KEMRI Bioethics Review

Volume V - Issue 3 2015

Ethical Issues in Human Genetics and Genomics Research

For questions and queries write to:

The KEMRI Bioethics Review

KEMRI-SERU P.O. Box 54840-00200

Nairobi, Kenya

Email: DDRT@kemri.org

Contents

The **KEMRI Bioethics Newsletter** is an iniative of the ADILI Task Force with full support of KEMRI. The newsletter is published every 3 months and hosted on the KEMRI website. We publish articles written by KEMRI researchers and other contributors from all over Kenya. The scope of articles ranges from ethical issues on **biomedical science, healthcare, technology, law , religion and policy.**
The chief editor encourages submisssion of articles as a way of creating awareness and discussions on bioethics

NEXT THEME- ETHICAL ISSUES IN REPRODUCTIVE HEALTH
please write to ddrt@kemri.org

Letter from the Chief Editor

Prof Elizabeth Anne Bukusi,
MBChB, M.Med (ObGyn), MPH, PhD , PGD(Research Ethics). MBE (Bioethics) , CIP (Certified IRB Professional).
Chief Research Officer and Deputy Director (Research and Training) KEMRI

I am pleased to present to you this third issue of 2015 on **Ethical Issues in Human Genetics and Genomics.** Inside this issue, we feature two articles: one is by a group of KEMRI-Wellcome Trust researchers, who share their experiences on the social and ethical issues in research on Sickle Cell Disease (SCD) in communities within Kilifi County. The second article is by Dr John Kiiru, a KEMRI molecular biologist, who highlights the Ethical challenges regarding genetics testing and genomic research with a special focus on studies conducted in low-income countries. We also continue to share the profiles of new reviewers of SERU committees.

Ever since the times of Gregor Mendel and Frienrich Miescher (founders of the modern science of genetics and genetic engineering), genetics and genomics have evolved into important aspects of medicine. Genomics is now used in molecular analysis of every cell to better understand its growth, how its environment is invaded, and how cells divide. This research is then applied to targeting the damage in cells with treatment or medications that may result in correction. Genetics testing has also advanced to the point where cutting edge technologies like Polymerase Chain Reaction (PCR) Gene Expert and other genetic testing techniques are used to yield important health information. These rapid developments in genetic testing and diagnosis driven by research and information technology has effects on individuals, families and society at a social, moral and ethical level.

Genetics research faces the same ethical dilemmas like other studies involving human subjects; however, a major challenge in genetics is that it has implications beyond the individual participant. With genetic research and testing, an individual's right may have to be balanced against the rights of others. Therefore, to achieve autonomy in genetic research, it is vital to provide adequate genetic counseling to the participants enable all them decide on the basis of detailed informed consent on the implications to others who may share

their genetic makeup. Researchers also need to guarantee confidentiality which is vital to ensuring the privacy of that decision-making.

Sharing of genetic information is another dilemma in studies involving genetic testing. The implication of sharing results of genetic tests with other family members can sometimes be uncertain or cause disharmony among families. How do researchers balance between the obligations to ensure that they act to benefit the good of the community without causing harm to individuals or vice versa? An example is where a test may elicit information that touch on other blood relatives; in this case the researcher must act in the best interest of the safety, privacy and confidentiality of the individual but also prevent harm or avoid seriously jeopardizing the health of others. Adequate counseling and information must be provided to participants and the larger community for them to appreciate the shared nature of genetic information within families. This will enable individuals to be mindful not only what genetic results mean for their own health, but also what that information may mean for their relatives, and their responsibilities towards those relatives.

It is difficult to identify all the legal and ethical implications of genetic research. Often there are more questions than answers. Genetic screening, testing, therapy, counseling, and genetic research are delicate themes. The continuous evolution of genomics demands that researchers and health professionals remain well-informed and up to date on scientific progress in this field. As with any other research, researchers must maintain professional attitude and protect confidentiality, ensure Informed consent in any procedure or testing done.

Prof Elizabeth A. Bukusi
Editor in Chief

A word from the Director KEMRI

Prof Solomon Mpoke, PhD, MBS
Director, KEMRI

Welcome to this issue on Ethical Issues in Human Genetics and Genomics. Human genomics forms a crucial component in current healthcare and health research. The application of genomics in healthcare involves use of genetic information to refine disease diagnosis, develop new therapies, predict drug effects and understand and possibly prevent diseases. Beyond healthcare, human genomics is also useful in criminology as a source of impeccable evidence for solving crime cases and parental disputes.

KEMRI scientists have been involved in molecular biology research that has led to improvement in health either through improved diagnosis of diseases or development of prevention and control interventions. Our researchers continue to conduct genetic research in order to use the information generated for development of novel interventions that will yield better drugs, better diagnostic methods and improved disease prevention strategies. Recognizing the unmet needs of the genetic testing services in the country, we recently commissioned a Human Identification DNA laboratory to provide DNA identification for maternity/paternity testing and forensic analysis. This laboratory is expected to supplement the existing services by the government chemist and other private laboratories within the country. Human DNA identity typing services can also be used to carry out donor matching where tissue or organ transplantation may be needed.

Despite the considerable benefits of genomics in healthcare, there are challenges that come with the application of these technologies in healthcare or other fields. One notable challenge of human genomics is the sharing of genetic information. This is an ethical issue that must be taken seriously not only because of the rights of individuals involved but also because genetic information is subject to interest from other parties, such as the family, the government, insurance, researchers and law enforcers. The ethical issues that might arise from sharing of genetic information include confidentiality, privacy, and informed consent.

KEMRI remains committed to ensuring that participants in genetic research and those who seek testing services access proper information and counseling so that utilization of these services is on the basis of informed consent. Such informed consent is expected to build confidence and ensure privacy of genetic information derived from those seeking the service. Given the shared nature of genetic information and conditions, what is to the good of one individual may be harmful to another. Therefore a balance of responsibility must be reached to ensure justice is served to the individual, the family and the public good.

KEMRI remains committed to ensuring that participants in genetic research and those who seek testing services access proper information and counseling so that utilization of these services is on the basis of informed consent. Such informed consent is expected to build confidence and ensure privacy of genetic information derived from those seeking the service.

Another drawback in the application of DNA technology in biomedical research field in Kenya is the lack of proper and clear legislation on the use of genetic information. It is urgent that necessary legislation be enacted on the use of human genomics in healthcare. Clear laws that guide the use of genomics in research, healthcare and even in legal disputes and forensics will ensure that the technology is applied appropriately for the intended purposes with adequate protection of individual rights as guaranteed by the constitution.

The benefits of human genetics and genomics in the advancement of human healthcare are immense. It is crucial to ensure that proper structures are put in place, including relevant legislation to ensure that this area of science is exploited optimally towards an improved healthcare delivery system in our country while adhering to attendant ethical requirements.

Genetics and Ethics

Learning from communities in Kilifi about social and ethical issues in research involving Sickle cell disease

Authors: Frances Kombe, George Mochamah, Thomas N Williams and Vicki Marsh

INTRODUCTION AND BACKGROUND

Genetic research focusing on individual and population-level genetic susceptibility or resistance to disease has attracted extensive attention in the public as well as the scientific media. Proponents of genetic research argue that it has the potential to develop or increase understanding of human disease mechanisms, improve diagnostic techniques and the development of rational strategies for minimizing or preventing disease phenotypes such as discovery of new targets for vaccines and drugs.[1, 2] At the same time, a range of ethical concerns have been raised for genetic and genomics research.[3, 4] This article, describes ethical issues in research involving screening or testing for a particular genetic condition, sickle cell disease (SCD), based on research conducted around a genetic birth cohort study: the Kilifi Genetic Birth Cohort (KGBC) study in Kilifi. The KGBC study aimed to assess inherited susceptibility and resistance to malaria and other common childhood illnesses.[5] Qualitative research conducted around the KGBC study examined a series of social and ethical questions before and during the cohort study[6-9]

The article draws together key findings from this research to highlight the nature of a set of important social and ethical issues that may occur in genetics and genomics studies in Kenya. The research was undertaken i) around forms of community and research stakeholder engagement in planning the KGBC study; and ii) in identifying and addressing ethical issues emerging during the KGBC study. We outline our responses to these findings, proposing recommendations for research practice that may be useful for other teams to consider in similar settings.

Sickle Cell Disease: A Brief Overview

Sickle Cell Disease (SCD) is a highly variable inherited condition, but often has high rates of morbidity and mortality, particularly in the early years of life and where there is low access to medical care to manage symptoms and reduce risks of complications.[10] Conditions of high malaria prevalence and over-stretched health resources exist in many parts of sub Saharan Africa, and the majority of the global burden of SCD is found in this continent.[10, 11] People with SCD often suffer repeated episodes of severe pain in different parts of the body, related to abnormalities in haemoglobin structure that lead red blood cells to temporarily change shape, or 'sickle'. In addition to episodes of painful sickling, SCD is associated with chronic anaemia and increased susceptibility to bacterial infections. Symptoms in affected children tend to emerge around the age of six months, when levels of foetal haemoglobin normally fall. SCD is inherited as an autosomal recessive condition. Affected individuals are homozygous, carrying two copies of the SCD gene (HbSS), one copy from each parent. Both parents of an affected child must either be carriers of the SCD gene (HbAS) or have HbSS.

The KEMRI Wellcome Trust Research Programme and the Kilifi Genetics Birth Cohort (KGBC) Study

The Kenya Medical Research Institute (KEMRI)-Wellcome Trust research programme (KWTP) is an international collaborative health research programme whose main centre is based in Kilifi County Hospital on the coast of Kenya. A long-term collaboration has been established between researchers and Ministry of Health managers and health providers in Kilifi. Through this partnership, KWTP supports clinical services in the hospital and some peripheral clinics, including supplementing staff, supplies and equipment and providing a paediatric high dependency unit at the hospital. Kilifi County's population includes rural and semi-urban populations with the majority of the residents being from the Mijikenda ethnic group. Statistics also indicate Kilifi has one of the highest poverty levels, lowest literacy rates and highest indicators of gender inequity nationally[12]

The KGBC study aimed to recruit 12,000 infants between the ages of 3 and 12 months into a longitudinal cohort to be followed passively through on-going clinical surveillance at the Kilifi County Hospital for the development of severe diseases or death, supported by a Health and Demographic Surveillance System.[13] The study also contributed to an international collaborative genome-wide association study (GWAS) on susceptibility and resistance to malaria, involving 20 developing and developed countries and including a focus on social and ethical issues in genetics and genomics research.[14] Initial activities in KGBC included collection of standardized data on disease risk factors and a 0.2ml blood sample for genetic analysis from participant infants. Capillary blood samples were removed from the heel to maximize safety and ensure an adequate volume was drawn rapidly with minimum discomfort. Prior to drawing the sample, informed consent was obtained by Mijikenda field workers who were fluent in local and national languages. The samples taken were screened for SCD as part of research on the health effects of the sickle cell gene. Results for children found to have SCD were returned within three weeks of testing, and parents were invited to attend a clinic (dedicated for SCD) for confirmatory testing and family counseling. Where the tests indicated a normal haemoglobin gene (HbAA) or carrier status (HbAS), families were informed of the negative results within three to four months.6

SOCIAL AND ETHICAL ISSUES AROUND SCD SCREENING IN KGBC

Difficulty in understanding the nature of SCD

Although the KGBC study demonstrated that around 1% of young children in the study area were affected by SCD and around 17% were carriers for this condition, engagement activities with community leaders and representatives before and during the study indicated low awareness and knowledge of SCD within the wider community. Many factors contributed to people's difficulties in recognising SCD in Kilifi. For children with symptoms, the intermittent and changing nature of these made a single causal 'condition' hard for parents to recognise. In addition, a common biomedical understanding of effective treatment as a 'cure' for illness led many families to underestimate the value of biomedical care given for this chronic condition, to manage symptoms and reduce the risk of complications. In any case, it was often difficult for parents to persevere with biomedical care if young children continued to suffer attacks of severe pain and emotional distress, instead preferring to try other treatment options.

In this traditionally patrilineal society, where mothers generally have primary responsibility for child care, mothers of a child with SCD were often blamed for their child's condition

An apparent low awareness of the condition amongst many primary care health providers contributed to challenges in recognising the condition. For example, families reported that during early visits to clinics health providers also often did not diagnose this condition, but would give treatment for 'fever', including 'fever of the bones' (homa ya mifupa was a common name for the condition amongst families), or malaria. Patterns of several family members being affected were often difficult to interpret, particularly given that young infants seemed healthy. Given the uncertainty about cause, and the lack of 'cure' in response to any treatments, many families delayed or mixed biomedical with traditional treatments, moving backwards and forwards between different types of providers in hope of curing their child. Traditional practices were used to treat symptoms and to try to tackle possible causes, including witchcraft, ancestral curses (particularly where more than one child in a family was affected) and/or evil spirits or devils.

The importance and challenges of sharing findings on SCD in research

A high importance of returning findings on SCD shown during research to parents of affected children emerged strongly from narratives of their mothers and community consultation activities. As before, given the high likelihood that SCD in young children will be undiagnosed, testing, counselling and initiating long term management are critically important to reduce morbidity and risks of mortality. In addition, we learned about the physical and emotional distress experienced by affected children and their parents who were unaware of the cause of their child's symptoms or how to find a solution. In this traditionally patrilineal society, where mothers generally have primary responsibility for child care, mothers of a child with SCD were often blamed for their child's condition. A good illustration of this attitude was given by a sister-in-law's claim about a mother of two affected children that: "All her children are born that way!" Further, many mothers carried particular burdens of care, being unable to undertake their normal household and/or farming duties or seek an essential supplementary income through petty trading or casual work, as is common in this community, because of their child's ill health.

"When I went to the doctor, the child was tested and…we were told that there was a condition from the father and me that caused the child to get that thing. So when we came back home, other people were saying that it was witchcraft…but, the two of us, we knew because the doctor had explained to us, and so we were not worried. So when the parents get information, it removes the fear."

Screening for SCD during the study presented an opportunity for researchers to share information on this condition to all families, as part of the informed consent process, but particularly to feedback information on children found to have the condition. Giving clear and convincing explanations about the nature and cause to parents of children found to be affected, and facilitating access to services that would improve conditions for the child and family, have an important potential to counter the family burdens described in the previous section. A young mother of two children with SCD explained the importance of knowledge clearly:

"When I went to the doctor, the child was tested and…we were told that there was a condition from the father and me that caused the child to get that thing. So when we came back home, other people were saying that it was witchcraft…but, the two of us, we knew because the doctor had explained to us, and so we were not worried. So when the parents get information, it removes the fear."

At the same time, the fact that SCD was inherited from both parents, who themselves had no symptoms, was alien and difficult for participants to comprehend, as was the possibility of one child having this condition while their siblings were unaffected. The quality of communication about this condition and availability of good supportive medical care are obviously central to ensuring that sharing SCD information is an overall benefit to the family. In this birth cohort study, where most children were under 1 year of age, some children had not yet developed symptoms – or had experienced only mild symptoms - at the time of study recruitment. For this group, high quality and careful communication and counselling are particularly important since there is a serious risk that parents will not accept the diagnosis in an asymptomatic child, and develop hostility towards the research team.

During the KGBC study, about 40% of children found to have SCD were not brought early to the SCD clinic, and a majority of these children have subsequently died at home. Some were brought once symptoms developed. Critically, an important and common challenge for many families who knew about the diagnosis was the affordability of access to services, given that these were centralized at the County General Hospital within a large and generally poor rural district.

More broadly, and in common with disclosure of any genetic information, sharing information on a child's SCD status raises the challenge that some genetic information on close blood relatives will also inevitably be disclosed, in both succeeding and preceding generations. For example - as described above - a positive SCD test implies that each of the child parents has a SCD gene. The effect of providing genetic information on the wider family can have an impact on how members relate, potentially strengthening some relationships and weakening others, and creating new, or removing existing, obligations towards family members. Challenges in maintaining privacy and confidentiality can lead to forms of genetic stigma for the child, the parents and the extended family. In the case of a child

affected by SCD, the burden of morbidity and mortality for an affected child strongly argue for disclosure despite potential risks to the wider family, but the way in which this is done is clearly critical. Genetic stigmatization and discrimination emerge as important concerns across all eras and in all settings, at the level of the individual within a family, for the family within a wider community and for communities themselves15

Risks of increasing gendered blame in families and requests for paternal SCD testing

In the study, a further risk of sharing genetic information about SCD with parents was the increased blame on mothers, as well as denial by fathers on their genetic responsibility. Denial may happen through misunderstanding or non-acceptance of the medical model of inheritance for this condition (that is, that both parents must be carriers or affected individuals). It can also occur where fathers deny their biological paternity of the child, and accuse their wives of sexual infidelity. We encountered situations where fathers demanded testing for SCD themselves, to demonstrate paternal responsibility and therefore paternity.

We encountered situations where fathers demanded testing for SCD themselves, to demonstrate paternal responsibility and therefore paternity. Drawing on community views, we argue that researchers should resist such demands from fathers, on the basis of high risks of very serious consequences to the mother and affected child from showing non-paternity.

Drawing on community views, we argue that researchers should resist such demands from fathers, on the basis of high risks of serious consequences to the mother and affected child from showing non-paternity. These risks include physical violence and the mother and affected child being thrown out of the family home. Of note, the researcher's primary responsibility in this situation is to the child, as study participant. Instead, researchers should focus on providing supportive communication about the inheritance of this condition, including the roles of both parents.

Should researchers' disclose SCD carrier status in studies like KGBC?

While there is clearly an important and urgent reason for researchers to share information on SCD in children tested during research, it is less clear how they should handle information on SCD carrier status. All the risks of gendered blame and misunderstanding would accompany providing this information, but the benefits (or clinical utility) of knowing about carrier status is very different. People who are carriers are not likely to experience ill health from their genetic status, but have a higher risk of having children affected by the condition if they later partner with another adult who is a carrier. Giving information on carrier status could therefore, in theory, influence an individual's choice of reproductive partner as well as showing respect for their autonomy.

Challenges in returning carrier information include that: i) Carrier status may often be misunderstood, with potential harms that include 'medicalisation' of a healthy child; ii) Information will be given to the child's parents who may not pass the information on to their child at a later stage; iii) the time at which the information becomes useful is many years in the future, increasing uncertainty that it will be remembered and accurately communicated; iv) currently in Kenya, adults do not have access to SCD carrier testing so the individual may not have this option open to them in future;

v) much higher numbers of children are affected than for SCD (17% vs 1%), importantly increasing the resources needed to share this information carefully. However, we argue that sharing of carrier status information in families already known to be affected by SCD (for example, where another family member is known to have SCD) has much greater importance. Families are likely to be more familiar with the condition, including the importance of carrier status, and the alternative of describing carrier status as a 'negative' result is likely to be highly misleading. At a minimum, all families should therefore be asked at the outset of an informed consent process if anyone within the family is affected by SCD before a decision is taken on whether or not to disclose SCD carrier status.

The importance of informed consent for SCD testing during research

Underlined by the principle of autonomy, researchers have an obligation to ensure those involved in research that includes screening or testing for SCD do so on the basis of prior understanding of what they will be involved in, including the implications of SCD testing. Particularly given challenges in explaining and understanding genetic research and SCD, researchers should develop careful

communication strategies, avoiding jargon and using local analogies where appropriate. In Kilifi, we developed a series of communication approaches, including visual aids to support explanations and as part of 'game' to demonstrate inheritance and the role of chance in SCD.

Other strategies developed to support ethical practice in KGBC

In addition to those described above, researchers in the KGBC study adopted a series of additional strategies to support ethical practice, many of which were developed, used and continuously modified throughout the study in response to emerging issues:

OTHER STRATEGIES DEVELOPED TO SUPPORT ETHICAL PRACTICE IN KGBC

1. From early on, researchers worked closely with County Health managers and providers to jointly strengthen services for recognising, diagnosing and managing SCD in the County Hospital and peripheral health facilities, including through in-service training activities.

2. Researchers worked closely with the research programme's Community Liaison Group to build community understanding of KGBC and SCD prior to initiation of the cohort study, including sessions on the inheritance, nature and management of SCD as an activity within the study. While important, there were many challenges in communicating complex and technical information in large scale public meetings, particularly since people commonly arrive and leave throughout these sessions. More emphasis was placed on giving detailed information to key community stakeholders likely to be asked questions about this study, including administrative leaders, health workers and other opinion leaders.

3. Emphasis was placed on the individual informed consent process, which – at the outset of the study - often involved prolonged discussions before a decision could be made. Over time, communication within the community about KGBC study created awareness of this study, but the component of SCD testing remained the most interesting and memorable part of this genomics study for most of the population.

4. Field workers in KGBC needed particular and specialised training on SCD and the cohort study to enable them to seek informed consent, collect data and capillary blood samples and return preliminary results. Early feedback on this informed consent process highlighted changes needed in the original approved information sheet. KGBC field workers developed a new version of this form at a participatory workshop to facilitate information sharing from their perspective. This amendment was later approved for use in the study. We also set up regular de-briefing sessions for KGBC FWs with an experienced programme community facilitator, separate to but in collaboration with study team, to listen to challenges experienced and offer advice.

Further recommendations based on our findings

1. Given low public understanding of SCD, patchy awareness of this condition amongst many health providers, and the common and serious nature of this condition, there are strong ethical and practical arguments for developing a national SCD control programme in Kenya, as has been done in other countries in Africa.16-18 SCD should be included in routine health monitoring activities within County and National reporting systems. An important component of this strategy is likely to be pre-marital voluntary counselling and testing for SCD.

2. Making medical and supportive SCD care available at peripheral health facilities, in addition to referral centres, has high potential to improve access to SCD management by increasing the uptake of services, and reducing physical and emotional burdens for affected families.

3. Researchers should carefully consider particular vulnerabilities of populations who might be involved in research, and ways these can be mitigated. Participant information and informed consent sheets should be clearly translated and as non-technical as possible, preferably using the local language-including using illustrations and visual aids. As much as possible, community representatives and field workers responsible for seeking informed consent should be involved in developing information sheets to ensure the community will understand them.

4. In Kilifi, mothers of children with SCD were able to provide important emotional and practical support to each other. Self-help groups may also be an important strategy to improve quality of life for affected children and their families.

5. Researchers should actively enquire about a family history of SCD when they recruit participants into studies that include SCD screening. A positive family history may offer a strong opportunity for introducing genetic counselling before marriage in regions where the gene frequency is high.

6. Most importantly, more public information on SCD across areas affected by this condition is critical to build understanding and optimise care. In the SCD clinic in Kilifi, after increased publicity through the media and the activities of field workers and community representatives in the KGBC study area, we have seen increased self-referrals, affirming the role of communication and the need for this to be strengthened.

Conclusion

SCD is commonly misunderstood in many areas of Kenya, with potentially devastating effects for many affected children and their families. While the main efforts to improve awareness and health care for people with SCD is the responsibility of government policy makers and providers, researchers should work closely with their Ministry of Health partners towards maximizing benefits and limiting harms, especially where studies involve genetic testing or screening or genomic analysis. More awareness and understanding of this condition is likely to improve outcomes for affected people, including reducing stigma and physical and emotional burdens. Researchers should also work with community representatives and affected families to address ways of improving care and quality of life for study participants affected by this serious and common genetic condition. As well as working with government health partners, this is likely to involve more community consultation in protocol development as well as public engagement to build understanding of the condition when research involves SCD screening or testing.

References

1.Collins FS. Shattuck lecture--medical and societal consequences of the Human Genome Project. N Engl J Med. 1999 Jul 1;341(1):28-37.
2.Risch NJ. Searching for genetic determinants in the new millennium. Nature. 2000 Jun 15;405(6788):847-56.
3.Pinto MC. [Ethical dilemmas in the field of genetics]. Acta Med Port. 1993 Jun;6(6):291-6.
4.Young ID. Ethical dilemmas in clinical genetics. J Med Ethics. 1984 Jun;10(2):73-6.
5.Williams TN, Uyoga S, Macharia A, Ndila C, McAuley CF, Opi DH, et al. Bacteraemia in Kenyan children with sickle-cell anaemia: a retrospective cohort and case-control study. Lancet. 2009 Oct 17;374(9698):1364-70.
6.Marsh VM, Kamuya DM, Mlamba AM, Williams TN, Molyneux SS. Experiences with community engagement and informed consent in a genetic cohort study of severe childhood diseases in Kenya. BMC Med Ethics. 2010;11:13.
7.Marsh VM, Kamuya DM, Molyneux SS. 'All her children are born that way': gendered experiences of stigma in families affected by sickle cell disorder in rural Kenya. Ethn Health. 2011 Aug-Oct;16(4-5):343-59.
8.Marsh V, Kombe F, Fitzpatrick R, Williams TN, Parker M, Molyneux S. Consulting communities on feedback of genetic findings in international health research: sharing sickle cell disease and carrier information in coastal Kenya. BMC Med Ethics. 2013;14:41.
9.Marsh V, Kombe F, Fitzpatrick R, Molyneux S, Parker M. Managing misaligned paternity findings in research including sickle cell disease screening in Kenya: 'consulting communities' to inform policy. Soc Sci Med. 2013 Nov;96:192-9.
10.Makani J, Williams TN, Marsh K. Sickle cell disease in Africa: burden and research priorities. Ann Trop Med Parasitol. 2007 Jan;101(1):3-14.
11.Weatherall DJ. Genomics and global health: time for a reappraisal. Science. 2003 Oct 24;302(5645):597-
12.Molyneux C, Hutchison B, Chuma J, Gilson L. The role of community-based organizations in household ability to pay for health care in Kilifi District, Kenya. Health Policy Plan. 2007 Nov;22(6):381-92.
13.Scott JA, Bauni E, Moisi JC, Ojal J, Gatakaa H, Nyundo C, et al. Profile: The Kilifi Health and Demographic Surveillance System (KHDSS). Int J Epidemiol. 2012 Jun;41(3):650-7.
14.A global network for investigating the genomic epidemiology of malaria. Nature. 2008 Dec 11;456(7223):732-7.
15.Phoenix DD, Lybrook SM, Trottier RW, Hodgin FC, Crandall LA. Sickle cell screening policies as portent: how will the human genome project affect public sector genetic services? J Natl Med Assoc. 1995 Nov;87(11):807-12.
16.de Graft Aikins A, Anum A, Agyemang C, Addo J, Ogedegbe O. Lay representations of chronic diseases in Ghana: implications for primary prevention. Ghana Med J. 2012 Jun;46(2 Suppl):59-68.
17.Kyerewaa Edwin A, Edwin F, Etwire V. Controlling Sickle Cell Disease in Ghana--ethics and options. Pan Afr Med J. 2011;10:14.
18.Adewoyin AS. Management of sickle cell disease: a review for physician education in Nigeria (sub-saharan Africa). Anemia. 2015;2015:791498.

THE HAVASUPAI GENETIC RESEARCH CASE.

Important ethical lessons from the diabetes research project.

By Timothy Kipkosgei
SERU

Havasupai people are american indian tribe that lives in the Grand Canyon, Arizona, United States of America. Arizona State University (ASU) conducted a research partnership with Havasupai tribe on diabetes in 1989. This project was carried out among members of this small tribe of approximately 650 people after its members approached ASU anthropology professor John Martin to conduct a genetic study on diabetes. The members of the community were concerned of the rising incidence of diabetes among the community and wanted to determine a possible genetic link. Professor Martin solicited the help of Therese Markow, a geneticist at the Arkansan University. Dr Markow research interest was on mental health specifically schizophrenia.

The study recruited approximately 400 tribal members who signed a broad consent document: "study the causes of behavioral/medical disorders". Most of participants were students who English was a second language. All of the tribe members believed they were donating blood solely for the purpose of research on the existence of a genetic link to the prevalence of diabetes that could possibly improve the health in their community. The diabetes project included health education, collecting and testing blood samples and genetic testing to establish possible genetic link with diabetes. The research went on for several years but was unsuccessful in establishing genetic link to Type II diabetes among the community. The researchers surprisingly did not end the study after the findings; instead, they continued researching into other areas that included schizophrenia, migration, inbreeding and alcoholism. These were obviously important areas in health but the community had not consented for use of the samples in these studies which they viewed as a taboo.

In 2004, Havasupai tribe sued the university and the researchers for misuse of their samples. In the case of Havasupai tribe vs the Arizona board of regents, six counts were listed: lack of informed consent, violation of civil rights, and intentional or negligent infliction of emotional distress, unapproved use of data, and violation of medical confidentiality. The university hired private investigators to keep the case out of court, after 7 years of legal battle a settlement was agreed upon. The members of Havasupai tribe in 2010 accepted a payment of $700,000, return of the samples and additional assistance that included scholarships and funding for health clinic for the tribe.

ETHICAL CONCERNS

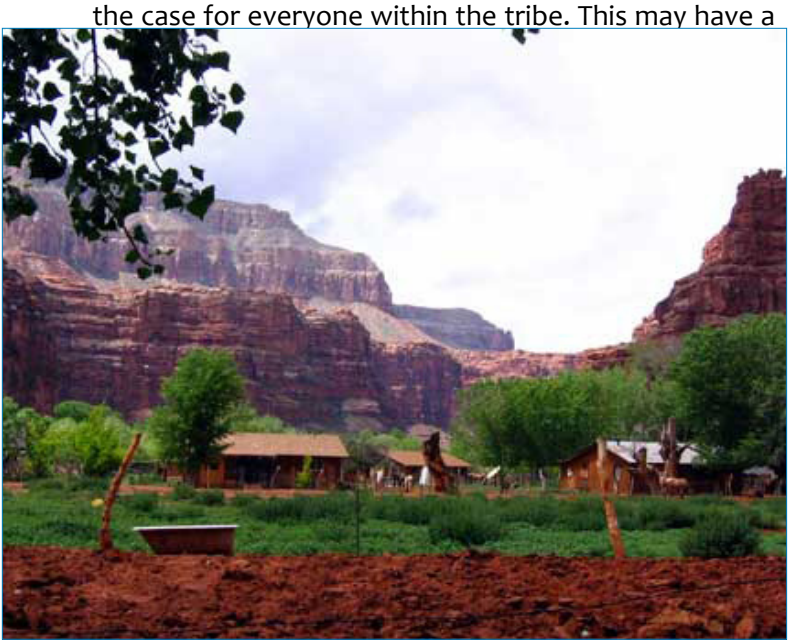
1. INFORMED CONSENT

A major concern in the suit was lack of informed consent in other studies done apart from diabetes. The informed consent in this study was obtained by oral statements to the tribe members asking them to participate in the research after which they were given forms to sign. Those who gave blood samples were informed that the samples would be used on genetic studies of type II diabetes. Although the consent mentioned research on behavioral and medical disorders, the members were not told of the specifics like schizophrenia.

The researchers needed to seek fresh informed consent for the specific studies other than diabetes research

2. STIGMATIZATION

The tribe was placed at a higher risk of possible stigmatization due to the concerns of inbreeding. The findings of the study indicated that inbreeding co efficient among this tribe was higher that other tribes. The way the results were communicated created an impression that this tribe inbreeds with each other which was not the case for everyone within the tribe. This may have a



Havasupai village overlooking the Grand Canyon

potential of ridicule and stigma on this tribe. Moreover, measuring inbreeding may not have benefited the community but may have caused more harm than good.

3. UNAUTHORIZED ACCESS TO MEDICAL RECORDS

The case of the Havasupai some researchers accessed the medical records without permission from the participants or other authorities in custody of the samples. Unauthorized access to private medical information is illegal. The researchers accessed information by using the samples to study other potential diseases, which was unrelated to the objective of the study-Diabetes genetic link. Medical records should be secured in a safe place where only authorized users can have access. It is very important to have a system in place to prevent researchers and other unauthorized users from accessing personal identifiers.

4. RISK OF LOSS OF PRIVACY

The researchers published manuscripts from the diabetes research. The appearance of the Havasupai tribe on scientific journals was a risk of identification to individual who participated. Although none of the participants was named, the Havasupai total population is approximately 650 while 400 of them provided samples making identification a concern.

5. BIO-BANKING: OWNERSHIP AND CONTROL OF SAMPLE USE.

Human samples can be used potentially by third parties for their own interest. Samples in the diabetes project were used for purposes beyond the consent of those who donated these samples. The samples from the Havasupai tribe could have been used in pharmacogenomics research or other genetic studies that could yield to benefits of improved treatments making the results profitable trough commercialization and gene patenting. However, what happens when a participant donates a part of body to for a particular purpose and more research beyond the initial purpose is done on the sample? Does it remain in the ownership of the participants? Could the tribe benefit from the results of the research for which they were not informed? When entering into a research agreement or when deciding whether to participate, tribes/communities should consider whether they will have control over how samples can and should be used, and dictate what can or cannot be done with samples.

CONCLUSION

The Havasupai case is an example of the ethical and legal dilemmas of genetic and genomic research. These issues apply to genetic research in any other setting of community based research. Researchers should always consult and agree with head of tribes and community advisory board where applicable before beginning a research project. Moreover, adequate genetic counselling must be provided, detailing the nature of genetic information to be collected and consequence of of sharing such genetic information. Institutional Review Board (IRB) must ensure all ethical and legal concerns of genetic research are addressed before approving such protocols. The researchers must be diligent in designing studies and ensure informed consent in all procedures of the study. Ultimately putting the interest of research participants at the forefront will avert harm on participants or exploitation of vulnerable population which can spoil the prospects of future research in such communities.

References

1. Indians NCoA. Havasupai Tribe and the lawsuit settlement aftermath 2012 [cited 2015 Sep 11]. Available from: http://genetics.ncai.org/case-study/havasupai-Tribe.cfm.
2. Budimir D, Polasek O, Marusic A, Kolcic I, Zemunik T, Boraska V, et al. Ethical aspects of human biobanks: a systematic review. Croatian medical journal. 2011;52(3):262-79.
3. Sterling RL. Genetic research among the Havasupai--a cautionary tale. The virtual mentor : VM. 2011;13(2):113-7.

Genetics Testing and Genomic Research

Ethical Challenges focussing on Studies Conducted in low-income countries

Kiiru John, PhD (BioSci Engr), MSc (Mol. Bio), MSc (Microb.), BSc (Biol. Sci)

The writer is a senior researcher at CMR-KEMRI and a member of S.E.R.U

Genomics is the study of all the genes in the (human) genome including their interactions with each other, the environment, and the influence of other psychosocial and cultural factors. On the other hand, genetics has evolved to encompass the impact of a person's entire genome, environmental factors, and their combined effects on health. New genomic discoveries and their applications bring great hope for a more tailored approach to treat diseases for each individual. By identifying the genetic factors associated with disease, it is possible to design more effective drugs, to prescribe the best treatment for each patient, to identify and monitor individuals at high risk from disease, and to avoid adverse drug reactions.

Genomic medicine has the capacity to revolutionize clinical practice. Recent advances in technology have made it possible to sequence an individual's entire genome for identifying variant genes or markers and investigating how these variants interact with environmental factors to cause diseases. Such studies also reveal how unique genomic variations are distributed among populations. The field of genetics, until recently, has focused on rare, single-gene diseases, such as muscular dystrophy. Mapping of the human genome therefore created new opportunities for genetic testing that can be used to predict, prevent and treat diseases. For example, it is now possible to conduct early and accurate screening for breast and colorectal cancer by screening for genetic markers such as BRCA 1/2 (human genes that produce tumor supressor proteins) and Hereditary Non- Polyposis Colorectal cancer (HNPCC) respectively. Other genomic tests can predict optimal chemotherapy regimens while others can predict the expected drug response and toxicities before subjecting populations to toxic materials during clinical trials.

The term "genetic testing" covers an array of techniques including analysis of DNA, RNA, or proteins. Genetic tests may be used as a health care tool to detect gene variants associated with a specific disease or condition and for non-clinical uses such as paternity testing and forensic investi-

Genomic medicine has the capacity to revolutionize clinical practice. Recent advances in technology have made it possible to sequence an individual's entire genome for identifying variant genes or markers and investigating how these variants interact with environmental factors to cause diseases. Such studies also reveal how unique genomic variations are distributed among populations

gations. In clinical setting, such tests can be performed to determine the genetic cause of a disease, confirm a suspected diagnosis, predict future illness, predict if an individual might pass a genetic mutation to his or her children, and to predict the expected response to therapy. The first genetic tests were for the detection of chromosomal abnormalities and mutations in single genes causing rare, inherited disorders such as cystic fibrosis. Today, genetic testing has expanded to include screening for multiple genes involved in heart diseases and cancer. There are also many tests for predicting the effectiveness of therapeutics and for guiding their administration. There exist a battery of tests applicable in screening for genetic defects in embryos, fetuses and newborns.

Examples of new and fairly advanced techniques for genomic research include Genome-Wide Association studies (GWAS) and next-generation-based sequencing strategies (NGS). These techniques, in particular, GWAS, have proven valuable in identifying regions of the genome that affect resistance or susceptibility to a wide range of common diseases. Today, researchers endeavor to combine large-scale epidemiological studies with GWAS as a strategy to study the causal mechanisms of this disease . A good example of how GWAS can be used is in the study of malaria. This complex disease involves various immunological pathways. Malaria also presents an intricate and dynamic relationship between the human, the mosquito vector and the malaria parasite .

EXAMPLES OF COMMON GENETIC TESTS

a. Carrier Identification.

These tests (e.g. screening for genetic markers for cystic fibrosis, Tay-Sachs disease, and sickle-cell trait) are popular among couples whose families have a history of recessive genetic disorders and who are considering having children. .

b. Pre-implantation Genetic Diagnosis (PGD).

These tests are carried out during the process of in vitro fertilization (IVF). After hormonal manipulation, multiple ova are collected from the woman and each ovum is screened for biological fitness before selecting one or two for implantation.

c. Prenatal Diagnosis is applied for genetic testing of a fetus.

This test is normally conducted to predict the chances of a child developing mental retardation or physical infamy or even for gender determination. Down's Syndrome is the most common genetic disease screened for using this method. This testing is highly controversial because pregnant mothers may opt for an abortion after finding out that their fetus is predisposed to an undesirable genetic condition

d. Newborn Screening

This is frequently done as a preventative health measure. Most of these tests (e.g. screening for phenylketonuria and congenital hypo-thyroidism) usually have clear benefit to the newborn because treatment is available.

e. Late-onset Disorders include adult-onset diseases such as Huntington's disease, cancer and heart diseases.

Some of these diseases are complex and have both genetic and environmental causes and the genetic result only gives an idea of possible predisposition to the condition and not a confirmation that such a condition will develop. Single genes may be responsible for conditions such as the Huntington's disease and therefore, a positive screening result are therefore highly predictive. These types of disorders can be tested for at any age. Some women from families with a history of cancer due to a mutated BRCA1, a gene that confers an 85% lifetime risk of cancer, have elected to undergo prophylactic mastectomy and oophorectomy (removal of the ovaries). However, it should be noted that such procedures may reduce but do necessarily eliminate the risk of cancer.

f. Mass population testing

This is a large scale testing usually of a particular ethnic group that shows a high rate of a specific genetic disorder. This type of testing has been both successful and unsuccessful. An example of this testing is the mass screening for Tay-Sachs disease among the Jewish people who have a high predisposition to this disease.

Although genetic and genomic testing raises hopes for disease prevention and treatment, they also bring challenging ethical issues to patients and healthcare providers alike

it is clear that as new and rapid technologies emerge, genetic testing is becoming more commonplace in the clinical and the probably in community settings. Yet, most genetic tests are not regulated and new tests may reach the market without proper analysis to verify and validate the claims of the seller. Furthermore, research participants' samples, genomic data, and associated health information are increasingly being stored and shared to maximize the benefit achieved through research.

What is a good genetic test?

A good genetic test should pass three key validity tests:
(i) is the test accurate and reliable? (Analytical validity),
(ii) Is the test result medically meaningful? (Clinical validity)
(iii) does the test improve healthcare? (Clinical utility).

Based on these criteria, genomics and genetic research raises a number of ethical challenges including the consent-seeking process , privacy of the participants, and the collection, storage and release of genomic data . Since genomics and genetic studies depend on the contributions of research participants, the rights and interests of human subjects who contribute samples and health-related information must be respected and protected. The first part of this article highlights the challenges encountered in genetic and genomic studies and testing while the second part focuses on key challenges faced when conducting genetic/genomic research in developing countries.

Part I

1. Pertinent issues in genomic research

Although genetic and genomic testing raises hopes for disease prevention and treatment, they also bring challenging ethical issues to patients and healthcare providers alike. These challenges include (i) Privacy and Confidentiality of patients and participants, (ii) possible discrimination arising from genetic testing, and (iii) Equitable Access to Genomic Technologies. This part highlights critical issues that relate to these challenges

1.1 Consent seeking process

It is important to ensure that forms used for seeking informed consent include information on any risks associated with participation in a study that involves genetic testing. The study objectives must be thoroughly explained and assurances given on how the confidentiality of records will be maintained. Since the terms used in genetic testing may be complicated, it is important to ensure that simple but accurate language is used during the consent-seeking process. A valid consent for research participation must be adequately informed and understood, voluntary, and should be obtained by someone who is competent to do so. In addition, the consenting should be done in conditions and in a language that is locally appropriate . Therefore, designing and obtaining consent for genomics research studies from a population characterized by lower average income and literacy levels presents many challenges. Such challenges include the need to explain concepts such as 'genetics', 'genomics', 'data release', and why there is a need to recruit a large numbers of healthy populations as controls .

1.2 Privacy of participants in a genomic research studies

Technological advances mean that it is now cheaper and easier than ever before to sequence and interpret genomic information for clinical and research use. It should be noted that sharing anonymous genomic data has a potential to facilitate major advances in science and this could in turn have immense benefits to human kind. It is however important to strike a balance between sharing this data and protecting the privacy of participants. Since individual's DNA may reveal the owner's health and pre-dispositions and those of his family members (especially among identical twins) it is important to ensure that the privacy of each participant is uniquely respected and protected.

One of the greatest challenges faced by genomic researchers, especially those involved in conducting Genome Wide Association studies (GWAS), is the need to link clinical data and genomic data when deriving the causal relationship between genes and diseases. The exercise of linking these two types of data presents vulnerability as far as protection of participants' identity is concerned. It is therefore important to minimize the possibility that any research participants are re-identified during this process. In order to protect the privacy of the participants, the NIH issues Certificates of Confidentiality to enable NIH-funded researchers to limit access to research participant infor-

The exercise of linking these two types of data presents vulnerability as far as protection of participants' identity is concerned. It is therefore important to minimize the possibility that any research participants are re-identified during this process. In order to protect the privacy of the participants, the NIH issues Certificates of Confidentiality to enable NIH-funded researchers to limit access to research participant information held at grantee institutions especially in the US.

mation held at grantee institutions especially in the US. Another challenge regarding privacy is often encountered when working with ethnically, geographically, and linguistically identifiable populations. Since individual's genomic data can be used to infer similar or identical traits in close relatives and tribesmen, working with such groups is particularly challenging with regard to guarding their privacy and protecting them from stigmatization, and discrimination. This is because there is a chance that a positive identification of undesirable genetic variation in an individual's genome that may be used as a basis for discrimination against him/her and the in some cases, the entire ethnic group.

1.3 Use of Clinical Samples in genomic Research

Specimens such as blood and tissue biopsies serve as important sources of material for genetic and genomic research and testing. The DNA extracted from such sources can be used in epidemiological and population-based studies on a wide range of infectious diseases and birth defects. In order to generate meaningful and reliable data, a common practice is to use de-identified blood spots obtained from a large population size. However, in such a study in the US, parents raised concerns regarding the use of their children's blood spots in genomic research without their consent. This research had utilized de-identified dried blood spots collected from neonates for routine screening. A lawsuit against this study lead to the destruction of five million stored blood specimen. Since then, various states in the US e.g. Minnesota, have passed laws regarding the use and retention of blood spots after newborn screening. The US congress has also passed a law requiring consent for use of blood spots from newborn screening.

1.4 Patenting genomic research

Patents are issued as an incentive to encourage innovation and to protect against infringement on the intellectual output of an investor or a researcher. This should in turn stimulate healthy competition that should ensure continuous investment in the field of science. Since the issuance of the first genetic patent in 1982, the core of the debate over genomic/genetic patents has been whether or not the discovery of a gene or a genomic sequence qualifies as a patentable invention. In the US for example, a patent may only be granted on "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof. As such, laws of nature, natural phenomena, and abstract ideas cannot be patented. Patentable items must also be novel and existence of "prior art' can be used as a basis to invalidate a claim to an invention. Those who oppose genetic patenting argue that genes are naturally occurring, and while much intellectual effort may go into discovering the genes, a discovery is not the same as an invention. It should however be understood that genetic technologies such as new methods of DNA sequencing are patentable. However, patents that limit the use of basic genetic information have a potential to inhibit progress in science and may assert unduly constrain on (medical) research

It has been feared that large numbers of patents associated with human genome have a potential to limit the integration of genomic medicine into health care. This is because such patents may impose major restrictions in knowledge sharing and may also result to prohibitive costs by other developers and consumers due to loyalty payments. One potential danger of patenting a gene is that if allowed, development and improvement of new diagnostic tests based on the patented gene will be impossible because the actual DNA sequence to be tested is claimed in the patent. In addition, multiple patent holders may lay claim to large sections of a genome and this could potentially inhibit translation of genetic discoveries into health care benefits. In order to avoid such a scenario, the Secretary's Advisory Committee on Genetics, Health and Society published a report, *Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* (oba.od.nih.gov) This report recommended that diagnostic (but not therapeutic) genetic tests, be exempted from patent infringement, along with a research use exemption.

1.5 Legal issues regarding the use of genomic/genetic data

In developed countries such as the USA, many people fear that participating in a genomic study or undergo-

ing genetic testing may expose them to discrimination based on the data derived from their own genetic mark-up. In order to avoid such scenarios and in order to encourage people to participate in studies that could lead to development of new tests and improved therapies, the US passed the Genetic Information Non-discrimination law (2008). This law prohibits discrimination in the workplace and by health insurance issuers based on genetic testing. As such, health insurance issuers cannot use genetic information as a basis to make decisions regarding the clients' eligibility to a policy, coverage, underwriting or for determining premiums rates. Furthermore, issuers may not request or require individuals or their family members to undergo genetic testing or to provide genetic information as a prerequisite to obtaining insurance covers.

It is important to note that according to this act, genetic information includes family medical history and information regarding individuals' and family members' genetic tests. This act further prevents employers from using genetic information in employment decisions such as hiring, firing, as a basis for promotions and determination of pay rates or when assigning jobs and tasks to their employees. Furthermore, it prohibits the employers from passing such information to third parties for whatever use. It is however important to note that this act does not apply to employers with fewer than 15 employees and that the rights expressed therein do not extend to the US military and do not cover long term care insurance, life insurance or disability insurance. It is however important to note that many developing countries lack such laws.

1.That genomic data can be stored and used indefinitely and that the interpretation of these results can change over time

2.That analysis of the data may reveal susceptibility to a broad range of conditions (some of which are unexpected given personal or family history) and therefore, a good decision should be made on whether to release this information to the participant or not. It is also important to determine what validations should be done before releasing data from exploratory studies because such results may only be preliminary pending further studies and validations.

3.That finding a gene considered to predispose to a disease does not always mean that the bearer will eventually develop the associated condition because phenotypic expression is influenced by diet, ethnicity, and the environment among other factors.

4.That release of genetic data raises privacy concerns because there is a possibility of re-identification of participants depending on the data structure and study design.

5.That depending with the target gene, results from an individual can be extrapolated to other members of the family/tribe with a fair degree of precision and this could expose an individual or an entire population to prejudice and discrimination

1.6. Genomic Data release and storage

One of the earliest principles agreed upon by the principal investigators of the Human Genome Project was that the DNA sequences generated should be freely available to the public. Later, in 1997, the Bermuda Principles were derived and these set forth the expectation that all DNA sequence information should be released into publicly available databases within 24 hours of being generated. Since then, many other genomic research studies have adopted similar principles. Decisions concerning storage and release of genomic data should be made after making the following considerations;

1.7 Predictive genetic testing in children

Parent may be eager to know about the genetic predisposition of their child during and after the gestation period. A technology called Tandem Mass Spectrometry is now being used in many states in the US for screening newborns for more than 24 different genetic disorders using one simple test. Although many developing countries lack laws governing genetic testing of children, the American Academy of Pediatrics (AAP) and the American College of Medical Genetics (ACMG) have provided new guidelines for the ethical issue of pediatrics genetic testing and screening of children in the United States. According to these institutions, performing pediatric genetic testing should be in the best interest of the child. The AAP and ACMG guidelines also recommend that unless testing during childhood can reduce morbidity or mortality, genetic testing for late-onset conditions should be put on hold until adulthood. They however allow testing for asymptomatic children who are at risk of childhood onset conditions. Among other tests that are allowed for children include histocompatibility testing, tests related to pharmacogenetics and a battery of tests for newborn screening. However, it is still important to put mechanisms in place in order to protect the minors from coercion and to safeguard their interests. The guidelines further discourage the use of home-based kits for self-testing because of the accuracy, interpretation and oversight of test content. These guidelines further state that the parents or guardians should be encouraged to inform their child of the results from the genetic test if the minor is of an appropriate age.

Although a minor of mature and appropriate age may request for his/her own genetic test, the health care providers are advised to be cautious in providing predictive genetic testing without the involvement of the parents or guardians. The health care providers have an obligation to inform parents or guardians on the implication of test results. The guidelines also state that any type of predictive genetic testing is best offered after genetic counselling by trained health care providers

1.8 Controversies surrounding genetic testing

It has been argued that results from genetic testing may have associated psychological, social, and financial risks. Psychological risks for parents who are carriers of a condition may include parental guilt of having passed an undesirable trait to their child. Furthermore, a child diagnosed with a genetic condition may face lowered self-esteem and may be vulnerable to discrimination in risk insurance and employment. Newborn screening may also present an advantage in that it can reveal a genetic predisposition to a condition for which the parents were not aware prior to the test and therefore, such parents may be in a position to make a decision before getting another child. However, identifying infants as carriers may interfere with the parent-child relationship leading to sibling discrimination. In order to avoid such scenarios, the Institute of Medicine and the American Academy of Pediatrics ruled that newborns should not be screened specifically to identify their carrier status. In addition, if the carrier status is noted in a child during screening, the results should only be given to parents who have had previous counseling and who had given their consent prior to the testing.

Other controversies in genetic testing include the fact that many genetic conditions are still difficult to treat or prevent and therefore, the test result may be of limited value. The American Academy of Pediatrics (2001) has therefore directed that "detailed counseling, informed consent and confidentiality should be key aspects of the genetic testing process, particularly when the benefits are uncertain". There is also the question on whether children screened for adult-onset disorders would want or benefit from such testing once they are adults. Therefore, at present, subjecting children and adolescents to predictive genetic testing for adult-onset disorders is deemed inappropriate unless the test can be used to reduce morbidity and mortality in childhood. Some experts are of the opinion that testing for adult-onset disorders in child eliminates the their right to informed choice especially where the results have a potential to subject the individual to lifelong stigma and discrimination. In 1995, the American Society of Human Genetics recommended that predisposition testing for their infant or child should be delayed until the child is old enough to make an informed choice

While working with these communities, it is important to recognize the need for relevant health research but still be awareness of the potential for exploitation in the context of potential vulnerability and inequality experienced by participants from such countries compared to those in the developing countries .

PART II.

2. ETHICAL ISSUES IN HUMAN GENOMICS RESEARCH IN DEVELOPING COUNTRIES

Genome-wide association studies (GWAS) provide a powerful means of identifying genetic variants that play a role in various diseases. Such studies present important ethical challenges. An increasing number of GWAS is taking place in low-income countries and there is a pressing need to identify particular ethical challenges arising in such contexts.

2.1 Participants from low-income counties are vulnerable

Due to the high investment costs and knowledge gaps, many genomic and genetic analysis strategies such as GWAS are yet to be applied to study diseases that primarily affect people in lower income countries . While working with these communities, it is important to recognize the need for relevant health research but still be awareness of the potential for exploitation in the context of potential vulnerability and inequality experienced by participants from such countries compared to those in the developing countries . When working with such communities, it is important to have excellent community engagement strategies in order to ensure fair, inclusive, accountable and appropriate studies . Genome-based research on (neglected) diseases in such countries is important because of relatively higher mortalities rates and lower "quality of life". In addition, low literacy levels make such populations difficult to work with as far as the consent-seeking process is concerned.

2.2 Regulating and approval of human genomics research in developing countries

The export of these samples presents many challenges including the fear that once samples have been exported, the local researchers may lose control over them . There is also a need to ensure that the samples will only be used for the intended purposes. It is therefore important to ensure that proper agreements are reached on export, sample handling and mechanisms for destruction of samples upon completion of the study

Where genomics research focuses on diseases affecting populations with low income and literacy levels, it tends to take place in collaborations between researchers from higher and lower income countries. It is also important to note that whereas the infrastructure for genotyping and whole genome analysis is usually based in laboratory in higher income countries, majority of patients affected by the diseases may be in lower income countries. This unequal distribution of research resources raises important issues concerning the use of archived samples, sample ownership and ethics review by multiple committees.

2.3 Protecting the interests of research participants in developing countries

The recruitment of participants regardless of where it is conducted, prospective participants in lower income countries are much more likely to be poor and to have limited access to healthcare, education and other resources. A balance must be attained between stimulating research in such regions and protecting the welfare, interest and privacy of the participant.

2.4 Sample export and ownership

Another challenge in genomic research using samples from low-income countries is the export and analysis of samples in laboratories only available in developed countries. Genomic research e.g. GWAS, require access to sophisticated laboratories and large-scale genotyping facilities and a set of dedicated and highly trained statisticians. Most of these requirements are only available in a few countries in the world. Therefore, majority of GWA studies require export of samples to laboratories in developed countries. The export of these samples presents many challenges including the fear that once samples have been exported, the local researchers may lose control over them . There is also a need to ensure that the samples will only be used for the intended purposes. It is therefore important to ensure that proper agreements are reached on export, sample handling and mechanisms for destruction of samples upon completion of the study .

2.5 Capacity building

A significant challenge for sustainable GWA studies in lower income countries concerns the development of research capacity across participating research sites. Where researchers are engaged in the collection of large numbers of samples, it is vital that they are also in a position to analyze research results, and to use their contribution for career development.

The fact that collaborative genomics research in lower income countries involves the establishment of large and diverse scientific networks bringing together diverse and interdependent forms of expertise and institutions in higher and lower income countries, the responsibility for the ethical dimensions of such research is inevitably shared among all key players in a study. For such studies to be successful, important issues such as ownership of samples and data and capacity to analyze genomic these data need to be addressed. In addition to establishing means of developing consensus onethical issues to be addressed in their research, such research networks need to determine how best to tailor the implementation of ethical principles to individual research sites. Therefore, the key challenge for genomics research conducted on populations with lower average income and literacy levels is how to ensure that local researchers and local research ethics committees feel confident on how samples and data will be used appropriately, and transparently.

Conclusion

Recent advances in genomic analysis have expanded possibilities of developing a wide array of genetic and genomic testing strategies. While such strategies have increased the precision for early screening of diseases and other conditions, there is a need for each country, especially developing or low-income countries, to formulate laws that will ensure that the interests, privacy and welfare of the study participants are protected and assured. Even with the availability of genetic tests for various conditions, the challenge remains in the interpretation of these results. It is particularly important to enhance counseling of patients or participants before and after genetic testing. Genomic researchers from developed and developing countries involved in collaborative genomic studies must cultivate trust,

respect and mechanism to share data, techniques and skills. Finally, it is important to realize that the final and the major beneficiary of genetic and genomic testing platforms should be the participant and society at large.

REFERENCE

1. Kwiatkowski D: How Malaria has affected the Human Genome and what Human Genetics can teach us about Malaria.American Journal of Human Genetics 2005, 77:171-190.
2.Greenwood BM, Bojang K, Whitty CJM, Targett GAT: Malaria.the Lancet 2005, 365:1487-1498
3.McGuire AL, Caulfield T, Cho MK: Research ethics and the challenge of whole-genome sequencing.Nat Rev Genet 2008, 9(2):152-156
4.Chokshi DA, Parker M, Kwiatkowski DP: Data Sharing and Intellecual Property in a Genomic Epidemiology Network: Policies for Large-Scale Research Collaboration
5.World Medical Association: Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects.2008.
6.Chokshi DA, Thera MA, Parker M, Diakite M, Makani J, Kwiatkowski DP, Doumbo OK: Valid Consent for Genomic Epidemiology in DevelopingCountries.PLoSMed 2007, 4(4):e95.
7.Rosenberg NA, Huang L, Jewett EM, Szpiech ZA, Jankovic I, Boehnke M: Genome-wide association studies in diverse populations. Nat Rev Genet 2010, 11(5):356-366.
8.Nuffield Council on Bioethics: The ethics of research related to healthcare in developing countries. Nuffield Council on Bioethics; 2002.
9.Chokshi DA, Thera MA, Parker M, Diakite M, Makani J, Kwiatkowski DP, Doumbo OK: Valid Consent for Genomic Epidemiology in Developing Countries.PLoSMed 2007, 4(4):e95.
10.Upshur R, Lavery J, Tindana P: Taking tissue seriously means taking communities seriously. BMC Medical Ethics 2007, 8(1):11
11.Langat SK: Reuse Of Samples: Ethical Issues Encountered By Two Institutional Ethics Review Committees In Kenya.Bioethics 2005, 19(5-6):537-549

New SERU Commitee Members.

Dr Peter Mwitari, PhD

Dr Peter Mwitari is a Principal Research Officer and Director of the Centre for Traditional Medicine and Drug Research (CTMDR) at the Kenya Medical Research Institute (KEMRI). Dr Mwitari holds a PhD in Pharmacology from Tianjin University of Traditional Chinese Medicine. He joined KEMRI in 1998 and has over 15 years' experience in the field of traditional medicine.

His career interests are on application and development of plant medicines in the management of communicable/non-communicable diseases, drug quality control, analysis and development and training & technology transfer. He is currently a Co-principal investigator in the pyrethrum as well as a co-investigator in the khat study funded by the Government of Kenya. He is a member of the Committee B KEMRI Scientific and Ethics Review Unit. Dr. Mwitari has published widely in the area of plant medicine and pharmacology.

Prof. Christine Sekadde-Kigondu, PhD

Prof. Christine Sekadde Kigondu is an Associate Professor in the Department of Human Pathology, School of Medicine, University of Nairobi. She holds a PhD degree in Clinical Biochemistry from State University of New York at Buffalo, New York, USA. She has taught in a number of universities over the years. Her main interests are Endocrinology and Laboratory Andrology.

Prof Kigondu has played a key role on international panels, facilitating the advancement of research in reproductive health for the Africa. She has published widely with over eighty publications in both local and international journals. She has supervised various students from different departments in the School of Medicine and other universities in their research work. Prof Kigondu has also received extensive training in Bioethics. She is a member of the Kenyatta National Hospital – University of Nairobi Ethics and Research Committee as well as the KEMRI Scientific and Ethics Review Unit (SERU) Committee. She actively participates in various training programs in bioethics for university students, scientists, medical personnel and academic staff. She has also served as a member of various committees in the University, regionally and internationally.

Dr Charles Obonyo, PhD

Prof. Obonyo is a Chief Research Officer at the Kenya Medical Research Institute (KEMRI), based at the Centre for Global Health Research (CGHR) in Kisumu, Western Kenya. He joined KEMRI in 1991. He trained in Clinical Medicine at the Kenya Medical Training College (1986-89), before embarking on a career in clinical research. He obtained a Master of Science Degree in Clinical Epidemiology from Erasmus University in the Netherlands in 1997, and a PhD in Clinical Epidemiology from Utrecht University in the Netherlands in 2006. He attended the New England Medical Center in Boston, USA as a Pre-doctoral Clinical Research Fellow between 2000 and 2001. He attended a course on Ethical Issues in Global Health Research at Harvard School of Public Health, Boston, USA.

In his research work at KEMRI, Prof Obonyo has focused on epidemiology and treatment of paediatric malaria, anaemia, schistosomiasis, impact of HIV-malaria co-infections on response to treatment and evaluation of new interventions against these conditions using the clinical trials and systematic review methodologies. As part of the Cochrane Collaboration, he has conducted systematic reviews to generate evidence for the effectiveness of conjugate Hib vaccine for pneumonia and meningitis, artesunate-based drug combinations and clindamycin plus quinine for malaria.

Prof Obonyo has an interest in the epidemiology and control of Non-Communicable Diseases in Kenya. He has published over 20 papers in peer-reviewed journals and also edited book chapters. On a part-time basis, he teaches Epidemiology, Bioethics, Research Methods and Systematic Reviews, at Jaramogi Oginga Odinga University of Science and Technology in Western Kenya. He is also the Kenyan coordinator of the Cochrane African Network as well as a member of the African Research Network on Neglected Tropical Diseases.

Prof Obonyo is the Chair of the Ethics Committee at the Great Lakes University of Kisumu, a member of the KEMRI Adili taskforce and the KEMRI Scientific and Ethics Research Unit. He is also a regular journal reviewer for the Lancet Infectious Diseases and American Journal of Tropical Medicine and Hygiene.

Dr Beatrice Wassuna, PhD

Dr. Beatrice M. Wasunna is a Research Scientist at the KEMRI's Eastern and Southern Africa Cent re of International Parasite Control (ESACIPAC). She holds a PhD in Public health (Infectious and Tropical Diseases) from the London School of Hygiene and Tropical Medicine, United Kingdom. Her PhD thesis investigated the impact of a complex behaviour change intervention implemented under routine operational conditions on prompt and effective treatment of children under five with fever in rural Kenya.

Dr. Wasunna has served as principal and co-investigator in various research activities undertaken in collaboration with national and international partners and institutions. Her current research interest is on community directed approaches to treatment of neglected tropical diseases. Since October 2013, she has been the lead core module developer of the World Health Organization's District Level Neglected Tropical Diseases course.

In addition to her research activities, she provides technical assistance to the Kenyan Ministry of Health in various projects and activities. In 2014, she provided technical assistance to the Malaria Control Unit in the planning, execution and subsequent report writing for the biannual Kenya National Malaria Forum.

Dr. Wasunna also represents ESACIPAC in the Community Health Services Unit Operations Research Technical Working Group. Her interests lie in operations research, using social science methods to design and evaluate complex health interventions that aim to improve access to quality healthcare

Ms Cynthia Kimani

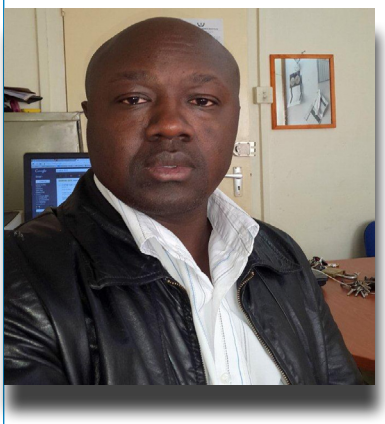
Ms Cynthia Kimani works for the Kenya Medical Research Institute Headquarters Library as a Librarian. She is the systems Librarian in charge of the digital library that entails the E resources, online databases and all ICT related issues in the Library. She holds a Masters in Development Management form the Open University UK, Masters in Library and Information Science (MLIS) from Kenyatta University, a Bachelor's degree in Technology Library and Information Science from the University of South Africa (UNISA) and a Diploma in Library and Information Studies from Inorero University, Kenya.

Cynthia is involved in capacity building through training on online information resources in relation to health information and Intellectual Property (IP) databases. Her training initiatives extend beyond KEMRI, through her Professional Associations. She is an active member of the Association of Health Information and Libraries in Africa (AHILA) where she serves as an executive member and Chief Editor, and Kenya AHILA country Chapter. She is a key trainer and facilitator in all Major Health Information training workshops held by KEN-AHILA.

Cynthia is an award winner of the 2013 "Unsung Heroes" Research4life Library Competition. Her story on her passion in the online training initiatives granted her this opportunity. She participated in this competition that was in recognition of the role of librarians in building research capacity and boosting output among scientists, doctors and policy makers especially through capacity building and training and creating awareness of the Research4Life databases. Through her participation, she was selected as one of the key trainers in the region as well as in the global Research4Life Programme Advisory Committee which oversees the needs of various training initiatives around the region.

In addition, Cynthia is a member of the KEMRI SERU Committee B, where she actively participates in the review process of research protocols. She also supports Cancer initiatives through the Twakutukuza trust, by annually singing in the Twa Choir concert that raises money in support of Cancer treatment to those who may not be able to afford the treatment.

Dr. John Ndemi Kiiru



Dr. John Kiiru is a Senior Research Officer at Center for Microbiology Research KEMRI with over 10 years of experience. He holds a PhD (Bio-Science Engineering, KuLeuven, Belgium), MSc (Molecular Biology, KuLeuven, Belgium), MSc (Microbiology, UoN) and BSc (Bio. Sci UoNairobi). He is currently a Post-Doctoral researcher in the University of Liverpool/KEMRI/UoN/ILRI Zoonotic and Emerging Diseases Program. His research objective has been to integrate epidemiology and Molecular Biology techniques for mapping the spread of infectious diseases with a special focus on multidrug resistant (MDR) strains.

Dr Kiiru has published extensively on Salmonella, E. coli, and Vibrio among other pathogens with special focus on mobile genetic elements and extended spectrum beta-lactamases. He is also a faculty member of the Wellcome Trust International Training Programs in molecular aspects of infectious pathogens. Dr Kiiru also teaches various themes in molecular microbiology at the KEMRI/JKUAT ITROMID post-graduate course and is an invited lecturer in JKUAT and University of Nairobi. He is a member of the National Infectious and Parasitic Diseases Research Program (IPDRP) and a committee member of the KEMRI Scientific and Ethics Review Unit.

Bridget Wanjiku Kimani

Bridget Wanjiku Kimani is a Research Officer at Kenya Medical Research Institute's (KEMRI) Centre for Microbiology Research (CMR). Ms. Kimani who joined KEMRI in 2007, holds a Bachelor's degree in Biochemistry and is currently pursuing her Master's Degree in Public Health at the Institute of Tropical Medicine and Infectious Diseases (ITROMID).

Bridget's research interest areas are on parasitology (Intestinal Helminthes, Lymphatic Filariasis and Schistosomiasis) and bacteriology (Escherichia Coli and Salmonella). In addition, she is actively involved in quality control and quality assurance in the CMR labs.

Ms. Kimani serves as a member in various Committees such as; the KEMRI Annual Scientific Health Conference Organizing Committee, the KEMRI Library Information Committee and the KEMRI Digital Repository Committee. She has attended in-house training on research ethics and written online research ethics courses with the Collaborative Institutional Training Initiative (CITI) by University of Miami. She is a committee member of the KEMRI Science and Ethics Review unit.

BIOETHICS SOCIETY OF KENYA

MISSION

Supporting the development of ethics in the life sciences and diffusion of knowledge for equity and progress in health care

Membership Drive Still On

CATEGORY	REGISTRATION FEES KSH	ANNUAL MEMBERSHIP FEES	TOTAL
STUDENT	500	1000	1500
INDIVIDUAL	1000	2500	3500
INSTITUITIONAL(IRB)MEMBERS	1000	2500	3500

NB- 20% discount on registration and annual membership fee will be granted for IRBs that register as a group

Registration and membership fee can be paid through
Account Name: Bioethics Society of Kenya.
Account Number: 01134696005500 Branch: Nairobi Business Centre
M-pesa number 0718703943.
For more inquiries contact BSK on: email address bsk@rctp.or.ke or call mobile number 0718703943
For more information visit http://www.bioethicskenya.org/

SERU MEMBERS TRAINING AND TEAM BUILDING IN NAIVASHA

The SERU Reviewers and the Secretariat attended a retreat from the 15th to 17th July, 2015 at the Sun Africa group of Hotels, Lake Naivasha Country Club. The retreat involved training, presentations and discussions on: study designs, Intellectual Property Rights, sampling and data analysis, research ethics, bio-banking and sample storage, closure and dissemination of study findings. This was also an opportunity to present to reviewers, their performance evaluation results. In addition, the reviewers also shared their observations on the developments made in the restructuring of KEMRI's research regulatory system.

SERU members perform a song during presentations

Dr Evans Amukoye makes his presentation

SERU members participate in team building sport activities

Case Challenge: Genetic research on an island population

Adapted from WHO CASEBOOK ON ETHICAL ISSUES IN INTERNATIONAL HEALTH RESEARCH, 2009, Case 45, pg 139

An island nation has a population of about 90 000, all of whom are of a single ethnic background. There is little or no immigration to the island and hence the genetic make-up of the population is quite homogenous. This presumed genetic homogeneity along with the high incidence of certain diseases in the population are seen as an advantage by some researchers who are looking for specific alleles associated with polygenic diseases.

The island's government is a monarchy, although it also includes a prime minister and a cabinet, a third of which is chosen by popular vote. A popular movement has been pressing for more democratic representation and a free press in the country. Most of the islanders belong to one of the several denominations of Christianity that spread during the active missionary movements led by European colonizers during their 100-year presence on the island, which ended 30 years ago. The island's economy is supported by a narrow base of agricultural exports and some tourism. The GDP is approximately US$ 1500 per person. Most food is imported and unemployment is about 15%. Literacy is almost universal, and health services are reasonably good and free. A growing concern, however, is the rising rate of diabetes and obesity; 18% of the population is estimated to have diabetes, which is twice the prevalence reported 25 years ago. Changes in diet and physical activity, including increased consumption of imported fatty foods overlaid on a possible genetic predisposition for the disease, are believed to account for the rising prevalence of diabetes.

In 2001, after negotiations with the government, a European biotechnology firm announced an agreement to conduct genetic research designed to identify disease-related genes in the relatively isolated and homogeneous island population. The company planned to target families with members who had already been diagnosed with diabetes for sampling and genetic analysis. A newspaper account in Europe described the arrangement as allowing the company "exclusive rights" to collect blood samples from the islanders, provided that islanders gave individual informed consent for genetic analysis. In fact, the word exclusive" does not appear in the agreement. The company has made a commitment to donate a certain amount of money to the country's ministry of health, including plans to construct a new research centre on the island, and to share some portion of any royalties generated by commercial products either developed for the project or as a result of it.

The agreement, first announced in the European press, was immediately criticized by the island's community groups. The head of the popular democracy movement stated several objections, including a lack of public discussion of the project; inadequate transparency on the part of the government about its actions; a failure to consider the privacy of those whose family members might participate in the project on the basis of individual consent; opposition to the notion of patenting DNA and other life forms; and the lack of guarantees of any benefits either for those who participate in the study or for the island population more generally. In addition, he contended that the benefits would be minimal compared with the material gain that might be realized by the company in attracting new capital and producing successful products. At the time, the country had no existing intellectual-property law or regulation of biological research, and thus had a limited ability to protect its own interests.

The island's organization of Christian churches published a statement in a journal of medical ethics that opposed the project on the basis of religious beliefs, namely that patenting of "life forms" was a violation of respect for the sanctity of life and fundamental religious principles. Shortly after the protests, the company withdrew its plans for the project and pursued agreements to gather samples elsewhere.

Questions

1 Does a group of people have collective ownership of their genetic heritage? If so, how could this ownership be defined?

2 What ethical concerns arise about the ability of national governments to negotiate and decide agreements for genetic research in their populations?

3 How can benefit-sharing arrangements be evaluated in terms of fairness, transparency, and responsiveness to national needs?

4 How can it be determined that benefits that might accrue to a body or governmental organization in the country best serve the interests of the population?

5 Would it have made any difference to the ethical implications if the genetic research project was carried out by a non-profit entity, as opposed to a for-profit commercial entity?

The first three respondents in will receive a prize.
The first correct response will also receive a prize.
Answers should be submitted to ddrt@kemri.org

LAST ISSUE WINNERS
Winner -Nicollate Akoko
Second -Moses Barasa
Third- Teresiah Njeri

Tersiah Njeri(Left) and Moses Baraza, third and second runners up respectively receive their prizes from the Deputy Director, KEMRI Prof Elizabeth Bukusi.