

## Newer doesn't mean better when it comes to type 2 diabetes drugs

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An inexpensive type 2 diabetes drug that has been around for more than 15 years works just as well and has fewer side effects than a half-dozen other, mostly newer and more expensive classes of medication used to control the chronic disease, new Johns Hopkins research suggests.

In their report, published online March 14 in the journal *Annals of Internal Medicine*, the Hopkins team found that metformin, an oral drug that was first approved by the U.S. [Food and Drug Administration](#) in 1995, not only controlled blood sugar, but was also less likely to cause weight gain or raise cholesterol levels.

"Metformin works for most people. It's cheaper, there's a generic form — it's tried and true," says study leader Wendy L. Bennett, M.D., M.P.H., an assistant professor in the Division of General Internal Medicine at the Johns Hopkins University School of Medicine. "Our study shows that even though there are all these newer drugs, metformin works just as well and has fewer [side effects](#)."

The study is an update of Hopkins research published in 2007 that also showed there were advantages to metformin. New classes of medication for adult-onset diabetes have been approved by the FDA since then, and Bennett and her colleagues wanted to know if the newer drugs were any better than the older crop. The research team also looked for the first time at the efficacy of two-drug combinations to treat the chronic disease, which has become increasingly common with more than one-third of diabetes patients needing multiple medications. Researchers

found that while two drugs worked better than one in those patients whose blood sugar remained poorly controlled on a single medication, there were also side effects associated with adding a second medication.

"Diabetes is an enormous public health problem, and patients have difficult decisions to make about what medications they should be taking," Bennett says. "Our study provides good information comparing drugs and can be used to inform those decisions."

Bennett and her colleagues reviewed 166 previously published [medical](#) studies that examined the effectiveness and safety of diabetes drugs, as well as their impact on long-term outcomes including death, cardiovascular disease, kidney disease and nerve disease. The team had previously looked at several popular classes of oral diabetes medication — metformin (sold as Glucophage, Fortamet and others), second-generation sulfonylureas (Amaryl, Glucotrol and more), thiazolidinediones (Avandia and Actos) and meglitinides (Starlix and Prandin) — and added two new classes of drugs, dipeptidyl peptidase-4 (DPP-4) inhibitors (Januvia and Onglyza) and glucagon-like peptide-1 (GLP-1) receptor agonists (Byetta and Victoza), which are given by injection.

No drug or combination of drugs was shown to have an advantage in improving long-term outcomes, Bennett says, primarily because there weren't enough long-term studies, particularly of newer medications.

While most drugs reduced blood sugar similarly, metformin was consistently associated with fewer side effects. Though metformin is associated with increased risk of gastrointestinal side effects, Bennett, an internist, says she finds many of her patients can overcome them by starting with a low dose and taking it with meals, though patients with severe kidney disease may avoid it. The sulfonylureas and meglitinides were associated with increased risk for hypoglycemia, or dangerously

low blood sugar levels. The thiazolidinediones increased risk of heart failure, weight gain and fractures. In September 2010, the FDA placed restrictions on the use of Avandia because of concerns that the drug increases the risk of heart attack.

Meanwhile, the new medications, because there are no generic options, are significantly more expensive than older ones. One hundred metformin pills cost about \$35.57, or 35 cents a pill, while 30 Januvia pills (a DPP-4 inhibitor) cost \$192.52, or \$6.42 a pill — nearly 18 times as much.

While the drugs all reduce blood sugar levels, Bennett says more research is needed into whether they actually improve outcomes for diabetics in the long run. It remains an open question as to whether patients with type 2 [diabetes](#) who have their [blood sugar](#) controlled by medication will reduce their chances of having complications associated with the disease, including eye, kidney and nerve diseases, she says.

"Some of the drugs haven't been on the market long enough to study the long-term effects or even some of the short-term rare side effects, so we need longer studies in patients who are at highest risk for complications" she says.

Provided by Johns Hopkins Medical Institutions

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