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Fast, cheap, and out of control? Speculations and ethical concerns in the conduct of outsourced clinical trials in India

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ABSTRACT

The globalization of biopharmaceutical clinical trials and their offshore outsourcing, from the West to low and middle-income countries, has come under increasing scrutiny from academic scholars, practitioners, regulatory agencies and the media. This article reports the results of a study conducted in Bangalore and Hyderabad between 2007 and 2009, to elicit the perspectives of stakeholders, concerning media representations of their work and the ethical issues that emanate from their engagement in the clinical trials enterprise. In acknowledging the inherently problematic nature of the outsourcing of clinical trials to low income countries, I argue that the practice of not prioritizing research on diseases that are most prevalent among communities, from which subjects are recruited, demands a coordinated and sustained critique. I propose that the critical discourse on the outsourcing of clinical trials should not only emphasize the perils of this practice, but also address some broader issues of equity and distributive justice that determine people's access to basic health care in low income countries. Close attention to the specific context of clinical trials in an increasingly neoliberal medical and health environment in emerging economies such as India can provide critical insights into the on-the-ground complexities and challenges of outsourced global clinical trials.

Introduction

The global pharmaceutical industry, which is increasingly offshoring and outsourcing biopharmaceutical clinical trials to emerging economies like Brazil, China and India, has been at the center of intense ethics and policy debates regarding its role in using trial subjects from the Third World to further consolidate its pharmaceutical research and marketing agenda (Glickman et al., 2009; Petryna, 2005, 2009; Prasad, 2009; Sariola & Simpson, 2011; Shuchman, 2007; Sunder Rajan, 2005, 2006, 2007). Proponents of outsourcing have pointed to several advantages it offers: substantial savings in operational costs while recruiting a large number of patients in a timely manner, speedy completion and approval, and more extensive validation of the trial drugs among genetically diverse and so-called treatment naïve populations. They also contend that clinical trials constitute a "social good" and not a "social evil" (Martin, 2006) that will ultimately bring unprecedented health benefits to the global community (Bhatt, 2004; Bobba & Khan 2003; Maiti & Raghavendra, 2007).

Critics, however, have contested these claims, arguing that the growth of clinical trials, particularly in developing countries, has resulted in exploitative and unethical practices such as "subject coercion, the lack of voluntary and informed participation, and inadequately informed consent" (Petryna, 2009: 124). Some have also documented case studies to show that these trials have resulted in deaths among trial subjects (Shah, 2006; Srinivasan, 2009a, 2009b). They have argued that it is mostly poor, disenfranchised and vulnerable people who are lured by pre-trial payments into participating in trials that ultimately contribute little or nothing to their health, let alone the health of the community from where they are recruited (Nundy & Gulhati, 2005; Sunder Rajan, 2007). Critics have argued that by conducting clinical trials in developing countries and among economically disenfranchised "ready-to-recruit" and "ready-to-consent" populations, and by offering these groups limited and problematic access to health care in exchange for their bodies as testing sites for new products (Fisher, 2009), pharmaceutical companies and Contract Research Organizations (CROs) abuse and exploit disadvantaged populations for the benefit of privileged groups (Abadie, 2010; Elliott & Abadie, 2008; Shuchman, 2007). Critics have emphasized the need to address the exploitative nature of global clinical trials, and the treatment of human subjects in Third World countries as "guinea pigs" or a "*sacrificial* population" (Srinivasan, 2004; Sunder Rajan, 2006). In the Indian context, for example, Nundy and Gulhati (2005) have described the outsourcing of clinical trials as a form of "new

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colonialism" in which poor and non-literate people are systematically exploited.

Amid the debates surrounding the advantages and disadvantages of the globalization of clinical trials, intense speculation has developed in the media and scholarly literature regarding the number of active clinical trials and investigative sites globally, and the actual number of international human subjects involved in these trials. This is especially true of the clinical trials offshored/outsourced by European and US-based multinational pharmaceutical companies (MPCs) to some of the large emerging economies. The emergent literature from science and technology studies and medical anthropology is only beginning to shed some light on the on-the-ground reality of clinical trials, especially in countries where they are being outsourced (Cooper, 2008; Petryna, 2009; Sunder Rajan, 2005, 2006, 2007).

Based on empirical research conducted in two cities in India, this article examines stakeholders' (sponsors, CRO executives, investigators and ethics committee members)[1] perspectives on the enactment of clinical trials in a new legal environment that has facilitated the offshore outsourcing of multicenter, multinational clinical trials from the West to India. While much of the existing social science literature on clinical trials has critiqued stakeholders' active utilization of speculative neoliberal capitalism to promote the outsourcing of drug trials, stakeholders' voices have been largely omitted in the critique. There is a need to bring the stakeholders' voices to the fore to better appreciate multiple perspectives on the outsourcing of clinical trials from the West to the Third World. As such, I juxtapose the media hype, speculation, and also the perils of clinical trials, with the perspectives discursively articulated in interviews by Indian stakeholders closely involved in the clinical trials enterprise. In acknowledging the inherently problematic nature of outsourcing of clinical trials to developing countries, I argue that the practice of not prioritizing research on diseases that are most prevalent among communities from which subjects are recruited, especially when these diseases cause high morbidity and mortality (Benatar, 2007), demands a coordinated and sustained critique. I also argue that standard of care, adequate compensation, health equity and distributive justice are key issues that are at stake in the outsourcing of clinical trials to an emerging economy like India. I propose that the current narrow debate on the effects of outsourcing of clinical trials to developing countries needs to be broadened to address not only the potential dangers and exploitative practices, but also engage some fundamental concerns regarding growing health inequalities, issues of global justice, the social determinants of health, and human development (London, 2005).

Clinical trials in India: new directions

The conduct of pharmaceutical clinical trials in India is not new. What is new, however, is that in the last decade, the focus has shifted toward global competition and global, multicentric clinical trials (Bhatt, 2004; Sunder Rajan, 2005). The Indian government has introduced crucial legal measures to facilitate the process of making India a global player in biotechnology and clinical trials. One of the most concrete changes is the inclusion of Schedule Y in the Drugs and Cosmetics Act (1945) in 2005, which allows MPCs to conduct Phase 2, Phase 3, or Phase 4 trials without any "phase lag." Prior to the new law's introduction, if a phase 3 study had been completed elsewhere, only a phase 2 study was permitted in India. Thus, the Indian nation-state has been a key player in creating a legal environment to facilitate the acquisition of clinical trials that MPCs in the West would like to outsource, and making Indian bodies necessary for testing (Prasad, 2009; Srinivasan, 2009b). As in many other emerging economies, speculations in the media regarding the nature and magnitude of clinical trials in India abound. These speculations frustrate attempts to draw specific conclusions about the industry's size, the diseases and experimental therapies trialed in the country, and to determine how the Indian terrain compares with that of other 'nontraditional' economies where multi-sited trials are increasingly being conducted (see Cooper, 2008 for a comparative situation in China). In 2006, for example, less than 1% of the commercially sponsored global clinical trials were being conducted in India. In 2007, there were only 757 sites in India with a trial density of 0.7, as compared to 36,281 sites in the US, with a trial density of 120.3 (Thiers, Sinskey, & Berndt, 2008).

There are many reasons why India's clinical trials enterprise is marked by hype, speculation and uncertainty. First, India has recently emerged as one of the fastest growing economies in the world. Therefore, while MPCs and CROs are keen to tap into the growing economy for profit maximization, Indian stakeholders (physicians, corporate hospitals, pharmaceutical companies and for-profit institutional review boards) are equally keen to partake in the profits. Second, as a signatory to the World Trade Organization (WTO) in 1995, India opened up its economy to foreign investors on an unprecedented scale; it made efforts to adhere to the 'product patent regime' by 2005. This has allowed MPCs to conduct global trials in India, while also being guaranteed patent protection under the Trade-Related Intellectual Property Rights (TRIPS) agreement. Third, while India has successfully established itself as one of the leaders in the global IT industry, it is keen on becoming a global player in the biotech industry before the initiative is lost to other countries, particularly China, its rival, "where the government is playing an active role in encouraging foreign companies to conduct clinical trials" (Cooper, 2008: 84). Finally, neither international nor Indian stakeholders are certain about the true scope of the country's clinical trials industry.

Buoyed by initial optimism, the Indian government put its resources behind the industry by describing it as a "sunrise industry" deserving of aggressive support through a "tax holiday" (exemption from service tax on drug testing) based on the expectation that it will attract huge foreign investment funds, leading to jobs in the biopharma industry and national prestige (Bhatt, 2004; Prasad, 2009). "This is very much in keeping with a post-1990s ideology of economic liberalization that has been prominent in Indian elite and policy circles whose idea of India is as India Inc" (Sunder Rajan, 2006: 68). At the time, proponents claimed that "the Indian clinical research industry could attract US $1.5 billion of revenue from U.S. and European sponsors by 2010, creating a demand for more than 10,000 investigators, trained in good clinical practice (GCP) and supported by nearly 50,000 clinical research professionals" (Sahoo & Sawant 2007: 51). The Indian pharmaceutical industry, members of the Indian clinical trials industry, CROs, Confederation of Indian Industry, corporate hospitals and research investigators, in particular, are eager to become part of the lucrative multi-billion dollar global pharmaceutical industry. They have repeatedly called attention to the so-called "spillover" benefits of clinical trials through related business opportunities that could make India a major hub for global biotechnology research.

Scholars contend that MPCs and CROs are keen to conduct clinical trials in settings like India because they are able to complete the trials speedily and cheaply, mainly due to the lower salaries of physicians, nurses, study coordinators, payments to trial participants and insurance premiums (Glickman et al., 2009). Simultaneously, critics have pointed out that the clinical trials outsourced to India are going ethically awry because of inadequate regulatory

[1] Other stakeholders such as patients, family members, nurses, and community leaders were not included in the study.

oversight (Jeffery & Santhosh, 2009: 23; Nundy & Gulhati, 2005; Srinivasan, 2009a). Unknown is how these contentious issues figure into stakeholders' perspectives in the local context. What do stakeholders have to say about media reports that characterize the conduct of clinical trials in India as fast, cheap and getting out of control? What factors do they think have driven the outsourcing of drug trials to India? How has the new "friendly" legal environment facilitated the outsourcing of global clinical trials to India? What kinds of ethical issues emanate from their engagement in the clinical trials enterprise?

Methods

Following a content analysis of media clippings/newspaper articles pertaining to India, and reports of several workshops sponsored by the Government of India in collaboration with WHO and the Indian Council for Medical Research (ICMR) (2005–2006) to train stakeholders, I held discussions with the Drug Controller General of India (DCGI), senior officials from ICMR, and those representing the regulatory authorities in New Delhi. Simultaneously, I prepared a list of all known key stakeholders (all Indian nationals), including CRO executives, investigators and chairpersons of independent ethics committees/IRBs – 34 in Bangalore and 30 in Hyderabad, and contacted them via letters, email and phone calls, and in person, inviting them to participate in the study.

I interviewed sponsors (CEOs) of clinical trials, CRO executives and clinical trial managers, physician-investigators working in for-profit corporate hospitals and public hospitals, and members of ethics review committees, medico-legal experts, social workers and journalists. I chose Bangalore and Hyderabad as field sites for this study because these two cities are internationally known for their thriving information technology industry, CROs, and also because they have several active sites for "outsourced" clinical trials. Most of the stakeholders who were contacted willingly agreed to be interviewed (audio-recorded); a few of them declined to participate, stating that they were either traveling, preoccupied with other commitments or in the process of changing jobs. I interviewed a total of 42 stakeholders: 3 sponsors of clinical trials, 7 CRO executives, 19 investigators, 13 ethics committee members, including a retired Supreme Court Justice, a high court judge, a medico-legal expert, a medical social worker and a senior bureaucrat representing the regulatory authorities. In this article I have not addressed the patient-subjects' perspectives on the conduct of clinical trials: what leads them to participate in clinical trials? Do they experience coercion or feel that they are being exploited? Such questions provide a critical complement to the present analysis and will form the focus of a follow-up study. The present study was approved by the University of British Columbia's Behavioural Research Ethics Board (#B05-0565).

The allure of clinical trials as "science"

All CRO executives and investigators had advanced medical degrees. They had received at least some training and hands-on experience in conducting clinical trials either in the United States, United Kingdom, Canada or Australia. The majority had less than 5 years of experience in participating in multinational trials that were designed in compliance with the International Conference on Harmonisation Guideline for Good Clinical Practice (ICH-GCP). A close analysis of the narratives regarding their professional histories revealed that the majority of the CRO executives and investigators were attracted to the clinical trials endeavor either during their training abroad or in the course of their decision to "take on something exciting and challenging." Asked whether "money" or financial incentives is the main reason why individuals are attracted to the clinical trials enterprise, one prominent female CRO executive based in Bangalore told me:

> If money was the primary motivation, I wouldn't be working here in India. I get several lucrative job offers from the US and UK, but I've chosen to work in India because I'm passionate about what I do here. That being said, I do want to be paid well, for the excellent quality I bring into my work. I want to make a difference.

For this CRO executive, invoking a discourse of career fulfillment and a strong desire to make a difference in India and in the world is a means to counter claims that those who work in the clinical trials industry are drawn to it mainly to make money. Another 38-year-old female investigator based in Hyderabad who had trained as a dentist felt that her job was not as exciting as she had hoped, and therefore she decided to switch her career to conducting clinical trials:

> For me it was not about money, because I knew that had I pursued my career in dentistry I would have earned a lot more money…Here, I feel like I'm doing something worthwhile. I'm not saying that it's not for monetary gains or anything like that, but clinical research is beyond money, it's about bringing something good to the society, and being a part of this thing called science.

In this investigator's case, a claim is made that the decision to switch a career path was prompted by her desire to contribute to the advancement of science and not primarily for monetary gains. Another senior male physician at one of the prestigious corporate hospitals in Bangalore reflected on his decision to pursue a career in clinical trials:

> I spent 15 years in the UK, doing full time clinical trials. I returned to India nine years ago for family reasons. Here I'm involved in a prestigious trial on the long-term impact of diabetes on the heart… Apart from seeing my patients, I like to do these clinical trials because I feel like I'm doing something different, otherwise my work becomes monotonous.

While this physician saw clinical trials as a respite from the monotony of routine medical practice, nearly every CRO executive and investigator downplayed the importance of money as the primary motivating factor in their decision to get involved in clinical trials. Instead, they emphasized that they had "sacrificed opportunities to earn a lot of money" in favor of "bringing the benefits of medical advances to the patients," "making a difference," "service to humanity," "desire to contribute to advances in medical treatment," and the "pursuit of science" as something that is indubitably good for humanity. Such claims are significant because being a medical researcher is not considered as prestigious and as rewarding in monetary terms as being a successful physician or a surgeon. Interviewees claimed that being involved in the clinical trials enterprise was an indication of their humility, the sacrifice they had made in order to serve humanity, and their desire to pursue excellence, and not a strategic career move to "get rich quickly." Their statements present multiple iterations of the proposition that clinical trials are intrinsic to advances in medicine and saving lives. As Melinda Cooper (2008: 78) notes, in the medical community, it is widely held that "Human subject experimentation is the *sine qua non* of biomedical invention. There is no medical efficacy, no patentable biomedical innovation, and thus no innovation value without the participation of living bodies in clinical trials."

Unsurprisingly, all the CRO executives and investigators took umbrage at the manner in which the news media portrayed their work and the suggestion that they were venal, rapacious, profit hungry individuals. Interviewees repeatedly stated that they were proud of their work and wanted to contribute to the advancement of science in India and improve global health in general (for similar observations in the United States and Poland see Fisher, 2009; Martin, 2006; Petryna, 2009). One investigator at a private hospital in Hyderabad provided an illustrative example of how he had sought to bring the benefits of medical advances to his patients:

> As doctors we have to be very careful about doing clinical trials in India because if something goes wrong, the media will exaggerate everything and the hospital will throw us out of our jobs. Imagine the stress I experienced when I gave the first trial injection to one of my patients who was suffering from rheumatoid arthritis. On that day, I prayed to all the Indian gods because I was going to inject the drug in the body of a Muslim lady…so [being a Hindu] if anything had gone wrong, the media would have blamed me for it and I would be dead!

In the above discourse, risk taking is simultaneously presented as an indication of the physician's concern for and dispassionate commitment to the patient's welfare, especially at a time when the social context was marked by ongoing Muslim–Hindu conflicts, and his concern to keep his job.

Despite their claims to the contrary, there is substantial evidence to suggest that many CRO executives, investigators, and their employers do see the monetary potential in the clinical trials enterprise. The proliferation of CROs in India, estimated at 150; the increasing number of investigators who are trained in GCP guidelines, estimated at less than 1000; the frequent announcements and press releases of new licensing agreements and "joint ventures" with international pharmaceutical companies (e.g., Ecron-Acunova in Bangalore); and the evaluation of the clinical trials' potential in India in financial terms all, underscore the financial attraction inherent in the clinical enterprise. The globalization of clinical trials and their outsourcing to India are part of the "neoliberal confidence" that speculative global market capitalism has generated in India, especially among middle class urban dwellers that are increasingly looking offshore to market themselves.

Prime destination

In the context of the media reports and published research articles, respondents were asked whether India has become one of the prime destinations for outsourcing clinical trials, mainly from MPCs. They were also asked to comment on the implications of this shift for Indian stakeholders. A majority of the respondents expressed their skepticism regarding this claim, suggesting that this was media hype and not a reflection of the on-the-ground reality. One managing director of a CRO in Bangalore told me:

> When I first took this job, everyone was saying, "Oh yes, we are going to be a one billion dollar industry by 2010" but where is all the money that we have been talking about? At least I haven't seen it! I would like to do many more trials, but there are not many companies that are keen to come to India. It's not only the big MPCs that are interested in clinical trials, there are also many smaller biotech companies; they are the ones that need help.

The interviewee's concern regarding the exaggeration about the magnitude of the clinical trials enterprise in India is consistent with the estimated value of clinical trials in the country, which was less than $100 million at the time of interview—a far cry from the most optimistic projections of $1 billion a year industry. Several other interviewees, including members of the ethics committees, shared this skepticism. They emphasized that the "reality" was not in consonance with the media hype (both foreign and local) regarding the nature and magnitude of clinical trials in India.

All the stakeholders acknowledged that since 2005, there has been a significant increase in the number of clinical trials outsourced to India, albeit not enough to substantiate the hype and speculation. CRO executives insisted that it is not just the cost effectiveness and India's "treatment naïve" population that MPCs and CROs find attractive, but also the quality of work that Indian researchers are able to produce. The briefest review of the variegated literature on clinical trials in India echoes these interviewees' observations (cf. Bobba & Khan 2003; Maiti & Raghavendra, 2007; Nundy & Gulhati, 2005; Sunder Rajan, 2006).

Fast, cheap and pragmatic

Cost considerations are often cited as one of the main reasons why MPCs are outsourcing clinical trials to developing countries. On the issue of low cost as a factor in the outsourcing of clinical trials to India, one investigator explained:

> If you conduct a phase 1 clinical trial in the US, it will cost you around $25,000 per case. But if you do the same study in India, we can do it for less than $1000 per patient. So the best thing about India is the low cost, and the treatment cost and consultant cost; everything is very accessible because of the high patient pool.

Another highly experienced CEO of one of the largest CROs in Bangalore framed his response more broadly:

> In the West it is becoming increasingly difficult to motivate investigators to conduct clinical trials because they have to confront various legal issues. In contrast, in India, where the clinical trials enterprise is still emerging, investigators think "Oh we are doing some world class clinical research" when in fact they are basically doing operational protocol that is developed by pharmaceutical companies in the West, and they are implementing that protocol in India. So we are a country of "enthusiastic investigators."

Yet another highly experienced physician-investigator who was trained in Scotland, articulated his thoughts on the reason why MPCs are increasingly conducting clinical trials in India by emphasizing the science as well as the pragmatism involved in their decisions:

> Extrapolating the data from trials conducted only in the West is becoming increasingly difficult. The pharmacokinetics or pharmacodynamics in a Caucasian individual may be different as compared to Indians or Chinese or Sri Lankans or Pakistanis due to genetic differences and diet. If pharmaceutical companies want to sell their drugs to these populations, they need to do multicentric clinical trials before they start using these drugs directly among patients who are non-White.

Most of the stakeholders, however, disagreed with the suggestion that India represents a "treatment naïve population" that pharmaceutical companies are keen to recruit as trial subjects. As one prominent CRO executive in Bangalore said to me:

> Who says Indians are a treatment naïve population (TNP)?! Here in India we can go to the pharmacy across the street and say "I have a cold…" and the pharmacist will happily sell you a high level antibiotic over the counter. So if you are looking for infections, then there is no TNP, but if you are talking about endocrinology and certain types of cancers, and some of the cardiovascular conditions, yes, we are a TNP, but as a population, we are not really TNP because for years we have been medicating ourselves with antibiotics and other drugs bought from retail pharmacies.

Given that several medical anthropologists have documented the ease with which people in urban India are able to buy antibiotics and other prescription-only drugs over the counter, there is some merit in the statement that India's population is not as treatment-naïve in terms of exposure to biopharmaceutical drugs as it is made out to be, particularly in urban areas where most of the trials are conducted (Kamat & Nichter, 1998). Still, the vast majority of the people in India are not as treatment-saturated as the people in the West, where "the average American is prescribed and purchases somewhere between nine and thirteen prescription-only drugs per year" (Dumit, 2012: 2).

In 2007, except one investigator who was conducting a phase 1 trial in collaboration with a Canadian university, all the others were involved in phase 2 and phase 3, and mostly phase 4 post-marketing studies, and bioavailability and bioequivalence studies for generics and "me-too" drugs already marketed in India. Thus, while most of the stakeholders acknowledged that India has become an important destination for the conduct of global clinical trials, they were quick to add that India's contribution to the total number of clinical trials across the globe was negligible, and that the country had a long way to go before becoming an important player in the global clinical trials market. Yet, the overall tone in the majority of the interviewees' responses was one of growing, but cautious, optimism, as exemplified by some speculative claims made in 2007 that by 2010, 10%–15% of the global clinical trials would be conducted in India.

Informed consent, ethics and distributive justice

Ethically legitimate informed consent is generally understood to be the *sine qua non* of human experimental research (Benatar, 2007; Fisher, 2009; Sariola & Simpson, 2011). For informed consent to be ethically legitimate, there should be no "therapeutic misconception" (Sankar, 2004). In other words, the patient-subject must understand that the procedure or medications used in the trial are experimental, and may not have a therapeutic purpose. The problem of obtaining ethically legitimate informed consent (verbally or in writing), and therapeutic misconception, becomes especially acute in resource-poor settings because of conceptual, linguistic, cultural and other barriers (Molyneux & Geissler, 2008; Molyneux, Peshu, & Marsh, 2004). While some critics have argued that in conducting research with human subjects in developing countries, the potential subjects are likely to be exploited because they may lack the necessary knowledge to make a reasoned decision—to participate or not to participate in a trial, others have argued that "being poor and having few health care options does not make a person stupid or unable to understand explanations of clinical research" (Hawkins & Emanuel, 2008: 8). Still, in some cases, the primary investigator may not provide information regarding potential risks in the subject's own language, leading to potential "misunderstanding" and exploitation – a diffuse and unclear ethical concept. However, as Fisher's (2009) study in southwestern United States revealed, the vast majority of the potential subjects she interviewed were generally uninterested in the information contained in consent forms. This is because most human subjects decide to participate in clinical trials in advance of the informed consent process. "In other words, the details contained in consent forms become irrelevant to patient-subjects who know they want to participate regardless of any risks, benefits, or inconvenience" (Fisher, 2009: 166; see also Abadie, 2010).

When posed with questions about the informed consent process, physician-investigators and ethics committee members provided anecdotes to illustrate the level of care and concern built into the process. They emphasized that subjects are clearly told that their participation is voluntary and they have the right not to participate in the trial, and/or choose to withdraw from the trial at any time. In describing in detail the care that goes into communicating effectively with the subjects, one site manager in Bangalore explained:

> We give our subjects complete information, and if the subject wants a family member to be part of the discussion, we welcome that. And after explaining the informed consent, the subject is given the option to go back home and think about it, and consult his family physician before making the decision whether to sign the form or not. If the subject has any doubts, we actually encourage him to ask us questions. When our subjects ask questions we try to give them the best answer, according to the current scientific literature; usually they take time and come back and sign the consent form. If they don't want to, they don't come back.

Nearly every investigator and ethics committee member fervently denied that it is usually the poor, unemployed working-class and uneducated people who are lured by pre-trial financial inducements or the promise of free treatment into participating in clinical trials, and ultimately treated as human "guinea pigs" by MPCs and CROs. The CEO of a well-known CRO in Bangalore, who had returned to India after ten years in the United States doing clinical research, forcefully articulated:

> My clients [sponsors], who are mostly from the West, bring with them the same level of diligence that they use in the West. No western client is going to say to the FDA "Hey, I did this trial in America with 50 clients at standard A, and I did this trial in India at 1/10 that standard." That simply won't work because they *have* to maintain the same standards. It's a self-regulatory process. There are no cowboys here. There are several in-built quality standards to regulate the clinical trials process… In India we are essentially testing the drugs that we know are safe; we need 10,000 patients; we can mobilize 20,000 patients in India… we need to do the trial to satisfy the FDA, for numbers, but over the next 5 years or so, the paradigm might change, people might die, issues might crop up, but right now, we are working in a safe environment.

According to this narrator, there is no ethical variability in India; investigators are currently working in a safe environment, with safe drugs and with the same level of diligence that investigators use in the West. However, the narrator also acknowledges that the future is uncertain and might prove to be potentially deadly.

Another senior female investigator at a large private hospital in Hyderabad who delinked the participants' poverty status from their willingness to participate in the trials, asserted:

> We have come across many patients who are poor and illiterate, but they are quite intelligent… They are the ones who ask us very decisive questions, whether to participate in something or

not, whether to get the procedure done or not, and then they give a clear-cut answer. So just because they are poor or illiterate does not automatically mean that they will agree to do whatever we tell them to do.

Contrary to the well-documented paternalistic notions of the doctor–patient relationships in the Indian sub-continent (Sariola & Simpson, 2011), the above investigator's disposition toward trial participants was seemingly anti-paternalistic. She depicted participants as individualistic, autonomous and rational individuals who exercised agency when making a decision whether to participate in a trial or not, regardless of their economic status. While investigators may discursively position themselves as not being paternalistic toward their patient-subjects, it is possible that in practice they may behave quite differently. However, determining the validity of such claims, in practice, is beyond the scope of this paper.

Insofar as the profile of patients-subjects who participate in clinical trials is concerned, one senior female investigator who was coordinating four major trials at a well-known corporate hospital in Hyderabad dismissed the claim that clinical trials in India are mainly conducted on poor patients:

> At this [corporate] hospital, the patients who enroll in clinical trials are neither upper class, nor very poor, most of them are middle class. We don't really get patients from both ends of the spectrum. Most of them are very aware that they have their rights; they are very conscious of their rights, and we also alert them to the rights. Some patients have refused to participate in our trials after taking the consent form to their family members. They call back to say that they have discussed the matter with someone, and that they have decided not to participate.

While the ethics committee cannot police every move an investigator makes, and dictate terms to him/her on the conduct of the research, it is widely acknowledged that the signatures on paper consent forms do not necessarily mean that subjects are well informed about the procedures and risks involved. The language of informed consent is complex, multilayered and prone to "misunderstanding" even among relatively affluent participants. As critics have pointed out, the subject's misconception often hinges on the belief that therapy is being provided, whereas the outcome of the clinical trials may have little bearing on an individual. Importantly, as Prasad (2009: 18) has noted, the "ethicality of drug trials cannot be narrowly focused around the issue of informed consent. The problematic of how to make the people on whom drugs are being tested receive juridical, social and economic protection against unethical exploitation has to be seen in a broader context."

Several interviewees acknowledged that the majority of the drugs tested in India as part of the global clinical trials do not address the real health needs of the vast majority of India's population. However, only few of them elaborated the point and fewer still spoke of the socio-political context of the conduct of clinical trials outsourced to India. One of the most senior investigators from a large public hospital in Hyderabad who participated in the study forcefully articulated his thoughts in the following words:

> Unfortunately, there is no correlation between our disease burden and the kinds of clinical trials we conduct in this country. The disease burden is mostly infectious diseases and malnutrition…the kinds of clinical trials that are being conducted in this country will not help the large segment of the population, which is suffering from both a disease burden and an economic burden...In a country like India, rather than testing new drugs, it is important to look into the deliverability of the existing drugs without compromising the efficacy of the delivery system…our research is concentrated on a small segment of the population; it's not bringing any benefits to the millions of poor people in the country.

On a similar note, the medical director of a large biotech company in Bangalore acknowledged:

> Currently, our company has about 200 investigative sites all over India, but to date we have not received a single request to do a trial for malaria or any of the tropical diseases. Nobody wants to develop drugs for these diseases because commercially it is not a very attractive proposition even though millions of people are suffering and dying from these diseases. All the drug development is taking place in diabetes, heart problems and cancer; this actually mirrors the disease profile in the West, which is now very similar to what we find in urban India.

The above comments from two senior people directly involved in the conduct of clinical trials in India, corroborate the discourse generated by critics who have equated the offshore outsourcing of clinical trials with "Third World dumping" and the broader globalization of clinical trials in general as a form of new colonialism (Nundy & Gulhati, 2005). Central to such comments is the concern that the conduct of clinical trials in India stands to benefit wealthy people in the West, and they are irrelevant to the health needs of the vast majority of Indians. These comments question the validity of the dominant self-sanctification narratives among the majority of the stakeholders, especially CRO executives and investigators, who claim that clinical trials constitute a "social good" to alleviate human ills and not a "social evil," and that their participation in the clinical trials enterprise represents their passion for science and excellence, rather than the pursuit of money.

Discussion

The Indian nation-state has played a key role in facilitating the conduct of global clinical trials in India by introducing crucial legal measures. In consonance with an ethos of neoliberal capitalism, the Indian nation-state has strived to create the necessary conditions "where a vision of the future is sold to create the conditions of possibility of the present" (Sunder Rajan, 2006: 136). As Sunder Rajan (2007: 75–76) has noted "the clinical-research landscape in India cannot be reduced to the neo-colonial exploitation of the local population as "guinea pigs" by rapacious multinational interests, where cutting corners is the norm and ethics easily sacrificed."

The conduct of global clinical trials in India is marked by hype and speculations of significant proportions, and the "truth" about the Indian drug companies, sponsors, CROs, investigative sites, and investigators lies somewhere in between credibility and incredibility. For one, most of the big MPCs (e.g., Astra Zeneca, Glaxo Smith Kline, Pfizer) conducting drug trials in India have had a long presence in India's complex pharmaceutical sector. These companies have been among the first to take advantage of the new regulatory environment, which is supportive of global clinical trials. While India is certainly emerging as an important site for the conduct of global clinical trials, with projected annual growth rates of up to 80%, "the anticipated surge in trial contracts to India remains speculative" (Sunder Rajan, 2007: 72). Claims such as India is "the most preferred location for contract pharma research and development" and that "nearly 20% of all global clinical trials will be conducted in India by 2010" (Maiti & Raghavendra, 2007) must be treated with skepticism because they lack credibility in the face of existing data on the relatively small number of investigators (less

than 800 compared to the 1000s in the US alone and 200,000 world-wide) who have been trained in GCP guidelines. They are also belied by the relatively small number of research centers that meet the criteria for the conduct of world-class clinical trials (about 800 or less than 1% of the total number of active trial sites in the world) and the generally poor presence and functioning of IRBs and ethics committees across the country (Jesani, 2009). In 2008, according to the Drugs Controller General of India (DCGI), there were 582 (registered) clinical trials being conducted in India, of which 72% were carried out by the pharmaceutical industry (Srinivasan, 2009a, 2009b).

Notwithstanding some of the indefensible, documented accounts of scandalous clinical trials that have resulted in serious harm and even death to unsuspecting subjects in India (cf. Maiti & Raghavendra, 2007; Nundy & Gulhati, 2005; Shah, 2006), far more rigorous empirical research is needed to demonstrate that "Indians are being treated as guinea pigs" more than subjects from elsewhere in the world, including China and the United States, where for many uninsured people, enrolling in a clinical trial is often the only way of gaining access to expensive medical treatment (cf. Abadie, 2010; Fisher, 2009; Shuchman, 2007; Srinivasan, 2009a, 2009b). While concerns regarding exploitation constitute an essential element of the discourse on the problems associated with globalization and outsourcing in general, anecdotal scandals and second-hand reports have been commonly equated with self-evident truth in journalistic accounts, and uncritically reproduced in subsequent publications. Clearly, many indigenous pharmaceutical companies are also involved in clinical trials in India and the Indian government has a regulatory framework in place that is meant to protect the rights of patients and subjects who participate in clinical trials. It has enacted measures to ensure that trials are conducted according to international ethical and methodological guidelines, and it has also set up a Clinical Trial Registry India (CTRI) in collaboration with the WHO. Moreover, the number of people who experience harm or even die as a result of their voluntary or involuntary participation in clinical trials needs to be put into context, especially in India where every year hundreds of thousands of people, mostly children, suffer and die due to avoidable causes, including lack of access to basic health care, safe drinking water, nutritious food and timely vaccinations.

None of this is to suggest that the dangers of clinical trials are 'trivial' because India has bigger issues of poverty, structural inequality and injustice to deal with and therefore there is no need for increased accountability and transparency in the conduct of global clinical trials. As one of the CRO executives who asserted that currently "there are no cowboys" in India's clinical trials industry, acknowledged that the future of clinical trials is unpredictable, and might prove to be potentially deadly for some participants. Indeed, there is a dire need to ensure that adequate safeguards are in place to protect the health and wellbeing of *every* trial participant, including healthy volunteers, and the country in general, including insurance and appropriate compensation of subjects for whom the drugs under study have serious adverse effects. There is a need to strengthen national and local oversight, and increase vigilance to ensure that only investigators who are trained in GCP are allowed to conduct trials at accredited investigative sites, and that itinerant investigators are prevented from getting involved in clinical trials. To that end, since 2005, the Central Drugs Standard Control Organisation (CDSCO), Government of India in collaboration with WHO-India Country Office, has sponsored a series of national workshops on GCP and regulatory requirements for clinical trials in India. Indian lawmakers (including the Supreme Court of India) in consultation with NGOs have been making efforts to prevent unethical and illegal clinical trials in the country and to ensure that sponsors of trials provide adequate insurance coverage and compensation to patient-subjects who suffer from serious adverse effects or die while participating in the trials. As Sunder Rajan (2007: 74) has noted, "India is the only country in the world where the violation of good clinical practice is a criminal rather than a civil offense."

An important issue at stake in regard to clinical trials outsourced to India is that of equity in the context of the World Medical Association Declaration of Helsinki (2013), which clearly states that "medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community..." Unfortunately, the overwhelming majority of the drugs for the treatment of common diseases are sold in the wealthiest countries, and, as in the West, in the Indian context as well, there is no guarantee that an experimental drug will necessarily be made available for those who participated in its trial after its approval, at an affordable cost (see Fisher, 2009; Glickman et al., 2009; Sunder Rajan, 2007).

When pressed to address this concern, the majority of the investigators and ethics committee members in the present study skirted the question of whether they were able to ensure that their trial subjects have continued access to the drugs tested on their bodies. Most of them regarded it as a business decision for the pharmaceutical company or the CRO to make—that it was beyond the investigator's and ethics committees' purview to ensure equity of that nature. Further ethnographic research is needed, with a focus on patients-subjects, including healthy volunteers, who participate in the trials, to document not only their socio-economic profiles and aspects of their consent and willingness to participate in the trials, but also their perspective on the question of equity—what motivates them? Do they see their participation as deriving from a sense of altruism, a moral imperative? What do they expect in return for offering their bodies to test investigational drugs or procedures? Such a study will demonstrate whether it is primarily the disadvantaged, vulnerable or marginalized individuals whose bodies are being exploited to test investigational medications that will ultimately benefit the socially and economically well-off people with certain disease profiles, particularly in the West.

Conclusion

In an era of international treaties like WTO, GATT and TRIPS, and the rapid advances made in the field of medicine, genomics, proteomics, and vaccines against life-threatening infectious diseases, the Indian nation-state is unlikely to restrict the conduct of global clinical trials on its citizens. Nonetheless, it is likely to implement measures to strengthen the local and national oversight to safeguard the patient-subjects' wellbeing. As with many critics, including some of the stakeholders interviewed for this study, I am concerned about the purpose for which local bodies are used—to experiment with a drug that may not be of relevance to the health of the subjects and their larger communities. Clinical trials conducted in the Indian context should address diseases that are endemic to the country such as malaria, dengue, leishmaniasis and drug-resistant tuberculosis, along the lines of recent initiatives by WHO, Wellcome Trust and CDC, and with reasonable standard of care. I am doubtful whether in the current neoliberal medical terrain, MPCs and India's corporate hospitals would undertake such 'socially oriented' trials even as part of their social responsibility.

The current discursive emphasis on the hype, speculation and dangers surrounding the offshore outsourcing of clinical trials to emerging economies like India has its limitations, in that it potentially distracts stakeholders, regulatory authorities and policy makers from attending to 'the real issues' of vast health inequalities. Clearly, there are no foolproof mechanisms to prevent

unacceptable practices in the conduct of clinical trials, even in the West where "payment to subjects has escalated, creating "shadow economies" in cities throughout North America and elsewhere" (see Elliott & Abadie, 2008: 2316; Glickman et al., 2009: 820). In the United States, the pharmaceutical industry continues to profit from disenfranchised *ready-to-consent* populations who do not have better alternatives than participation in clinical trials as a means to access treatment and also some income (Fisher, 2009). Therefore overemphasizing the particularities of the dangers of clinical trials in developing countries can dampen our analysis of key issues, which come under the rubric of ethics, distributive justice and human rights. Ultimately, clinical trials represent only one facet of global health; most of the health problems in the developing countries can be addressed with effective interventions that already exist.

In sum, the debate on the nature and scope of clinical trials in poor and developing countries needs to be broadened to address the social determinants of health, and global justice (London, 2005). As Benatar (2002: 1136) has argued: "If it is insisted that the best standard drug regimen must be used …Why not include the best standard medical, nursing and hospital facilities, and follow up care?" Only in addressing some fundamental questions about equity and social justice as they relate to the conduct of global clinical trials in developing countries, can we expect to create a more balanced global health research agenda that addresses the needs of industrialized countries and the disease burden of the majority of the poor (Petryna, 2009: 96). To that end, this article is an attempt to reconfigure the narrow, discursive focus, away from the hype and speculation surrounding clinical trials, and to consider broader issues that are fundamental to human development – socio-political global inequities and global justice.

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