Five Lessons from Niaspan's Disappointing Study

Adapted from a post on Dr. Harlan Krumholz's Outcomes blog at Forbes.com

Comparative effectiveness research has attracted attention in the healthcare debate. Critics charge that these studies are designed to restrict choice, stifle innovation, and keep useful but expensive therapies from patients. But when this research is done well, it can overturn conventional wisdom about understudied drugs and demonstrate that patients are receiving ineffective — or even harmful — treatments. Isn't more knowledge about benefits and harms of treatment alternatives just what patients need?

Last month, we saw a widely publicized example of comparative effectiveness research done well. The National Institutes of Health (NIH) produced a gem of a study with critical implications for clinical decision making and future research. In the study, called AIM-HIGH, researchers sought to determine whether adding Niaspan (Abbott Laboratories' extended-release niacin) to statin therapy benefits patients with cardiovascular disease.

The AIM-HIGH investigators enrolled 3414 patients with cardiovascular disease, low HDL cholesterol levels, and high triglyceride levels. All patients received simvastatin and additionally were assigned randomly to Niaspan or placebo. In apress release, the investigators announced that the trial was stopped after average follow-up of about 3 years (more than 1 year earlier than planned) because no hint of benefit was seen at this point. Although the results have not yet been published, enough information has been released to give us a good picture of the study. There was even a suggestion of harm — more strokes in the Niaspan group — but that might have been a chance occurrence.

This study exemplifies comparative effectiveness research that should be embraced by patients, clinicians, industry, payers, and government. Here are five reasons:

1. The study targeted an important area of uncertainty for patients. Niaspan is a popular drug that raises HDL cholesterol levels and lowers triglyceride levels. In 2010, its worldwide sales approached US$1 billion. Unfortunately, we do not know whether the drug lowers risk for heart disease or stroke — or lengthens survival — when added to statins and other modern cardiovascular therapies. The only large study of niacin (not the extended-release formulation) was conducted more than 30 years ago. Drugs that modify risk factors do not always affect clinical outcomes in predictable ways.

2. Too often, studies compare one therapy with an inferior therapy. But in this study, Niaspan add-on therapy was compared with an appropriate alternative — simvastatin therapy, designed to achieve LDL cholesterol levels between 40 and 80 mg/dL. The study replicated a typical clinical scenario in which clinicians and patients must decide whether adding an unproven medication to an already proven therapy is worthwhile.

3. The conclusions of the study did not go beyond the evidence. The press release focused on the absence of benefit with Niaspan but did not generalize further to other drugs that might raise HDL cholesterol levels. Each drug must be tested separately because it could have distinctive effects on human biology. Even within a class, we have seen marked differences in risk profiles of drugs: Consider the recent examples of rosiglitazone (Avandia) and pioglitazone (Actos). Also, the investigators noted that the results should not be extrapolated to other patient populations. What this study can say is that niacin was not beneficial in a relatively high-risk population.

4. Both the NIH and Abbott were involved in the study. The investigators were wise to include Abbott, because the company tested its own product and relieved taxpayers from paying the entire bill (Abbott paid more than half the $52 million in study costs). Abbott should be commended for supporting the study: No pharmaceutical company should want to sell a product that does not help patients. Abbott has not criticized the study.

Involvement of the NIH was also important, because it assured the study's credibility. The NIH has impeccable research credentials, with policies and procedures that protect scientific integrity and transparency. Unfortunately, concerns about misbehavior in data manipulation and the publication process have tainted many industry-sponsored trials.

5. The study had close oversight by a data safety monitoring board. Members of the board were the only people allowed to see results as the study progressed. Their decision to stop the study was based on statistical certainty that Niaspan would not show benefit with further follow-up. Oversight by an independent group, which is not controlled by the sponsors and is accountable to participants, is essential.

The challenge now is to act on the AIM-HIGH findings. The released information should be considered to be reliable enough to inform patients that adding Niaspan to statin treatment does not lower risk, regardless of its effects on HDL cholesterol and triglyceride levels. Although we will learn more details when the results are published formally, every patient on this drug — and every patient for whom this drug is contemplated — should be aware of these findings.

This is exactly the kind of comparative effectiveness study that we need. We are now better informed about Niaspan than we were just a few weeks ago. Better information should lead to better decisions: That's an outcome we should all embrace.

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