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Editorial

Keep the pressure on for more transparency of clinical trials on endometriosis

In the past decade, about half a dozen books have been published that are very critical of the pharmaceutical industry, some of them scathingly so. They include Merrill Goozner's *The $800 Million Pill*, Jerry Avorn's *Powerful Medicines*, John Aramson's *Overdosed America*, Jerome Kassirer's *On the Take*, Marcia Angell's *The Truth About the Drug Companies*, and, very recently, Ben Goldacre's *Bad Pharma*. From various angles, these books provide an unflattering—sometimes disturbing—but consistent portrait of drug companies' behaviors.

The seeming deluge of these books on a similar topic cannot be dismissed offhand as a pharma-bashing fad, because these books appear to be well researched and based on credible sources. A few of them are written by former editors of some prestigious medical journals who witnessed firsthand some high-profile cases of clinical trials sponsored by the industry, such as the Vioxx saga. One troubling behavior is the selective publication and the suppression of "negative" information arising from clinical trials funded by drug companies.

Against this foreground is the enactment of several legislations in the United States (U.S.) mandating more openness in clinical trials and the birth of a handful of clinical trial registries. Notably, Section 113 of the Food and Drug Administration Modernization Act (FDAMA 113) was enacted by the U.S. Congress in 1997. Section 113 ultimately led to the creation of ClinicalTrials.gov as an Internet-based public depository for information on studies of drugs (including biological compounds) that are conducted under the FDA's investigational new drug regulations.[1] In 2007, the U.S. Congress enacted the FDA Amendments Act of 2007 (FDAAA), or Public Law 110-85. On the same day, the FDA Revitalization Act was signed into law, with the aim of improving the FDA's ability to ensure the safety of the nation's drugs and medical devices. Section 801 of the FDAAA mandates the expansion of ClinicalTrials.gov and provides for the first federally funded trial results database. These legislations and trial registries are intended to encourage and promote openness in clinical trials.

As elaborated in these books, the selective reporting and the suppression of "negative" data are quite ubiquitous and pervasive across the entire industry. Not surprisingly, endometriosis trials are no exception. In a survey conducted 4 years ago, it was found that 57 endometriosis-related clinical trials were registered at ClinicalTrials.gov.[2] Among the 15 completed Phase II or Phase III trials that evaluated the efficacy of various promising compounds, only three (20%) had published their results, but the remaining 12 (80%) did not. In other words, most endometriosis trials were shrouded in secrecy.

Four years have since passed. A recent analysis of trials registered at ClinicalTrials.gov found that the situation has changed very little.[3] Specifically, it reports that among 35 completed trials on endometriosis, only 11 (31.4%) published their results, which is below the 66.3% reported in a recent survey of nonendometriosis trials.[3] More disturbingly, trials sponsored by industry were about four times less likely than those sponsored by nonindustry to publish the results, even though they were typically larger in size and completed quicker—likely because of more resources. Industry-sponsored trials that did get published were those that led to the regulatory approval for marketing. Conspicuously, no "negative" trials sponsored by industry have ever been published. Such an abject failure to publish and selective reporting pose a serious threat to professional access to all trial results and to the validity of evidence-based medicine. It also goes against the mounting pressure around the globe for greater transparency of clinical trials.

One can argue that the ultimate goal of disease-focused research such as endometriosis research is better clinical care of patients through providing better diagnosis, treatment, or even innovative ways of prevention. Toward this goal, one important intermediate linking basic research and clinical practice is randomized clinical trials that evaluate the safety and efficacy of compounds deemed to be promising in preclinical research. Results from successful clinical trials may also be submitted to regulatory agencies to obtain approval for marketing.

Clinical trials are known to contribute to our knowledge base in evidenced-based medicine. Yet, this hinges critically on the timely public release and dissemination of findings from such trials, which are considered to be key principles in the proper conduct of clinical research.[4] Indeed, clinicians, policymakers, and even patients learn of evidence-based medicine primarily through peer-reviewed biomedical journals. The apparent opaqueness of endometriosis trials is certainly a disservice to the public.

At the time when there is a palpable disappointment over the slow progress in developing novel therapeutics for endometriosis,[5] this opaqueness is an added hindrance to drug development, because it impacts negatively on basic research scientists. When everybody is holding their cards close to their chests, nobody will benefit from hard-earned lessons, and everybody will be condemned to repeat others' mistakes, miscalculations, or missteps. It also exposes trial participants to the unnecessary risk of receiving inferior treatment or having an adverse effect since different drug companies may test slightly different drugs that belong to the same class of drug (such as selective progesterone receptor modulators). Above all, it betrays the wish implicitly or tacitly expressed by the trial participants that their participation will generate generalizable medical knowledge that might benefit not only themselves

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but also other and future patients, scientists, and physicians so that collectively the trial and other scientific research will ultimately improve patient care.

Given this apparent opaqueness in endometriosis trials, pressure needs to be kept on to change this situation. More transparency not only is a moral imperative to researchers, sponsors, reviewers, and journal editors alike, but also should help researchers, healthcare providers, policy-makers, drug companies and, above all, patients with endometriosis.

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Despite mounting pressure on more transparency of clinical trials, the current state of transparency, or lack thereof, of clinical trials on endometriosis is worrisome and does not benefit the trial sponsor or women with endometriosis. We need to change this! Professor Sun-Wei Guo, Fudan University, China. In the last decade, about half dozen books have been published that are very critical of the pharmaceutical industry, some of them scathingly. They include Merrill Goozner's The $800 Million Pill, Jerry Avorn's Powerful Medicines, John Aramson's Overdosed America, Jerome Kassirer's On the Ta Clinical trial data transparency enables qualified researchers to verify clinical trial results, improve the efficiency of clinical trials and ad-vance medical knowledge. In addition, data sharing has the potential to improve public health, while also increasing public trust in clinical research and the life sciences industry.Â â€¢ SAS is the de facto industry standard for clinical trial data analysis and reporting. â€¢ For more than three decades, life sciences companies have trusted SAS to derive greater insight from information. â€¢ Today, SAS has customers at more than 65,000 sites worldwide. Learn more about SAS software and services for life sciences at: sas.com/lifesciences. The argument for more transparency. Transparency advocates say clinical study reports need to be made public in order to understand how regulators make decisions and to independently assess the safety and efficacy of a drug or device. They also say the reports provide medical societies with more thorough data to establish guidelines for a treatment's use, and to determine whether articles about clinical trials published in medical journals â€" a key source of information for clinicians and medical societies â€" are accurate.Â One analysis showed that only about half of clinical trials examined were written up in journals in a timely fashion and a third went unpublished.Â The FDA does not keep track of how many clinical study reports it has released through FOIA, says Walsh. Clinical suspicion of reb-leeding was defined as any one of the following three signs: (i) vomiting of fresh blood, (ii) insufficient increase in haemoglobin or increase in need for blood transfusions, or (iii) haemodynamic instability (two of the following: decrease in haemoglobin to <10 g/dL or a drop â‰¥2 g/dL, increase in heart rate >100 beats/min or of >.Â The results were also analysed a posteriori according to the more commonly used outcomes of clinically suspectedÂ In keeping with the original protocol specifications, the primary endpoint (overall outcome ordinal score) is reported for the ITT population.Â Focusing on trials that used high-dose intravenous bolus and continuous Guidance on the management of clinical trials during the COVID-19 (coronavirus) pandemic. Version 3 28/04/2020.Â The impact of COVID-19 on ongoing trials, on opening new trial sites in an existing trial, on ongoing recruitment and continued involvement of participants in the trial, or on starting of new trials needs to be considered. This evaluation should take into account national recommendations and measures including travel restrictions and confinements of trial participants and trial staff and the availability of trial staff to perform visits, enter data in the Case Report Form (CRF), notify serious adverse events and, more generally, follow the protocol.