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## Q/ Is metformin effective for reducing weight in obese or overweight adolescents?

### EVIDENCE-BASED ANSWER

**A/** YES, to some degree—but it is of uncertain clinical significance. Over a period of 6 months, metformin modestly reduced weight (-2.1 kg) and body fat mass (-1.9%), but not body mass index (BMI) or lean body mass, in adolescents who were overweight or obese. This is comparable

to lifestyle interventions (diet and exercise) supported with > 26 hours of counseling, which modestly improved BMI but not weight. (Strength of recommendation [SOR]: A, based on a large meta-analysis of randomized controlled trials [RCTs] of variable quality).

### Evidence summary

#### Metformin has modest effects on body weight

A large systematic review and meta-analysis (38 RCTs; n = 2199) published in 2020 evaluated metformin therapy in children and adolescents (including those with metabolic disease, growth problems, and psychological disorders in addition to obesity and overweight).<sup>1</sup> Over an average of 6 months, metformin use modestly reduced BMI (weighted mean difference [WMD] = -1.07 kg/m<sup>2</sup>; 95% CI, -1.43 to -0.72 kg/m<sup>2</sup>) and body weight (WMD = -2.51 kg; 95% CI, -3.14 to -1.89 kg) for all participants.<sup>1</sup>

However, the authors also performed a meta-analysis of trials involving obese or overweight youth without other comorbidities. Participants in these trials ranged in age from 7 to 17 years (mean not supplied; most trials, 12-15 years), had a BMI greater than the 95th percentile for age, and took doses of metformin ranging from 1500 to 3000 mg (most trials, 1500-2000 mg/d for 24 weeks).<sup>1</sup> In this analysis, metformin reduced body weight (8 trials; n = 616; WMD = -2.06 kg; 95% CI, -3.47 to -0.65 kg) and body fat mass (-1.9%; 95% CI, -3.25% to -0.56%). But it did not reduce BMI (12 trials; n = 826; WMD =

-0.76 kg/m<sup>2</sup>; 95% CI, -1.61 to 0.08 kg/m<sup>2</sup>) or improve lean body mass (2 trials; N = 98; WMD = -0.74 kg; 95% CI, -2.4 to 0.91 kg).<sup>1</sup>

The authors of this meta-analysis did not include an evaluation of the quality of the individual RCTs.

#### Metformin has benefits but also adverse effects

A 2016 Cochrane systematic review and meta-analysis assessed 8 trials (total n = 543) evaluating metformin vs placebo in adolescents prescribed exercise and lifestyle support.<sup>2</sup> This meta-analysis included 4 trials (n = 294) with obese or overweight adolescents that were also included in the newer meta-analysis,<sup>1</sup> as well as 4 trials involving obese adolescents with insulin resistance. The authors did not assess the effects of metformin on obese or overweight adolescents separately.

Over 6 months, metformin use reduced BMI (WMD = -1.35 kg/m<sup>2</sup>; 95% CI -2 to -0.69 kg/m<sup>2</sup>).<sup>2</sup> Metformin commonly produced gastrointestinal symptoms: diarrhea, flatulence (rates not given), and nausea in 15% to 42% compared with 3% to 21% with placebo (no comparison statistic supplied),

however rarely to the point of discontinuation (< 5%).<sup>2</sup> Nine participants withdrew due to adverse effects: 5 in the metformin group and 4 in the placebo group. The authors rated the quality of the included trials as low to moderate.

An evidence report and systematic review (42 RCTs; total n = 6956) compared the efficacy of several approaches for weight loss in adolescents, including metformin (6 of the 8 RCTs included in the 2020 meta-analysis<sup>1</sup>) and lifestyle interventions.<sup>3</sup> Interventions comprising exercise and diet counseling for > 26 hours over 6 to 12 months produced decreases in BMI (-0.86 kg/m<sup>2</sup>; 95% CI -1.44 to -0.29 kg/m<sup>2</sup>) but not weight (-2 kg; 95% CI -3.2 to 1.2 kg).<sup>3</sup>

### Recommendations from others

The US Preventive Services Task Force states that metformin treatment in adolescents who are overweight or obese produces a small reduction in BMI when compared to placebo,

but the clinical significance of this reduction is unclear.<sup>3</sup>

### Editor's takeaway

The idea of using medications for weight loss remains seductive, given how hard it can be for patients to achieve significant, lasting weight loss through lifestyle modification. Evidence suggests that metformin can help in this regard but not enough to recommend it. In addition, metformin therapy is associated with gastrointestinal adverse effects. **JFP**

### References

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