Research ethics review – protecting participants in research

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The global proliferation of medical research has imposed a huge responsibility on research ethics committees (RECs). While South Africa has a climate conducive to serious growth in research, it is also home to a large number of vulnerable groups of poor populations. The potential for misuse of power in research cannot be ignored. Stipulations within the National Health Act now make the ethical practice of research a statutory requirement in South Africa. Commitment to REC support by institutions will be reflective of their commitment to ethical research. However, currently RECs are overworked and understaffed. Regrettably, protecting participants in research has not kept pace with the rapid increase of research in the country.

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The past few decades have witnessed a global proliferation of medical research including multicentre, international and pharmaceutical studies.[1] South Africa, with its sound infrastructure, medical expertise in science and technology and well-equipped research institutions, is a country of immense research potential. While the clinical research industry has existed in South Africa for about 30 years, it has experienced rapid growth over the past decade,[2] increasing by 40% between 1997 and 1998,[3] with the total budget during 2000 being in the region of R826 million (M Joffe – unpublished data). Reasons for this include researchers being able to meet patient recruitment timelines and targets consistently. More recently, South Africa has been viewed as a valuable 'gateway' for launching clinical research efforts northwards into the rest of Africa.[2] In addition, in 2003 South Africa was rated 4th as a top international National Institutes of Health (USA) grant recipient by country, with Canada, the UK and Australia in 1st, 2nd and 3rd places respectively[2] (see Table I for an example of the increasing number of reviews at an institutional level).

While South Africa has a climate conducive to serious growth in research, it is also home to a large number of vulnerable groups of poor populations who have limited or no access to education and health services and who accept authority without question.[4,5] Fifty per cent of South Africans live below the poverty line.[6] As a country we suffer from several of the health burdens of a developing nation and are still recovering from the many years of oppression under apartheid. This, together with previous tragedies, makes clear that potential for misuse of power in research cannot be ignored. Accordingly, the promotion of high ethical standards to protect participants in research is imperative. Currently, research ethics committees (RECs) are assigned this duty. However, protecting participants in research has not kept pace with the rapid growth of research.

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Historical perspective

That medical research has resulted in improved well-being cannot be disputed. However, over time, medical research has also violated the rights and dignity of participants, with the first transgressions being documented in the 19th century.[7] Many of the now well-known brutalities on Jews and other victims in the name of medical research were exposed in the aftermath of World War II during the Nuremberg Trials, and by the late 1960s medical research had undergone several scandals and tragedies.[7] Beecher's landmark article 'Ethics and clinical research'[8] in 1966 in the *New England Journal of Medicine* resulted in ethical issues in research receiving much more attention. Twenty-two studies that violated the basic standard of ethical research with human beings were described. These studies were performed by respected researchers at leading medical institutions and were published in reputable medical journals. Reports in 1972 revealed extensive violations of human rights in the Tuskegee Syphilis Study which was initiated in Alabama in 1932.[9]

South Africa has also had its fair share of scandals. While the Truth and Reconciliation Commission in 1994 did not specifically address research issues, it highlighted the human rights violations inflicted on many South Africans by members of the medical fraternity, some of whom were active researchers.[10] In December 1990, randomised trials assessing the efficacy of high-dose chemotherapy in metastatic and high-risk primary breast cancer were begun by Werner Bezwoda at the University of the Witwatersrand. Impressive results, showing that patients in the high-dose group had survival significantly superior to that in the standard-dose group, were presented at two international oncology meetings in 1999. Some oncologists adopted the Bezwoda approach as standard therapy and an onsite review of his data was undertaken before embarking on an international multicentre confirmatory trial. Sadly, the review revealed vast disparity between the records and the data presented at the international meetings, there was no signed informed consent and the institutional REC had no record of the study being submitted for ethics clearance.[11]

Table I. Breakdown of protocol reviewed by the Biomedical Research Ethics Committee at the University of KwaZulu-Natal over a 5-year period*

	2004	2003	2002	2001	2000
Investigator-driven studies (*N*)	186	166	116	97	108
Studies for higher degrees (*N*)	65	39	36	37	29
Industry-related trials (*N*)	23	35	29	27	36
Total studies reviewed (*N*)	274	240	181	161	173

* The author thanks Cheryl Borresen (administrator University of KwaZulu-Natal Biochemical REC) for facilitating access to the figures in the protocol breakdown. Permission was obtained for use of these data from the REC on 1 March 2005.

Research participant protections – process

In response to Beecher's landmark paper, from 1966, individual institutions in South Africa constituted review bodies to appraise the ethical aspects of research, and provide ethics clearance before undertaking research.[12] However, while there are various codes elucidating fundamental protections and oversight bodies to guide the ethical practice of research, exploitation of participants' vulnerabilities has continued, as evidenced by the above examples.

In 1998, a process to develop guidelines to promote good practice and standards in the conduct of clinical trials in South Africa was started by the National Department of Health. This resulted in the production of a conceptual framework by the end of 1998, and a final document in 2000, 'The Clinical Trials Guidelines', guided by and based extensively on international documents.[13]

In 2000 the Interim Ministerial Committee on Health Research Ethics was appointed and it has functioned since to review the guideline documents of 2000 and to act in an advisory capacity to local RECs. The National Health Act[14] requires the establishment of the National Health Research Ethics Council (NHREC), its functions being to: 'a. determine guidelines for the functioning of health research ethics committees; b. register and audit health research ethics committees; c. set norms and standards for conducting research on humans and animals, including norms and standards for conducting clinical trials; d. adjudicate complaints about the functioning of health research ethics committees; e. hear any complaint by a researcher who believes that he or she has been discriminated against; f. institute disciplinary action against any person found to be in violation of any norms and standards, or guidelines, set for the conducting of research; and g. advise the national department and provincial departments on any ethical issues concerning research.'

The Act further affirms that every institution, health agency and health establishment at which health research is conducted must either establish or have access to a health REC, which is registered with the National Health Research Ethics Council. Hence ethical practice of research is now a statutory requirement in South Africa.[15] Moreover, the emphasis on RECs, together with the need for central audit, clearly implies that these committees may be viewed as the main protectors of human research participants. If implemented appropriately, central registration could also lead to systematic collection and dissemination of performance data. Currently, records are lacking on the number of health-related projects and people participating in health-related research in the country, the number of research participants suffering serious adverse events each year, and the number who sustain permanent disabilities or die unexpectedly from their involvement in research.

Research participant protections – some challenges

While recent legislative changes mandate ethical rigour in research, there are challenges to implementation. Financial implications of protections programmes may result in RECs not doing justice to their protections role. This is true even in resource-rich regions. Deficiencies in institutional review board (IRB) procedures led to the suspension of clinical trials programmes at several institutions in the USA. Strengthening these processes increased their operational costs substantially.[16] While there has been some mobilisation in the USA to address meaningful reform, including federal oversight, IRB members continue functioning under demanding conditions, juggling IRB membership with numerous other responsibilities. This, together with a lack of recognition of their communal contributions, communicates to them a devaluation of their commitment to ethical research. Not only is this demoralising to IRB members, but there are damaging implications on a practical level as chairs of these bodies have difficulty securing and retaining qualified members. In addition, lack of resources compromises administrative and support staff.[17] Currently, South African RECs, with their increasing workload, find themselves in a similar situation. Nevertheless, increased research is usually commensurate with increased funding to institutions that have an obligation to apportion part of this to REC support. It will require more than just legislative changes to ensure research participant protection.

Among the multiple duties of RECs is the post-approval responsibility of monitoring approved protocols. Lack of REC support also means that in most instances the committees are unable to fulfil this obligation adequately. Post-approval monitoring includes annual review, consent monitoring, monitoring of adherence to protocol and monitoring of data integrity.[18] Many problems uncovered with current research practices arise after continuing review and might have been avoided with thorough and careful monitoring and continuing review.[17]

Conflicts of interests involving RECs can occur at multiple levels. It has been suggested that by virtue of their constitution and location RECs in academic institutions are remarkably close to the scientific community whose research they review. This could possibly result in institution and investigator protection at the expense of subject protection.[19,20] RECs need to protect and maintain their independence within organisational structures so as to reduce the risk of compromising participant protections in favour of institutional interests.[21]

Conclusion

The need for registration with the NHREC, and the stringent requirements for accreditation, means that the REC can no longer be regarded as 'just another administrative committee' within the institution. The National Health Act has set the rules for research involving humans. REC accountability is no longer limited to the institution only. The time has come for appropriate recognition and support to be accorded to RECs and research ethics as a discipline if RECs are to function as protectors of human research participants.

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