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## [November 1, 2007 Table of Contents](#)

### FPIN's Clinical Inquiries

#### Metformin Therapy and Diabetes Prevention in Adolescents Who Are Obese

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### Clinical Question

Does metformin (Glucophage) therapy reduce the likelihood of obese adolescents developing diabetes?

### Evidence-Based Answer

No studies have addressed the question of whether metformin reduces development of diabetes among adolescents who are obese. Metformin treatment in adolescents who are obese can modestly reduce risk factors for type 2 diabetes, including elevated body mass index (BMI), fasting insulin levels, and fasting glucose levels. (Strength of Recommendation [SOR]: C). However, metformin treatment is associated with nausea, abdominal pain, and diarrhea. (SOR: A). Because of the limited available data, metformin is not recommended for diabetes prevention in adolescents. (SOR: C).

### Evidence Summary

Overweight and obesity are associated with an increased likelihood of type 2 diabetes, hypertension, hyperlipidemia, cardiovascular disease, osteoarthritis, and several other conditions.<sup>1</sup> Of particular concern is the rapid increase in the prevalence of overweight among children, which rose from 5 percent in persons 12 to 19 years of age in 1976 through 1980 to 17.4 percent in 2003 through 2004.<sup>2</sup> Severe childhood overweight (greater than 95 percent of BMI for age) is associated with adult obesity and its sequelae. Type 2 diabetes is rapidly becoming the most common type of diabetes in children.

The Diabetes Prevention Program (DPP), a three-year study of 3,234 obese, nondiabetic adults with elevated fasting blood glucose, showed that metformin treatment can prevent the development of type 2 diabetes. The DPP study also found that drug treatment was less effective than lifestyle modification; 58 percent of participants in the lifestyle modification group did not

develop diabetes compared with 31 percent in the metformin group.<sup>3</sup> There are no studies that specifically address the use of metformin for the prevention of diabetes among adolescents.

Three small randomized controlled trials evaluated metformin for the treatment of obesity among adolescents. However, the studies are limited by short duration (nine weeks to one year), small sample size (22 to 29 patients), and a failure to measure anything other than physiologic end points (e.g., BMI, fasting blood sugar levels, fasting insulin levels). Although these studies did see modest reductions in BMI (approximately 1 to 2 mg per kg<sup>2</sup>) and weight (3 to 4 kg), the long-term safety and clinical effectiveness of these drugs in adolescents is unknown.<sup>4-6</sup> Furthermore, nausea was a common adverse effect of treatment; in one study, 40 percent of treated participants experienced abdominal discomfort or diarrhea.<sup>5</sup>

#### Recommendations from Others

The American Diabetes Association recommends lifestyle changes and avoiding weight gain for diabetes prevention in adolescents.<sup>7</sup> There are no professional organizations that endorse the use of metformin in adolescents who do not have polycystic ovary syndrome or type 2 diabetes mellitus.

#### Clinical Commentary

The use of metformin in adults who are obese helps to reduce weight and to delay the development of diabetes. However, compliant patients willing to take a long-term medication that may cause nausea are likely to also follow advice about exercise, a reduced-calorie diet, smoking cessation, and, if needed, taking blood pressure medication. The real issue in clinical practice, therefore, is how to treat those patients who are obese and have little or no genuine motivation to make a lifestyle change. A diabetes diagnosis is clearly a marker for increased risk, but simply giving medication in the short term to temporarily reduce the blood sugar will likely accomplish nothing. What physicians really need to see is evidence regarding how to best motivate adolescents who are overweight to adopt a significant long-term lifestyle change; this is what will likely result in improved patient-oriented outcomes.

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Clinical Inquiries provides answers to questions submitted by practicing family physicians to the Family Physicians Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group ([http://www.cebm.net/levels\\_of\\_evidence.asp](http://www.cebm.net/levels_of_evidence.asp)).

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