



Contents lists available at ScienceDirect

Contemporary Clinical Trials Communications

journal homepage: www.elsevier.com/locate/conctc

The role of corruption and unethical behaviour in precluding the placement of industry sponsored clinical trials in sub-Saharan Africa: Stakeholder views

Efe Egharevba^{*}, Jacqueline Atkinson

Glasgow University, Institute of Health & Wellbeing, 1 Lilybank Gardens, Glasgow, G12 8RZ, United Kingdom

ARTICLE INFO

Article history:

Received 27 December 2015

Received in revised form

23 April 2016

Accepted 26 April 2016

Available online 30 April 2016

Keywords:

Clinical trials

Ethics

Sub-Saharan Africa

Corruption

Pharmaceutical

ABSTRACT

Clinical trials still represent the gold standard in testing the safety and efficacy of new and existing treatments. However, developing regions including sub-Saharan Africa remain underrepresented in pharmaceutical industry sponsored trials for a number of reasons including fear of corruption and unethical behaviour. This fear exists both on the part of pharmaceutical companies, and investigators carrying out research in the region. The objective of this research was to understand the ethical considerations associated with the conduct of pharmaceutical industry sponsored clinical trials in sub-Saharan Africa.

Corruption was identified as a significant issue by a number of stakeholders who participated in semi-structured interviews and completed questionnaires. Additionally, fear of being perceived as corrupt or unethical even when conducting ethically sound research was raised as a concern. Thus corruption, whether actual or perceived, is one of a number of issues which have precluded the placement of a greater number of pharmaceutical sponsored clinical trials in this region.

More discussion around corruption with all relevant stakeholders is required in order for progress to be made and to enable greater involvement of sub-Saharan African countries in the conduct of industry sponsored clinical trials.

© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Background

1.1. Introduction

Clinical trials are the mainstay in new drug development processes, as well as for product license extensions for existing therapies [1]. Despite the fact that developing countries are usually under-represented in research due to a lack of commercial viability and trained researchers, Africa is emerging as an important destination for clinical trials [2]. Sub-Saharan Africa has largely been excluded from industry sponsored clinical trials for a number of reasons. Whilst many of these reasons are related to commercial and practical concerns, there are also a number of ethical issues which have precluded the placement of industry sponsored research in this region to date. These issues include concerns around the appropriate mechanisms for delivering informed

consent, fear of being considered exploitative particularly with the conduct of randomised placebo-controlled studies, as well as other considerations around continued access to medicines once the trials are complete [3,4].

The use of placebo in clinical trials is an arguably contentious benefit of conducting research in developing countries. On one side placebo-controlled trials are easier to implement in developing countries due to less availability of standard of care treatments and a greater number of treatment naïve patients and thus the ability to produce less ambiguous data which might reduce the time it takes to approve a new drug [5]. However, there are obvious ethical concerns with conducting studies in developing countries which would not be approved in developed countries and it could be argued that the conduct of such research would only be appropriate if reduced timelines to drug availability would be relevant for participating subjects. This is an important point to consider as there are a number of examples of drugs which have not been marketed in the developing countries in which they were tested. Limaye et al. assessed the relationship between the number of clinical trials conducted and the number of new drug approvals

^{*} Corresponding author.

E-mail address: efe.egharevba@googlemail.com (E. Egharevba).

(NDAs) issued in India and South Africa and described a gap between the number of studies conducted and marketed availability of these new drugs in these two developing countries. The study concluded that of trials conducted with sites in India and South Africa, approximately 40% and 60% respectively led to a market authorisation in the EU or US without an approval in India or South Africa [6]. Homedes & Ugalde discuss similar issues in Latin American countries where sponsor organisations have conducted pivotal clinical trials and either failed to subsequently market the drug in that country or have marketed the drug at a prohibitively high cost, precluding access to treatment for many patients in that country [7].

Another significant concern on the part of pharmaceutical companies, however, is that of corruption. The African Development Bank estimate that corruption costs the continent of Africa around \$148 billion per year [8]. In comparison, developed countries gave \$22.5 billion in aid to sub-Saharan Africa in the year 2008 [9]. These concerns around corruption and the associated implications for patient safety, data integrity, and the industry's reputation have all played some role in preventing pharmaceutical companies from placing more clinical trial work in the region, despite Africa's strengthening healthcare systems and growing economies. There are equally, however, concerns around corrupt or unethical industry practices on the part of healthcare professionals based in the region. These concerns are particularly relevant for countries where there are historical cases of pharmaceutical corruption. For example, in Nigeria where the impact of the meningococcal meningitis outbreak and subsequent trial of trovafloxacin by Pfizer [10] in 1996 during which 11 children died and many more were left disabled after receiving the experimental treatment trovafloxacin (Trovan) received much attention [11]. More recent examples of unethical behaviour in the conduct of clinical trials in developing countries include that of a trial which ran from 1997 to 2003 in Uganda sponsored by Boehringer Ingelheim who were testing nevirapine for the treatment of HIV. During this trial investigators failed to obtain patients' consent regarding changes in the experimental design and administered incorrect doses of the drug [12]. More recently the DART trial conducted in Uganda, Zimbabwe and the Ivory Coast which compared structured treatment interruption (STI) with continuous therapy (CT) in patients receiving anti-retroviral therapy for the treatment of HIV highlighted unethical behaviour wherein patients who were on the STI arm of the trial were not switched back to the CT arm of the trial, despite the Data Safety Monitoring Board (DSMB) finding that treatment interruption was associated with a higher risk of disease [12].

Clinical trials can potentially play an important role in helping to contribute to the development of a country's healthcare system in a number of ways including raising research standards, exposing physicians to new diagnosis and treatment modalities and bringing health improvements as well as badly needed investment [13]. Angwenyi and colleagues describe the benefits of investment from clinical trials in studies that were conducted in Ghana, Kenya and Burkina Faso, summarising how all three countries benefited from upgrades and renovations to the physical infrastructure, additional medical supplies and medical equipment [14]. It is also important, however, to note that despite the potential collateral benefits of clinical trials, the benefit of faster access to drugs may not always be relevant as a recent paper by Hay et al. reported that only 10.4% of drugs entering into phase I clinical trials are approved by the US Food & Drug Association [15]. However, in order for sub-Saharan Africa to increase its footprint in the clinical trial space, the topic of corruption, whether actual or perceived, and its associated impact on data quality, patient safety and pharmaceutical engagement in the region needs to be further explored, understood

and addressed. Whilst corruption represents just one of a number of challenges related to conducting trials in the region, it represents arguably one of the most significant and therefore needs to be addressed before other more practical topics can be discussed.

1.2. Objectives

This is part of a larger study of stakeholders' views on the benefit, if any, to the population and the ethical implications of conducting industry sponsored clinical research in the sub-Saharan region of Africa.

This article presents those research findings which are associated specifically with corruption and unethical behaviour.

2. Methods

The study involved two parts. Since there is little research on views of stakeholders interviews were conducted to explore issues. These were then used to develop a questionnaire.

2.1. Choice of countries

For the interviews Nigeria and Ghana were chosen as the two sub-Saharan countries from which health care professionals would be contacted due to their size, economic status, and relative stability at the time the research was planned. Existing links to health care professionals also existed Pharma respondents were in Europe (UK & Switzerland) and South Africa. For the questionnaire study the countries targeted for pharma respondents were the UK, US, and Switzerland however through snowballing questionnaires from pharma were also completed in France and Spain. For the healthcare professional group the countries in Africa were expanded to include were expanded to include South Africa however through snowballing respondents from Uganda, Egypt, and Liberia also completed the questionnaire.

2.2. Chronic versus infectious

The reasons chronic diseases were chosen are twofold; firstly, there is evidence within the literature which illustrates increasing levels of chronic disease in the region [15,16]. Secondly, infectious disease rates are higher in developing countries (and therefore unbalanced when compared to the disease profile of Western countries). In order to compare the issues related specifically to the conduct of trials in a like for like manner, focusing on chronic disease allows comparison of patients in both the developed and developing world.

2.3. Identifying stakeholders

Two groups of stakeholders were involved; industry professionals and health care professionals in the relevant countries. Stakeholders were identified from a variety of sources including literature reviews and internet searches. For healthcare professionals this was largely done through academic journal review contributions. No specific journals were targeted however search efforts focused on contributors to articles related to clinical trials conducted in patients in Ghana and Nigeria. Healthcare advocacy and government websites were used to identify potential government respondents. Some stakeholders from the pharmaceutical group were identified through existing professional links as well as via snowballing techniques. Although not specifically targeted, snowballing also led to the inclusion of a Non-Government Organisation (NGO) respondent with experience in clinical trials.

For the interviews, senior pharmaceutical representatives

(Associate Director level or above) were targeted as they were felt to be most influential on the direction of their respective organisations and therefore have greater influence on the direction of the industry as a whole.

For the questionnaire, respondents from the same group of stakeholders were contacted, although the requirement for pharma respondents to be senior was relaxed. This criterion was relaxed as it was felt that senior staff members were more likely to influence the direction of their respective companies and therefore have a greater influence of the direction of the industry as a whole. As the issues which senior pharmaceutical representatives believed to be most relevant had already been elucidated during the interviews, the aim of the questionnaire was to explore those themes in greater detail. Additionally, relaxing the criterion allowed for a greater number of respondents from various functional areas to be identified and approached.

2.4. Interviews

A semi-structured interview was developed based on issues raised in academic papers, industry press and past informal conversations with colleagues. It was piloted with a few industry colleagues.

2.4.1. Contacting stakeholders

Potential interviewees were contacted by email with a copy of the Research Participant Letter of Invitation which outlined the study in more detail and explained what would be required in the event they chose to participate in the study.

2.4.2. Interview conduct

Due to the distances involved semi-structured interviews were conducted either by telephone, Skype, or face to face and recorded using a Dictaphone. Each interviewee was informed that their responses would be recorded and transcribed and asked to provide informed consent before recording began. Interviewees were questioned about the ethical issues that they associated with the conduct of clinical trials in sub-Saharan Africa. All interviews were conducted in English.

A copy of the interview schedule can be found in [Appendix I](#).

2.5. Questionnaires

A questionnaire was developed created using the thematic outputs from the interviews, resulting in 21 questions. It was piloted with several pharmaceutical industry colleagues and minor amendments were made following feedback. Changes were mostly typographical and grammatical. Some changes were required additional language to be added for clarity. The questionnaire could be reached online and was hosted by Survey Monkey.

A copy of the questionnaire can be found in [Appendix II](#).

2.5.1. Contacting stakeholders

Potential respondents were contacted by email. The email contained a short outline of the study and included an ethics approved plain language statement which contained more detailed background information as well as information related to what would be required if they decided to participate in the study. The email also contained a direct link to the questionnaire.

Consent was taken as implied by the return of the questionnaire.

2.6. Analysis

2.6.1. Interviews

The data from the audio recordings were analysed using

thematic analysis facilitated by the use of a qualitative data analysis (QDA) computer software package, Nvivo[®]. The resulting codes were sorted into themes. In some instances codes fell into multiple theme categories. Using the codes that fell under each of the initially identified overarching categories, a number of more detailed themes were derived. The initial coding was performed by EE and then reviewed by JA and a colleague. There were no discrepancies identified. Only the themes related to corruption are considered in this paper.

2.6.2. Questionnaires

Outputs from the survey software were transferred into Nvivo[®] and thematic analysis was performed on any free response comments which were submitted alongside questions. Basic calculations were performed on the numeric outputs of each question for the purpose of descriptive statistics.

2.7. Ethical approval

Ethical approval for the study was given by University of Glasgow College of Medical, Veterinary and Life Sciences Research Ethics Committee.

3. Results

Only results relating to corruption and/or unethical behaviour are presented here.

3.1. Interviews

3.1.1. Respondents

Ninety-eight emails were sent out to various stakeholders from whom twenty-two responses (22%) were received. After further contact sixteen (16%) interviews were conducted. A breakdown of the number of planned and actual interviewees can be found in [Table 1](#). High level information of each respondent can be found in [Table 2](#).

Most of the interviewees fell into one of two groups; Health Care Professionals based in Ghana or Nigeria, or pharmaceutical professionals. Only one government respondent was involved in the interviews.

3.1.1.1. Pharma respondents. At the time of interview, all respondents in the pharma stakeholder group worked at manager level or above and had roles in the research and development arm of their respective organisation. Most ($n = 8$ or 89%) held a position equivalent to Associate Director or above. One respondent, whilst currently not working for a pharmaceutical organisation, had done so previously and at the time of interview was working for an NGO which manages and develops a research and development portfolio and was therefore deemed suitable for interviewing.

3.1.1.2. HCP respondents. Five out of the six respondents (83%) falling under this stakeholder category were physicians. The one respondent who was not a physician was a patient facing member of clinic staff (i.e. a member of staff who is not a medic but still has direct interaction with patients). This persons responsibilities were to perform basic tasks associated with collecting patient samples for research trial participants. All were based in either Ghana or Nigeria.

3.1.1.3. Government/policy maker respondents. Despite contacting six individuals within this particular stakeholder group, only one responded and was interviewed. The interviewee was based in Ghana and was working for the country's Food and Drugs Board.

Table 1
Number of planned and actual interviewees.

Stakeholder group	Number from Nigeria (planned)	Number from Nigeria (Actual)	Number from Ghana (planned)	Number from Ghana (Actual)	Total (planned)	Total (Actual)
Government representatives	2	0	2	1	4	1
Local HCP's	3	3	3	3	6	6
Patient advocacy group representatives	2	0	2	0	4	0
Pharmaceutical industry representatives	–	–	–	–	10	9
Total					24	16

Table 2
High level overview of interview participants.

Unique identifier	Role	Years in current role	Clinical trial experience?	Method of interview	Location
HCPN_1	Physician/Clinical Pharmacologist	10+	Yes – as Research Physician	Skype	Nigeria
HCPN_2	Radiologist	30+	Yes – as Research Physician	Telephone	Nigeria
HCPN_3	Surgeon	15+	No	Telephone	Nigeria
HCPG_1	Radiographer	20+	Yes	Telephone	Ghana
HCPG_2	Research Fellow	15+	Yes	Telephone	Ghana
HCPG_3	Clinical Oncologist	15+	Yes	Telephone	Ghana
REG_1	Food & Drugs Board	10+	Yes – Regulatory	Telephone	Ghana
PHARM_1	CEO Strategy & Business Development	20+	Yes – Pharma	Face to face	UK
PHARM_2	Operational Leader [Pharmaceutical Company]	10+	Yes – Pharma	Face to face	UK
PHARM_3	Non-executive Chairman, [Clinical Research Organisation]	20+	Yes – Pharma	Skype	South Africa
PHARM_4	Operational Leader, [Pharmaceutical Company]	20+	Yes – Pharma	Face to face	UK
PHARMA_5	Executive Director, Operations, [Pharmaceutical Company]	5+	Yes – Pharma	Face to face	UK
PHARMA_6	Medical Research Manager, [Pharmaceutical Company]	15+	Yes – Pharma	Telephone	UK
PHARMA_7	Interim Clinical Director, [Pharmaceutical Company]	15+	Yes – Pharma	Telephone	UK
PHARMA_8	Medical Director, [Pharmaceutical Company]	20+	Yes – Pharma	Telephone	UK
PHARMA_9	Head of Translational Medicine, [Non-Profit Foundation]	15+	Yes – Pharma	Telephone	Switzerland

3.1.2. Themes

Corruption was identified as a significant barrier to the conduct of clinical trials in sub-Saharan Africa across stakeholder groups. The types of corruption that stakeholders were concerned about differed based on which stakeholder group the interviewee fell into.

3.1.2.1. Perception of corruption. Pharmaceutical industry stakeholder members were concerned about not just the corruption which could occur during the set-up and conduct of the trial but also held fears around perception – in particular being perceived as corrupt and/or exploitive even when conducting ethically sound research.

I know there's been a number of countries who have ... very high profile criticism for having been accused of exploiting populations. Some of this has been well grounded but it has caused a lot of concern about reputation risk about being seen to be exploiting a population who may be considered vulnerable based on their background or education. And the reputational risk is so high that it's actually not worth taking." (PHARM_8)

"Because you do a study where there may ... not be ethical concerns but ethical issues which are addressed ... the fear is that they'll just get ... be spun out of context which wouldn't happen in a European or North American or even an Asian environment. And so there's this fear of reputational damage by doing legitimate clinical research in a developing country such as many of those in sub-Saharan Africa." (PHARM_8)

During a number of interviews, pharmaceutical stakeholders (i.e. those working in the pharmaceutical industry) raised the issue of whether or not the idea of significantly higher levels of corruption in sub-Saharan Africa is a perception or a reality. A

pharmaceutical industry respondent who was actually based in sub-Saharan Africa substantiated the claims from other pharmaceutical stakeholders around corruption but argued that it is for the individuals involved to decide whether or not to participate in it, describing it as being exaggerated in some instances.

"There is corruption. I'll be open about that. And it depends on whether you participate in it or not. Whenever I went to a Ministry of Health and they've said; 'well what will you pay us for this? [...]' We've got to get over this misconception ... it's a conception and a misconception of corruption in the rest of Africa." (PHARM_X¹)

3.1.2.2. Responsibility of pharmaceutical companies. The complexity of issues around corruption became evident when discussions progressed onto the topic of the structure of pharmaceutical companies. Publicly traded companies have a responsibility to shareholders and the importance of ensuring their buy-in to any efforts to engage countries perceived as corrupt was a topic which was raised through the interviews as well. The amount of resource required to track the flow of equipment and investigational product was also a topic that was raised. This is relevant particularly when considering the earlier referenced transparency index metrics, an objective measure of corruption, for the countries who were represented by those involved in these interviews [9].

"... you know and you hear, you know, even with aid that's been given you hear about it being misappropriated and going to ... and that isn't going to resonate well with shareholders if you

¹ Identifier left out to protect anonymity of respondent due to sensitive nature of comment.

say, you know; 'well we're giving all of this to sub-Saharan Africa and then, you know, you've got to actually track it. It's not just enough to make a donation, you have to check it's actually getting to where you think it's supposed to be getting and stuff like that.' (PHARM_4)

Concerns of corruption were not just directed toward those who are involved in the region. Several pharmaceutical interviewees were critical of the industry and raised issues around the potential for pharmaceutical companies to behave in a corrupt way if working outside the more closely regulated confines of the West's regulatory and ethical oversight;

"... basically I would think that the major pharmaceutical companies in the West are behaviourally very poor. They are extremely cynical in the way that they conduct studies in the West, in the way they publish data in the West, and do not publish data where they withhold data. The way they manipulate clinical studies to profoundly alter the outcome of those medicines to make them much more favourable than they would otherwise be. If they were doing this in third world countries, they probably would do more of that." (PHARM_1).

"... although I do work in the pharmaceutical industry, I am quite cynical that no successful pharmaceutical companies operate within a capitalist society where they're out to make, you know ... where their reason for being is to make a profit and my personal view is sometimes apparently philanthropic acts that pharmaceutical companies announce are really attempts to you know, they're marketing attempts to make them look good so at the end of the day you know there's the potential ... you know the profit might not be there but the profit's there in intangible assets". (PHARM_7)

3.1.2.3. Historical corruption. Health care professionals were focussed on the troubling history of clinical trials in developing countries. There are high profile historical examples of pharmaceutical companies behaving inappropriately in developing countries. Just as some pharmaceutical representatives had concerns that stakeholders involved in the trial process in sub-Saharan Africa may not behave ethically, healthcare professionals in the region also had their own concerns about potential corruption on the part of pharmaceutical companies. These fears around the legacy of corruption in Africa and its potential consequences on the conduct of ethically sound clinical research in the region suggest that trust is a mutual concern and will be an important factor if countries in sub-Saharan Africa are to participate in more industry sponsored research;

... there is an issue of trust and an issue of exploitation or non-exploitation. People are usually really suspicious you know but I think you need a lot of public enlightenment and you need very good policy structure in place which can be enforced because now the problem with most of sub-Saharan Africa ... Nigeria, let me use Nigeria for example is that you have very good policies but they're not enforced. So people come in and do whatever, like the Pfizer trial that took place in Nigeria some years ago that was very scandalous. (HCPN_1)

"Most people in Nigeria just think that if you say 'trial', they'll say 'oh they're using you for guinea pigs' OK?" (HCPN_1)

3.1.2.4. Unethical behaviour of healthcare professionals. There was

recognition on the part of the healthcare professionals based in the region that they were perceived by some externally as corrupt. Comments suggested that some of the training groups operating in the region have started to include discussions around transparency and corruption as part of the training provided to further educate potential researchers.

"... so they have no reason not to understand the importance of being absolutely precise in whatever they're doing and to report exactly what they are doing and not to doctor results and the importance of the informed consent process and that it's not just a document for participants to sign, but a document for you to ensure that they understand everything that is within the informed consent, it's a process, rather than just a, you know, a mere signature, bribe type of event. So they know all this and they understand all of this ..." (HCPN_2)

Healthcare professionals based in the region also expressed concern regarding the potential for healthcare professionals to coerce potential trial subjects into a study which may not be right for them. The socioeconomic conditions which exist in many parts of this region make subjects more susceptible to being unduly coerced and potentially impact a potential subject's ability to make an informed decision in the presence of an insistent investigator. Investigators may stand to benefit from enrolling as many patients as possible into clinical trials for a number of reasons, for example for financial gain or professional notoriety etc.

"Again for sub-Saharan Africa why it's particular is because you have a group of vulnerable people and when I mean vulnerable people I'm not thinking about children or women or pregnant women alone or disabled or prisoners, I'm thinking of ... because of the economic problems I actually put Africans as vulnerable and especially when it comes to research because most of the people you're going to be doing the research with ... the clinical research, the clinical trials, they're not the people in the blue chip companies in their offices, you're going to go to the communities and these are the people that are poor, that are managing to survive so any help, in quotes, that they are getting from you, you're not sure if you're inducing them or not." (HCPN_1).

This susceptibility to coercion is also made worse by the dynamics of the physician: patient relationship in this part of the world where doctors enjoy a higher social standing and are therefore less likely to be challenged by their patients.

"... because in this part of the world most patients just believe that the doctor knows what is best for them so when you tell them that; "OK, so I'm doing this study, do you want to join?" they'll tell you "Ah, doctor, you know what is best for me – I will do it!" (HCPN_1).

Transparency and open dialogue from investigators is one way through which this behaviour can be countered and trust can be built with patients in the region, particularly following incidents such as the trovafloxacin (Trovan) trial which increase the levels of distrust.

So, now, when you tell people that OK, this is essential for your health or for the health of your children. That the drugs we're using now are not working. You need to get new drugs and this is the only way you can find out so I think you just need to talk to people. Once you talk to them and you assure them that their health and safety is taken care of and they will get insurance and

nothing is not ‘this thing’ is going to be done to them I think a lot of people will ... because I've done trials, like I told you with my boss before and you see most times once you talk to them, they agree. They agree, but again you need to build trust.” (HCPN_2)

The topic of corruption and unethical behaviour is a complex one. The results from the interviews evidenced mutual suspicion and concern on the part of both pharmaceutical companies in the West and healthcare professionals based in Ghana and Nigeria. The concerns around corruption appear to be genuine although potentially exaggerated, however historical examples on the part of the pharmaceutical companies such as the Pfizer Trovan incident in Kano, Nigeria are still recent enough to cause concern for some of those treating patients in sub-Saharan Africa.

3.2. Questionnaire

3.2.1. Respondents

Two-hundred and thirty-seven emails were sent out to potential respondents and seventy-five questionnaires were eventually completed (32%).

Of the 75 respondents, the largest percentage, 77% (n = 58) were from the pharmaceutical industry followed by 15% (n = 11) from healthcare professionals and 4% (n = 3) were from a group which was labelled other but included; a Lawyer, Investment Director and a Managing Consultant. The regulatory group comprised only a small percentage of those surveyed (1%, n = 1).

3.2.2. Themes

Five questions were related to corruption and unethical behaviour and are presented here. The quantitative responses for these questions are given in Table 3. Each question gave respondents the opportunity to comment, those relevant to the theme of corruption are presented as they were entered (verbatim).

3.2.2.1. Corruption and/or fraud are NOT likely to impact the conduct of clinical trials in sub-Saharan Africa. The first question related to corruption asked respondents to indicate whether they agreed with a statement which suggested that corruption and fraud were unlikely to impact the conduct of clinical trials in sub-Saharan Africa. The results indicate that fraud is perceived to be a significant potential issue as (63%, n = 47) either strongly disagreed or disagreed. Of the four respondents who agreed (n = 3) or strongly agreed (n = 1), only one respondent was an HCP based in sub-Saharan Africa.

Disagree;

“Unfortunately, some persons are motivated by profited and would aim for profit at any cost. The tobacco industry comes to mind” (REG/HCP)

“Corruption is a universal thing” (HCP(2))

Neutral;

“The (sic) hits all walks of life” (PHARM(57))

The universality of corruption and fraud at numerous levels was a sentiment which was echoed throughout the supplementary comments. Many respondents lacked experience working in the region, however the role of the media in shaping the perception of those in the West was also evident.

Disagree;

“Without firsthand (sic) knowledge I cannot say with any certainty but my impression from media representation of the region is that governmental corruption is rife and assuming that to be correct I would assume it could extend to the regulatory environment and healthcare services that might be involve in trials.” (PHARM(11))

3.2.2.2. Pharmaceutical companies are likely to exploit patients involved in clinical trials in sub-Saharan Africa. In response to this question 43% (n = 32) of respondents disagreed. Over a fifth of respondents either agreed (13%, n = 10) or strongly agreed (8%, n = 6) with the statement, the majority being HCPs working in the region. This finding represents an arguably unsurprising disconnect between the perceptions of the pharmaceutical industry between stakeholder groups. Comments left in response to this question point quite clearly to the Pfizer trovafloxin (Trovan) trial as the biggest example in recent history;

Agree;

“there are examples from Nigeria I am sure you are aware of” (HCP(3))

There were also some respondents from the pharmaceutical stakeholder group who believe that pharmaceutical companies are likely to take advantage of clinical trial subjects in developing countries. This echoed some of the comments made during the interview part of study.

Table 3

Responses to questionnaire questions related to corruption and unethical behaviour.

	1 (strongly disagree)	2 (disagree)	3 (neutral)	4 (agree)	5 (strongly agree)	Responses	Average
1. Corruption and/or fraud are NOT likely to impact the conduct of clinical trials in sub-Saharan Africa	15 (20%)	32 (43%)	24 (32%)	3 (4%)	1 (1%)	75	2.24/5
2. Pharmaceutical companies are likely to exploit patients involved in clinical trials in sub-Saharan Africa.	13 (17%)	32 (43%)	14 (19%)	10 (13%)	6 (8%)	75	2.52/5
3. Investigators (clinicians) in sub-Saharan Africa are more likely than those in the West to exploit patients in clinical trials.	8 (11%)	21 (28%)	26 (35%)	17 (23%)	2 (3%)	74	2.78/5
4. Investigators in sub-Saharan Africa are more likely than those in the West to falsify data for financial gain.	7 (10%)	24 (33%)	22 (30%)	17 (23%)	3 (4%)	73	2.79/5
5. Pharmaceutical companies in the West do not always conform to GCP	7 (10%)	24 (33%)	17 (23%)	22 (30%)	3 (4%)	73	2.86/5
6. Pharmaceutical companies do not want to engage in research in sub-Saharan Africa over fears of being considered exploitative.	2 (3%)	21 (28%)	23 (31%)	26 (35%)	3 (4%)	75	3.09/5
							2.71/5

Most common response is bolded.

Agree;

“I would like to disagree with this - but can't!” (PHARM(20))

3.2.2.3. Investigators (clinicians) in sub-Saharan Africa are more likely than those in the West to exploit patients in clinical trials. In response to the next statement suggesting that investigators treating clinical trial patients in developing countries were more likely than their counterparts in the West to exploit patients in clinical trials, 39% (n = 29) of respondents either strongly disagreed (11%, n = 8) or disagreed (28%, n = 21). 35% of respondents (n = 26) were neutral whilst 23% (n = 17) and 3% (n = 3) agreed and strongly agreed, respectively. The overall results suggested that HCPs mostly disagree with the statement. There were, however, some HCP respondents who strongly agreed (n = 1) and agreed (n = 3) with the statement.

Disagree;

“I think investigators will exploit patients (if given the opportunity) anywhere.” (PHARM(32))

Neutral;

“I hope/ don't think there would be an intent to do this on a wide basis but societal norms are different and this would be likely to influence some investigators” (PHARM(44))

This is relevant because one could argue that there is an element or aspect of corruption which is subjective. This will be discussed in further detail later on in this article.

3.2.2.4. Investigators in sub-Saharan Africa are more likely than those in the West to falsify data for financial gain. Of the seventy-three respondents who responded to the question asking them to indicate their agreement with the following statement; Investigators in sub-Saharan Africa are more likely than those in the West to falsify data for financial gain, approximately 30% (n = 22) were neutral and a third (33%) disagreed with the statement. A further 23% (n = 17) and 4% (n = 3) agreed or strongly agreed, respectively, indicating that some felt investigators would potentially falsify data.

Neutral;

“I think there is more motivation in any developing country to falsify data than developed countries. I don't feel this is Africa specific” (PHARM(45))

3.2.2.5. Pharmaceutical companies in the West do not always conform to GCP. The next statements asked respondents to indicate whether or not they believed that pharmaceutical companies in the West do not always comply with GCP. Approximately a third (n = 24, 33%) of all seventy-three respondents disagreed with this statement. A further 10% (n = 7) strongly disagreed indicating that many believe that pharma is largely compliant with GCP. However, an observation worth noting (particularly considering the pharma bias sample population) is that over a fifth (23%, n = 17) agreed that pharma does not always comply with GCP in the West and a further 4% (n = 3), all of whom fell under the pharma stakeholder group, strongly agreed with the statement.

Disagree;

“On the whole they do!” (PHARM(14))

Neutral;

“true, any audit finding is a non-conformance to GCP. But if this question is seeking my thoughts on wilful non-conformance, then I'd be inclined to disagree, these days” (PHARM(12))

Strongly agree;

“Fact of life, sometimes intentionally, sometimes not” (PHARM(8))

3.2.2.6. Pharmaceutical companies do not want to engage in research in sub-Saharan Africa over fears of being considered exploitative. The final question around corruption and unethical behaviour asked respondents to indicate their agreement with the following statement; Pharmaceutical companies do not want to engage in research in sub-Saharan Africa over fears of being considered exploitative.

Of the seventy-five respondents, (35%, n = 26) agreed with the statement – three of these respondents fell under the HCP stakeholder group. This was followed by 31% (n = 23) who were neutral. One respondent who was in agreement went as far as to liken (in what may or may not be tongue in cheek) some of the people working in the region to the secret police of Nazi Germany commenting;

Agree;

“Agree. Many self-appointed “ethicists” in the region bear more resemblance to the Gestapo than to Ghandi.” (PHARM(30))

Disagree;

“I do not think it is this fear that drives it, but the regulatory expectations, ethics, and reliability of data” (PHARM(11))

4. Discussion

The findings from both parts of the study will be treated together since there was no real disparity between them. The majority of the pharma industry respondents did not have experience of working in developing countries and the responses from this stakeholder group should be viewed with this in mind. Nevertheless, their views, irrespective of how they have been reached, are likely to be important within the industry especially given the seniority of pharma stakeholder groups involved in the interviews.

The responses from both the interviews and questionnaires highlight that there are still concerns from healthcare professionals in developing countries due to the conduct of some contentious trials in the past, more specifically the Pfizer Trovan trial in Nigeria [10]. This has led to questions around pharma's presence in the region because of the conduct of potentially unethical or corrupt studies. Healthcare professionals also highlight patient concerns around industry sponsored clinical trials with some believing that they're being used as guinea pigs by pharmaceutical companies. There appeared to be mutual suspicion between stakeholder groups with each concerned about the other's potential behaviour when conducting trials in sub-Saharan Africa.

On the part of pharma, there were several concerns around corruption and unethical behaviour, the first of these being around

perception. More specifically, concerns that even in instances where research is conducted ethically, there is a chance that it will still be perceived as exploitative simply because the trials are being carried out in this developing part of the world. The influence of media, whilst not explicitly mentioned, was evident throughout the interviews with pharma respondents as many had not worked in the region but had concerns based on things they had seen and heard in the media. The power of the media to influence perception is an important point to note on both sides the media could likewise influence healthcare professionals and the general public likewise by painting pharmaceutical companies engaging in research in this part of the world in a negative light.

Another concern on the part of pharma was around the misappropriation of resources (e.g. equipment, payments etc.) which may be given to hospital sites and investigators for the conduct of trials and where they would potentially be directed to. Although the majority of pharma representatives who were interviewed and who completed the questionnaire did not have experience working in the region, many were under the impression that there were higher levels of corruption in sub-Saharan Africa than in Western countries. This could lead to equipment and material not reaching its intended destination and being sold privately. It could also lead to experimental medicines being unlawfully sold on, which could have more serious consequences.

The research also showed that many feel as though pharmaceutical companies are largely compliant with ethical standards when conducting research in the West, however there were concerns even from pharma representatives themselves that companies may not be so compliant when conducting trials outside of the more closely regulated Western countries which are typically represented in industry-sponsored clinical trials. The research also highlighted the cynical views that members of the pharmaceutical group hold about current industry practices which are of concern and may indicate that current stringent regulations and self-policing of the industry are not producing the desired results.

4.1. Recommendations for moving forward

It is important that as discussions around sub-Saharan African countries participating in clinical trials begin to gain traction, issues such as the potential for corruption do not become the proverbial elephant in the room². The findings here suggest that there is some suspicion by all parties involved of the other groups, whether this be around corruption or exploitation. This might suggest that discussions need to be held openly with solutions around creating transparency and accountability mutually agreed by all parties. This mutual agreeability is an important component to making progress as it will demonstrate that pharma companies are avoiding the adopting of imperialistic strategies which fail to take into account the cultural and practical differences that exist between developing countries and the West.

It is important to note that many companies are beginning to take steps towards ensuring the conduct of ethical trials in developing countries and are benchmarked against one another. The Access to Medicines Index [17] assesses companies on their compliance to ICH-GCP standards and the Declaration of Helsinki [18,19], as well as companies' processes for monitoring compliance and taking disciplinary action when necessary, for both in-house and outsourced trials. Additionally, it examines companies' criteria for selecting Clinical Research Organisations (CROs) as well as compliance with WHO's 2005 Technical Consultation of Clinical

Trial Registration Standards [20] to ensure that trials are registered centrally and that results are published irrespective of outcomes. The selective registering of results of trials was a concern which was raised by a pharma respondent during the interviews and so compliance with these guidelines will help redress this concern. The Index's 2014 report showed that most pharmaceutical companies are generally setting high standards for trial conduct with a handful being exceptional in respect of high levels of transparency and clinical trial codes of conduct [17]. It is worth noting, however, that the Access to Medicines Index ratings are based on self-reporting, and not on actual inspections of the trials.

Taking into consideration the legacy of the historic examples of corrupt and unethical behaviour pharmaceutical companies ought to ensure they are conducting themselves with the same level (if not greater) of transparency and ethical integrity that they would when conducting trials in the West. This includes developing appropriate trial designs for this part of the world and ensuring that they do not compromise the health and wellbeing of patients due to corrupt business practices and ethically questionable research. This, along with education, two-way discussions and an appropriate code of conduct should help overcome the fear (and actuality) of being perceived as exploitative and/or corrupt simply by conducting research in developing countries. This will require further discussion on sensitive topics such as corruption – more specifically, conversation around whether or not the definition of 'corruption' is universally applicable or whether there are/should be allowances from Western interpretations of corruption in recognition of cultural or societal norms.

The countries which comprise sub-Saharan Africa are each unique in their landscape and in their cultural norms and this should be taken into account when engaging the relevant stakeholders in these various countries. The only way to effectively achieve this is to ensure those on the ground are engaged and consulted and that flexibility to allow for cultural nuances and norms is permitted, so long as they do not compromise the health and wellbeing of research participants nor the integrity of the data produced.

4.2. Limitations

4.2.1. Limitations of interviews

Numbers were not as high as originally planned for and only two of the stakeholder groups were well represented. A higher number of interviews with a more varied group of stakeholders based in the countries of interest might have been achieved either by travelling to the countries (which would have been prohibitively expensive) or recruiting a local interviewer. Whether the interviewer came from a drug company, was based in the West or was local there was the possibility they would always be seen as biased in some way by different groups.

Another limitation was the way in which interviewees, particularly those in the HCP group, were identified. These were mostly identified through academic journals and snowballing and as such, can be assumed to have at least some interest in clinical research. It would have been preferable to have had a mixed sample of HCPs from the region (i.e. those with and without research interests) however many of the HCPs contacted who were not identified through other methods such as internet searches did not respond to requests to participate in the interview. The findings may have been different if the HCPs did not have an interest or working knowledge of clinical research. Conversely, one could argue that HCPs with no research interest may not have been able to identify the relevant issues due to unfamiliarity with some of the relevant topics. This potential bias means it is difficult to ascertain whether or not the results of this study are representative of the general

² 'Elephant in the room' refers to an obvious problem or difficult situation that people do not want to talk about.

feelings towards research that most HCPs in the region hold.

4.2.2. Limitations of questionnaire

The low overall response rate to the questionnaire was a limitation for this study. Furthermore, a similar and greater number of respondents across each stakeholder group would have allowed for a more balanced comparison. Within the pharma stakeholder group, it would have been preferable to have had greater cross functional representation. More specifically, the involvement of more respondents who work in, for example, commercial operations as opposed to the almost exclusively R&D based group of respondents who were contacted to complete the questionnaire.

Also, it is difficult to know whether the responses which indicated a neutral position were truly neutral or whether respondents did not know the answer and therefore chose a neutral response. In retrospect it may have been better to have added an option for respondents to indicate they did not know the answer to the question in order to gain a better understanding of how neutral responses should be interpreted. This was not raised in the piloting of the questionnaire.

5. Conclusions

Set against a context of under-representation in clinical trials and raising prevalence of chronic disease in sub-Saharan Africa this study looked at stakeholders' perceptions of corruption and unethical behaviour in such trials.

The main findings around corruption which came out of this research showed that there appears to be an element of mutual suspicion on the part of the two stakeholder groups best represented in both parts of this research. The perception of pharma respondents seemed to have been largely influenced by media, and important point to note, as many did not have any experience working in the region yet their responses indicated suspicion. Healthcare professionals in the region were suspicious of the pharmaceutical industry largely because of historical examples of corruption, most notably the Pfizer experiments.

There were concerns on both parts that patients may be exploited either by pharma companies conducting poorly designed or unethical studies or by healthcare professionals falsifying data or misappropriating resource intended for clinical trial use. Additionally, the fear of being perceived as corrupt plays a significant role in precluding the placement of trials in this part of the world as the risk of reputational damage may be greater than the reward.

Opening up the debate between pharmaceutical companies and local stakeholders would seem to be the first step to developing the clinical trial research capacity in the involved countries.

Appendix A. Supplementary data

Supplementary data related to this article can be found at [http://](http://dx.doi.org/10.1016/j.conctc.2016.04.009)

dx.doi.org/10.1016/j.conctc.2016.04.009.

References

- [1] G. Puppallwar, M. Mourya, G. Kadhe, A. Mane, Conducting clinical trials in emerging markets of sub-Saharan Africa: review of guidelines and resources for foreign sponsors, *Open Access J. Clin. Trials* 7 (2015) 23–24.
- [2] T. Lang, S. Siribaddana, Clinical trials have gone global: is this a good thing? *PLoS Med.* 9 (6) (2012).
- [3] C.S. Molyneaux, et al., "Even if they ask you to stand by a tree all day, you will have to do it (laughter)...!": community voices on the notion and practice of informed consent for biomedical research in developing countries, *Soc. Sci. Med.* 61 (2005) 443–454.
- [4] E.W. Emanuel, What makes clinical research in developing countries ethical? The benchmarks of ethical research, *J. Infect. Dis.* 189 (2004) 930–937.
- [5] A. Schulz-Baldes, E. Vayena, N. Biller-Andorno, Sharing benefits in international health research. Research-capacity building as an example of an indirect collective benefit, *Sci. Soc.* 8 (1) (2007) 8–13.
- [6] D. Limaye, J.M. Langer, T. Ruhling, G. Fortwengel, A critical appraisal of clinical trials conducted and subsequent drug approvals in India and South Africa, *BMJ Open* 5 (8) (2015).
- [7] N. Homedes, A. Ugaldé, Availability and affordability of new medicines in Latin American countries where pivotal clinical trials were conducted, *Bull. World Health Organ.* (2015) 674–683.
- [8] AfDB, Corruption and fragile institutions: mutual accountability between Africa and its partners as cited in Africa economic & financial brief, *Afr. Dev. Bank. Chief Econ. Complex* 4 (40) (2010), 2013.
- [9] Transparency International, Corruption Perceptions Index 2014: Results, 2014. Retrieved June 16, 2015, from Transparency International: <http://www.transparency.org/cpi2014/results>.
- [10] J. Wise, Pfizer accused of testing new drug without ethical approval, *BMJ* 327 (2001) 194.
- [11] Pfizer: Nigeria Drug Trial Victims Get Compensation. Retrieved from BBC News: <http://www.bbc.co.uk/news/world-africa-1449327>.
- [12] SOMO & Wemos, SOMO Briefing Paper on Ethics in Clinical Trials, 2008.
- [13] E. Brouwner, Clinical trials in developing countries: Unethical Practice or a Product of Necessity, *Global Medicine*. Available from: <http://globalmedicine.nl/issues/gm5/article2.pdf>.
- [14] V. Angwenyi, K.-P. Asante, A. Traore, L.G. Febir, C. Tawiah, A. Kwarteng, et al., Health providers' perceptions of clinical trials: lessons from Ghana, Kenya and Burkina Faso, *PLoS ONE* 10 (5) (2015).
- [15] a M. Hay, D.W. Thomas, J.L. Craighead, C. Economides, J. Rosenthal, Clinical development success rate for investigational drugs, *Nat. Biotechnol.* 32 (2014) 40–51;
- [16] World Health Organisation, Preventing Chronic Disease: A Vital Investment. Geneva, 2005.
- [17] Trading Economics, Life Expectancy at Birth; Total (Years) in Sub-Saharan Africa, 2010. Retrieved March 16, 2013, from, <http://www.tradingeconomics.com/sub-saharan-africa/life-expectancy-at-birth-total-years-wb-data.htm>.
- [18] Access to Medicine Foundation, The Access to Medicine Index, 2014. Retrieved from http://www.accesstomedicineindex.org/sites/2015.atmindex.org/files/2014_accesstomedicineindex_fullreport_clickablepdf.pdf.
- [19] International Conference on Harmonisation, Guideline for Good Clinical Practice, 2014. Retrieved from Guidelines: <http://www.ich.org/products/guidelines.htm>.
- [20] World Medical Association, Ethical Principles for Medical Research Involving Human Subjects, 2013, October. Retrieved December 8, 2014, from WMA Declaration of Helsinki: <http://www.wma.net/en/30publications/10policies/b3/index.htm>.
- [21] World Health Organization, WHO Technical Consultation on Clinical Trial Registration Standards, April 25–27, 2005. Geneva, Switzerland. Available at: http://www.who.int/ictrp/news/ictrp_meeting_april2005_conclusions.pdf (accessed 09.03.16).