Adults with Down Syndrome: Grading the Evidence and Identifying Research Gaps

Judy Kim, MD, John Berens, MD, K. Jordan Kemere, MD, Elisha Acosta, MD, Ellen Fremion, MD
Baylor College of Medicine, Houston, TX

DSMIG-USA Down Syndrome Medical Interest Group-USA

Authors' disclosures: none

BACKGROUND

The prevalence of obesity is higher among adults with Down syndrome (DS) compared to the general adult population and to adults with intellectual disability not due to DS[1-3]. Obesity confers an increased risk of comorbidities including: obstructive sleep apnea, diabetes, osteoarthritis, mobility impairment, mental health concerns, and low quality of life. Obesity management guidelines have been established for the general population, and include strategies such as lifestyle intervention, pharmacotherapy, bariatric surgery, and nutrition/appetite control[2]. Guidelines for management of obesity in adults with Down syndrome, however, are lacking.

OBJECTIVES/AIMS

Evaluate the quality of the existing evidence in peer-reviewed journals regarding the treatment of obesity in adults with DS and identify research gaps to direct future study and guideline development.

METHODS

A literature search was performed using Medline OVID, Embase, and PsycINFO. MeSH terms "Down syndrome" and "obesity" were combined in the title and abstract search fields. Filters included: human subjects, English language, age > 18, and start date > 1960.

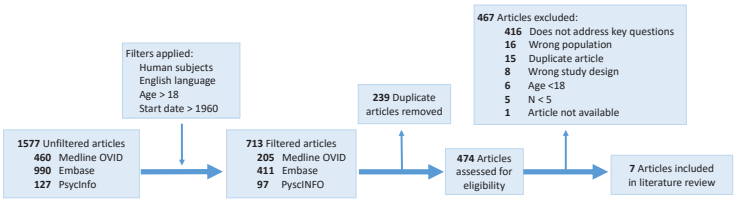
By group consensus the following key questions (KQ) were formulated:

1) What interventions have been studied for its effect on weight in adults with Down syndrome and obesity?
2) In addition to weight change, what other secondary outcomes have been studied in interventions used in adults with DS and obesity?
3) What interventions resulted in statistically significant weight loss?
4) What interventions resulted in statistically significant changes in secondary outcome measures?
5) What are the financial costs, potential adverse effects of the intervention?

Two investigators independently reviewed titles and abstracts. Articles were excluded if: subject age was < 18 years, no key questions were addressed, case series or reports with N<5 individuals with DS, wrong study design (review articles, opinion piece, non quantitative), wrong population, duplicate article, or article not available. Discrepancies were resolved by a third reviewer.

Each included study was assigned to a primary and secondary reviewer. The primary reviewer extracted information regarding: patient population, methods, study design, USPSTF evidence category for research design and quality of evidence for internal and external validity, and findings related to key questions. The secondary reviewer reviewed for accuracy and completeness. Discrepancies were resolved by a third reviewer.

RESULTS/SUMMARY



Key Findings
(see associated bibliography for list of articles reviewed)

	USPSTF Category of Research Design by Article #	USPSTF Quality of Evidence for Internal Validity by Article #	USPSTF Quality of Evidence for External Validity by Article #
KQ1: What interventions have been studied for its effect on weight in adults with Down syndrome and obesity? 1) **5 Physical activity (PA) intervention studies**[1,3,4,5,7]: 2 studies with treadmill-based aerobic training, 1 study with combined aerobic and plyometric jump training, 1 study comparing continuous aerobic training (CAT) vs. interval training (IT), and 1 study with Wii-based exercise training. 2) **1 Dietary + PA intervention study**[6]: 1 study using enhanced Stop Light Diet and controlled diet per USDA MyPlate recommendations + encouraged 30 min/day of moderate intensity physical activity 5 days/week 3) **1 Multicomponent intervention study (using 3+ components)**[2]: 1 study comparing effect of nutrition/activity education (NAE) alone vs. NAE + parental behavioral intervention training 4) No studies involving pharmacotherapy met inclusion/exclusion criteria 5) 4 case reports/case series on surgical interventions (3 using gastric sleeve, 1 Roux enY gastric bypass) were excluded due to N < 5.	Level I: 1,2,3,5,7 Level IIb: 4,6	Good: 1,4,5,6,7 Fair: 2,3	Fair: 1,2,3,4,5,6,7
KQ2: In addition to weight change, what other secondary outcomes have been studied in interventions used in adults with DS and obesity? 1) **Anthropometric measures**[1,2,3,4,5,7]: fat mass percentage, fat mass, lean mass, waist circumference (WC), hip circumference (HC), waist to hip ratio, systolic/diastolic blood pressure 2) **Fitness measures**[1,4,5,7]: VO_2 peak, relative peak VO_2, time to exhaustion, 6 min walk 3) **Strength measures**[1,4,5,7]: sit to stand in 30 seconds, hand strength grip, standing broad jump 4) **Functional measures**[1,4,5,7]: 8 feet up and go, timed up an go, bean bag throw, response speed subset of Bruininks-Oseretsky Test of Motor Proficiency 1st edition 5) **Laboratory measures**[1,4,5]: total cholesterol, glucose, TNF alpha, IL-6, hsCRP, fibrinogen, alpha 1 antitrypsin 6) **Lifestyle measures**[1,6]: physical activity frequency, daily vegetable/fruit intake, energy intake, treat intake	Level I: 1,2,3,5,7 Level IIb: 4,6	Good: 1,4,5,6,7 Fair: 2,3	Fair: 1,2,3,4,5,6,7
KQ3: What interventions resulted in statistically significant weight loss? 1) 1 PA intervention study[4] showed statistically significant decrease in weight and BMI with interval training (IT) and decrease in weight with continuous aerobic training (CAT) after 12 weeks. Body weight and BMI decreased significantly more in IT compared to CAT. 2) 1 Multicomponent intervention[2] found that nutrition/activity education (NAE) + parental behavioral intervention training resulted in more weight loss than NAE alone at 6 months (-2.7 kg vs. +0.5kg) and 12 months (-1.9 kg vs. +1.7kg). ** Note: 1 Dietary + PA intervention[7] reported "clinically significant" weight loss at 6 and 18 months but statistical significant was not reported*	Level I: 1,2	Good: 1 Fair: 2	Fair: 1,2
KQ4: What interventions resulted in statistically significant changes in secondary outcome measures? 1) **Anthropometric measures:** 1 PA intervention[3] showed an increase in whole body lean mass and lower limb lean mass after 21 weeks of combined conditioning and plyometric jump training. 2 PA studies[4,5] showed decrease in % fat mass. 1 PA study[5] showed decrease in waist to hip ratio; 1 PA study[7] showed decrease in waist circumference. 2) **Fitness measures:** 2 PA studies[4,5] showed improvement in VO_2 max. 1 PA study[4] showed increased time to exhaustion. 1 PA study[7] showed increased distance walk in 6 minute walk test. 3) **Strength measures:** 1 PA study[4] showed improvement in leg strength (sit to stand in 30 seconds) after 12 week of continuous aerobic training. 1 PA study[7] showed improved hand strength (hand grip test) and leg strength (standing broad jump after 2 months Wii based exercise training. 4) **Functional measures:** 1 PA study[4] showed improvement (decreased time) in 8 feet up and go test after 12 weeks of continuous aerobic training. 1 PA study[7] showed improvement in response in the speed subset of the Bruininks-Oseretsky Test of Motor Proficiency (1st edition) after 2 months of Wii based exercise training. 5) **Laboratory measures:** 2 PA studies[4,5] showed decrease in TNF alpha levels. 1 PA study[5] showed decrease levels of multiple inflammatory markers: TNF alpha, IL-6, hsCRP, and fibrinogen. 6) **Lifestyle measures:** 1 multicomponent intervention[2] showed significant differences in daily moderate/vigorous physical activity (MVPA) time in the group receiving nutrition/activity education (NAE) + parental behavioral intervention (BI) training compared to the NAE only group. The NAE+BI group increased MVPA time while the NAE only group decreased time. 1 Dietary + Physical activity[6] study showed significant reduction in energy intake.	Level I: 1,2,3,5,7 Level IIb: 4,6	Good: 1,4,5,6,7 Fair: 2,3	Fair: 1,2,3,4,5,6,7
KQ5: What are the financial costs, potential adverse effects of the intervention? 1) No adverse effects were reported in any of the included studies. 2) Financial costs of treatment were not discussed in any of the included studies	None	None	None

CONCLUSIONS

Key Conclusions

- Physical activity (PA) interventions[1,3,4,5,7] were the most frequently studied interventions. However, only 1 of 5 PA studies showed statistically significant change in weight/BMI[1]. All PA studies demonstrated statistically significant changes in various secondary outcomes (ex: fitness, strength, function, and inflammatory markers). More studies are needed to evaluate the effect of PA on weight/BMI, but other health benefits of PA are promising.
- Dietary interventions were used in 2 studies[2,6], and the effect on weight was inconsistent. One multicomponent intervention study showed statistically significant weight loss when parental behavioral intervention training was included[2]. This finding highlights that caregivers may play an important role in supporting lifestyle changes.
- Bariatric surgery in DS is under studied. Potential benefits must be weighed against ethical issues (ex: consent/assent for procedure), short term risks (ex: post surgical complications), long term adverse effects, and need for adherence to lifelong lifestyle changes.
- There were no studies to guide use of pharmacotherapy for treatment of obesity in adults with DS.

Limitations

This review is limited by the small number of studies that met inclusion/exclusion criteria. Most studies had small subject numbers (average n = 41), thus limiting the generalizability of findings and the external validity of the studies.

Research gaps

Future studies for treatment of obesity in adults with DS should address:

- How effective and safe are weight loss medications for adults with DS?
- How effective and safe is bariatric surgery for adults with DS?
- How do dietary interventions differ in effect on weight and in patient adherence to diet?

Directions towards practical guidelines

The following recommendations may be considered for guidelines:

- Considerations for obesity management in adults with DS include a combination of dietary control, behavioral modification, physical activity, and caregiver counseling.
- More research is needed to guide the use of pharmacotherapy and bariatric surgery in this population.

REFERENCES

1. Capone, G. T., Chicoine, B., Bulova, P., Stephens, M., Hart, S., Crissman, B., Videlefsky, A., Myers, K., Roizen, N., Esbensen, A., Peterson, M., Santoro, S., Woodward, J., Martin, B., Smith, D., & Down Syndrome Medical Interest Group DSMIG-USA Adult Health Care Workgroup (2018). Co-occurring medical conditions in adults with Down syndrome: A systematic review toward the development of health care guidelines. American journal of medical genetics. Part A, 176(1), 116–133. https://doi.org/10.1002/ajmg.a.38512
2. Ryan D. H. (2016). Guidelines for Obesity Management. Endocrinology and metabolism clinics of North America, 45(3), 501–510. https://doi.org/10.1016/j.ecl.2016.04.003
3. Wong, C., Dwyer, J., & Holland, M. (2014). Overcoming Weight Problems in Adults With Down Syndrome. Nutrition Today, 49(3), 109–119. doi: 10.1097/nt.0000000000000029.