REVIEWS

An industry without borders

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Adriana Petryna. *When experiments travel: clinical trials and the global search for human subjects.* Princeton, NJ: Princeton University Press; 2009. 258 pp

The words "randomised controlled trials" have taken on new meaning for me. In *When experiments travel,* Adriana Petryna reveals the experimental machinery manipulated by the globalising clinical trial industry in the quest for blockbuster drugs. She chronicles interviews of people who are not so much heroes or villains but ordinary actors engaged in a partly dirty business across national boundaries.

In this anthropological account, Petryna explores how the research industry has mastered the science of "evidence making", which includes configuring to which countries to offshore clinical trials, teasing out the loopholes of existing regulatory frameworks and seeking out "foolproof, treatment-naïve, steroid-naïve, statin-naïve" clinical trial populations in the most ailing healthcare systems.

Through her interviews of clinical trial industry players in Eastern Europe and Latin America, the author weaves an intricate web of issues involved in the politics of pharmaceutical globalisation. She reveals a paucity of accountability, oversight and transparency. She expresses concern over "commodified patients" and exploitation of the vulnerable, raising questions about the scientific integrity of research, wondering whether ethics is simply "workable documents on paper".

The author describes how the epidemic of cardiovascular diseases in Poland in the 1980s and 1990s was the pull factor leading to a "gold rush" of drug and surgery trials in cardiac care in that country. According to the director of a global contract research organisation (CRO), Poland among other Eastern European countries was used as a "rescue country" where failed projects of me-too drugs were often dumped. Salvage research and floating "garbage trial" protocols to low-income countries began to be seen as a profitable form of rescue for pharmaceutical companies. The author flags concerns about the aftermath of these trials which leads to the worsening of health inequities, complicated by the lack of post trial access to treatment.

While in Brazil, healthcare is the duty of the state. Pharmaceutical access is a cornerstone of healthcare coverage providing for all kinds of medicines – whether they are on the country's essential drug list, part of specialised programmes or even in experimental stages not yet approved for marketing. This "pharmaceuticalisation" – a term coined by medical anthropologist Joao Beihl – paved the way for a strained health system offering too much. The irony is obvious; "you might be out of work and hungry but you could still claim your free anti-anxiety pill" at the local health post, writes Petryna. In Brazil's context of poverty, people die mostly of infectious diseases while the consumption of drugs for lifestyle diseases soars. The apparent disconnect between clinical experimentation and local health needs is starkly evident. "We have no idea what their value is for our patients. All we know is that many of the new drugs can't kill, but we don't know if they can save" explains Dr Andry Costa, a cardiologist and researcher. She goes on to explain the exploitation of Brazilian real-life patients who are much sicker than the ideal patients in clinical trials and in these scenarios biased data is an inherent flaw. They use human subjects not only to generate drug value through R&D, but they also turn them into vociferous consumers of treatment via the state, creating a dangerous "public health trial".

A running theme through the book is that of cold blooded research at the hands of CROs, the data generating enterprises working on behalf of sponsor companies. They care most about getting the data, ensuring their "integrity," "engineering out" the possibility of adverse events by including a "randomised" (read "highly edited" and cautiously selected) patient population and making data from international sites portable and usable within the US drug approval process. In the unsettling words of a CRO professional, "I don't see patients, I see data." The benefit of this lop-sided approach, he claims, is that while data are transferred out of the country, a lot of clinical investment comes back in.

Providing context, Petryna highlights a notable event for the clinical trials research industry: the International Conference of Harmonization's Good Clinical Practice (ICH-GCP) guidelines. Their main aim was to make clinical data from international sites transferable and acceptable to regulatory authorities in the US, Western Europe and Japan. They also served to undercut the regulatory significance of the 2000 revision of Helsinki Declaration regarding placebo-controlled trials. The Helsinki Declaration requires a new drug to be tested against the best or standard treatment for a particular indication. ICH-GCP on the other hand allows placebo-controlled trials. The experimental drug can be tested against "equivalent medication", not necessarily standard or best treatment, but whatever was locally available and accepted by local review boards – which could be no treatment, or a placebo. This ethical

variability allowed pharmaceutical companies to bypass ethics in the developing world. Placebos also happen to reduce trial costs and provide better evidence.

Though India's clinical trial scenario receives nothing more than a few passing references, one can't help but draw parallels and wonder about the fate of pharmaceutical research in this country. How is India going to respond in the wake of being dubiously hailed as the "global clinical trials hub"? With the inflow of clinical trials investments, will the Drugs Controller General of India beef up regulatory mechanisms? Or will clinical trials become a part of healthcare delivery for disadvantaged groups? At present, one can only guess.

How to catch a thief

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Frank Wells and Michael Farthing, (eds). Fraud and misconduct in biomedical research. London: The Royal Society of Medicine Press; 2008, pp 300 (paperback) Paperback ISBN 978-1-85315-786-8 45 £ UK

Fraud and misconduct have probably always existed in biomedical research and, as is evidenced by recent events, they are here to stay. Witness, for example, two recent cases, one in basic science from 2006, that of the Korean stem cell researcher Hwang Woo-Suk, and the other from clinical medicine in 2009 (after the book under review was published), that of Scott Reuben, the anaesthesia and pain researcher. Both of them published papers in leading journals in their field which changed the way we think about and practise science and medicine – until their fraud was detected. Thus, the authors begin the book with these appropriate words in the preface: "It is with some regret that a fourth edition of this book still has relevance today."

Fraud and misconduct in biomedical research, in its earlier avatar (with the redoubtable Stephen Lock as one of the editors) has been acclaimed as a masterpiece and this edition, which is largely rewritten, is meant to be a textbook for dealing with fraud. In this, the editors of the book have succeeded. The six sections of the book deal with the basics of fraud (value systems, issues in publishing and a definition of misconduct), a review of the history of fraud in North America and Europe, the prevention of fraud, how to detect fraud, how to investigate it and, finally, the way ahead.

The book reiterates that fabrication, falsification, plagiarism and theft are the four cardinal examples of fraud. Much of this is to achieve fame, financial gain, promotions and at times, to use Stephen Lock's term, because of a "Messiah complex". However, our changing values and a changing society have dictated that many things which would once have been considered entirely acceptable are now looked upon entirely differently. Richard Smith, ex-editor of the *BMJ*, discusses some of these ethical issues that arise in publication. These include, among other things, failure to obtain informed consent for research, failure to publish (!) or publishing too much. Informed consent is perhaps the best known aspect of research ethics and needs no elaboration. But failure to publish, particularly if the results are negative, also constitutes misconduct. This is because, it is argued, it is the researchers' duty to publish, and because negative results rarely get published, this can result in a bias in favour of a treatment – which would be unscientific. Journals nowadays insist on patient consent even for the publication of case reports. I must confess that I had never understood the logic of this, but Smith explains why the *BMJ* started asking for this – and I now see the logic of it. Yet, Smith himself admits that they sometimes felt they were going too far in this and thus, there are still many unanswered questions about the appropriateness of consent in all cases.

About one third of the book deals with the methods of detection of research misconduct – appropriate indeed for a textbook. The means of doing this are varied and at many levels – right from using the electronic media to identify fraud to the use of audits to the use of appropriate statistical analysis to unearth fraud. There are explanatory examples - but the authors do not divulge all details. Of course, it makes sound sense not to reveal your hidden strengths to the enemy. It is interesting to learn that most cases of misconduct are brought to light because of whistleblowers. Yet most of these whistleblowers – as seen in numerous anecdotes in the book – suffer financially, professionally and mentally after blowing the whistle. Other thought-provoking bits of information in the book were these: research fraud is not considered by many, it appears, as heinous as financial fraud; none of the 26 cases of fraud in the UK (p 73) are by women; and as recently as 2007, 41% of over 200 leading biomedical journals gave no instructions about authorship criteria.

Can this book be improved further, in the next edition, perhaps? My only wish, or perhaps grouse, is that the book is largely West-centric. It is, of course, entirely up to the editors to decide who they wish their target audience to be (European and American), but given that they intend this to be a text, I believe they should address a larger, global audience. Indeed, while the preface states that the contributors are "from all corners of the world", I could only see contributors from Europe and the USA. Even the excellent histories of fraud are largely about cases from North America and Europe. Surely South America, Africa,