DISCUSSION

Storm in a teacup? General implications of the Cochrane crisis

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Abstract

The crisis that has emerged around the expulsion of Peter Gøtzsche from the Cochrane Board seems at first sight to be the outcome of a typical power play. However, the structural issues that have led to the crisis have emerged in a more technical criticism. These include lack of transparency, lack of cooperation of the pharma industry and hostility of institutions. Thus, the watchdog institution for efficacy and effectiveness of pharmaceutical drugs has itself now been hobbled by inefficacy and lack of effectiveness in its operation. What the confrontation shows us is how little control or understanding we (ordinary people) have over what we are given as curative and preventive biomedicine. It demonstrates how we are ignorant about the treatment of our sick bodies by expertise, pharmaceutical industry and medical institutions. The problem is not one of a particular evil actor. It is a problem of our medical culture. While we struggle to find our way through this overall historical situation, we need to listen to ethical experts like Peter Gøtzsche who are willing to stick their necks out and speak the truth.

The expulsion of Peter Gøtzsche from the Cochrane Collaboration had all the signs of a storm in a teacup at first glance.

Gøtzsche's writing in his popular book (1) on the unstated dangers of psychotropic drugs for the mentally ill coming into the market had all the finesse of a bull in a china shop. He has clearly used populist phrases to describe the authoritarianism of experts who ran the psychiatric profession, worst of all, calling them "silverbacks", likening them to alpha male gorillas. Gøtzsche's argument against psychotropic drugs is that the system of production and marketing pushes flawed products that harm the mentally ill: including increasing the risk of chronic diseases, having debilitating side effects and failing in their primary curative purpose.

While this book's perspective was informally referred to (2) as one element in a trail of reasons for the expulsion, apparently going as far back 2003, the last flap of the butterfly's wing that caused the storm was Gøtzsche and others' "excessive" criticism (3) of the Cochrane review of the human papilloma virus vaccine for adolescent and young adult women which promised to cut down the incidence of cervical cancer. So, it is indeed understandable that Gøtzsche was sacked because of his outspoken, loose cannon style. The "proper" voice of the Cochrane board described the criticism of the review as "overstated" (4). The implicit charge to me was that he was arrogant, self-indulgent, irresponsible and excessively polemical in his statements. These seemed without doubt the personal stylistic reasons that accompanied the substantive reasons for the sacking: that his pronouncements put millions of patients at risk. Good riddance, I thought!

Gøtzsche responded by writing a public letter (5) that charged the Board with acting in a dictatorial manner, arguing that, with his expulsion, "the Cochrane Collaboration has entered an unchartered territory of crisis and lack of strategic direction. A recovery from this dire situation would call for the dissolution of the present board, new elections and a broad-based participatory debate about the future strategy and governance of the organization". So far, it seems like a typical power play between the "haves" and the "wanna haves", ho hum!

What is at stake? On the one hand, if the Cochrane Board is right, Gøtzsche's pronouncements, under the garb of Cochrane authority, unethically mislead doctors and the people at large by misinforming them about false flaws in these drugs, thus putting many young girls at risk of preventable cervical cancer. On the other hand, if Gøtzsche et al are right, the Cochrane reviews of the HPV vaccines are faulty. These vaccines can cause serious iatrogenic disability: postural orthostatic tachycardia syndrome (POTS) and complex regional pain syndrome (CRPS), are two documented side-effects of the vaccine (6). The disagreement between Gøtzsche and the Board is regarding the relative risk and benefit.

Gøtzsche's charge is that these problems arise because the Cochrane Review Board which had started out as a noble institution to ensure the truth of medical research is corrupted by the pressure of pharma. So, the storm in this teacup has some potentially serious repercussions on our lives. For example, doctors blithely recommend the use of HPV vaccines ignoring (or perhaps in genuine ignorance of) doubts about their side effects (7). How do we decide what to do?

While the Cochrane charge against Gøtzsche and the latter's original announcement of his termination seem a run of the mill power battle, a publication by Gøtzsche and his colleagues

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shows the matter in a different light (6). This substantive essay describes clearly the intentional and structural roadblocks that go against any independent evaluation of a Cochrane review. It also highlights the shortcomings of the review. The main issues summarised:

- Public confidence in vaccines hinges on reliable assessment. The Cochrane review is no longer reliable.
- Clinical study reports that are kept by manufacturers contain more information than journal publications but are harder to access. The Cochrane review of the HPV vaccine studies didn't use the manufacturers' clinical study reports. They were not allowed access to this data.
- In general, regulators did not have the full data and the manufacturers place restrictions on the dissemination of industry data.
- The European Medicines Agency too did not initially permit free access of data to Gøtzsche and his colleagues, and when they ultimately did, the data was incomplete, scattered and difficult to use. Only half of potentially eligible reports for a systematic review of HPV vaccines had been delivered to the authors of the essay cited after three years of their efforts: this data was incomplete and contained extensive redactions (blanked sentences to ensure pharma knowledge secrecy).
- The process for releasing clinical study reports should be improved to make it faster and more complete.

This paper is far more convincing than the statements that exchanged blame and underlines the real problem for the doctor who prescribes and recommends based on faith in the system.

Clearly the doctor must be well informed. But how many of our doctors have the time to be well informed; and what happens to this "well informedness" if their continuing education is by the medical representative of precisely the pharmaceutical companies that have pushed these vaccines and drugs into the market? How do mere mortals find out what the truth is here, when even the privileged authors Jorgensen, Gøtzsche, Doshi and Jefferson say that it is difficult to get information from the regulatory agencies and the manufacturers?

So then, this is the size and extent of the crisis: Cochrane, the global watchdog of effective and efficient drug discovery and use has now been hobbled by inefficacy and inefficiency.

The problem clearly seems to be that of a pharmaceutical industry (as any other industry) which seeks to find ways to profit from its business. Naturally it tries to sell more medicines. And as with any other industry, it finds loopholes to do so. The problem with medicine is that it is not a simple sale between a buyer who knows what she wants and a seller who is open about the information. In medicine, the ignorant patient, ie, the "buyer" trusts, and is at the mercy of the doctor, who prescribes what he thinks the buyer needs, *often based on "knowledge" he receives from the seller's representative*. Not only this, the buyer is often in a catastrophic or critical situation where she must accept the doctor's prescription, or expect to suffer a dire and painful future if she refuses medical advice! This then is the larger trap we are in with respect to our approach to medical care and health. Despite obvious "villains", the situation is larger than individual wrong doing or corporate greed alone. This is the medical culture we are born into.

It bodes ill that this knowledge-industry-specialist medical culture we live in has fully taken the health of people into its hands. Medicine has become increasingly specialised and remote, yet it reaches into our daily lives with terrifying alacrity to promote health, to prevent disease and to cure our bodies with its alien expertise. If it fails, and it has so often, we have no recourse. Industry wants to profit and grow and, in the process, is losing sight of its primary responsibility as part of medicine: not to harm people knowingly while selling them cures for their illnesses. Governments seem, on the one hand, to depend indiscriminately on the specialists, and on the other, to encourage pharmaceutical industries to do whatever they want to, to boost economic growth indices. And in the middle of this global morass of interests and priorities, the watchdog institution, the Cochrane Collaboration, has dealt itself a potential death blow, abetted by pharma pressure. How do we retrieve our wellbeing from this dead end?[1]

While our medical culture struggles to find its feet, there is no doubt that we must listen to the likes of Gøtzsche and his colleagues. These are the few experts who remember their responsibility to the people and fight institutional failure and corporate greed. For those like them, it is a fundamental ethical responsibility to do so. For those like us-people, patients, caregivers-it is a matter of survival and wellbeing.

What then is the professional responsibility of a doctor in this uncertain situation? The average Indian patient will continue to put his life in the doctor's hands in implicit and explicit trust. But perhaps we should begin to think for ourselves a little more; find ways to survive, as a people, this trap we are in. Perhaps we need to strengthen models of local knowledge and sharing of insights, depending on ethical critics like Gøtzsche and colleagues, to find ways to survive this unhealthy regime of healthcare. It is here that organisations like Medico Friend Circle of India need to continue to prove their role as places of exchange and mediation between expertise and activism.

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Note

[1] For an earlier and more general version of this argument, see the "Introduction" in Zachariah A, Srivatsan R, Tharu S, editors. *Towards a critical medical practice: Reflections on the dilemmas of medical culture today*. Hyderabad, India: Orient Blackswan; 2010. Pp 392.

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The crisis in Cochrane: Evidence Debased Medicine

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Abstract

The mission of the Cochrane Collaboration, established in 1993, was to systematically review medical evidence with a view to producing the best quality and trustworthy evidence. Twenty-five years later, it is in a crisis that centres on the dismissal one of its founders and the question of access to clinical trial data. The original mission aimed at improving health. In the face of stalling life expectancies, the stakes in the current crisis could not be higher. This essay looks at the crisis in the context of the disastrous effects of medication for paediatric depression on children as a consequence of the suppression of adverse findings from clinical trials.

The first article by Iain Chalmers announcing the Cochrane Collaboration appeared in 1992 (1), with its mission being to systematically review medical evidence with a view to producing the best quality and trustworthy evidence (2). Writing *The Antidepressant Era* in 1995, I characterised systematic reviews as a logical, and necessary medical development (3). Although the founders came from Canada (Sackett and Enkin), the United States (Dickersin), Denmark (Gøtzsche) and elsewhere, from the mid-1990s, the United Kingdom (UK) became the home of the Collaboration. From the very start, there was a tension between a renegade disruptive element in Cochrane and an establishment function (2).

The idea of embodying Evidence Based Medicine (EBM) in Guidelines also took shape at this time. In Britain, in 1997, a Labour government created a National Institute for Clinical Excellence (NICE) which began issuing Guidelines underpinned by Cochrane methods and in some instances with Cochrane collaboration. The NICE process was and still is highly regarded, sufficiently so for the Labour government to issue a new plan for Britain's National Health Service (NHS) which, on the basis of newly-minted standards of care, set about standardising the health service in a manner that embraces continuity of data with an interchangeability of personnel, rather than continuity of care (4).

In 2004, a world no-one anticipated came into view. As part of an FDA review of paediatric antidepressant trials at this point, it became clear that all trials in paediatric depression were negative, that all published studies were ghost or company written, in all cases the data were inaccessible and in the case of the published studies, the publications were at odds with the data regulators revealed. The data on both benefits and harms was systematically distorted in publications even in the leading medical journals (5). This came to a head over the issue of suicide in 2004, when New York State filed a fraud action against GlaxoSmithKline (GSK), primarily on the basis that a ghost-written publication of Study 329[1] claimed paroxetine worked for and was safe for children who were depressed, when in an internal review it had recognised it didn't work and had opted to pick out the good bits of this study and publish them (6).

This led reviewers within NICE, then compiling Guidelines for the treatment of paediatric depression, to publish an editorial "Depressing research" which raised a question as to whether it was possible in the circumstances revealed by these trials to undertake systematic reviews or write guidelines (7).

The issue of lack of access to the data and ghost writing of publications was therefore "known" within the Cochrane Collaboration and guideline apparatus as of 2004. This is not a feature of paediatric antidepressant trials alone, as what had been revealed appears to be standard industry operating mode (8).

Cochrane, NICE, and other guideline bodies, however, suppressed this awareness. Peter Gøtzsche, and later Tom Jefferson, have been the exceptions to this rule. Beginning in 2009, Gøtzsche began to lobby the European ombudsman for

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