

# Professional Abstract

## Objective

To compare the effectiveness of using metformin plus an educational program about healthy eating and exercise versus using the educational program alone in managing short- and long-term weight and metabolic health for youth with overweight or obesity and bipolar spectrum disorders (BSD) who take second-generation antipsychotic medications

## Study Design

Design Element	Description
Design	Randomized controlled trial
Population	1,565 youth ages 8–19 with overweight or obesity and a current or past diagnosis of BSD who were taking or starting a second-generation antipsychotic medication and who were receiving care at 1 of 64 clinics in 11 states across the United States
Interventions/ Comparators	<ul style="list-style-type: none"><li>• Metformin plus educational program on healthy diet and exercise</li><li>• Educational program on healthy diet and exercise alone</li></ul>
Outcomes	Primary: change in BMI z-scores, which is a measure of relative BMI adjusted for age and sex  Secondary: metabolic parameters; adverse events; treatment satisfaction and adherence; weight satisfaction; psychiatric symptom burden; psychotropic treatment changes; and quality of life
Timeframe More Information	6-month and 24-month follow-up for primary outcome

This randomized controlled trial compared the effectiveness of two approaches in managing weight among youth with BSD who were taking antipsychotic medications. The study also assessed metabolic parameters, adverse events, satisfaction with and adherence to antipsychotic medication treatment, and other patient-reported outcomes.

Researchers randomly assigned youth to receive a metformin prescription plus an educational program on healthy diet and exercise or the educational program alone. In the educational program, youth and their caregivers viewed a video and received materials about making healthy eating plans, exercising regularly, and avoiding sedentary activities.

The study enrolled 1,565 youth who were ages 8–19 and who had a diagnosis of BSD and were receiving care at one of 64 clinics in 11 states. All had overweight or obesity and were receiving or starting treatment with a second-generation antipsychotic medication. Of these youth, 67% were White, 17% were Black, and 12% were Hispanic. The average age was 14 years, and 53% were male.

From baseline through 24 months, clinicians recorded weight and height for youth at checkups. Also, youth and their caregivers completed a survey about adverse events, such as gastrointestinal symptoms; medication adherence; overall quality of life; and psychiatric symptoms. Researchers reviewed bloodwork results to monitor metabolic parameters, such as high-density lipoprotein levels.

Youth with BSD, their parents, and clinicians helped design the study.

## Results

Compared with youth receiving the educational program alone, youth receiving metformin plus the educational program:

- Had greater reductions in their body mass index (BMI) z-scores at 6 months (95% confidence interval [CI]: 0.15, 0.37;  $p < 0.001$ ) and 24 months (95% CI: 0.00, 0.22;  $p = 0.044$ ). At both time points, the average effect of metformin was modest ( $d = 0.11$ – $0.26$ ).
- Were more likely to report mild to moderate gastrointestinal adverse events, including nausea, diarrhea, vomiting, cramps, and flatulence at 24 months (all  $p < 0.001$ ).
- Had greater improvement in caregiver-reported quality of life at 24 months ( $p = 0.030$ ).

Youth did not differ significantly in most metabolic parameters, reports of other adverse events, or adherence to their antipsychotic medications.

## Limitations

Because most youth were already taking second-generation antipsychotic medications when they started the study, researchers could not determine metformin's effectiveness in preventing weight gain associated with starting antipsychotic medications.

## Conclusions and Relevance

In this study, compared with youth with BSD receiving the educational program alone, youth with BSD receiving metformin plus the educational program had greater reductions in their BMI at 6 and 24 months and improved quality of life at 24 months, and were more likely to experience gastrointestinal symptoms at 24 months.

### **Future Research Needs**

Future research could examine whether metformin prevents weight gain in youth with BSD who are starting second-generation antipsychotic medications.