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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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In response to the pressing need for more efficacious and safer therapeutics for endometriosis, there have been numerous reports in the last decade of positive results from animal and in vitro studies of various compounds as potential therapeutics for endometriosis. A handful of these have undergone â€¦Â A handful of these have undergone phase II/III clinical trials. Since the announcement of the International Committee of Medical Journal Editors that mandated registration as a prerequisite for publication, 57 endometriosis-related clinical trials have been registered at ClinicalTrials.gov, an Internet-based public depository for information on drug studies. Among them, 25 are listed as completed, and 2 as suspended. Endometriosis sometimes gets better by itself, but it can get worse if it's not treated. One option is to keep an eye on symptoms and decide to have treatment if they get worse. Support from self-help groups, such as Endometriosis UK, can be very useful if you're learning how to manage the condition. Pain medication. Anti-inflammatories, such as ibuprofen or paracetamol, may be tried to see if they help reduce your pain.Â For more information, read about pain relief for endometriosis on the Endometriosis UK website. Hormone treatment. The aim of hormone treatment is to limit or stop the production of oestrogen in your body, as oestrogen encourages endometriosis tissue to grow and shed. Limiting oestrogen can reduce the amount of tissue in the body. 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. See more of GCT on Facebook. Log In. or.Â We launched 2 new gynecology studies in Endometriosis and a Phase II study in idiopathic pulmonary fibrosis (IPF), a rare pulmonary indication. GCT team was also awarded a trial in COVID-19 infected patients to contribute to the global search for treatment options. ðŸ”·Among other #projects, we are presently in the active start-up phase and opening 25 sites for a large global study in non-small lung cancer patients. ðŸ”·It is our pleasure to announce that we are moving to a new.Â New recommendations for Sponsors on how to manage clinical trials have been published by the European Commission, #EMA and national #HMA. Endometriosis is a disorder in which tissue similar to the tissue that forms the lining of your uterus grows outside of your uterine cavity. The lining of your uterus is called the endometrium. Endometriosis occurs when endometrial tissue grows on your ovaries, bowel, and tissues lining your pelvis. Itâ€™s unusual for endometrial tissue to spread beyond your pelvic region, but itâ€™s not impossible. Endometrial tissue growing outside of your uterus is known as an endometrial implant.