

Evolution of Research Ethics in a Low Resource Setting: The Case of Uganda

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Abstract

Background: The globalization of clinical research in the last two decades has led to a significant increase in the volume of clinical research in developing countries. As of 2016, Uganda was the third largest destination for clinical trials in Africa. This requires adequate capacity and systems to facilitate ethical practice.

Methods: This was a retrospective study involving review of laws, guidelines, policies and records from 1896 to date.

Results: Modern medicine evolved from 1896 and by the time of Uganda's independence in 1962, a 1500 bed national referral hospital was in place and a fully-fledged medical school was established at the Makerere University. As the practice of medicine evolved in the country, so did medical research that addressed priority health issues.

The growth in modern medicine was not matched with development of research infrastructure and regulatory systems. The first documented regulation of research activities was in 1970 while the first research ethics committee established in 1986 was to facilitate review of research related to the HIV/AIDs pandemic. In 1990 an Act of Parliament was passed to facilitate development and implementation of policies, hence the development of the national guidelines in 1997, training, establishment and accreditation of research ethics committees, conferences and research site monitoring.

Conclusion: Over the past 120 years, the implementation and structural aspects of research ethics in Uganda have evolved through 70 years of no regulation, followed by 30 years of rudimentary regulation while the last 20 years have shown significant growth in the regulatory system associated with supportive laws, institutionalization of regulatory and training processes.

KEYWORDS

evolution, research ethics, Uganda

1 | INTRODUCTION

The globalization of clinical research in the last two decades has led to a significant increase in the volume of clinical research in developing

countries. By 2016, Uganda was the third largest destination for clinical trials in Africa after South Africa and Egypt.¹ Ethical conduct of such numbers of research projects necessitated availability of

¹Clinicaltrials.gov. Available from: www.clinicaltrial.gov. Retrieved 18 Jul 2016.

adequate capacity and systems to facilitate the effective ethical review, regulation and implementation of research.^{2,3,4,5,6,7,8}

Though the practice of modern medicine in Uganda is credited to Sir Albert Ruskin Cook starting in 1896, documented regulation of research activities in the country is traced to as late as 1970 with the formation of the National Research Council (NRC). This implies that a number of recorded research activities in the country between 1896 and 1970 did not benefit from a formalized research regulatory system. In 1990 the NRC was transformed into the Uganda National Council for Science and Technology (UNCST) with a broader mandate to guide and coordinate all research and development programs throughout Uganda.⁹

It should be noted that research ethics to a great extent has been informed by international ethics scandals and documents like the Nazi experiments, Tuskegee syphilis studies, Thalidomide experience, Declaration of Helsinki and issues that gave research ethics a global revolution. There are several ethical challenges in research in low resource settings as evidenced by the numerous gross violations that have been documented.^{10,11,12,13,14}

²Potash S. Fogarty Program Develops Bioethics Expertise in Uganda. *Global Health Matters*. 2016;15(5)

³Uganda National Council for Science and Technology. National Guidelines for Research Involving Humans as Research Participant. 2014. Available from: www.uncst.go.ug. Retrieved 28 Oct 2016.

⁴Council for International Organizations of Medical Sciences. International Ethical Guidelines for Health Research Involving Humans. 2016. Available from cioms.ch. Retrieved 22 May 2018.

⁵The World Medical Association. Declaration of Helsinki. 2013. Available from: www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/. Retrieved 22 May 2018.

⁶Nuffield Council on Bioethics. The Ethics of Research Related to Healthcare in Developing Countries. 2002. Available from: <http://nuffieldbioethics.org/project/research-developing-countries>. Retrieved 22 May 2018.

⁷Belmont Report. Ethical Principles and Guidelines for the Protection of Human Subjects of Research. 1979. Available from: www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html. Retrieved 22 May 2018.

⁸WHO Expert Committee. Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products, the Use of Essential Drugs. Sixth Report of the WHO Expert Committee, WHO Technical Report Series. 1995. Available from: <http://apps.who.int/medicinedocs/en/d/Jh3009e/22.9.html>. Retrieved 22 May 2018.

⁹Uganda National Council for Science and Technology Act. Cap. 209 of the laws of Uganda. 1990. Available from: www.ulii.org/ug/legislation/consolidated-act/209. Retrieved 28 Oct 2016.

¹⁰Angell M. Investigators Responsibilities for Human Subjects in Developing Countries. *N Engl J Med*. 2000;342(13), 967–9.

¹¹Mudur G. Johns Hopkins Admits Scientist Used Indian Patients as Guinea Pigs. *BMJ*. 2001;323(7323), 1204.

¹²Wise J. Pfizer Accused of Testing New Drug Without Ethical Approval. *BMJ*. 2001;322(7280), 194.

¹³Kovac C. Nigerians to Sue US Drug Company Over Meningitis Treatment. *BMJ*. 2001;3239(7313), 592.

¹⁴Lenzer J. Secret Report Surfaces Showing that Pfizer was at Fault in Nigerian Drug Tests. *BMJ*. 2006;332(7552), 1233.

Additionally, development of the field of research ethics has been hindered by inadequate financial, human resources and lack of infrastructure.^{15,16,17,18}

The globalization of clinical research calls for improved standards in the research environment to ensure that harm, exploitation and the abuse of research participants in low resource settings are minimized. This is also associated with the need for equitable sharing of research benefits by the research communities. In order to address these challenges, several projects have been implemented over the last two decades with a goal of providing human resource development and increasing the capacity for ethical review of health research in Africa through a number of international partnerships.¹⁹ Though many countries have benefitted from these initiatives, the developments that resulted from such initiatives are not uniform across sub-Saharan Africa.

This study describes the implementation and structural aspects of research ethics in Uganda since the introduction of modern medicine in 1896 up until today. We present the case of Uganda, a low resource country, which has gradually registered significant progress in developing research ethics capacity despite the wide spread challenges in the field. The achievements have unique features which may have enabled such developments in the research ethics enterprise constituting a Ugandan model of research ethics architecture involving a combination of policy and capacity development, coupled with effective oversight and continued dialogue.

2 | METHODS

This was a retrospective study. Data were collected through review of records, laws, guidelines, policies, publications and evaluation of documented practices covering the period from when modern medicine was first established in Uganda (1896) to date. A data collection tool from a related study was adopted and adapted.²⁰ The documents reviewed are summarized in Table 1.

¹⁵Ikingura J, Kruger M, Zeleke W. Health Research Ethics Review and Needs of Institutional Ethics Committees in Tanzania. *Tanzan J Health Res*. 2008;9(3), 154–8.

¹⁶Matar A, Silverman H. Perspectives of Egyptian Research Ethics Committees Regarding their Effective Functioning. *J Empir Res Hum Res ethics JERHRE*. 2013;8(1), 32.

¹⁷Ijsselmuiden C, Marais D, Wassenaar D, Mokgatla-Moipolai B. Mapping African Ethical Review Committee Activity onto Capacity Needs: the MARC initiative and HRWeb's interactive database of RECs in Africa. *Dev world bioethics*. 2012;12(2), 74–86.

¹⁸Kadam R, Karandikar S. Ethics Committees in India: Facing the Challenges. *Perspect Clin Res*. 2012;3(2), 50.

¹⁹Ndebele P. et al. Research Ethics Capacity Building in Sub-Saharan Africa: A Review of NIH Fogarty-Funded Programs 2000–2012. *J Empir Res Hum Res Ethics*. 2014;9(2), 24–40.

²⁰Ochieng J. et al. Research Site Monitoring for Compliance with Ethics Regulatory Standards: Review of Experience from Uganda. *BMC Med Ethics*. 2013;14(1), 23.

TABLE 1 Research ethics documentary review

Activity	Documents reviewed	Observations
Ethical review	Ethical guidelines Policies Regulations Establishment of Research Ethics Committees Research and Publications	Nature of policies and regulations Year of publication Nature of study Presence of regulatory system and RECs Content of the publications Indication for ethical review
Research regulation	Research regulatory documents Guidelines Research policies NRC documents Research ethical review minutes	Year of establishment Content of the policy documents Mandate for the institutions Number of review committees, individuals trained in bioethics and presence of guidelines Content of the research reviews reports
Enactment of supportive Laws for ethical conduct of research	UNCST Act UNCST statute National Drug Authority (NDA) Act NDA statute	Year of enactment Content of the Act Mandate for the institution
Establishment of research regulatory institutions	UNCST documents NDA documents	Year of establishment Mandate of the institution Operating procedures Evidence of operational institution activity reports Annual reports
Development of research oversight capacity	UNCST guidelines Accredited RECs REC Chairs forum NDA guidelines National conference reports Bioethics working group activities reports Research site monitoring reports	Institutions with RECs Year of accreditation Presence of SOPs Minutes of meetings Conference proceedings, themes and number of participants MOUs and minutes of meetings Number and content of site monitoring reports
Training in bioethics	Training curricular Training materials Trainings records	Number of individuals with long term training Number of individuals with short term training Duration of training Content of the training curricula Activities of trained graduates

2.1 | Ethical Review

Since the study involved review of public records with information already available in the public domain, ethical review was not required.

3 | RESULTS

3.1 | Research Regulation 1896 to 1970

The practice of medicine evolved over time and by the time of Uganda's independence in 1962, the New Mulago national referral hospital, a 1500-bed capacity facility, and a fully-fledged medical school at the associated Makerere University were in place. As the practice of medicine evolved in the country so did medical research

including but not limited to research in the early 1900s by Albert Cook, research on the Zika virus in 1947 and 1948, research on Burkitt's lymphoma in the 1960s, Bululi ulcer in the early 1960s and Busoga hernia in 1964.^{21,22,23,24,25} However, the growth in modern

²¹Cook AR. The Role of the Trypanosomiasis in African Ecology. Oxford Clarendon Press 1945; Cook AR. Uganda Memories (1897-1940), Uganda Soc Kampala, 1945.

²²WHO. The History of Zika Virus. Retrieved October 28, 2016 from: <http://www.who.int/emergencies/zika-virus/timeline/en/>

²³Burkitt D, Hutt MS, Wright DH. The African Lymphoma: Preliminary Observations on Response to Therapy. *Cancer*. 1965;18, 399-410.

²⁴Clancey J, Dodge R, Lunn HF. Study of a Mycobacterium Causing Skin Ulceration in Uganda. *Ann Soc Belg Méd Trop*. 1962;4, 585-90.

²⁵Eckhart P. The Incidence of Strangulated Hernia in Busoga, Uganda. *East Afr Med J*. 1964;41, 59-62.

medicine was not matched with the development of research infrastructure including the lack of research regulatory systems.

3.2 | Research Regulation 1970 to 1990

The first documented regulation of research activities in Uganda is traced to 1970 with the formation of the National Research Council (NRC). This implies that the recorded research activities in the country between 1896 and 1970 did not benefit from a formal research regulatory system. However, even with the formation of the NRC, research ethics committees (RECs) to review research protocols and national guidelines to guide the review process were non-existent. Review by the NRC was guided by the Declaration of Helsinki that was not adapted or tailored to the local context. The first REC, the National HIV/AIDS Research Committee was formed in 1986 in order to facilitate review of research related to the HIV/AIDS epidemic that was then at its peak in the country. The operations of the REC were not guided by any national guidelines for conduct of research involving humans as participants.

In 1990 the laws regulating research in the form of the Uganda National Council for Science and Technology (UNCST) Act was established. The UNCST Act provided a formal basis for development and implementation of policies. This gave birth to the first Uganda national guidelines for research involving humans as research participants in 1997.²⁶

3.3 | Research Regulation 1990 to present

The development of research ethics in Uganda since 1990 has been spearheaded by the Uganda National Council for Science and Technology in conjunction with major research partners, particularly Makerere University. Currently, the UNCST is a major coordinating centre for research ethics and research regulation and works in collaboration with a diversity of academic, health and research institutions to strengthen the capacity as well as implement the relevant policies.

The following achievements have been made since 1990. It should be noted that timing of some of the activities does overlap.

3.4 | The UNCST Act

In 1990 Government of the Republic of Uganda enacted the Uganda National Council for Science and Technology (UNCST) Act, a law that mandates the UNCST to oversee research and development in Uganda. This law enables the UNCST to develop policies and regulations aimed at improved regulation of science nationally. Following the approval of this law, the UNCST developed and implemented a number of activities related to research ethics including; developing the Uganda national guidelines for research involving humans as

participants; regulation of research ethics committees (RECs); developing curricular and conducting ethics trainings; research clearance; and provision of research oversight as well as promotion of ethical conduct of research.

The mandate of the UNCST has been strengthened from a unit under the Uganda Government Ministry of Finance, to a directorate at the Ministry of Education, Sports, Science and Technology in 2014; and finally, in 2016 as the newly created Ministry of Science, Technology and Innovations.

3.5 | National Guidelines for Research Involving Humans as Participants

Since its establishment in 1970 the National Research Council (NRC)'s role was to review of research protocols based on the 1964 Declaration of Helsinki. Thus, the NRC provided general but lacked a locally-adapted guidance for ethical review, approval and regulation of research.

The Uganda national guidelines for research involving humans as participants were first developed in 1997 in response to the increased demand for improved research ethics review and regulation of international collaborative research projects in the country, particularly HIV vaccine trials and other related HIV/AIDS research. These guidelines have since been revised in 2007 and again in 2014 in accordance with the emerging issues in research ethics. The revisions include the addition of new chapters that cover areas such as community engagement; data ownership, sharing and result dissemination; and traditional and complementary medicine research. Other changes improved on aspects such as vulnerable populations in research; care for research participants; ethical review by only a single REC in the country; incorporation of REC accreditation committee; insurance coverage for clinical trial participants and monitoring of approved research. In addition, a section on oversight was provided by the Uganda National Health Research Organization (UNHRO), a new research regulator for all health research in the country. Improvement and clarity on the language and stressing on the importance of particular aspects were also added. Finally, some chapters were removed including one concerning Ethical Considerations in the Review of Research Protocol and had its contents merged with the chapter on Establishment and Functions of Research Ethics Committees. The guideline development involved the UNCST and representatives from the research fraternity, academicians, policymakers, other research regulators including the National Drug Authority, Uganda National Health Research Organization and officials from the Uganda Ministry for Health. However, the guidelines have not been translated into regulations which would be prescriptive in terms of enforcement. Hence interpretation of action to be taken in case of violation of the guidelines is usually based on other nationally-applicable laws such as the Constitution and the Penal Code which are not specific to research ethics.

²⁶Uganda National Council for Science and Technology. National Guidelines for Research Involving Humans as Research Participant. 2007. Available from: www.uncst.go.ug. Retrieved 28 Oct 2016.

3.6 | Long Term Training

Since the early 2000's many individuals have benefitted from the National Institutes of Health (NIH) funding for long term training in bioethics for mid-career faculty which has been conducted in collaboration with Ugandan institutions like Makerere University. Such training has resulted in a critical mass of nine individuals trained at masters' level and others at postgraduate diploma level.

In 2011, Makerere University won an NIH planning grant that resulted in a larger award in 2014 to implement an International Health Research Ethics Training Grant which includes a Masters of Health Sciences (MHSc) program in bioethics at the university.²⁷ Twenty five individuals have so far been trained at the master's level in bioethics. Because of locally available expertise, the need to outsource foreign expertise to conduct both short term and long term training has been significantly reduced over the past ten years.

Despite the sustained capacity building, there has not been a proportionate growth in the numbers of bioethics experts in the country until the establishment of local training programs.

3.7 | Short Term Training

Short term training of up to five days have been conducted by Makerere University and the UNCST addressing topics such as research ethics, human subject protection, responsible conduct of research, good clinical practice and clinical ethics. Participants included individuals receiving such training for the first time and those that required refresher training. The training is contextualized, affordable and conveniently conducted close to or within participants' places of work. As highlighted above, the International Health Research Ethics Training Program at Makerere University runs three courses including RCR, Research Ethics and Clinical Ethics and has trained 451 individuals. These include 175 individuals trained in RCR, 216 individuals in research ethics and 60 individuals trained in clinical ethics for a total of 451 individuals that have been trained in short courses by the International Health Research Ethics Training Program since 2014. The individuals trained in the short term courses include researchers, clinicians, graduate students, research ethics committee members, research regulators and research administrators.

Other short term trainings including Human Subject Protection (HSP), RCR and Good Clinical Practice (GCP) have been conducted by the UNCST in conjunction with the Uganda Society of Health Scientists and the Bioethics Working Group. As a result, more than 1000 individuals have benefitted from the training since 2007. The individuals trained included researchers, REC members, REC administrators and graduate students. As a result of short term trainings,

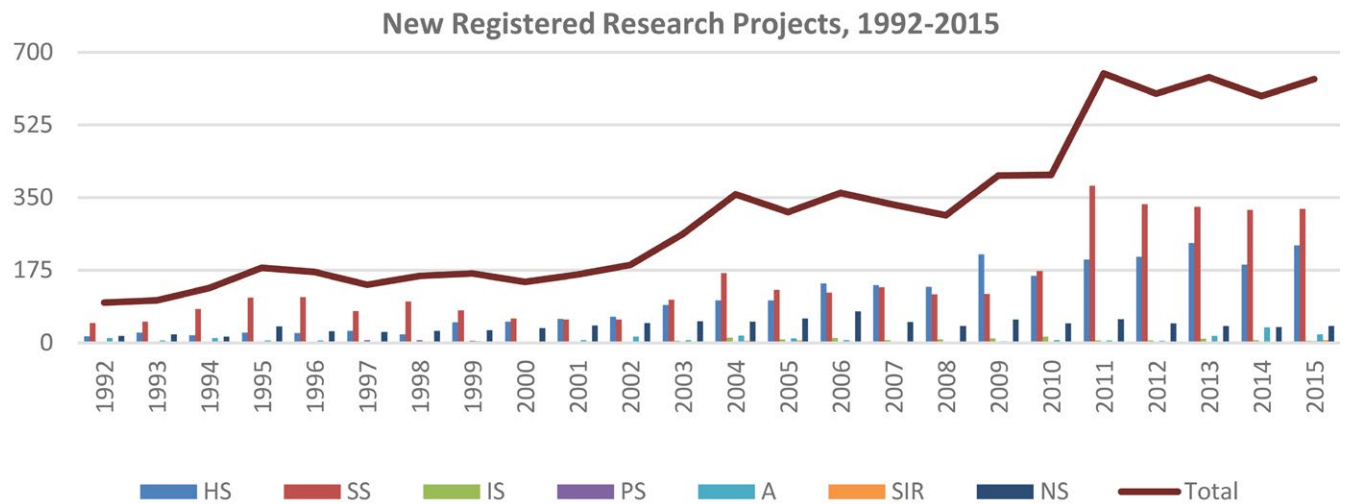
TABLE 2 Accredited Research Ethics Committees in Uganda

Number	REC	Institution of affiliation
1	National HIV/AIDS Research Committee	Uganda National Council for Science and Technology
2	Uganda Virus Research Institute	Uganda Virus Research Institute
3	Joint Clinical Research Centre	Joint Clinical Research Centre
4	Mbarara University of Science and Technology REC	Mbarara University of Science and Technology
5	School of Medicine REC	Makerere University, College of Health Sciences
6	School of Biomedical Sciences REC	Makerere University, College of Health Sciences
7	School of Public Health REC	Makerere University, College of Health Sciences
8	TASO REC	TASO
9	Mbale Regional Referral Hospital REC	Mbale Regional Referral Hospital
10	School of Health Sciences REC	Makerere University, College of Health Sciences
11	Mengo Hospital REC	Mengo Hospital
12	St Mary's Hospital Lacor Hospital REC	St Mary's Hospital Lacor
13	Mild May Uganda Research and Ethics Committee (MUREC)	Mild May Uganda Hospital
14	Mulago Hospital Research and Ethics Committee (MHREC)	Mulago National Referral Hospital
15	International Health Sciences University REC	International Health Sciences University
16	Hospice Africa Uganda REC	Hospice Africa Uganda
17	Gulu University REC	Gulu University
18	Vector Control Division REC	Vector Control Division
19	Uganda Cancer Institute REC	Uganda Cancer Institute
20	St Francis Hospital Nsambya REC	St Francis Hospital Nsambya
21	Kampala International University REC	Kampala International University
22	Makerere University School of Social Sciences REC	Makerere University, College of Humanities and Social Sciences
23	THETA Uganda REC	THETA Uganda

the level of awareness of the relevancy of ethics training and consequently its demand by institutions and research groups have increased. This enhances potential for improved ethical conduct of

²⁷Makerere University. The International Health Research Ethics Training Program. Available from: <http://chs.mak.ac.ug/ihret>. Retrieved 28 Oct 2016.

Trends in New Research Projects Registered at UNCST



Registered Research Projects, 2015 - 2017

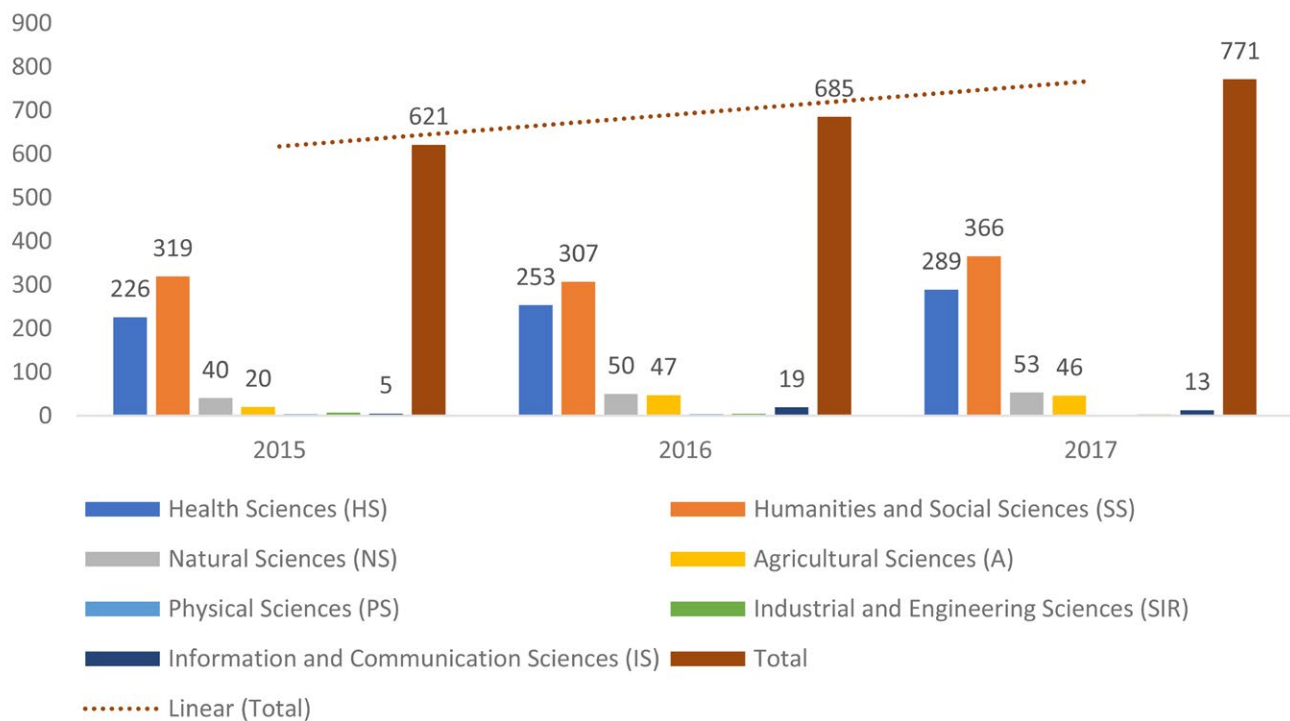


FIGURE 1 Trends in New Research Projects Registered at UNCST

research. Local training programs have made research ethics related training much more affordable, and increasing access to ethics training has changed the way research ethics has been looked at.²⁸ The trainings have also increased awareness about research ethics as

well as demand because more individuals are requesting and actually attending these trainings.

3.8 | Establishment of Research Ethics Committees (RECs)

The first recognized REC in Uganda was the National HIV/AIDS Research Committee, established in 1986 through a difficult process

²⁸Uganda National Council for Science and Technology. Available from: www.uncst.go.ug. Retrieved 22 May 2018.

complicated by the absence of specific laws, policies or guidelines in the country to govern the formulation and functioning of RECs. Following the adoption of the UNCST Act in 1990 and the launching of the first national guidelines for research involving humans as participants in 1997, a number of RECs have been established and operationalized in the country. These RECs conduct initial and continuing ethical review and oversight of research on behalf of the UNCST. As a measure to maintain standards, ensure quality ethical review and enhance the protection of human participants, the National Guidelines requires all Research Ethics Committees (RECs) operating in Uganda to be accredited by UNCST. Accreditation by the UNCST is done by the Accreditation Committee for RECs that has been active since 2010.

Currently, 23 RECs have been accredited nationally and are functioning (see Table 2)

The geographically closer the REC is to a potential researcher, the higher the chances that ethical review and approval will be sought. Additionally, if an institution hosts a REC, it creates awareness about the roles of RECs and is more likely to encourage its staff to submit their research protocols to the REC. All these have contributed to an increase in number of protocols reviewed by RECs as well as those cleared by the UNCST from less than 175 in 1992 to close to 800 in 2017 (figure 1) and, with time, this is expected to translate into improved ethical conduct of research in Uganda. The highest rise in the number of protocols cleared by the UNCST was in 2011, most likely because the process of accreditation of RECs started in 2010 which resulted in improved regulations of RECs and hence their numbers and activities.

Additionally, about 300 research protocols approved by the RECs have not been cleared by the UNCST and are not a part of Figure 1 because they are masters and undergraduate student protocols most of which do not require such clearance.

However, there are variations in the capacities of RECs, consequently, their effectiveness in the review process is not at the same standard as others that are more advanced.

3.9 | Bioethics Working Group

In 2007, bioethics experts in Uganda in collaboration with the Uganda National Council for Science and Technology and the Uganda Society of Health Scientists constituted the Bioethics Working Group (BWG) whose aim was to promote regular discussions on contemporary ethical issues, identify and contribute to addressing bioethics needs and provide consultancy services and mentorship. This team meets thrice a week and is instrumental in research ethics development.

Think tanks have been found to be instrumental in fostering change in a number of aspects and the BWG has made contributions through development and implementation of training curricula, guideline improvement and implementation, initiation of the research site monitoring program and provision of consultancy services among others.

The BWG teamed up with Makerere University and over the past eight years contributed to the development and implementation of the curricula for Responsible Conduct of Research (RCR), research ethics, clinical ethics and the Masters of Health Sciences in Bioethics.

However, despite the valuable contribution made by the BWG, there is still a significant lack of bioethics scholarship in Uganda. This needs to be developed as well.

3.10 | Research Site Monitoring

Since 2007, the UNCST, the National Drug Authority (NDA) and some RECs have conducted on-site monitoring of research projects across the country aimed at promoting ethical conduct of research. This achievement is important since site monitoring is performed by few regulatory agencies yet it can be very efficient in minimizing unethical conduct research. As capacity for research site monitoring grows, coupled with the requirement by the UNCST REC Accreditation Committee that all RECs monitor

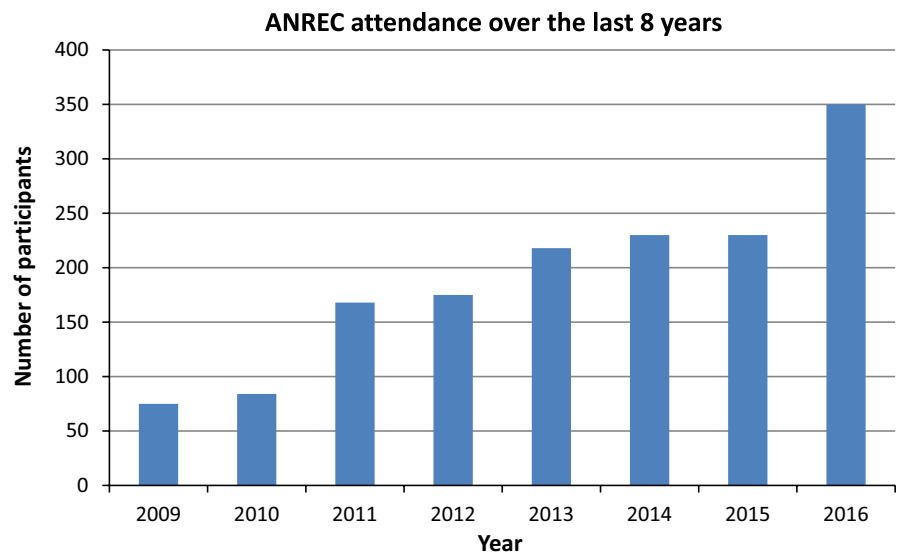


FIGURE 2 ANREC Attendance over the last 8 years

implementation of the research they approve, more RECs have become actively engaged in this regulatory process. This is important because it reduces on unethical conduct and promotes sharing of best practices. It is feasible in a limited resource setting and a great stride towards improved ethical conduct since individuals tend to be more compliant if they know their activities can be monitored or audited.

3.11 | The Annual National Researcher Ethics Conference (ANREC)

The annual National Research Ethics Conference is an initiative of the UNCST with the aim of promoting interaction and dialogue between researchers, research regulators, policy makers, research users and other stake holders in the field of health research. This is envisaged to help the different players appreciate each other's roles, improve understanding of research ethics and thus the protection of the rights, interests and wellbeing of the human research participants. The number of conference participants has increased from 75 in 2009 to 350 in 2016, indicating a positive trend and growing interest in research ethics as seen in Figure 2. Conference themes have also gained depth, generating more exciting and richer discussions.

The conference themes are broad, covering important topics such as balancing science and human research participant protection in Uganda; promoting responsible conduct of research in Uganda; communities as partners in research; issues in post-trial access to interventions; research ethics in cross-cultural settings; strengthening research ethics in Uganda; vulnerability in research; and respect for research participants.

The conferences are sponsored by the UNCST in partnership with its stakeholders and this consequently contributes to providing answers to ethical challenges faced by the participants.

3.12 | REC Chairs' Forum

In order to promote the ethical discourse and mentorship to upcoming RECs, the UNCST facilitated the formation of a discussion forum for REC chairs in the country. Quarterly meetings have been held since 2010 with the aim of sharing experiences and best practices that address issues associated with ethical review of research.

3.13 | The UNCST REC Accreditation Committee

In order to promote high standards of ethical review and oversight of research in Uganda, the UNCST formed the REC Accreditation Committee whose role is to monitor and guide RECs. Only accredited RECs are authorized to conduct the ethical review and approval of research. The accreditation of RECs has to be renewed every three years and for a REC to become accredited, it must meet some minimum standards. These include institutional commitment by the host institution, availability of members of staff, appropriate standard operating procedures as well as acceptable membership.

The Accreditation Committee is comprised of five members appointed on individual merit by the Executive Secretary of UNCST. Members of the Accreditation Committee are appointed for a three year renewable term limit; they work together as a committee of the UNCST and report to the Executive Secretary of UNCST. Their Terms of Reference are to review REC applications for accreditation in accordance with accreditation standards established by UNCST; and conduct periodic assessment of performance of RECs.

The Accreditation Committee reviews the organization's application, and if satisfied, will accredit the REC after inspection of the REC's host institution, ensuring that the REC is well constituted and its members have received training in basic research ethics.

Inspection of the host institution involves meeting with institution officials responsible for establishing the REC, the REC Chairperson, members and staff, in addition to assessment of facilities for the REC's operation such as office space, meeting space, documentation and storage facilities and standard operating procedures. Only accredited RECs are recognised by the UNCST and the Accreditation Committee can revoke accreditation in case of non-compliance.

However, the accreditation process does not evaluate how the REC reviews protocols making it possible for institutions with adequate infrastructure to have their RECs accredited even when such RECs may be incompetent when it comes to effective ethical review of research.

3.14 | Establishment of the Centre for Bioethics

The Makerere University College of Health Sciences recently finalized its plans to establish a Centre for Bioethics. The Center is in its early phases of operationalizing structures which will enable it to act as a coordination centre for all bioethics-related programs. It will also serve as a resource Centre for health-related bioethics information and link trainees to experts and other relevant individuals in the field of bioethics. This centre has been accredited and has been appointed to host the Uganda Unit for UNESCO Chair in Bioethics.

However, the centre needs sustained funding to be effective in promoting bioethics works by attracting the best expertise to participate in the ethical discourse on pertinent issues affecting society.

4 | DISCUSSION

This article describes the development as well as the implementation and structural aspects of research ethics in Uganda. The field has significantly evolved over the past 120 years with many initiatives all aimed at sustained improvement.

In the initial period between 1896 and 1970, ethical regulation was challenged by the lack of regulatory systems or formal structures coupled with limited knowledge and capacity in research ethics rendering research ethics activities quite difficult. This situation was not unique to Uganda. Around the world, research ethics

became more significant after the World War II when development of the initial international guidelines took place.^{29,30} However, even after the formation of the National Research Council in Uganda in 1970, its activities were limited by the initial challenges. The lack of national guidelines was an impediment to the development of research ethics. Similar challenges have faced other countries including our economically-developed counterparts, for example, the United States of America, which commissioned and published the Belmont Report in 1978. The enactment of the UNCST law enhanced UNCST's performance and boosted its command of authority.

The UNCST Act and the development of the national guidelines that are regularly reviewed have been instrumental in enhancing ethical conduct of research. Regular review and improvement of the guidelines is an international standard and helps the document to stand the test of time in the rapidly evolving field of health research. International guidelines are also reviewed whenever need arises. Since the Uganda National Guidelines have not been translated into regulations, interpretation of the action to be taken in case of a violation of the guidelines is usually based on other national applicable laws like the Constitution and the Penal Code which are not specific to research ethics. Translation of national guidelines into regulations is essential as is the practice in comparable settings.³¹

Long term training of individuals and nurturing of career tracks in ethics are essential components of capacity building without which the discipline may not grow. Capacity development has contributed significantly to the development of ethics in Uganda and is a key ingredient for sustainability. The number of bioethics experts has grown significantly since training has been offered locally, a situation similar to how other disciplines have evolved.

Short term training in research ethics is essential and feasible for researchers or research regulators. These trainings provide an opportunity for individuals to learn and share experiences as part of continued training and professional development. It would be impossible to conduct ethical research or regulate research without adequate knowledge of what constitutes acceptable ethical behavior. Hence trainings provide a framework upon which individuals base their judgment. Additionally, training is an essential component of capacity building and continued professional development. Bioethics training has contributed significantly to the development of the field in Uganda and elsewhere. Such trainings have increased awareness about the need for research ethics among the research fraternity which if sustained can contribute to improved ethical conduct. Short term training can be enforced by requiring every individual involved in research to undergo such training. Such enforcement

has been adopted by institutions like the National Institute of Health in the USA whereby those researchers who have been funded by the institution are required to undergo training in Protecting Human Research Participants.

The objective of the annual National Research Ethics Conference to a large extent is addressed satisfactorily as the number of the conference participants keeps growing (Figure 2), and we hope the increased awareness will contribute to improved ethical conduct during research. These developments are similar to what has been experienced in the USA by PRIMER, 'The Global Forum for Bioethics in Research and the International Association of Bioethics'.^{32,33,34}

In order to ensure compliance, enforcement of ethical conduct is complemented by research site monitoring. Though the practice of research site monitoring is not common in many parts of the world, it has taken shape in Uganda, and has been incorporated into the guidelines and to a large extent accepted by both the regulators and the researchers.

The formation of the RECs demonstrates a positive trend and attitude towards improved ethical conduct of research by research institutions. However, the effectiveness and efficiency of such RECs needs to be continually monitored in order to maintain the required standards. Additionally, adherence to the required standards calls for regular internal and external evaluations. This could be addressed through accreditation. This is an audit process where the performance of RECs is evaluated against expected indicators of quality by the regulator. However, assessment of the actual processes by which RECs conduct their business is currently not practiced, while auditing of the REC review document is still lacking.

The REC Chairs Forum is instrumental in generating consensus on approaches to addressing challenging research protocols. These committees are at varying levels of development and their capacity in terms of expertise is different implying that the well-developed and experienced committees could in some way mentor the upcoming RECs. Our research has not discovered any such forum or practice of mentoring anywhere around the globe.

Policy development as well as coordination of research ethics regulation is spearheaded by the national regulator, the UNCST, in collaboration with the major partners like Makerere University as well as other academic, health and research institutions as implementers. This model of research ethics capacity development and regulation is effective and sustainable since it involves the critical stakeholders.

Many Low and Middle Income Countries (LMIC) including those with socio-economic and cultural similarities to Uganda have benefited from NIH funded training programs, with a good number developing their own local short and long term training programs. If a critical mass of individuals has been trained, they can work in

²⁹Nuremberg Code. Nuremberg. 1947. Available from: https://en.wikipedia.org/wiki/Nuremberg_Code. Retrieved 16 Jun 2017.

³⁰The World Medical Association. Declaration of Helsinki Guidelines. 1964. Available from: www.wma.net/en/30publications/10policies/b3/. Retrieved 16 June 2017.

³¹Federal Code of Regulations. USA. Available from: <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/>. Retrieved 16 Jun 2017.

³²Public Responsibility in Medicine and Research: PRIM&R. Available from: www.primr.org/. Retrieved 28 Oct 2016.

³³The Global Forum for Bioethics in Research: Available from: <http://www.gfbr.global/>. Retrieved 22 Jun 2017.

³⁴International Association of Bioethics. Available from: <http://www.bioethics-international.org/>. Retrieved 22 Jun 2017.

collaboration with their national regulators, to build their research ethics capacity based on the Ugandan model.

With the consolidation of capacity development through continued long term training of experts in bioethics, short term training for a wider community, research on research ethics and research regulation as well as policy reviews and improvements, we anticipate that the future for research ethics in Uganda is bright. And this will go a long way in developing research ethics scholarship which is still underdeveloped in the country.

It is evident that adequate research ethics capacity development can be achieved even in a low resource setting provided appropriate structures are put in place to facilitate such development. Finally, foreign support from high income countries if appropriately utilized can significantly aid development of research ethics capacity in LMICs which has been the case in Uganda.

4.1 | Lessons learnt

Research ethics capacity development requires and takes time, significant financial resource commitment and effective collaborations both at the local, national and international levels.

Clear policies and effective coordination are essential for development, implementation and sustainability of research ethics regulatory systems.

Local capacity development is an essential component of research ethics development and sustainability.

Uganda now has extensive infrastructure and lots of trained people and attracts lots of foreign funded research studies. So it is time for Ugandan ethics scholarship to be developed as well.

4.2 | Challenges

Attracting individuals into the field of research ethics with no clear career path is an ever menacing challenge because people need training that would readily result in employment.

Research ethics has been rapidly changing and this requires practitioners to keep up with the pace of change if any standards are to be maintained.

4.3 | Limitations

The study was a retrospective records review and the challenges of incomplete/missing records especially for work that was done so many years back are always present.

The review did not assess the impact of this bioethics development on actual practices. There is a need to assess the extent to which these developments have been translated into practice.

5 | CONCLUSION

Over the past 120 years, the implementation and structural aspects of research ethics in Uganda have evolved through 70 years of no

documented evidence of research regulation, followed by 30 years of rudimentary regulation while the last 20 years have shown significant growth in the regulatory system associated with supportive laws, policies, formal education and the institutionalization of regulatory processes and training programs.

LIST OF ABBREVIATIONS

ANREC	Annual National Research Ethics Conference
BWG	Bioethics Working Group
LMIC	Low and Middle Income Countries
NDA	National Drug Authority
NIH	National Institutes of Health
NRC	National Research Council
RCR	Responsible Conduct of Research
REC	Research Ethics Committee
PRIMER	Public Responsibility in Medicine and Research
UNCST	Uganda National Council for Science and Technology
UNHRO	Uganda National Health Research Organization

ETHICS

Not applicable.

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COMPETING INTEREST

The authors declare that they have no competing interest.

AUTHORS' CONTRIBUTION

Joseph Ochieng performed Literature search, study design, data collection, data analysis, data interpretation, drafting, writing, proof reading and approval of manuscript; Erisa Mwaka performed data analysis, data interpretation, proof reading and approval. Betty Kwagala performed data analysis, proof reading and approval. Nelson Sewankambo performed study design, data analysis, data interpretation, proof reading and approval. All authors read and approved content of the final manuscript.

AVAILABILITY OF DATA AND MATERIALS

Data used to derive conclusions for this study was captured from publicly available information as shown in Table 1.

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