

Commentary

## Independent Analysis of Industry Data Necessary for Promoting Collaborative Science

By Harlan Krumholz, MD, SM, FACC



Clinicians and their patients make decisions every day without knowing that some of the information about the risks and benefits of drugs and devices are never published and are out of public view. We depend on literature and systematic reviews to provide us with a synthesis of the medical literature, yet we are often getting only a selective view of the evidence. In some cases studies are never published, while in other cases not all the relevant information is presented.

Several high-profile legal cases have led to agreements compelling companies to share all their study results and the information was surprising. For example, the release of all published and unpublished data on Vioxx revealed evidence of cardiovascular risk as early as 2001 – the drug was not withdrawn from the market until 2004. For rosiglitazone, evidence of cardiovascular risk emerged from an analysis of published and unpublished studies released by GlaxoSmithKline released as a result of litigation. In both cases, problems would not have been apparent if the focus were only on published studies. Systematic reviews of the published literature would have been falsely reassuring. There are many other examples.

This is not just an issue with companies, a review of registered trials recently showed fewer than half are published within 30 months of their completion – and it seems that many are never published. Many of these

studies are funded by the National Institutes of Health. There is a need to focus attention on missing information, timely reporting of results and the sharing of data. If we are to trust and accelerate the science of medicine, then we need to ensure that there are opportunities for others to investigate the findings of others, replicate their results, and provoke new questions.

In August, the Yale group initiated the Yale Open Data Access (YODA)

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Project, an effort to develop a model that would encourage industry to share data about their products. The YODA Project is committed to sharing of data, but also seeks to be attentive to legitimate concerns of industry about the potential misuse of their data.

Medtronic has a product, INFUSE (rhBMP-2), which is used in spinal surgery to promote bone growth. Some investigators are raising questions about the safety of the product. YODA approached Medtronic with a proposal that they release all their human subject data on INFUSE for analysis and then subsequent public release. To provide some distance between Medtronic

and the analyses, we indicated we would seek proposals from leading organizations that conduct systematic reviews and award contracts to the two organizations with the best applications. The reviews which are expected to be completed by next summer, are being conducted in parallel. The idea of having two organizations is to strengthen public confidence in our approach and to assess the agreement of independent reviews. We have asked the organizations to determine the quality of the evidence, its appropriateness to answer questions of efficacy and safety, and what can be inferred from it. Meanwhile we are working on a process that would subsequently result in all of the data being made available to investigators and others who request it. Our intent is to promote the use and analysis of the data.

This effort is intended to serve as a model for other companies to participate in data release and the external, independent evaluation of the totality of data. Through these efforts we hope to leave behind an era where clinicians and patients assume that all study results are available, to a time when results of all studies are made available in a timely way and there is a spirit of data sharing that promotes collaborative science.

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**Disclosures:** Krumholz previously worked on the Vioxx litigation and has received a grant from Medtronic to pursue the project described in this article. He also chairs a scientific advisory board for United HealthCare.