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REVIEW ARTICLE

Human dignity as a basis for providing post-trial access to healthcare for research participants: a South African perspective

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Abstract This paper discusses the need to focus on the dignity of human participants as a legal and ethical basis for providing post-trial access to healthcare. Debate about post-trial benefits has mostly focused on access to products or interventions proven to be effective in clinical trials. However, such access may be modelled on a broad fair benefits framework that emphasises both collateral benefits and interventional products of research, instead of prescribed post-trial access alone (Legal and ethical regulation of biomedical research in developing countries p. 134, 2016). The wording of the current version of the Declaration of Helsinki could in fact be interpreted to broaden the scope to include other collateral benefits by applying such a broad fair benefits framework. We argue that this possibility should be utilised by low and middle income countries' (LMICs) health research ethics committees (RECs) in order to ensure that research participants who enrol in clinical trials so as to receive medical care continue to access care after the trial is concluded, as befits their dignity. Although each LMIC has unique concerns, nonetheless there are common challenges based especially on emerging issues, such as post-trial access to healthcare. Accordingly, the South African perspective is used to draw lessons that can benefit other LMICs.

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Introduction

Current literature on the increased globalization of clinical research has mostly focused on the factors driving this phenomenon, and its ethical implications (Richter 2014; Lang and Siribaddana 2012; Glickman et al. 2009). The protection of the dignity of clinical trial participants in this evolving context remains underexplored. It is in this perspective that Kamat has suggested the consideration of "broader issues that are fundamental to human development" since the narrow focus on the dangers of offshore outsourcing of clinical trials distracts stakeholders from the real issues particularly of vast health inequalities (Kamat 2014, p. 55).

Human dignity and post-trial access to healthcare are proposed herein as two of such broader issues. Since there is no consensus on how these two issues should be appropriately addressed, we build on the valuable work that Cook et al. have done in assessing the "presence or lack of consensus over the ethical nature of the obligation to provide post-trial access" and additional benefits (2016, p. 71). Our paper seeks to contribute to the discourse by emphasizing the dignity of human participants as an ethical basis for post-trial obligations, and, subsequently broadening such obligations to include other collateral benefits that can foster the provision of healthcare, rather than a limited focus on access to post-trial products.

This paper additionally highlights the underexplored issue of targeting easy recruitment of participants in developing countries like South Africa, its link to post-trial access to healthcare, and how this impacts on the dignity

of trial participants. The first section provides background information on the globalized context in which health research is conducted, its implications regarding post-trial access to healthcare and the unique challenges RECs have to contend with. The second section highlights the vital albeit complex role of RECs in ensuring respect and protection of human dignity and compliance with post-trial obligations in a globalized context. The challenges that South African RECs face in performing their role of ensuring such compliance are discussed in the third section, which paves the way for some suggestions on the way forward in the conclusions.

We have chosen South Africa for the purposes of this paper for two reasons. First, it was the first African country to establish a REC in 1967 (Kass and Hyder 2001; Rwabihama et al. 2010). It has also strengthened the ethical and regulatory frameworks by requiring all health research that is conducted in the country to be approved by an accredited health REC.[1] Secondly, South Africa presents an ideal destination for clinical trials due to the diversity of the population and burden of variety of diseases (Wemos Foundation 2013, p. 5). An additional reason for its popularity is succinctly captured in the statement by Catherine Lund, Managing Director and founder of OnQ:

> Patient recruitment is easy in South Africa. People are motivated by access to drugs, the fact they will be seen quickly, the doctors will be nice to them, they won't have to queue all day. But I don't see these factors as coercive. Our informed consent process is very robust...[2]

The statement reaffirms the common trend in literature which equates the procurement of informed consent to an expression of human dignity (Rheeder 2014). It also assumes that a robust informed consent process is capable of ensuring the protection of human dignity.

South Africa is a popular choice for international pharmaceutical companies that conduct clinical trials (Wemos Foundation 2013, p. 5). Notably, the statement by Lund above shows how trial participants are attracted by the immediate benefits of having access to medical care during the trial; the crucial issue of post-trial access does not seem to be addressed at that stage and instead is left to RECs to deal with (Wemos Foundation 2013, p. 33).

The globalized health research environment and its implications for post-trial access to healthcare

The increase in international collaborative research in LMICs has been attributed to scientific and socio-economic factors such as the need to generate data for supporting licensing applications in different countries and the ease of recruiting trial participants in some countries (Lang and Siribaddana 2012). Other significant economic factors are low labour costs in developing countries as well as moving from the increasingly bureaucratic and expensive regulatory environments in the high income countries (Glickman et al. 2009, pp. 816–817). A recent study established that this increase in international collaborative research has in turn significantly increased the workload of some biomedical RECs in South Africa (Silaigwana and Wassenaar 2015). Other authors have underscored the need to maximize protection of human participants due, similarly, to "the growth in volume and complexity of international collaborative biomedical research involving human participants" (IJsselmuiden et al. 2012).

Before discussing specific complexities of international collaborative research, it is helpful to mention several principles of international research collaboration as identified by Caballero (NRC 2014, pp. 16–17).

- Study design should be "...relevant for the local population, local scientists, and for the national Ministry of Health...it cannot be just for convenience, cost, or expediency";
- Risk-sharing "either by using a combined population or a protocol designed to minimize risk";
- A regulatory framework acceptable internationally and going beyond culture; and
- Strong local ethical expertise and unbiased funding driven by the study size, not the operations or convenience.

Although compliance with the above principles in a globalized research context can be demanding, they are still useful for addressing weaknesses of the fair benefits framework that critics (Ballantyne 2008; London 2005) have highlighted as discussed further in this section of the paper. Some of the challenges that have been identified in current literature are diverse ethical practices that may create tensions between universal principles and local approaches, and "ethics-free zones" that arise from severely limited or non-existent ethical oversight, leading, as a consequence, to the importation of unethical research (European Commission 2009). The other challenges are the apparent vagueness associated with the concept of dignity (Lang and Siribaddana 2012), as well as the lack of participants' post-trial

[1] S 73 of the National Health Act no.61 of 2003.

[2] Quoted in Wemos report, 2013 p. 12.

access to beneficial medical treatments (Cook et al. 2016). The challenges that directly affect post-trial access to health care are further discussed below.

Ethics governance

As noted already, the increasingly bureaucratic and expensive regulatory environment in the high income countries has led to more international collaborative health research being conducted in developing countries. This may be problematic for LMICs without proper ethics governance. Dhai observes that governance "is often absent in developing countries, and when it is present the standards differ markedly across countries." In addition, even when ethics governance does exist, implementation is a problem, given the general lack of financial support for such initiatives (NRC 2014, p. 18). In this regard, Dhai suggests "the possibility of creating a global minimum standard for regulatory activities that both parties in research collaboration would have to meet before a project could begin and that both parties can sustain throughout the project" (NRC 2014, p. 18).

The other challenge related to governance is *ethical imperialism*, which tends to undermine local philosophies and cultures (NRC 2014, p. 18). Ethical imperialism can lead to the importation of unethical research when the international guidelines that prescribe minimum ethical standards are inconsistently applied in a globalized context, without giving due consideration to the local philosophies and cultures. A related issue, particularly in a collaborative context, is a culture of mistrust and suspicion that is attributed to a history of exploitation that is closely linked with that of international research. Dhai observes that "when there are differences in what a local ethics committee decides compared to the decisions made by its developed country collaborators, these [local] decisions are often looked upon negatively" (NRC 2014, p. 18).

There has equally been a trend where even stringent ethical requirements are ignored in national or regional guidelines. For example, the 2004 revision of the Declaration of Helsinki (DOH) requiring post-study access to the intervention products[3], was deemed by the USA's Food and Drug Administration (FDA) to have excessively increased the responsibilities of trial sponsors towards research participants. The FDA accordingly excluded any reference to this revised version of the DOH in its regulations and instead made reference to a version that was no longer valid (Wolinsky 2006, p. 670). Notably, paragraph 34 of the current version[4] of the DOH requires "sponsors, researchers and host country governments [to] make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial." Such information should be disclosed to the participants during the informed consent process and in advance of the trial. This is considered important especially for participants from limited-resource settings (Ndebele 2013).

Post-trial access to healthcare

Providing post-trial access to an intervention identified as beneficial is admittedly very complex and there are diverse views on the issue (Cook et al. 2016; Usharani and Naqvi 2013; Emanuel et al. 2004b). Attempts should however be made to adhere to the ethical requirement of ensuring that the study itself is responsive to the health needs of the participants. The main challenge that should be noted at the outset is that although RECs may strive to ensure that the approved protocol includes a post-trial access plan, nonetheless as Saver has rightly concluded, it would be difficult to monitor and enforce such an ethical requirement (2009, p. 427). Saver argues in this regard that RECs cannot take any action in respect of a trial that has already been concluded except threatening not to approve future protocols from the same sponsor (2009, p. 428). This difficultly notwithstanding, Sanmukhani and Tripathi (2011) have recommended that RECs should consider plans for post-trial access since, as Usharani and Naqvi precisely observe, this can facilitate delimiting the access period, and even the possibility of the REC waiving the obligation for a good cause (2013, p. 60). Ross has also correctly argued that research that does not consider such needs is unethical (Ross 2014, p. 1423). He suggests that RECs should reject applications from researchers who are not willing to accommodate the needs of local participants. The main reasons for supporting these arguments are presented in the section of this paper that focuses on dignity as a basis for claiming post-trial access.

A fundamental issue that remains unsettled in the current discourse is the legal and/or ethical validity of the claim for post-trial access. Usharani and Naqvi (2013) have attempted to delve into this issue by making an analysis of the regulatory guidelines and major stakeholders' perspectives, while other authors have proposed the fair benefits framework as an alternative approach (Nwabueze 2016; Emanuel et al. 2004b). These contributions are analysed below for purposes of laying the foundation for the detailed discussion on the dignity of research participants as a basis

[3] The revision introduced paragraph 30 stating that "at the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study."

[4] Adopted by the 64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013.

for the validity of the claim for post-trial access and reliance on the fair benefits framework to satisfy this claim appropriately.

The legal and ethical basis of the claim for post-trial access

As noted already, paragraph 34 of the DOH outlines the ethical requirements of post-trial access. In addition, the ethical obligation not to do harm to research participants by stopping the medication that has been proven to be effective once the study is over, has been used to justify the claim for post-trial access (Grady 2005; Millum 2009). Although the DOH neither explicitly grants research participants a clear entitlement to post-trial access nor specifies who is responsible for ensuring access, courts in countries such as Brazil have enforced guidelines[5] that oblige sponsors and the government to provide post-trial treatment (Wang and Ferraz 2012, p. 192). Surprisingly, no case has been decided by the Brazilian Federal Supreme Court in which it has recognised a legal duty to provide post-trial access, although the guidelines have generated heated debates (Wang and Ferraz 2012, p. 192). The position in Brazil therefore remains unsettled and continues to be debated in most other jurisdictions (Saver 2009, p. 426 and p. 438).

Furthermore, though Brazil has successfully based post-trial access on the constitutional right to health,[6] the state has ended up suing the sponsors of trials claiming that the state should not be compelled to take over the sponsors' responsibilities (Wang and Ferraz 2012, p. 193). This is not surprising considering the prevailing lack of consensus on the explicit legal or ethical basis for claiming post-trial access. The difficulty in reaching a consensus is evident from the diverse rationales that Cook et al. established in their review of the current academic literature (2016, p. 74). Four rationales are worth highlighting here: the need to foster fairness and avoid exploitation of participants; considerations of beneficence and reciprocity; justice and fiduciary relationship between the researcher and the participants. These are further discussed in the section herein that focuses on dignity. It suffices to mention at this point that lack of consensus on the ethical or legal basis for post-trial access has led to participants being referred to either the public health system or their regular healthcare for post-trial access. Wang and Ferraz have correctly argued, however, that this may not be viable in cases where these options are either inexistent or ineffective (2012, p. 192).

Modelling post-trial access on a broad fair benefits framework

The fair benefits framework was proposed by Emanuel et al.[7] to supplement ethics review and informed consent, thus offering "a more reliable and justifiable way to avoid exploitation" (2004b, p. 17). Their formulation of the framework emphasises collaborative partnership with the participating population, which negotiates the fairness of benefits with the researcher or sponsor (2004b, p. 22). The main criticism against this formulation, which was subsequently endorsed by Gbadegesin and Wendler (2006), is that it focuses on a procedural account of fairness and offers no substantive normative principle for determining fair distribution of benefits (Ballantyne 2008, pp. 241–243). The procedural account accordingly offers a thin principle of fairness, relying solely on "the information/consent aspect of decision-making" such that one can only object "to transactions that occur without the fully informed consent of the weaker party" (Ballantyne 2008, pp. 241–242). Informed consent alone is not capable of protecting participants from exploitation, as noted by London (2005, p. 31) in his criticism of Emanuel and colleagues' formulation of the framework:

> Since [the] framework defines as 'fair' any outcome the host community is willing to accept, it recognizes no moral grounds on which to object to lopsided divisions of benefits that reflect. .. dramatic imbalances of power.

An equally problematic aspect of the framework is the emphasis that Emanuel and colleagues place on the micro-level interaction, focusing on study-related benefits that are due to individual study participants, while ignoring the current broad agreement on a fair benefits framework based on both micro-level and macro-level benefits (Njue et al. 2014). We accordingly use the fair benefits framework in this broad sense while acknowledging, as Ballantyne rightly observes, that attempts to "stipulate normative standards of fairness to protect research subjects in developing countries have been deeply controversial" (2008, p. 243). Such controversies are evident from the heated debates that ensued following the 2000 revisions to the DOH through which the World Medical Association introduced paragraphs 29 and 30 in a bid to stipulate universal standards of care and assurance of post-trial access respectively (Wolinsky 2006). Ballantyne correctly concludes that the disagreements indicate that further conceptual and empirical work needs to

[5] The Brazilian National Health Council. Resolution 251/1997, Article IV.1, cited in Wang & Ferraz 2012.

[6] Brazil, Federal Constitution Article 196 provides that "Health is a right of all and a duty of the State."

[7] Participants of the 2001 Conference on Ethical Aspects of Research in Developing Countries.

be done to develop robust standards of fairness that can be applied in international research (2008, p. 244).

Nwabueze has proposed the broad framework because of its emphasis on both collateral benefits and interventional products of research, instead of prescribed post-trial access alone (2016, p. 134). He argues that a mandatory prescription of post-trial access ignores the fact that "the distribution and administration of drugs are matters subject to the requirements of a particular country and therefore beyond the control of an investigator or sponsor" (2016, p. 134). He further asserts that insistence on post-trial benefits ignores other significant benefits such as training of healthcare personnel, provision of healthcare facilities or infrastructure and collateral benefits such as employment (2016, p. 134), or, as stated by Sanmukhani and Tripathi (2011), establishment of counselling centres, clinics and education on maintenance of good health practices. These may be more feasible for sponsors and still beneficial to the entire community.

The proposal for a broad fair benefits framework makes sense particularly bearing in mind that phase I to III clinical trials only provide preliminary evidence, not proof of safety of the drug (Usharani and Naqvi 2013, p. 59). Consequently, if the trials are terminated during any of these three phases, no efficacious product can be expected from such trials in order to fulfil the post-trial obligation of making the product available to the participants. Additionally, other equally relevant types of research that are conducted in LMICs such as "Phase I and II drug and vaccine testing, or to genetic, epidemiology, and natural history research" may not yield immediate efficacious products (Emanuel et al. 2004b, p. 21). In this regard, Usharani and Naqvi correctly argue that "post trial access is not valid when the investigational treatment does not provide benefit over standard treatment" (2013, p. 60).

The fair benefits framework would be useful in a country like South Africa where the huge gap between the rich, and the poor who are unable to afford medical care, motivates the latter group to enrol for clinical trials with a view to receiving free medical care (Wemos Foundation 2013, p. 1). The main challenge of participating in clinical trials in such situations is the lack of guarantee of post-trial access to drugs that are proven to be effective and even basic healthcare for such poor participants. Such inaccessibility may amount to an affront to the dignity of the poor after they have sacrificed to make the trials possible. In this regard, it is worth noting that lack of access to the benefits of research is one of the basic markers of harm and exploitation (Arnason and Schroeder 2013, p. 15).

In advocating for a broad fair benefit framework, which includes collateral benefits, we are not oblivious of the concerns that have been raised regarding the risks of extending such benefits to poor participants. Emanuel et al. argument in this regard is that "collateral benefits will be escalated to induce the population to enrol in excessively risky research" (2004b, p. 21). An empirical study by Njue et al. (2014) generated very useful views from low-income settings stakeholders on which they base the following insightful argument: "…international researchers working in low-income settings should consider the potential for underestimating indirect costs as a more likely and serious risk than that of undermining free choice." This essentially means that international researchers in such circumstances cannot disregard the possibility of providing macro-level benefits as a result of focusing on micro-level interactions as proposed by Emanuel et al. (2004b, p. 20). Accordingly, Njue et al. (2014) correctly conclude that "a potentially more substantial way in which researchers can respond to structural inequities in this context is through the provision of community-wide benefits, including strengthening community-wide medical services within studies and across the programme in collaboration with the Ministry of Health."

Although post-trial access is a complex situation to address, Wemos' position that "the well-being and rights of the individual trial subjects must always take precedence over all other interests", nevertheless makes a lot of sense, and RECs should pay particular attention to this issue in the globalized research context (Wemos Foundation2013, p. 2). In view of this complexity, Schroeder has suggested that post-trial access should be addressed at the level of providing suitable healthcare since the success of the trial drug cannot be guaranteed.[8] Wemos' report confirms that South African participants are more vulnerable compared to high income country participants as they have no guarantee of continued medical care once the trial has ended (Wemos Foundation 2013, p. 32).

The protection of human dignity by RECs in the globalized health research environment: which interpretation of dignity, and why?

This section tries to show how RECs can contribute to a richer understanding of the concept of human dignity, beginning in a local context then with subsequent application in a globalized health research environment. This perspective will thereafter be applied specifically to the protection of dignity in the post-trial phase.

Dignity: a multifaceted and contested concept

"Dignity" is a concept in long usage albeit with varying meanings and nuances (McCrudden 2008). During the

[8] Quoted in Wemos Foundation 2013, p. 30.

classical Roman times, Cicero was one of the few outstanding exponents of dignity as characteristic of human beings as such (McCrudden 2008, p. 657). In the middle ages, it was used to distinguish human beings from other species (McCrudden 2008, p. 658) and in the Renaissance period and thereafter, the capacity and use of reason was deemed a characteristic feature (McCrudden 2008, p. 659). In modern times, human autonomy and capacity to determine one's future were considered its foundation, while during the Enlightenment era the Kantian sense stood out (McCrudden 2008, p. 659). The core of Kant's thinking may be said to be that dignity requires that human beings be treated as ends, not means to an end, an interpretation that is quite useful for REC purposes, as further discussed below. Dignity, Kant affirmed, has its source in the moral law dictated by our intellect, and its bearers are distinguished by their rationality (Schulman 2008, p. 10).

The concept took on a more communitarian connotation due especially to the philosophy of Rousseau (McCrudden 2008, p. 660). In the nineteenth century, it was the "slogan" of social and political movements advocating for social reform, and, in Europe and Latin America it was particularly associated with the abolition of slavery (McCrudden 2008, p. 661). From the end of the nineteenth century onwards, the Catholic Church employed the concept to address the threats of socialism, communism, and totalitarianism (McCrudden 2008, p. 662). Jacques Maritain, who was actively involved in the drafting of the UN Charter and the Universal Declaration of Human Rights (UDHR),[9] was also among its key proponents. In the twentieth century it has featured in the reaction to Nazism, in the American civil rights movement and in the fight for gender equality (McCrudden 2008, p. 663).

More importantly for purposes of this paper, dignity currently has a major role in the field of biomedical research and bioethics, so as to safeguard the basic characteristics of the human species (Andorno 2009). It is described as the *shaping* or *overarching principle* of global bioethics, and the ultimate rationale behind the rules, for example, in the UNESCO Declaration on Bioethics and Human Rights (UDBHR) (Andorno 2009, p. 227). It is also popular among Continental European ethicists who have challenged the particularly American and individualistic principles of autonomy, justice, beneficence, and nonmaleficence (Häyry 2004).

The 60th anniversary of the UDHR saw renewed emphasis on the role of dignity as one of the uniting factors in the human family (Nowak 2011). During this occasion, the Eminent Persons Panel (EPP), whose members are renowned for their extensive human rights experience, reiterated that dignity is *inherent* in all human beings and remains the moral and philosophical *basis for equality* and other universal human rights. With this they were underlining the continued relevance of the UDHR in which dignity is understood to refer to a *permanent* and *unconditional* attribute (Nowak 2011). In this regard, another way of understanding dignity, as per Andorno (2009, p. 231), one of the drafters of the UDBHR, is in its primary sense of the *intrinsic value of human beings* making it *the ultimate rationale for human rights* and *the basis for the prohibition of discriminatory practices*, degrading treatment and the 'instrumentalization' of people. This latter description carries a lot of weight in favour of the discussion herein on post-trial access to healthcare.

Other interpretations of dignity can be problematic. Among these is one caused by the ambiguous wording of Article 1 of the Universal Declaration on the Human Genome and Human Rights, which may be misunderstood to ground dignity in the human genome.[10] The misunderstanding can be avoided by reading Article 1 together with Articles 2 and 6 of the same Declaration, which prescribe respect for human dignity irrespective of genetic characteristics and prohibit discrimination on the basis of such genetic characteristics. Utilitarianism, on the other hand, associates dignity or moral worth of sentient beings with the ability to suffer (Häyry 2004, p. 10). Another view is that dignity has several levels and even contradictory meanings, which depend on the culture or sub-culture found in specific social contexts (Shultziner 2003). A more recent construal of human dignity is that shown by the advocates of human enhancement, but whose critics argue that such liberties actually harm rather than foster human dignity (Chapman 2015).

An additional challenge arises from the use of human rights as synonymous with human dignity, or its being reduced to a list of rights. Section 37(5) (c) of the South African Constitution, for instance, lists human dignity as a non-derogable right. Shultziner (2003), quoting Donnelly (1982), argues that human dignity is not expressed and assured universally by human rights alone because some spheres may correlate human dignity equally or more with duties than rights. Insofar as human dignity's content and meaning is determined in separate legal documents, its perceived content or meaning can change over time.

[9] Universal Declaration of Human Rights (UDHR), G.A. Res. 217 A (III) (1948). Available at http://www.un.org/en/documents/udhr/.

[10] UNESCO, Universal Declaration on the Human Genome and Human Rights, 1997, Arts 1 and 2. Available at http://portal.unesco.org/en/ev.php-URL_ID=13177&URL_DO=DO_TOPIC&URL_SECTION=201.html.

Dignity in the health research context

The above and other interpretations of dignity do not facilitate the already distorted understanding of the concept. The questions raised by the deliberation on human dignity have in fact not generated any consensus regarding the precise meaning, content, and requirements of this term (Chapman 2011, p. 3). The varied use of this concept has, as a consequence, attracted its share of critics in recent history for its apparent vagueness, lack of clarity, content and intelligibility (McCrudden 2008, p. 661). In philosophical or bioethical circles some consider it of little use in solving specific bioethical questions (Andorno 2011), consequently calling for its elimination on the grounds that its repeated usage adds little or nothing to the understanding of the topic (Macklin 2003, p. 1419). Others think, however, that such elimination is both unlikely and inadvisable (Brownsword 2010). Still, although the EPP affirms that human dignity is a universal concept transcending cultural differences (Nowak 2011), in actual fact varying interpretations prevail, depending on the underlying philosophy (Brownsword 2010).

The dominant modern interpretation of dignity as *individual autonomy* or empowerment is reflected in the above-mentioned EPP report (Nowak 2011, 38). It asserts that philosophers grounded the claim of human dignity and the uniqueness of human beings in *human free will, with the capacity for moral choice, and individual autonomy* (Caulfield and Chapman 2005, p. 736). Dignity as empowerment, or the right to make autonomous choices, is most apparent in the context of research ethics documents and informed consent policies where human dignity is treated as a means to make *autonomously chosen goals* (Caulfield and Chapman 2005, p. 736). Human rights theorists fall in this category (Brownsword 2010). Despite its limitations, some thinkers in fact see this as the only application of the concept, as shown below.

Andorno (2009, p. 230) advances a broader position that assures the protection of those who *do not* or *cannot* enjoy such autonomy because of their actual intellectual or moral abilities. Genuine consent to participate may also be hindered by limited or inaccurate knowledge regarding the true nature of clinical trials, such as the likelihood of abrupt study termination by the sponsor or the subtle but real implications of the distinction between clinical care and medical research (Saver 2009). These perspectives can greatly inform the RECs' role since informed consent is likely to be a somewhat relative concept or limited reality, where these and other constraints 'disempower' a priori those likely to be recruited in the trial.

The limited capacity to give or uphold genuine consent does not diminish inherent dignity, yet it could lead to increased vulnerability—understood here as the inability either to give adequate consent (Saver 2009), or to *sustain* or *extend* it—during and after the trial (Cash et al. 2009, p. 208). The dignity of research participants nonetheless transcends the fact and the moment of giving consent. We argue therefore that a correct interpretation of human dignity should extend to the *consequences* of making those choices, that is, to the post-trial phase. Here the dignitarian or duty-driven ethical position may be said to prevail in as much as consent does not eliminate the duty to respect human dignity (Brownsword 2010).

Andorno (2009, p. 231) also suggests a richer rendering of the above-stated Kantian notion of dignity. He refers to this approach as the *non-instrumentalization* or *non-commodification* of persons who deserve instead to be treated with the greatest respect and care. The post-study access to interventions proven to be effective in clinical trials or indispensable healthcare is an appropriate test in the latter interpretation of dignity as autonomy. The dignity of trial participants would entail more than being attended to so as to achieve the aims of the trial and instead would further ensure that their ill health is addressed even when the trial is over. Drawing from the South African experience, this approach would be pertinent in other LMICs since participants typically have limited options upon completion of the trial.

This paper therefore seeks to illustrate both the particular relevance of the concept of dignity in the context of international health research and subsequently its practical applicability specifically in the post-trial phase. Far from considering it redundant, all health research stakeholders need to keep working at the contextualization and application of this term, (Nowak 2011, p. 13) more so when it comes to thorny and context-sensitive issues like post-trial access in LMICs. The *unconditional value* of each and every human being needs to be underlined and reflected *in actu* once a 'researcher-participant' relationship is established. Human dignity makes it unthinkable that a research participant in a precarious health situation could later be left to his own devices because he or she is no longer 'useful'. The following quote from a LMIC research participant emphasises the point: "Because I will get into this trial, I get better, and then afterwards I am going to die. You have promised me life and then you take it back; that's not fair."[11]

[11] HIV/AIDS Clinical Trial Participant, Kenya 2006, quoted in Colona and Schipper (2015, p. 1).

How RECs can protect the dignity of health research participants

Gabr (1997, p. 5), a distinguished figure in Egypt's healthcare system, pointed out the lack of a coherent framework of human dignity violations in the field of health and the yet unidentified damage to wellbeing for as long as an adequate understanding and application of dignity remains unachieved. The crucial role of RECs could not be clearer in this light, keeping in mind that the concept of human dignity is often used in a manner to suggest that social consensus exists and its consequences fully assimilated, whereas, as just explained, this is far from the case (Caulfield and Chapman 2005, p. 737). South African REC members, like their global counterparts, have the responsibility to discern, judge and communicate effectively how human dignity is infringed upon or degraded, particularly in the context of emerging scientific advances (Caulfield and Chapman 2005, p. 736). In their evaluations, they have to be cognisant of the ongoing challenge of lack of unanimity regarding its interpretation and how human worth might be degraded by a given technology or scientific activity. The diverse meanings and content associated with the concept have to be pondered upon in relation to the values and background of the respective communities. Lack of clarity has the potential to hurt policymaking, and ultimately degrade the substantive value of the principle (Caulfield and Chapman 2005, p. 736). Greater attempts need to be made—as this paper tries to do in one specific sense—to show why and how dignity is threatened, over and above conveying a sense of general social unease or threats to the basic human condition.

The challenges outlined above can be dealt with in part by using this concept to facilitate policy debate (Caulfield and Chapman 2005, p. 737). This is particularly important in the context of globalized health research which is trans-cultural in nature. Häyry sees this as a way to foster increased understanding between people and cultures, with no attempts to monopolize the use of the term (2004, p. 11). RECs could contribute to clarifying the perceived or real vagueness so that human dignity remains a unifying concept rather than a controversial one (Shultziner 2003, p. 18). Taking cue from Gabr (1997, P. 11), efforts should additionally be made by RECs to identify still undetermined types of vulnerability, and to develop what he called a *taxonomy and epidemiology of violations of human dignity in health*. Since one of the more notable forms of vulnerability in South Africa is caused by unequal access to healthcare making those affected resort to free treatment through participation in the numerous clinical trials (Wemos Foundation 2013, p. 1), local RECs can lead the definition of a 'taxonomy of violations' suitable for LMIC contexts.

In order for human dignity to be better protected, therefore, these RECs will strive to contribute to a deepened understanding of the concept, and point international researchers to its practical application and rationale in specific circumstances. This would entail, in part, possession of the expertise and contextualized knowledge needed when reviewing protocols, and during their subsequent monitoring. Capacity building in this precise sense should be a given, further strengthened by the ideally multi-disciplinary nature of the RECs, with ethicists included (Silaigwana and Wassenaar 2015). Actual or potentially disadvantaged communities should also be represented (SA Medical Research Council).[12] In the African context, it is advisable that non-clinical members also be relied upon, especially on issues of consent and information to participants (SA Medical Research Council).[13] South African RECs in this way contribute to the formulation of ethical regulations and policies suited to the local setting.

As also indicated by the SA Medical Research Council, committees should command technical competence and judgement to reconcile the *physical* and *psychological* consequences of participation with both the welfare of the research participants and the research objectives.[14] We argue that post-study access to healthcare is one such scenario worthy of being addressed in this perspective, more so where the investigational health intervention is unlikely to be available to the research participants.

A national accreditation process may help to promote consistent application of ethical principles in this regard (Omosa-Manyonyi et al. 2015). This approach would moreover uphold the rationale of the UDBHR, which deliberately gave no precise definition of this term on the basis that it is best left to courts' interpretations (Andorno 2007). RECs—or the national accreditation body—could play this role by fostering a more precise interpretation of human dignity in the given social, economic and cultural context. Strong local ethical expertise could in consequence be nurtured and further guaranteed, thus ensuring that vulnerable persons are actual beneficiaries of relevant research (NRC 2014, 16–17).[15]

The next discussion outlines in practical terms the rationale for the post-trial provision of healthcare, and how this best responds to the dignity of any research participant in need of this intervention. It is compatible with other collateral research benefits and does not substitute the government and international community in their duty to provide healthcare to their citizens/members.

[12] *General Principles*, para 9.9.2 vii.

[13] *General Principles*, para 9.9.1.3.

[14] *General Principles*, para 9.9.1.1.

[15] See also s 4b of the National Health Act.

Dignity as the foundation of post-trial access and the respective REC role

The above description of dignity has significant implications in the context of international health research, and specifically in what has been termed *post-trial ethics* (Mastroleo 2015). Dignity requires respect and care for persons as subjects, not objects (McLean 1997), or segments of a production line (Mano et al. 2006). This approach is somehow alluded to by Saver (2009) when he suggests that the research relationship begins and ends with the study protocol. Dignity, nevertheless, characterizes the research endeavour above all as a relationship between persons, rather than a mere business transaction (Zvonareva et al. 2015).

Regard for dignity will lead the health researcher to adhere consistently to the ultimate purpose of his or her task, which is to solve specific health problems and to strengthen links between research and healthcare (Benatar and Singer 2010). The social value of research will be specified and enhanced (Emanuel et al. 2005; Lairumbi et al. 2011), not being overtaken or undermined by mundane reasons such as cheaper, faster and more abundant and varied research (Shapiro and Meslin 2001; Kass and Hyder 2001; Ballantyne 2005; Saver 2009) or less stringent ethical requirements (Benatar and Fleischer 2007). The knowledge obtained is not intended to be an end in itself (Haire 2011) or for the sole benefit of the sponsors' country (Saver 2009); rather it should be generalizable and translatable into better health all round (Glantz et al. 1998), thus contributing to the achievement of health as a basic good (Ballantyne 2010) and a human right (Haire 2011) for everyone. Studies that do not respond to health needs (Millum et al. 2013) and redress health disparities (Haire 2011) would otherwise make little or no sense (Glantz et al. 1998; Lairumbi et al. 2011).

The international health researcher is aware that the research project is not carried out in a vacuum (Benatar and Fleischer 2007) and that reference to context is indispensable (Pratt and Loff 2011). Where the research participants face limited or non-existent access to healthcare and/or are suffering a severe health condition, for which no immediate treatment or healthcare is accessible, the researcher is bound to acknowledge and address *that* particular situational vulnerability (Glantz et al. 1998; Benatar and Fleischer 2007) with particular sensitivity to past or current complicity by the West in the perpetuation or exacerbation of the pervasive poverty that is driving it (Shapiro and Meslin 2001; Benatar 2002; Benatar and Fleischer 2007; Zong 2008; Leisinger 2009). Such circumstances inevitably imply a high probability of individual or community exploitation (Gbadegesin and Wendler 2006; Shaffer et al. 2006; Benatar and Fleischer 2007; Zong 2008), due in part to the subsequent unavailability of medication and health services (Okpechi et al. 2015). It would otherwise be unethical to ignore that vulnerability (Pratt and Loff 2011), not even with the excuse of favouring research participants over other community members (Saver 2009), although it will vary in nature and intensity.

Additionally, the researcher cannot forget that although at times undesirable (Annas and Grodin 1998; Schroeder and Gefenas 2012), it is to be expected that there will be research participants who will enrol in the trial for purposes of obtaining treatment (Busse 1997; Saver 2009; Okpechi et al. 2015), just as happens in the West (Hebert-Croteau et al. 2005; Bois et al. 2005; Mano et al. 2006). In addition, the health researcher cannot entirely dissociate health research from medical care (Annas and Grodin 1998; Miller et al. 2003; Grady 2005; Haire 2011, 2013) or clinical practice, and the researcher role (Angell 2000) and development work (Resnik 2001; London 2005; Benatar and Fleischer 2007) although it is understood that research per se is neither about providing healthcare (Miller and Rosenstein 2003) nor restoring global socioeconomic inequality, much like the pharmaceutical industry has profit as one its chief aims (Leisinger 2009). The health researcher - especially in an LMIC context—nevertheless has a broader role as regards duty of care (Haire 2011), even though his/her post-trial responsibilities will somehow 'only' be an extension of research, and not its equivalent (Zong 2008; Haire 2013). The welfare of their patients is still a priority (Angell 1997, 2000; Shaffer et al. 2006) more so where the participants require continuing medical attention, as Saver (2009) rightly points out.

The health needs and limited health services of the research population obliges the health researcher to do everything possible to make the necessary research project realizable in the first place since it does not have merely one-sided aims. LMICs benefit from research in numerous ways (Annas and Grodin 1998) that are better off enhanced (Emery and Cooper 1997), not diminished or arbitrarily disregarded, as may happen with some pharmaceutical companies (Colona and Schipper 2015). Post-trial access is not an encumbrance to be avoided at all costs, as Saver (2009) advises. A compelling reason for pursuing a project against the existing or foreseeable odds is therefore the health benefits that are likely to accrue in a given context, without of course overlooking the needs of the sponsoring country. Funds can be earmarked (Essack 2014) with the joint efforts of trial sponsors and donor agencies (Berkley 2003), and/or raised in creative ways (Ananworanich et al. 2004; Grady 2005; Benatar and Fleischer 2007; Ballantyne 2010; Schroeder and Gefenas 2012; Ross 2014). This will in turn boost research initiatives that factor in the post-trial needs of the research participants, without disincentivising the researcher (Brody 2002; Berkley 2003; Colona and

Schipper 2015). Ultimately, healthcare could, at the very least, be provided at an affordable price (Pace et al. 2006) and in this way post-trial benefits can be extended to needy non-research participants.

Insofar as better health/healthcare is the health research goal per excellence, the international researcher needs to identify with the health priorities of the target population (London 2005), just as pharmaceutical innovation is supposed to be aligned to the common medical needs of both the sponsor and the host countries (Nathan 2007). This should be reflected in the drafting process and in the ethical section of the study protocol (Páez et al. 2009). The research project is, properly speaking, a collaborative endeavor aiming at common problems (Knoppers 2000; Chadwick and Berg 2001; Resnik 2001; London 2005), a fact that has been found implicit in South Africa for example (Zvonareva et al. 2015). Research participants generally intend to cooperate in a mutual act of solidarity (Benatar and Singer 2010; Schroeder and Gefenas 2012; Zvonareva et al. 2015) for the global wellbeing and common good (Berkley 2003). This point has a lot to do with context because the potential/actual research participants have certain expectations rooted in their specific moral viewpoints (Zvonareva et al. 2015) that deserve not only respectful acknowledgment, but also a sensitivity that shows appreciation and understanding of diversity across cultural contexts. Researchers' responsibilities in such a context are not reduced to resolving technical issues such as more accurate and complete disclosure prior to obtaining consent, as Saver (2009) proposes. Research participants are in turn expected to embrace the value and aims of the scientific endeavor and do all that is in their power to bring the research project to fruition. That, too, could be said to be a manifestation of their human dignity.

Despite the uneven legal landscape (Sofaer et al. 2013; Colona and Schipper 2015), and although few examples of good practice exist (Grady 2005; Shaffer et al. 2006; Schroeder and Gefenas 2012; Colona and Schipper 2015), post-trial access is still an ethical issue of global concern (Bois et al. 2005; Hebert-Croteau et al. 2005; Sofaer et al. 2013; Haire and Jordens 2015). This does not mean that it is not at times regarded as undesirable for reasons such as undue inducement (Macklin 1981; Emanuel et al. 2005), delay or prevention of trials (Brody 2002; McMillan and Conlon 2004; Saver 2009), and, likelihood of misuse as a marketing tool (Taylor and Wainwright 2005).

The right and duty of post-trial access to healthcare is nonetheless more evident in the perspective of mutual solidarity, and one can more easily comprehend why a research participant who has persisting health needs (Mastroleo 2015) and no suitable healthcare upon the completion of the clinical trial will feel exploited and resentful (Emanuel et al. 2004a, b), unfairly treated (Shaffer et al. 2006), or abandoned (Shapiro and Meslin 2001), if medical care is cut off abruptly. It would seem that their vulnerability has been manipulated simply to achieve the unilateral aims of the researcher and analogous foreign needs (Varmus and Satcher 1997; del Rio 1998; Shaffer et al. 2006). This is more lamentable and out-rightly unethical (Emery and Cooper 1997; McLean 1997) where it is likely to lead to clinical deterioration (Grady 2005; Shapiro and Meslin 2001; Zong 2008) and even death (Doval et al. 2015). Similarly, the duration of post-trial access to healthcare cannot be calculated a priori as it will depend to a great extent on the real-life situation of the individuals or communities concerned (Shaffer et al. 2006; Zong 2008) and the trial in question (Saver 2009). It is argued, besides, that the researcher should not apply lower ethical standards under the pretext of divergent political and economic conditions in a given region as compared to the sponsor country (Angell 2000).

There seems to be a growing sensitivity (Nuffield Council on Bioethics 2002; Shaffer et al. 2006; Zong 2008) and even legislation (Schroeder and Gefenas 2012) regarding post-trial access albeit without a consensus on the relevant modalities and duty-bearers (Cohen et al. 2009). *Access to healthcare*—where called for—is recognized in literature as one of its distinctive dimensions (Loue and Okello 2000; Berkley 2003; Mastroleo 2015). As earlier discussed, it is differentiated and sometimes preferred to the investigation drug due to the complexity associated with the latter measure (Schroeder and Gefenas 2012). Furthermore, although other benefits are welcome and usually necessary, they should not be deemed to be a suitable replacement of the basic one of responding to the health needs of the research population (Berkley 2003); this might be a form of double standards (Zong 2008). The dignitarian approach could be applied to rebut the argument by Saver (2009) that subject autonomy suffices in situations where a prospective research participant prefers to forfeit post-trial access rather than the research project as a whole. Their desperation should not be used against them, nor their dignity compromised, even if it is considered that they have given informed consent (Brownsword 2010) and are content with collateral benefits.

Researchers have actually been found to have a 'post-trial access' mentality even in the US (Shah et al. 2009) even though its rationale varies and remains debatable (Sofaer and Strech 2011; Sofaer 2014). For this reason, human dignity is proffered here as a plausible basis for this noble approach to international health research, with the overall aim of not only aspiring to, but also proactively attaining the highest ethical standards (Angell 1997) in all places where health research is carried out. Bilateral agreements and the elevation of post-trial access to an international human right (Pratt and Loff 2011) would be

a laudable milestone and useful tool to clarify and enforce post-trial obligations (Schroeder and Gefenas 2012).

The conviction of the worth of this endeavour will lead the researcher to carefully and realistically plan in advance for post-trial access (Glantz et al. 1998; Grady 2005; Mano et al. 2006; Zong 2008; Shah et al. 2009; Ibia et al. 2010) and remain undeterred by difficulties and the complexity of the issue (Leisinger 2009; Haire and Jordens 2015). As will be elaborated ahead, he or she will first and foremost consult and engage the community through dialogue (Lairumbi et al. 2011), informed and transparent discussions (Slack et al. 2005) appreciative of respective positions (King 1997) and worldviews (Pace et al. 2006; Shaffer et al. 2006; Weijer and LeBlanc 2006; Zvonareva 2015), in order to jointly identify their health priorities (London 2005), seek to clarify mutual expectations from the onset (Essack et al. 2010), and perceive the pursuit of scientific knowledge with more realistic lens (Jasanoff 2007). Where appropriate, the researcher could respectfully negotiate or bargain (Grady 2005; London 2005; Weijer and Le Blanc 2006) for desirable terms since it is understood that needs vary and thus no single recommendation is valid for all situations (Ciaranello et al. 2009). Some compromise may be necessary though (King 1997). Communal/cultural values and needs will, however, be recognized at all times.

Additionally, they will do all that is possible to mobilize a multi-stakeholder approach (Leisinger 2009; Benatar and Singer 2010) leading to the establishment of partnerships (Shapiro and Benatar 2005; Zong 2008; Leisinger 2009; Shah et al. 2009) and strategic alliances (King 1997; Benatar and Singer 2010). They will also challenge the pharmaceutical industry to fulfil its corresponding moral obligations (Leisinger 2009). Above all, they will do what is necessary to encourage responsible health governance (Pace et al. 2006; Leisinger 2009; Colona and Schipper 2015) inter alia by affirming and fostering the role of the state and the international community vis-à-vis the right to health of their citizens/members with the support of physicians and researchers (Haire 2011; Schroeder and Gefenas 2012). This includes averting corruption (WHO 2000) and instead pushing for adequate allocation of resources (Leisinger 2009) and the required input from national drug regulatory authorities (Okpechi et al. 2015), so as to progressively and sustainably (Berkley 2003) realize the rights (Leisinger 2009) of all people in developing countries.

The nature and scope of the RECs' role can be discerned in the above discussion. It needs to cut across the whole study itinerary, from the design stage until healthcare provision after research, if applicable. The REC needs to be part of the discussions (King 1997) regarding research priorities and questions (London 2005) and to firmly play its corresponding vetting role such as ensuring that post-trial access is not perceived as an afterthought, or some vague commitment (Grady 2005). Insofar as informed consent is a widely held means to safeguard human dignity, the expectations of prospective research participants in relation to care after research need, at least (Ciaranello et al. 2009), to be clarified prior to commencement of the trial and if deemed necessary, strategically implemented as the project draws to a close. Informed consent ought not to even implicitly override the right to post-trial care (Cleaton-Jones et al. 1997) and a compelling justification would be required for discontinuing treatment (Grady 2005). The REC could also ensure that its approval criteria is aligned with the national health strategies and goals as then the arising healthcare needs have better chances of being funded by government (Haire and Jordens 2015). It is understood that the REC would tap into the expertise of 'post-trial access-minded' stakeholder representatives, including local health authorities (Ibia et al. 2010), in order to provide a holistic host-country ethical perspective that their international counterparts need to count with from the onset (Schroeder and Gefenas 2012). In these and other ways, the LMIC RECs would boost its capacity and thus play an even more leading role in the delicate yet vital protection of the human dignity of international health research participants drawn from their countries/jurisdictions.

The following section addresses the challenges that South African RECs face in discerning and effecting measures needed to ensure the protection of dignity in the post-trial phase of international health research.

Challenges facing South African RECs

International ethics guidelines, namely, the Declaration of Helsinki (DOH) and the Council for International Organizations of Medical Sciences (CIOMS) guidelines provide for the protection of human dignity (WMA 2013; CIOMS 2002). Both have directly shaped the development of the South African ethical-legal framework. Paragraph 9 of the DOH obliges physicians who are involved in medical research to protect the dignity of human participants. Paragraph 23, which prescribes the functions of RECs, on the other hand obliges committees to "take into consideration the laws and regulations of the country or countries in which the research is to be performed, as well as applicable international norms and standards." CIOMS guidelines in turn emphasize the need for RECs to include members who are sensitive to issues of human dignity and to ensure that the process of obtaining informed consent manifests respect for the participants' dignity.[16]

[16] Commentaries on Guidelines 2 and 4, respectively.

Human dignity is one of the values of the South African democratic state, and is also contained in the bill of rights, which provides that "everyone has inherent dignity and the right to have their dignity respected and protected."[17] Consequently, the South African ethical-legal framework recognises "respect for the dignity of persons" as a fundamental ethical principle (National Department of Health 2006).[18] One of the roles of RECs as stipulated in the national guidelines on clinical trials, is "ensuring that humans involved in research are treated with dignity and that their well-being is not compromised…"[19] Paragraph 2h of the national regulations relating to research with human participants equally provides for the "respect [of] participants' rights, including, but not limited to, rights to dignity, privacy, bodily integrity and equality."[20]

As already established in the preceding section of this paper, part of the challenge from the onset is that there are multiple interpretations of dignity prevailing, which means that what an African REC may consider to be dignity, might differ to a lesser or greater extent if, for instance, the applicant is coming either from the United States of America (USA) or from a European country. There could also be discrepancies among the REC members themselves regarding the understanding of this concept.

The specific challenges that RECs face in South Africa can be gleaned by considering some of the relevant findings from a 2012 audit of 33 RECs registered with the South African National Health Research Ethics Council (NHREC).[21] The audit was conducted in terms of the National Health Act (NHA)[22] with the objective of testing the compliance of RECs with international and national guidelines (2004). Notably, the national guidelines stipulate that "respect for the dignity, safety and well-being of participants should be the primary concern in health research involving human participants."[23] The National Department of Health hopes that the results will help in the protection of human participants and training of RECs. We identified the relevant audit findings based on the three challenging considerations that Cook and colleagues made in their assessment of the academic arguments in support of post-trial access. These are: the specific benefits that should accrue to the participants to make the researcher-participant relationship less exploitative; the relevant people that should benefit, and, identification of the relevant parties that should provide the benefits (Cook et al. 2016, p. 71). In order to address the said considerations, we consider monitoring of approved research projects, fair research contracting, community consultation, and training, to be especially applicable to RECs.

Monitoring approved projects

The national guidelines require RECs to ensure "that the conduct of all research approved by the ethics committee is monitored." Apart from passive monitoring through reliance on the annual reports from principal investigators, mechanisms considered appropriate for active monitoring are "random inspection of research sites, data and signed consent forms, and records of interviews, with the prior consent of research participants."[24] Dhai gives examples of passive and active post-approval monitoring by the University of the Witwatersrand. "Passive monitoring involves reviewing reports from the sponsors' monitoring agents and data from safety monitoring boards, while active monitoring involves site visits." She states that "there have been instances… where active monitoring identified problems that required fixing before enrolment could continue"(NRC 2014, p. 18). This essentially shows that the rights of participants could be violated in the absence of active monitoring.

The NHREC audit established that 61% of the audited RECs include monitoring in their standard operating procedures, although this mainly refers to passive monitoring. Additional monitoring is mostly done in reaction to reported adverse events that could present additional risks that are noted in the reports that are submitted by the investigators in the course of passive monitoring (National Department of Health 2012).[25] Lack of capacity within the RECs was cited as the main reason for not including active monitoring. The report accordingly recommended that RECs ensure that all research that has been approved is actively monitored.[26] Active monitoring would be helpful for identifying the specific benefits that should accrue to the participants, as well as the ones that are likely to require post-trial access to healthcare. It is also useful for dealing with the related issue of determining who should actually benefit.

[17] The Constitution of South Africa, ss 1 (a) and 10.

[18] Para. 1.2.

[19] Para. 8.1.

[20] No. R. 719, issued in terms of Sect. 71 read with Sect. 90(1) of the National Health Act on 19 September 2014.

[21] National Department of Health, *Audit of health research ethics committees project, final report*, (September 2012).

[22] s 72 (6) (b).

[23] Guiding principle 2.1.

[24] Guiding principle 4.7.

[25] Para 3.1.8.

[26] Para 3.2.

Fair research contracting (justice)

Dhai considers this relevant "in terms of how the burdens and benefits of research are distributed among the collaborators and how decision making occurs" (NRC 2014, pp. 18–19). This ties with the question of post-study access, which in the current version of the DOH is deemed to include research participants who are not necessarily involved in clinical trials; it has also broadened the scope of benefits beyond products or interventions that result from the research (WMA 2013).

Paragraph 20 of the DOH, provides as follows:

> Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

Although the paragraph is rather vague in its stipulations, it allows for a range of benefits beyond products or interventions that result from the research. We envisage situations where such an interpretation may cover post-trial access to healthcare within poor communities.

In view of the circumstances that prevail in South Africa, participants who are motivated by access to medical care are susceptible to undue influence and can be classified as vulnerable. RECs are obliged to ensure that such participants benefit from the research (Andanda et al. 2013, p. 47). Vulnerability is a contested concept, but in this context the definition suggested by Schroeder and Gefenas is helpful for clarifying why the South African participants qualify as vulnerable. They define vulnerability to mean facing: "...a *significant probability* of incurring an identifiable harm, while substantially *lacking the ability and/or means to protect oneself*" (Schroeder and Gefenas 2009, P. 117).[27] The South African Regulations relating to research on human participants closely reflect most of the elements in the above definition: "…persons at increased risk of research-related harm, or who are limited in their freedom to make choices, or relatively incapable of protecting their own interests."[28] Poor South Africans who cannot afford healthcare and are motivated to join clinical trials as the only possible way of getting such care fit within the definition of vulnerability. The situation is clearly unjust (Dhai and Veriava 2012, p. 520).

Lack of community consultation and involvement of local researchers in the study design

A related challenge identified in the audit report is that although research proposal reviews were done to a satisfactory standard, there were some concerns with the process, that is, lack of evidence of community consultation and a communication plan for some approved research proposals where research involved communities (National Department of Health 2012).[29] This situation clearly needs to be addressed with a view to engaging with communities and ensuring that their circumstances are taken into consideration in approving proposals. Considering that concerns have already been raised regarding the exclusion of local researchers in developing the study design, lack of consultation with the community only compounds the problem further. Consultation with the communities will go a long way in helping RECs to contextualize the contested concept of dignity. It is the only way in which RECs can reckon with the values and backgrounds of the respective communities, as discussed in the previous section, in order to protect the dignity of research participants.

Lack of involvement of local researchers in designing the protocol may lead to undesirable consequences for the local trial participants. The South African national guidelines underscore the need to modify research protocols to suit the situation in local communities (National Department of Health 2004).[30] Indeed, one of the suggestions for improving the quality of international collaborative health research is "rigorous training in the design, conduct, and ethical oversight of trials…" to enable LMIC investigators "to engage more fully in multinational clinical research at a leadership level" (Glickman et al. 2009, p. 820). The reality, particularly in LMICs like South Africa, however raises serious concerns that can be discerned from the following extract from Wemos' report:

> A disturbing issue for both [private and public] sectors is the fact [that] most trials are designed and finalised before they are brought to us, with little if any room for changing the design or inclusion/exclusion criteria. … Really they are using us for our numbers, they are not interested in any intellectual input we make in the developing world; it is only about the number of patients we can recruit...[31]

The situation confirms our earlier observation that having a robust ethical-legal framework is not sufficient and that RECs should actively intervene to ensure that protocols suit local needs.

[27] Emphasis added.

[28] No. R. 719, issued in terms of Sect. 71 read with Sect. 90(1) of the National Health Act on 19 September 2014.

[29] Para 3.1.7.

[30] Principle 2.13.

[31] Professor M Tikly, quoted in the Wemos Foundation 2013, p. 31.

Training

Training and induction of newly appointed members to RECs is not common and the NHREC's audit recommended that this should be done. The prevailing obstacles are:

- Budget constraints;
- Lack of guidance regarding training requirements for members;
- Absence of a national standard;
- Most members are experts in their fields; and
- Most members are trainers (National Department of Health 2012).[32]

The above scenario clearly shows the need for training, as we earlier pointed out, in order to ensure that RECs have the expertise that is indispensable for reviewing protocols and monitoring approved research. This seems to be the relevant guidance that is missing from the training requirements for REC members. The complexities of a globalized health research context should be the main reason for encouraging RECs to undertake regular training as suggested in the audit.

Conclusion

We have highlighted some of the key challenges that can be encountered in attempting to justify the claim for post-trial access to health care in a globalized context and analysed how these can be countered based on human dignity. After highlighting the challenge of reaching a common understanding of dignity on a global platform, we conclude that a robust ethical-legal framework in itself is not sufficient to guarantee protection of clinical trial participants' dignity. RECs should play a more active and informed role in interpreting the contextual meaning and application of human dignity, and thus compliance with the post-trial obligation of providing access to healthcare to needy participants. The main suggestions from our discussions are summarized below.

It is important to involve the local researchers and communities in designing protocols and RECs should actively intervene in cases where protocols are pre-designed by international collaborators with a view to ensuring that local needs are met adequately. Such interventions will ensure that the research project will also take care of the immediate healthcare needs of the research participants based on human dignity and using a broad fair benefits framework. Equally, through such a strategy, a post-study access to healthcare can be secured for the local communities.

Active monitoring of approved research projects is crucial for ensuring compliance with ethical principles and standards so as to protect the dignity of human participants. The current trend of relying exclusively on passive monitoring is certainly undesirable as it does not assure the adequate protection of research participants' dignity.

Ongoing training of REC members is crucial because competent RECs can make an essential contribution towards specifying what constitutes a violation of human dignity in the context of health research. In this way, they will help to refine and possibly unify the understanding and practical application of human dignity in and from the given context. Importantly, dignity should be understood to include not only the reasonable and just benefits of autonomous choices, but also the corresponding duty to respect it regardless of the circumstances. It should be the bulwark against any attempt to use vulnerable research participants merely as a means to attain scientific goals that exclude their overall well-being, even where consent is believed to have been given freely.

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[32] Para 3.1.4.

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