ETHICAL CHALLENGES IN DISCLOSING GENOMIC RESEARCH RESULTS IN A DEVELOPING COUNTRY

By

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ABSTRACT

Genomic research results may reveal conditions which the researchers and the participants did not set out ab initio to discover but which may have health implications for the participant. Ethical guidelines require the disclosure of research results to participants although disclosure of such results may impose undesirable responsibilities and consequences on the participants. Unlike in developed nations, locally and culturally applicable guidelines for the protection of research participants from the harmful effects of disclosure of such results of genomic research have been not enunciated in developing countries. Establishment of such guidelines needs to be guided by expectations and preferences of the indigenous research participants. This study therefore attempts to determine potential research participants understanding and expectations of disclosure of genomic research results and its implications to participants in genomic research in Nigeria.

The study design is cross sectional descriptive study using quantitative approach. The participants were selected by systematic sampling from patients attending the laboratory of Adeoyo Maternity Hospital in Ibadan. A semi structured interviewer administered questionnaire was used to collect information on socio-demographic characteristics of participants, awareness of genomic research studies, awareness of possible consequences of disclosure of genomic results, preferences on the mode of disclosure of their result and the recipients of such disclosure. Data were analyzed using the SPSS version 17 and presented with the tables of frequencies

The study found out that the participants in this study were aware of genomic identification of diseases (68%) , and the prediction of likelihood of genomic diseases (60.5%). The main advantage expected from undergoing genomic testing is awareness of health status (58.7%) and main disadvantage is psychological trauma (71.0%) . The study participants want the findings from the genomic research to be communicated to the individuals involved in the research (94%) and certain third parties (86.7%), mostly next of kins (30.7%) and spouses (20%). Main reason for seeking disclosure is to obtain social (37.3%) and medical (22%) support. Participants suggested that guidelines for the disclosure process should consider issues of confidentiality and privacy (31.2%). The Participants also suggested that there may be reasons to withold the research results which include consideration of the mental health status of the

recipient of the disclosure (10.7%), curability of the disease (8.7%) and social consequence of the disease (8.7%).

The findings from this study suggests that the process of obtaining consent for participation in genomic research should put emphasis on informing the patient about the possible consequences of receiving their research result and obtaining consent on the type of result preferred to be disclosed. Participants may be required to indicate the third party to which the result should be provided.

Keywords: genomic research, disclosure of results, third party,

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Above all thanks and honour, be to the Almighty and Eternal God in with whom all things are possible

DECLARATION

I hereby declare the works presented here are to the best of my knowledge original except as acknowledged in the text and referenced. I have not submitted this material either in whole or part for another degree or certification in this or any other university.

Dr Dairo Magbagbeola David

CERTIFICATION

I certify that this study was carried out by Dairo Magbagbeola David, in the Department of Surgery, Faculty of Clinical Sciences, College of Medicine, University of Ibadan, Nigeria

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DR T. O OGUNDIRAN

Supervisor

DEDICATION

This work is dedicated to all my teachers, past and present.

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LIST OF ABBREVIATIONS

APOE	Apolipoprotein E
BRCA	Breast Cancer Gene
CIOMS	International Council for the Organization of Medical Sciences
CLIA	Clinical Laboratory Improvement Amendments Act
HIPAA	Health Insurance Portability and Accountability Act
NBAC	National Bioethics Commission
NHBLI	National Heart, Blood and Lung Institute
NRC	National Research Council
IOM	Institute of Medicine
IRB	Institutional Review Board

CHAPTER ONE

Background

The abuse of research participants and the consequent harm resulting has lead to the articulation of several declarations and statements on the rights of research participants and the enunciation of codes, guidelines and protocol on their protection. Historically, efforts to protect research participants began with the trial of investigators involved with the Nazi abuse of research participants during the Second World War. The trial lead to the development of the Nuremberg code which appears to be the first public effort to proffer guidelines for the conduct of scientific researches (Shuster 1997; Weindling Paul 2001). The Belmont report followed about thirty years later, having been spurred by the recognition of abuse of black research participants in the Tuskegee Study of Syphilis in the Negro Males (National Commission 1979; NCPHSR 2004). Other protocols such as the World Medical Declaration at Helsinki, the CIOMS, have followed and expatiated, elucidated and elaborated on the provisions of the earlier declarations (CIOMS 2002; WMA 2004). Each of these protocol developed recognized and advanced on the three principles to guide the conduct of research. These principles are respect for persons, beneficence and non maleficence, and justice (McGuire & Beskow 2010). Although these principles were not advocated with a hierarchical order intended, the principles of respect for persons appears to be the overarching principle incorporating all other principles (Gillon 2003).

The principle of justice imposes the obligation to share the benefits of research with those who provide the resources for the research. Implementation of this principle requires that the results of research should be shared with the society as a whole and with individual participants specifically. Sharing the results with the society as a whole can be accomplished by sharing the

results with the scientific community and the health care system. Sharing the results thus consummates the reciprocal relationship that exists between the research participant and the investigator on one hand and the society who provides the public fund for the research on the other hand.(Lévesque et al. 2011). Thus return of results implies the return of individual and general results.

The principle of respect for persons requires that individuals should not be treated solely as means to an end. Application of the principle of respect for persons requires that consent must be obtained from each research participant before the commencement of research. The investigator have to ensure that consent for participation in the research are made under conditions of clear understanding, free from all coercion and undue control ((Beauchamp 2003; Childress 2000). McGuire noted that there are three elements of informed consent. These elements are required to make consent obtained from research participants to be regarded as valid consent. These are documented in the Belmont Report as the applications of the principles of the respect for persons and are information, comprehension and voluntariness (McGuire & Beskow, 2010). As noted by Beauchamp, legal, regulatory, philosophical, medical and psychological literatures tend to favour the following as the components of informed consent: competence, disclosure, understanding, voluntariness and consent. However, Beauchamp and Childress advocated an analysis of informed consent as being composed of seven elements further grouped into three categories; threshold elements, information elements and consent elements. Threshold elements are preconditions for providing consent and are competence (to understand and decide) and voluntariness (in deciding). Informational elements include disclosure of material information, recommendation of a plan and understanding of the foregoing. Consent elements include decision in favour of a plan and authorization of a chosen

plan. Implicit in consent elements are refusals of participation in a research. However, it should be stated that refusal in itself constitute a decision and is viewed as the opposite of consent.

Disclosure of information is a major fulcrum upon which the information elements of the principles of informed consent rests. Most codes guiding ethical conduct of research requires that there must be specific items for disclosure to the participants in a research endeavour. Such items includes but is not limited to the research procedure, purpose of the research, risks and benefits, alternative procedures statement offering opportunity to ask questions and to withdraw at any time from the research. Authors of the Belmont Report however noted that the list cannot be exhaustive, and there needs to be standards regarding what information requirements for disclosure are appropriate for each research endeavour. While reporting on subsisting standards, the authors noted that there are limitations to the standards. One standard such as the one often accepted as guide in malpractice suite is that information should contain all that the patient needs to guide his decision in medical care. Thus is called the reasonable person standard. However this cannot be applied to research situations since the participant has a right to seek more information than is required in clinical care as his participation may be based on the self imposed need to know (Black & Mcclellan 2011). Proposing the reasonable volunteer standard, some authors recommend that "the extent and nature of information should be such that persons knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether to participate in furthering of knowledge" ((NCPHSR 2004; National Commission 1979). Thus disclosure of information, a major fulcrum of the informed consent procedure and thus also the principle of respect for persons, is a crucial aspect of research endeavor requiring attention and consideration.

The principle of beneficence imposes the obligation on the researchers to maximize the benefits that can be derived by research participants. Disclosure of results has thus been considered as a kind of benefit to the research participants(CIOMS 2002).

Disclosure of information from genetic and genomic research

Genomic research broadly include analysis of DNA collected from humans that has Implications for human health (even if the purpose of the study is not medical) [(Kaye et al. 2010)]. In the past, genetic studies have been limited to search for particular genes in certain individuals. The benefits of such identification are numerous and include the delineation of groups at risk of certain diseases such as the breast cancer. Identification of genes in families and communities is now possible. The development of technologies for genomics has enabled the determination of the whole genome of individuals through personalized kits. Information on risks and other health conditions thus can be determined by repeated examination of the genomes. Several genome wide association studies had been carried out in developing countries and more are ongoing. There has been the establishment of data banks for the storage of tissues, enabling future use of these specimen for further analysis and determination of susceptibilities now and in the future. Further, although data protection policies exist in the developed countries, there is the possibility of linkage through current technologies.

Ethical challenges can arise in all stages in the collection of genetic information. The challenges may arise from the demand creation for the testing, the process of collection and the revelation and disclosure of the result of the tests. Alongside the advancements witnessed in genetic research, ethical challenges became an issue of concern given the identity specifications that attend the discovery of the genetic traits in individuals, community and other groups. Disclosure of genetic information of an individual could lead to various types of harm which

affects not only the individual but also the community. Mc Guire Dunn et al (2002) noted six different types of harm that could result from inappropriate revelation of the result of genetic research in an individual. These are general anxiety, suicide, depression. Unsolicited discovery of genetic linkage between individuals may bring up unexpected issues about the lineage of individuals involved. Third party disclosures may lead to stigmatization, discrimination, stereotyping, denial of insurance and employment. Identification of certain genes in community groups may lead to discrimination and stigmatization. Insurance and other economic institutions may become unwilling to enter into transactions with individuals and groups with unfavourable genetic information. Group harm may occur on communities and families. There may also be social, economic and dignitary harm.(Brief et al. 2012; Fullerton & Lee 2011)

Another challenge of genetic testing is risk interpretation. Certain genetic information provides only an estimate of risks of certain diseases, which differs from population to population. For example, for BRCA 1 mutation, it has been found that individuals in which this gene were isolated have risk of breast cancer which vary with the age at estimation and by the population of reference. However this variation with age is not found for BRCA 2 mutation(Antoniou et al. 2003). In families the risk for developing breast cancer may be up to 85%, while population based screening programmes lower rates may be found and vary between 35 -50%. In clinic based evaluation programmes , by age 70, female breast cancer risk was 72.8% (95% confidence interval [CI] = 67.9% to 77.7%) in those with BRCA1 compared to those in which it was not isolated(Brose et al. 2002). Other investigators found lower risks for breast cancer among those with BRCA 2. In a review of 22 studies The average cumulative risks for breast cancer in *BRCA1*-mutation carriers by age 70 years were 65% (95% confidence interval 44%–78%) and the corresponding estimates for *BRCA2* were 45% (31%–56%)(Antoniou et al. 2003) . Given this magnitude of estimated risk, certain ethical questions arise on the next course of action on

the part of the investigator. Should the investigator disclose the result to the individual? What course of action will he recommend to the person? How does he intend to address the ranges of reaction that the individual may manifest upon knowing the result?

The ethical challenges of genetic research are present in other forms of research endeavours, but are amplified due to the sensitive nature of genetic information. On the basis of this nature of genetic research, proponents had argued in favour of genetic exceptionalism which is an advocacy that it should be undertaken in a different manner form other researches not involving the study of genes ((Sarata 2008). The basic concerns of these advocates are the potential ramifications of revelation of the genetic information about an individual.

The recognition of these possible harms informed the concern on the ethical soundness of genetic research in the past. However, the research communities has now embraced the advantages provided by genetic research and now are more concerned about the need to protect study volunteers from the possible harm that may result. Harms that could arise from participation, disclosure and interpretation of genetic result requires careful consideration if they are to be minimized or prevented. The array of genetic information available in genomic banks and the arrival of genomic testing in individuals highlight the challenge of disclosure of genetic information.

Geneticists and genomic researchers appear to have arrived at some common understanding regarding disclosure of results of genomic research. There seems to have been agreement that results of genomic research should be disclosed to participants (Zawati & Knoppers 2012). Ethicists had argued that ethical principles of justice, respect for persons, beneficence and reciprocity provides for routinely offering research results to participants. Other authors also concurred that at the international level, there now exists an ethical duty to return individual genetics results (Knoppers et al. 2006).

However, how disclosure of genomic research results should be done remains a study in progress (Zawati & Knoppers 2012). Certain rules or guideline have been proposed locally, nationally and internationally prescribing standards of conduct for researchers and investigators on the process for disclosing results; internationally the following bioethics have provided guidelines for researchers: Ethical and Practical guidelines for reporting genetic research results to participants: updated guidelines from a National Heart, Blood and Lung Institute Working Group; Pharmacogenetics: Ethical issues and International Bioethics (B. E. Bookman et al. 2008; Dressler 2009; Fabsitz et al. 2010). While some of these guidelines have been general on all types of research in the last one decade they have become more specific on genetic studies and genomic research. These guidelines appear to be in agreement on certain elements. The return of genetic research results should meet the criteria of existence of proof of validity, significance and benefit. Where these criteria are fulfilled, then the right of the research participant not to know has to be taken into consideration.

Rationale for the study

Procedures and regulations on disclosure of results of medical test and investigations are well known and applied in medical practice and have been well developed in the practice of medical ethics. Clinical medical ethics emphasizes the protection of the privacy of the patient and confidentiality of information provided in the course of physician patient interaction. Procedure and guidelines have also been developed to direct conduct and action in such circumstances where there is a necessity to breach such confidentiality, for example for the benefit of the public health, for the protection of a third party which may be harmed by the withholding of such information and for the protection of the public in criminal proceedings in the court. Research

enterprise however presents a different scenario from clinical medical practice. The relationship between the physician and the patient, described as fiduciary relationship, clearly offers from that of the researcher / investigator and the research participant. Extant rules and regulations are however being developed for disclosure of information in research endeavour. Rules have been developed about disclosure to living participants and relatives (Renegar et al. 2006).

Although guidelines for the disclosure of genetic and genomic information exists there are grey areas that requires clarifications. For example current US regulation is not implicit on disclosure of research results about deceased participant((Roberts et al. 2010)).

Detailed information and guidelines about the collection, storage and further management of genomic data in developed countries are available. The several ethical problems arising from the collection of such genomic data have stimulated debate with consequent enactment of legislations and Acts to tackle the ensuing challenges. However in developing countries such information and response is grossly deficient. Extant legislation and codes of ethical conduct of research and clinical care may be nonexistent, inadequate or unenforceable. International codes of ethical conduct of research such as the CIOMS, Helsinki Declaration, are being used to guide conduct of research in some developing countries, however nationally derived codes with local cultural relevance are nonexistent and may not have the force of law. Thus breaches of such guidelines attract no sanction within the countries and victims of unethical research can only get justice outside their country. In countries where ethical guidelines are available, the application of these to genomic research protocols is guided by the ethical committee discretion and precedents from other developed countries. Yet genomic testing is now available for residents of developing countries who can afford it and actually they are already being demanded. In addition, genomic researches are already being carried out in some developing countries and promises to scale up. Given the cultural differences and world view of populations in the

developed countries, the impact of these rapid development and availability of genomic testing, there is a need for studies to determine research participants expectations on disclosure of genomic research results and participants perception of such, so as to provide an evidence base for the development of nationally and culturally relevant guidelines.

Research Questions

1. What do potential research participants in a developing nation such as Nigeria understand by genomic research?
2. What are their appreciation of the potential consequences and impact of undergoing a genomic test during a research engagement?
3. What are the expectations of the potential participants on the disclosure of their genomic research results?

General Objectives

To determine the understanding of genomic research, expectations on the disclosure of the results and its implications among potential research participants in Ibadan, Oyo State, Nigeria

Specific Objectives

The study specifically aims to

1. To explore awareness of genomic research studies among patients presenting for various laboratory tests in a secondary hospital setting in Oyo State
2. To determine participants awareness of possible consequences of disclosure of genomic results.
3. Determine participants' preferences on the mode of disclosure of their results.
4. Determine the willingness of the patients to accept the disclosure of their genomic result and the recipients of such disclosure.

CHAPTER TWO

LITERATURE REVIEW

The recent years have witnessed the explosion of genomic research on complex conditions and diseases such as autism, breast cancer and others. Such investigations may underpin the refinement in the interpretation of disease taxonomy and aetiology, and may support the improvement of treatment modalities. It may also provide genetic pool of information to families, to explain the cause of diseases, explain associated reproductive risks and guide lifestyle decisions such as choice of marriage partner and decisions to procreate by couples. The explosion of genomic research and its development have been accompanied by requirements and demand to codify ethical obligations on researchers to disclose research results to participants. Two levels of disclosure have been proposed the one on the part of all the participants as a group or community and second, individual results.

2.1 The meaning of disclosure and clarification of concepts:

Knoppers and Dam reviewed the use of the term *results* in various national and international policies and recommended certain guidelines in the use of the lexicon *results*. They observed that the term *results* are not universally used in ethics guidance documents, and this reflects the multidisciplinary nature of the committees preparing the guidance documents(Knoppers & Dan 2011). Alternative terms, such as *findings* and *information* are used interchangeably with *results*. In this write up, the term results will be used to include information on groups of persons, that is general or aggregate, *results*. The term will also be used to include information or data on individuals. The term *findings* will be used as an alternative and this includes a broader meaning encompassing both general and specific results, incidental findings and pertinent. Levesque et al also refined the definition of *general results* further as those that are generalisable to a group of persons, and are those results normally linked to a research

hypothesis(Lévesque et al. 2011). Individual research results are defined as those that are associated directly with an identified individual and may or not be linked with the research objectives and hypothesis. Incidental findings are those that are incidental to the original aims of the research study and unforeseen at the time that the participant gave consent. Thus they are not linked with research hypothesis. Pertinent findings are those which "pertain to the disease being researched in each project". Clinical findings are usually those that have significant implications for the subject's health concerns or simply "any finding that relates to individual health" status (Knoppers & Dan 2011; Lévesque et al. 2011).

In the same manner the process of return of results appears to have been described in ethics literature with alternative or synonymous terms such as feedback, disclosure, reporting back and sharing. The authors also noted that feedback is commonly used to describe the immediate feedback provided to participants during initial assessment at recruitment centres. It also covers the general ongoing feedback provided to participants throughout the existence of a biobank (such as bulletins, on aggregate findings) (Knoppers & Dan 2011). Schulte and Singal also defined disclosure as the act of informing or notifying study subjects (as a group or individually) of the test or study results and the risks implied by those results. In this perspective disclosure is regarded as a form of risk communication. The authors defined disclosure to include broad communication of research results and information through relevant forms of publication and news. Disclosure of information in research thus encompasses; subject recruitment and informed, privacy and confidentiality, interpretation of test and study results, communication of test results, and communication of study results(Schulte & Singal 1996). In this dissertation, the scope of the review will be limited to the communication of the research results in genomic studies to the participants.

2.2 Should genomic research results be disclosed?

Arguments for disclosure have accumulated proponents and opponents although current consensus favours disclosure of research results, and guidelines, although inadequate, have been provided on the process.

In the past investigators had reasoned that despite the seemingly compelling nature of a research subject's request, there are a variety of reasons why researchers should not provide individual results to subjects before a study is completed. First, the validity of the results requires confirmation. Research projects that do not intend to provide results are not required to meet quality assurance guidelines that clinical laboratories do, and thus they may not be able to assure the quality of their testing procedures. Thus revealing the research result prematurely may lead to the participant being given results which may change later and might lead a subject to take drastic, inappropriate action. Secondly, research projects that have not been designed to include disclosure of results may not have appropriate adjunct services available, including referral for genetic counseling. These deficiencies are likely to be magnified by the fact that once one family member has received her results, others (who perhaps have given the matter less careful thought) may want their results as well. Third, there may be no treatment for the condition which was revealed by the genomic research or testing. Thus the participant suffers avoidable psychological harm resulting from the disclosure of the result. Even if the test is one for a disorder in which corrective treatment is available, the fact that the research test might not be adequately validated or quality controlled could lead to individuals receiving treatment unnecessarily. These conditions seem to some investigators to be compelling reasons for withholding research results from participants.

Proponents of disclosure based their arguments on specific ethical principles, while critics have questioned the coherence of the obligations and the implications of enforcing on the investigators; a uniform duty of disclosure for the results. Proponents of disclosure have advanced the practice as a general requirement of research ethics. Opponents of disclosure however argued that specific issues arising from different contexts presented by different diseases are neglected by proponents of disclosure even though the issues arising are substantial. For example in some diseases standards that are sensible may make no meaning or may even be absurd in other diseases. Furthermore it is not clear in many contexts what information the research participant will prefer to receive. Ethical obligation of the right to know, associated with demanding the researcher to disclose, also requires the researcher to ensure no harm to the participants, imposing a conflict of obligations. However whatever the researcher determines as harm may be different from the participant's perception(Affleck 2009). Thus participants understanding of disclosure of results and its implications must be understood to ensure participants derive maximal benefit from disclosure and minimize the possible harm.

However, current position of the research community is that research results should be communicated to participants and every research protocol must indicate specific plan to do so.((G Dressler 2009). However the right of the research participant to decide not to know also needs to be respected. (Knoppers et al. 2006) It is therefore generally recommended that investigators should communicate their plans for informing, or not informing, potential participants at the outset, and not deviate from that position. If they plan to inform research subjects, they should assure the validity of the test (Shalowitz & Miller 2008), (Andrew LB 1997).

Ethics guidelines on disclosure stipulates when individually relevant genetic research results should be disclosed to individuals and these are: when results identify serious and

avertable health risks, have significance for life and reproductive planning and are simply of interest to the individual. This is in addition to the specifications of the quality of the research result, the interest of the research participant and the logistics and procedural requirements that ensure beneficial disclosure.

Shalowitz and Miller reported that a review in the year 2006, identified 30 national and international guidelines concerning return of results , and that 21 of these (60%) were published in the last decade, highlighting the worldwide interest in the discourse (Beskow & Burke 2011; Shalowitz & Miller 2008). However they noted that current policy recommendations did not synthesize the views of participants and investigators and does not pays attention to data and the potential consequences [negative or positive] that communicating results may have for both the participant and the investigator. It is also widely acknowledged that there is little guidance on the return of research results to various interested parties especially family members (Megan et al. n.d.; Black & Mcclellan 2011)

2.3 Participants' response to disclosure of genetic information

The literature is replete with examples of unpleasant effects of disclosure of genetic results. Disclosure of results to participants in a research has been found to have different impact on the recipients. Researchers and bioethicists have suggested that research participant may suffer harm due to awareness of the results of the research in genetic studies. Impact have been found upon the individual, the relatives and the communities. Reported findings have been classified as psychological, social economic and dignitary. Psychological harm has been widely reported by investigators. Affleck reported that Ashburn and colleagues have documented cases of insurance and employment discrimination based on genetic information(Affleck 2009). Awareness of result have also been shown to positively influence the uptake of further genetic tests as

documented by Green and his team. Findings on psychological risk have not been consistent from study to study and appear to be influenced by the nature of the result and other factors related to individual characteristics, disclosure process and follow up after disclosure. In a study of children of patients with Alzheimer disease, disclosure of the APOE genotype induced no change in anxiety scores of their adult children, indicating no significant short term psychological risk. Although those who were APOE €4 negative had significantly lower anxiety score than those who were positive, high levels of emotional stress before undergoing the test was associated with emotional distress after the test indicating that previous emotional stability is more important as a mediator of psychological response than the nature of the result (Green et al. 2009). In another study by Ashida and colleagues, in which adult children of Alzheimer disease patients from a randomised clinical trial involving genetic testing for apolipoprotein E were followed up for specified period of 6 weeks and 12 months after disclosure, it was discovered that nature of the result, process of its disclosure and follow up, and sharing with health professionals and friends mediated the levels of distress experienced after the disclosure and the psychological adaptation to the result one year after (Ashida et al. 2010). Mundroyd et al highlighted some other factors associated with patients reaction to disclosure result. His findings suggest some preparations that may be embarked upon by researchers who deserve to comply with the emergent ethical duty to disclose results of genomic study. His findings also highlights why some patients/participants may not want to be engaged with the results of the genomic study. Ormondroyd et al found that a higher risk perception resulting from participants awareness of family history of cancer, or experiential knowledge of cancer in the family, tended to improve or enhance adjustment to disclosed results (Ormondroyd E, Moynihan E, Watson M, Foster C, Davolls S, Ardern-Jones A 2007). Thus, full awareness of the result of BRCA2 genetic study was regarded as a benefit. Further, the authors found that anxiety among the participants

was alleviated by post study genetic counseling. Age of the participants and fear of cancer and skepticism related to the relative disclosing the result are associated with non engagement with the result.

2.4 Participants' attitudes to disclosure of results: do participants want results?

Argument has been advanced that participants may not want to know the results of genetic and genomic tests and studies. Such arguments are predicated on the patients fear and anxiety over the discovery of an adverse trait. Indeed, authors have reported instances where disclosures of adverse traits have lead to suicide, increased anxiety and other unpleasant effects. However, other studies have pointed out that despite these possibilities, many individuals, groups and communities still prefer to know their results. Such preference is an exercise of personal autonomy which includes the right to know and be informed about oneself. In an ongoing genetic epidemiology study among a Japanese population participants were asked at entry point about their preferences with regards to being contacted by researchers in the future and whether they are willing to receive reports on their individual genetic results, if problems relevant to their health are discovered for which efficacious interventions might be available ((Matsui et al. 2008). Analyses of the responses revealed that most of the participants wish to be contacted and receive reports. Those who wish to be contacted are characteristically younger, current drinkers and former drinkers and have at least one parent who had cancer. Those who had one sibling and with a medical history of cancer were less than likely to want results.

Similar findings that participants want to receive results were found by David Wendler and Rebecca Pentz (Wendler & Pentz 2007). The authors noted that collection of results increases the individual desire to know the results themselves. Some respondents reported reasons for this desire include the awareness that the result exists and the desire not to know less about

themselves than the investigators. Only a small proportion are less inclined to know less about themselves. Generally, even in culturally divergent settings such as America and Hawaii, participants generally desire to receive the results of research carried out on them whether genetic or otherwise. (Megan et al. n.d.; Black & Mcclellan 2011; Shalowitz & Miller 2008; Matsui et al. 2008; Murphy et al. 2009). However reasons for such a similar desires differ in different cultural contexts, and may be essential to understanding how the results should be communicated.

In a review of published research works on return of result in clinical trial, Shalowitz et al found reasons for desiring the return of results to include clinical significance of results, pressures from relatives, the curiosity to know any information possessed by a physician on a participant which they are not yet privy to was a contributing factor for desiring to receive individual result of a study. However, Fernandez has suggested the possibility of distress to families as the reason for desiring non disclosure. Further certain individual characteristics may also be associated with the desire to want to know the results. For example, in a Japanese Population based genetic cohort study it was found that while most of the participants want to know the results personal habit such as drinking alcohol and family characteristics such as having parent with cancer was associated higher odds wanting to know the result(Matsui et al. 2008) compared with having a sibling with past medical history of cancer. Furthermore, Murphy et al in their study of genetic predisposition to asthma, noted that the nature of the result is also an important factor determining the desire to want to know the results(Murphy et al. 2009). Participants were concerned about the accuracy of the result and whether the result is actionable or not. Focus group members revealed an understanding of the iterative nature of scientific research, the need for replication of findings, and that early findings are later disprove or contradicted by later

studies. Inaccurate, invalid or inconclusive findings are viewed as not useful and misleading and sometimes even harmful.

The clinical utility of the result or the ability to do something about it was also raised by some of the respondents in the focus group discussion. Categories of responses to actionable findings raised by respondents include getting prevention or treatment, communicating the finding to relatives, making reproductive decisions, life and financial planning and participating in further research and taking community action to remediate the environmental hazard. It is instructive that some other participants would still prefer disclosure of the result even when no remediable actions are available. The basis of such preference being the hope for a treatment or remediable action in the future.

These divergent preferences on the return of results underscore the need to seek participants' opinion and consent in the decision to return results. It is advocated that plan for the return of results be made in the research protocol. Participants preferences should be ascertained during the recruitment period and the preferences should be complied with during and after the research engagement.

Shalowitz also reviewed the preferred medium of receiving the results on research results and found this to be dependent on the positivity or otherwise of the result. In general while participants desire to receive result through mails, about half are comfortable with receiving the result face to face. The preferred medium of communicating result appears to be dependent on the type of result- participants will prefer to receive negative result face to face rather than by mail. Evaluation of the disclosure procedure indicates that participants will prefer to have a feedback on the result communicated. Thus up to 40% will prefer to have a telephone number to call to ask questions (Shalowitz & Miller 2008; Roberts et al. 2010).

2.5 Regulations and guidelines on disclosure of results

Traditional dichotomy between research and clinical care is being challenged. Some findings of urgent clinical significance may be discovered during research. Managing such findings challenges the current dichotomy between clinical care and research. Furthermore, the rise in translational concept of genetics and genomics has brought into focus how research and clinical care have become part of a spectrum that moves research insights into clinical use. The translation is happening not just for populations but also for individuals. Personalized medicine necessitates that research confront the question of how and when research information should be offered to individuals because of its potential clinical significance. Thus the traditional silence of researchers on the issue of disclosure is being challenged. However a noted by Susan Wolf, 'too much of research information remain uncertain or even mistaken to dump it all on research participants" thus the scope or responsibility to return research results at this point is limited. Thus the emphasis on the need to meet certain criteria before return is undertaken(Wolf 2012a).

Recommendations found in the guidelines for the return of research results are based on the United States Federal Law and Regulations and guidelines on certification of laboratory to offer results which are for use in clinical care; ownership and control of specimens and data. There is none yet on the disclosure of genetic results. No legal precedent is existent. However there are legal precedent related to disclosure of result in clinical care. Thus there is potential and actual risk of law and legal liability in the developed countries thus provoking the interest of bioethicists on the guidelines for the return of results of genetic researches.(Wolf 2012b).

Renegar et al after careful review of existing regulations, summarized some points to consider in returning genetic study results to individual (Table 1). These considerations include: clinical relevance of the data, laboratory qualifications of the data, participants consent to be informed consent, Medical information confidentiality issues, and competence of persons providing the results to participants (Renegar et al. 2006).

Table 1: Summary of main recommendations in some guidelines on the return of results

Year	Organization	Main issues addressed and recommendations
2001	NBAC	Return results if the result is -valid and confirmed - have health implications -the result is actionable (National Bioethics Commission(NBAC) 2001)
2004, 2010	National Heart, Blood and Lung Institute working group	The recommendations specified when results should be offered and when they may be offered to research participants(Fabsitz, McGuire, Sharp, Puggal, Beskow, Biesecker, Bookman, Burke, Burchard, Church, et al. 2010)
2014	National Research Council and Institute of Medicine	The duty to return the research report depends in large part on the reliability of the findings and the significance to human health(National Research Council 2014)
2008	Susan et al (Working Group)	The 21 author consensus recommendations on return of results in incidental findings (Wolf et al. 2008)
2008	Caulfield et al	Recommendations on return of results and incidental findings in whole genome studies (Caulfield et al. 2008)
2012	Susan Wolf Working Group	Second consensus recommendation paper on return of results in whole genome research involving biobanks and archival data sets (Wolf et al. 2012)

Van Ness expatiated further that clinical relevance includes that the risk of disease is significant, disease must have important health implication and there must be proven therapeutic or preventive intervention. Thus to be precise, the use of the data must lead to some improvement in the outcome of the disease. Knoppers and Dam provided a review of the various scope of the use of the term clinical utility which is provided Table 2.

Table 2: Definition of clinical utility of a result

"Contribute to the current disease status or alter assessment of the future disease risk of the research participants"
"Information relevant to the health and wellbeing of the person"
"Relevant to their welfare"
"Clinically relevant to for individuals or their biological relatives in treating or alleviating health conditions or risks"
"Important health implications i.e fatal or substantial morbidity or should have significant reproductive implications [and] proven therapeutic or preventive interventions should be available"
"Information vital to the subjects life"
"Immediate and clear benefit to identifiable individuals [that] will avert or minimize significant harm to the relevant individuals"
"Pertinent to the improvement of health and /or the prevention of disease"
"Significant implications for the subject's health concerns" and "a course of action to ameliorate or treat these concerns is readily available"
"Clinically actionable" ... the result might not lead to cure, but it could help the participant better understand a clinical condition or plan for the future"

Source: Return of Results: Towards a Lexicon? (Knoppers & Dan 2011)

It had been argued by other authors that the criteria of clinical utility of the data supposes the existence of fiduciary relationship which is not present in research engagement (Knoppers & Dan 2011)

The NHLBI guidelines (2004) and the CIOMS of 1991 [revised 2002] recommended that individual subjects be informed of any findings that relate to their health status. It also acknowledge that subjects have a right to know. The consortium on Pharmacogenomics in 2002

noted “that researchers are obligated to offer the research participants the option of disclosure of research information when its reliability has been established and when the disclosure is of potential benefit. The American Society of Human Genetics and the Canadian College of Medical Geneticists both recommended that the process of disclosure should be accompanied with counseling.

The guidelines recommended that there must be estimate of standards of genetic associations with a disease in the general population. There should also be established reliable information and data management systems that clearly identify risks of each genetic variant included in the research studies. This will guide the researcher to review potential risks and benefits of genetic screens at time of submission of the protocol to IRB. The researchers should include the proposed pathways for the disclosure of incidental findings in their protocol. Finally, such reporting plan must have been included in the study protocol and approved by an institution review board (Ferriere & Ness 2012).

On laboratory qualification, only CLIA certified results should be reported as valid results that merit consideration for return to the participant.

Some authors argued for a result evaluation approach that assesses the expected information and the context of the study in order to decide whether and how the result should be offered. They answer the question how should result be offered. They noted that different results require different decision even within the same study. They argued that for each result the parameters to be evaluated should include establishment of the clinical utility threshold; that research utility may be lower that for clinical use of the result. Other criteria they advocated include personal meaning of the result and third, the clinical utility of the study must be evaluated.

Dressler also concurred that the findings of a genetic study must be analytically and clinically validated to merit disclosure (G Dressler 2009). Supporting the position of Lavier, Dresser also argued that the context of disclosure matters and the investigator or researcher should not make the decision alone but in consultation with the IRB ((Dressler et al. 2012).

Thus it is evident that recommendations on the return of results are usually premised aligned with and reconciled with the informative sources such as the Clinical Laboratory Improvement Amendments (CLIA) Act and Health Insurance Portability and Accountability Act (HIPAA) [(Nosowsky & Giordano 2006)]

However, Clayton and McGuire cautioned that there is a growing consensus on the return of results and that it may become a standard of care which could lead to legal duty to offer and return results (Clayton & McGuire 2012). The authors based their caution on the following premises. Research and clinical care are not the same although the reason for research is to seek knowledge that may directly or indirectly impact on clinical care in the future, the clinical impact of new research findings are almost never clear. The growing interest in translational and personalized endorses an obligation to offer individual research results may encourage therapeutic misconception about research by supporting the belief that research participation can and should provide personal benefits. Secondly, research results are different from clinical tests. Clinical tests are used to alter clinical care and are to be carried out in approved laboratory which meets standards prescribed by the CLIA and interpreted by qualified clinicians. While some research laboratory may meet and comply with these standards and be so certified, it is still to be noted that the availability of a research test does not and should not make its clinical muse compelling or even appropriate. Finally physician's obligations to patients are rather different from that of researcher's obligations to research participants. The ethical decision to offer research results to participants is often premised on the appeal to ethical principle of beneficence.

The authors argued that beneficence is role specific and that there is a debate on whether researchers owe such obligations to participants in a research. Investigators are not expected to act primarily for the benefit of the individual research participant. However, this freedom is confounded where the investigator has a dual role of physician and scientist. In this case the physician-scientist has clinical obligation to follow up if the result is valid and reliable. However this premise does not apply to investigator and scientist who have no dual role.

2.6 Approaches to disclosure

2.6.1 Researchers' approaches to disclosure

The dilemma of the researcher in the disclosure of result is aptly illustrated by the discovery of the incidentalome during genomic research. Incidentalome have been so called by Kohane and are findings which are unanticipated during genome testing but which may be highly significant to health(Kohane et al. 2012). Broad genome testing may lead to their discovery. Researchers are usually neither prepared nor qualified to deal with these findings of genetic abnormalities. However while incidental findings may not have known impact today, in the future they may be so. Thus they are time sensitive(Van Ness 2008; Kohane et al. 2012). The challenge of disclosure of an incidental finding discovered in the course of clinical research is quite different form that found during research. For example, discovery of a misattributed paternity, which has been reported in about 10% of pedigree analysis, presents the researcher with the dilemma of how to fulfill his duty to report his finding to the subject especially when the finding is associated with health implications. Accurate genetic counseling becomes impossible without addressing the issue of the misapplied paternity.

Furthermore, additional genetic variations may be uncovered by the researcher either deliberately or incidentally, since identical genetic variations often can lead to multiple outcomes

by deregulating the common pathways in the tissues. In addition, uncovered incidental genetic variations which appear unimportant today may become important when associated with 2, 4 or 24 other genetic variations. Also, incidental findings which have no know intervention today might become amenable to clinical intervention in the future. Thus disclosure of incidental findings presents a complex ethical dilemma for the genomic researcher.

2.7.2 Institutional Review Board (IRB) approaches to disclosure

The regulations under which most IRBs operate were established over 25years ago and have not been substantially altered in the intervening years. (Keane A. Moira 2008). In the United States for example, regulations requiring that all federally funded research should be reviewed by properly constituted ethics board was formulated in 1974, while the current set of regulations were established in 1983. The research technology available during these formative years did not envisage the development that research enterprise has so far witnessed. In particular, the revelation of incidental findings in research and the revelation of genome wide association's studies presents ethical challenges which the current regulations did not envisage and are therefore not adequate to address. Thus current regulations offer no guidance to IRBs.

The challenge of IRBs in reviewing studies of genomic research may be considered as that associated with making the research to conform to each of the principles outlined in the Belmont Report. IRBs are obliged to ensure that researchers include in their protocol plans to ensure the protection of the rights and welfare of their participants, as enshrined in the Belmont Report. The principles outlined in the Belmont Report are respect for persons, beneficence and justice.

The principle of respect for persons require that individuals have the right to true and continuing informed consent, IRBs are faced with the quandary of what to do with information about incidental findings. Existing guidelines for IBS have not addressed the questions on what

to tell the research participants, when to tell them, who should convey the information, in what form it should be communicated or retained in a record and under what circumstances the information should be withheld. (Keane A. Moira 2008).

A cardinal distinction made in the Belmont Report is that between research and therapy. In research, the participants have no expectation of benefits whereas in therapy, the principle of beneficence stands very strong and clear. Thus researchers are constrained to draw this distinction to their participants to avoid the problem of therapeutic misconception.

Genomic studies however represent an interface between therapy and research. Genomic findings are being applied in various therapeutic situations. Pharmacogenomics currently provides guidance in the development of drugs. Other applications of genomics to therapy are replete in Gene Therapy. The blurring of the distinction between research and therapy is made more pronounced where patients are recruited as research participants. Thus the IRBs decision will be further influenced by the type of subject recruited into the research, whether they be patients or healthy volunteers.

Further challenges to IRBs emanates from the consideration of the principle of beneficence. IRBs are required to ensure that research endeavours under their oversight provides maximizes benefits to the participants while minimizing the risks to every extent possible. They are also to ensure that the research provides enough justification for the risks to which the participants have been exposed. These considerations are not easy to navigate in genomic researches and may generate considerable discussion in IRB meetings. In some instances incidental findings may be revealed which have no known certainty of risk to the participant, and thus becomes unclear whether to inform the patient or not. In others there may be known risk, for which intervention is either not available or outside the reach of the participant. Further, findings which are thought of no risk today may become potential or actual risk in the future. Thus IRBs have to balance their

assessment of risk within certain realities which may often be changing. The question for the IRBs then becomes who decides whether incidental finding should be disclosed to the research subject and what information should be disclosed.

Keane (2008) posited that for the evaluation of risks and benefits effects of the research, IRBs should concern themselves only with risks that are of immediate or short term. These are risks that may result from the research itself and are distinguished from those which arise even when the participants are not engaged in the research(Keane A. Moira 2008).

2.8 IRB professionals views on the return of results

Despite the availability of guidelines on ethical conduct of research and disclosure, the prescriptions of these guidelines are not specific and thus IRB professionals are left on their own to navigate the perplexing route of decisions on disclosure practices. There exist no valid consensus on definition of several terminologies and descriptions related to return or disclosure of results. For example, there exists no consensus on what constitutes a valid result, neither has consensus been achieved on what should be the determinants for the disclosure of a result. Thus there is a necessity to clearly explicate and develop a framework that addresses existing uncertainties in disclosure practices. The involvement of the IRB professional and the community of researchers and participants in the explication of these parameters is very necessary.

The general consensus in the literature is that IRB members favour the return of research results. Dressler interview of IRB members revealed that the professionals articulated the moral and ethical justification for the return of research results. The emergent position agreed is that return of results should be based upon the principle of validated result, although there was no clarity on what constitute a validated result. The second criteria for determining result to be returned by the IRB professionals is the balance of weight of consequences on the individual, of

return of a potentially negative result and the anticipated benefits. The third criteria are the respect for persons, which is embodied in the right to know of the research participants and also include his right to decide not to know.

Other varying themes that emerged in the study and merits consideration includes the consideration for the future significance of the result. Also concerning incidental findings, IRB members prefer to invoke the principle of invoking the participants' desire and right to know or not to know, if the result is validated.

Generally IRB professionals perceive the return of results as the responsibility of the IRB. However, most perceive the responsibility as a perplexing endeavor. The underpinning of this perception is the rapidly evolving nature of the field of genomics research, which is described by some of the participants as " fast paced" and "broad scoped"(Dressler et al. 2012).

Reports on the actual practices reveal that the members of the IRB only abide by the guidelines when the genomic research results are from a CLIA certified laboratory. However, in many other instances the technology for the assay of the genomic research is only available in the researchers laboratory since it has been specifically developed for the research by the investigators, it under trial and thus is not widely available for use. In such instances the CLIA certification rules cannot be applied and enforced.

Identified concerns of the IRB members are consistent with the documentation on the literature and include concerns about risks consequent to return of the results and how the research participants will respond or act on the result. Specific concerns include emotional and psychosocial consequences, lifestyle changes and decisions, reproductive choices, impact on employment and potential for economic harm.

2.9 Investigating disclosure: approaches and techniques

The research endeavours to investigate disclosure practices have adopted various designs. The qualitative approach is often adopted by some researchers to explore pertinent issues that merit further investigations.

In FGDs, certain personnel must be present. These are the discussion leader, the note taker and the voice recorder. Issue of anonymity of responses are crucial to free and unhindered responses by the participants. Therefore, personalized data, master lists and other identifying parameters are not collected in focus group discussions. However, for representativeness of the findings of the discussion groups, social stratification is employed in the constitution of the members of the FGDs. Thus some demographic characteristics of the members of the population of reference will be required and collected from the participants in the FGDs. An average size of six members is optimum for a focus group discussion. Data from different strata of the respondents may be required and thus several focus discussion groups may be constituted on the basis of age, sex and other parameters that may determine the freedom of expression and participation by the respondents.

Qualitative data obtained from the respondents are recorded, transcribed and then analysed thematically. Recurrent themes, including major and minor themes are presented. Appropriate summary and reflections on the responses are presented and relevant conclusions drawn and reported.

Focus group discussions has been used by Dressler et al to explore IRB perspectives on the return of results to participants(Dressler et al. 2012). Such approach involves the use of interview guide containing themes to which participants are required to provide responses in the form of discussion. In the Dressler study, participants were required to provide responses to themes such

as perception on the necessity to return results of genomic studies, conditions required for the return of the results, and more(G Dressler 2009).

Other authors have adopted quantitative approach to the study of participants preferences to the disclosure of results from genetic studies(Matsui et al. 2008; Megan et al. n.d.). These studies used self administered interview schedules or interviewer administered interview schedules to obtain participants responses. The responses were precoded and structured to enhance analysis.

There appears to be some advantages in the use of qualitative methods for studied of genomic and genetic issues. In the first instance, the subject of genomics are not very clear to many participants and there are misconceptions that may need to be clarified. Secondly, the are sensitive issues which are easily clarified in a qualitative study but which may not be feasible in a quantitative approach.

CHAPTER THREE

METHODOLOGY

3.1 Study Area: The study Area is Adeoyo Maternity Hospital in Ibadan, Oyo State. Patients attending the laboratories of these institutions for various haematological tests shall be recruited into the study.

3.2 Study Population: Participants in the study are those who presents for haematological test in the respective centres. They must be adults above the age of eighteen years and must have consented to participate in the study

3.3 Study Design: The study design is cross sectional descriptive study.

3.4 Sample size:

The formula for the calculation of sample size for determining proportions is engaged for the determination of the sample size. The percentage of research participants willing to have their results disclosed to them (p) is assumed to be similar to one from a previous study ((Matsui et al. 2008) in which a preference for the disclosure of results of a genetic test was found to be 90.8%. This proportion is fitted into the formula shown below, to obtain the sample size of 128.4.

$N= z^2pq/e^2$

where

N= the sample size

Z = percentage point of the normal distribution corresponding to the 95% confidence level

P= proportion of mother accessing genetic counseling for their newborn

q = 1-p

e= the maximum tolerable error in the estimate

The corresponding values for the parameters are p=p.5, q =0.5, e = 0.05.

Substituting the corresponding values a sample size of 128.4 is obtained. An adjustment of 10% for non response to some of the variables is made. Thus a final sample size of 143 participants is obtained.

3.5 Sampling Technique

Systematic random sampling was used to determine the participants to be recruited into the study. The total number of the participants attending the laboratories for any test was used as the study population. This total attendance was determined from the clinic register. Sampling interval was calculated through the division of the laboratory attendance by the sample size calculated. Using the laboratory register, participants that fall on the calculated sampling interval will then be enrolled in the study until the sample size is achieved.

3.6 Data collection

3.6.1 Development and Translation of the questionnaire

The questionnaire was developed by a thorough review of the literature on the subject matter**.** The interview schedule and questionnaire were translated into the Yoruba language for the understanding of the research participants. The translated schedules was back-translated to English by another person to ensure the validity of the questionnaires schedules.

3.6.2 Training

Five research assistants were recruited for the study. The field research assistants were managed by one lead interviewer. These research assistants attended one day training on interviewing techniques. The skills imparted during the training include how to select the research participants, courtesy and rapport with the interviewee, questioning techniques, probing and observation of verbal cues.

3.6.3 Pretesting the data collection instruments

3.6.3.1 Pretesting the Questionnaire: The questionaire were administered to a sample of twenty patients attending a medical clinic in the Adeoyo Specialist Hospital. The responses of the participants were analysed to gain insight into the validity of the questionnaire. The questionnaire were then refined to improve upon its validity.

3.6.2 Data Collection Procedures:

The quantitative phase used interviewer administered questionnaires to explore the socio-demographic characteristics, awareness of genomic transmission of diseases, perception on the benefits and disadvantages of the tests, family experiences of diseases transmitted through genomic pathways, knowledge of genomic detection and prediction of likelihoood of diseases, perceptions on the return of the results of genomic research results and perceived consequences of disclosure, preferred disclosure processes and cultural viewpoints on the use of these disclosure of the results. The questionnaires are semi structured and interviewer administered.

3.7 Data Analysis and Management

3.7.1 Quantitative data

Quantitative data were analyzed using the SPSS version 17. Descriptive data were presented with the tables of frequencies while the associations between variables were explored using the chi square statistics. All levels of significance were set at a p- value of 0.05.

3.8 Ethical Matters

3.8.1 Ethical Approval: The protocol was reviewed and approved by the Oyo State of Ministry of Health Institutional Review Board for ethical quality.

3.82. **Informed Consent**: The consent of the participants were obtained before the interview. The rationale for the research, the contents of the questionnaire and the participants rights to participation and withdrawal from the study at any stage were explained to them in Yoruba. The consent to participate was then verbally requested. They were required to sign the consent form or thumbprint the consent form if they are not literate.

3.83 Privacy of the participants were assured during the interview by conducting the interview in a designated room away from the interference of others. The respondents were interviewed individually.

3.84: **Confidentiality**: The information provided were kept strictly confidential. The responses of the participants would be disclosed to any other party by the investigators except on the full consent of the individual participants. No effort shall be made to link the responses of the participants to the individual identity. Strict confidentiality was maintained during and after the survey. The filled questionnaire were kept locked in iron cabinets within the investigators office and the computer file of the analysis was provided with a password to keep it secure from

intruders. The password was kept strictly confidential. The participants were informed of their right to decline responses to any question during the interview and their right to withdraw from the study at any time

3.85 Non Maleficence: the study provided no harm to the participants. No tissue sample were taken

3.86 Beneficence : participation in this study offers the respondents the benefit of sensitization to the issues of genomic research. It promoted their awareness about their rights to research results and empowered them to demand same in the future. Participants also had the opportunity of referral for any other medical challenges that were brought to the notice of the investigators.

CHAPTER FOUR

RESULTS

4.1 Characteristics of respondents

Table 4.1 shows the demographic characteristics of the respondents in the study. Most were aged 20-29 years (40%) and 30-39 years (40.7%). Majority were females (80.7%), Yorubas (94%) and Muslims (62%). Over half (54%) had some high school education while about one third (36%) had university or other tertiary education.

About three quarters (78.7%) were married and 80% had at least one child. Most (26%) had only one child and 22.9% had just two children. Most (66.7) were self employed and average monthly income were mostly below the national minimum wage of eighteen thousand naira (62.7%). Majority (78%) of the respondents do not take alcohol, smoke cigarettes (91.3%) or use any other stimulants (92.7%). (Table 4.2)

Table 4.1: Demographic characteristics of the respondents

Characteristics	Frequency	Percentage
Age (in years)		
<20	8	5.3
20-29	60	40
30-39	61	40.7
40-49	12	8
50 and above	9	6
Sex		
Male	29	19.3
Female	121	80.7
Ethnic group		
Yoruba	141	94
Hausa	6	4.0
Ibo	2	1.3
Edo	1	0.7
Religion		
Christianity	57	38
Muslim	93	62
Education		
Nil formal education	3	2.0
Primary	12	8.0
Secondary	81	54
Tertiary	54	36

Table 4.2: Family characteristics employment status and income and lifestyle habits

Characteristics		
Marital Status		
Single	20	13.3
Married	118	78.7
Divorced/ Separated	12	8.0
No of children		
Nil	30	20
1	39	26
2	36	24
3	22	14.7
4 and more	23	15.3
Employment status		
Informal self employment	100	66.7
Formal sector employment	26	17.3
Not employed	24	16.0
Income (Naira)		
<5000	33	22
5000-17,999	61	40
18,000-29,999	27	18
>30,000	21	14
No response	8	5.3
Alcohol consumption		
Yes	33	22
No	117	78
Cigarettes smoking		
Yes	13	8.7
No	137	91.3
Use of other stimulants		
Yes	11	7.3
No	139	92.7

4.3: Awareness of genetic transmission of diseases

About two thirds of the respondents were aware that diseases can be transmitted to offsprings through genetic pathways. Diseases identified as following genetic inheritance were hypertension (16.7%), diabetes (14.7%), cancers (1.3%) and asthma (0.7%), and multiple or complex diseases (34%). (Table 4.3). However, about one third are not aware of diseases that can be transmitted through genetic pathways.

Only one third (32%) knew one person who contracted these diseases through genetic inheritance. Those so identified were parents (72.9%), other relatives (39.6%) and self (29.1%).

Table 4.3: Awareness of diseases transmitted through genetic pathways

Characteristics	Frequency	Percentage
Diseases		
Hypertension	25	16.7
Diabetes	22	14.2
Heart Diseases	1	0.7
Cancer	2	1.3
Complex diseases	51	34
Dont know	48	32
Knowledge of somebody with diseases transmitted through genetic pathways		
Yes	48	32
No	102	68
***Relationship with person with genetically transmitted diseases N= 48**		
Self	14	29.1
Parents	35	72.9
Sibling	2	4.2
Relatives	19	39.6
Friend	2	4.2
Aquaintance	6	12.5

- Multiple responses provided

3.4 : Family history of diseases transmitted through genetic pathways

Hypertension and diabetes were the diseases mostly reported by respondents as transmitted through genetic inheritance which the participants have experienced in their family. These diseases were found in the participants themselves (78.63%), their fathers (81.3%) and and mothers (78.9%). Diabetes and cancers were less experienced. (Table 4.4)

Table 4.4 : Family history of of diseases transmitted through genetic pathways

	Person with the diseases [No (%)			
Disease	**Self**	**Father**	**Mother**	**Siblings**
Hypertension	11(78.6)	13(81.3)	15(78.9)	11(78.6)
Diabetes	3(21.4)	2(12.5)	3(15.8)	3(21.4)
Cancers	0(0)	1(6.3)	1(5.3)	0(0)
Total	14(100)	16 (100)	19 (100)	14 (100)

4.5 Knowledge of genomic detection and prediction of likelihood of diseases

Most of the respondents were aware that possibility of developing some complex diseases can be made from genomic examination of body tissues. Diseases so identified as being possibly predicted are hypertension (16%) and diabetes (19.3%).

Most of the respondents (60.5%) were very certain of the likelihood of the prediction while only 42 (33.9%) were just certain. Only a minimal 7 (5.6%) were uncertain of the likelihood of the prediction.

4.6 Benefits and disadvantages of genomic testing

Majority (86%) of the participants expected to derive some benefits from undergoing a genomic testing. Expected benefits includes personal health status awareness (58.7%), early detection of hidden diseases (14.0%) and opportunity to commence early prevention and treatment of identified diseases (16%). Only a few indicated that it helps participants to make decisions related to lifestyle, reproduction or social lives (1.4%).

The main disadvantages reported was psychological trauma (71%) and possibility of developing psychosomatic diseases (16.1%).

Table 4.6: Expected Benefits and disadvantages of genomic testing

Expectation of respondents	Frequency (%)
Expected benefits (N=129)	
Awareness of health status	88 (58.7%)
Early detection of hidden diseases	8 (5.3%)
Motivation seek early treatment and prevention	24 (16)
Motivation to make personal decision on reproduction and social lives	2 (1.4)
No response	7 (4.7)
Expected disadvantages (N=31)	
Psychological trauma	22(71.0)
Development of psychosomatic diseases	5(16.1)
Suicide contemplation	1(3.2)
Stigmatization	1(3.2)
Possibility of contracting hospital acquired infections	2(6.5)

4.7: Opinion of respondents on the return of the results of genomic research which are negative

Overall 141(94%) opined that results of genomic research should be returned to the participants in the research. Reasons given for the necessity to return results includes to make the person aware of his health status (77, 51.3%), to motivate the person to seek treatment (34, 22.7%), and prevention 13, 8.6%), and lifestyle adjustment (13, 8.6%). About 13(8.6%) provided no reason.

Some respondents provided reasons why results should be withheld in certain situations. Such situation include when the disease detected is not curable, the patient is not mentally sound and so may react inappropriately to the disclosure. The results should also be withdrawn where the patient has debilitating health condition so as to prevent the worsening of the condition. Likewise when the disease is stigmatizing and the patient has comprehension problems

Table 4.7: Perception of respondents on the return of genomic results

Perception	Frequency	Percentage
Return of results		
Yes	141	94
No	9	6
Reasons for return of results		
Need to know	77	51.3
To motivate treatment decision making	34	22.7
To motivate prevention seeking	13	8.6
To motivate lifestyle modification	13	8.6
No reason	13	8.6
Reasons for withholding results		
Disease characteristics (incurable)	15	8.7
Patients health (mental well being of patients)	16	10.7
Comprehensibility	4	2.7
Patients physical health	5	3.3
Social consequences of the disclosure	13	8.7

4.8: Consequences of disclosure

The main consequence the respondents expected following disclosure was psychosomatic problems such as anxiety, depression, low self esteem and related symptoms (48%). A significant percentage expected development of psychosomatic diseases especially hypertension. Surprisingly, family crises is expected by only a few (2%), and a significant percentage (28%) expected no problem at all.

Expected consequence	**Frequency**	**Percentage**
Psychological problems	72	48
Psychosomatic diseases	28	18.7
Family crises	3	2.0
No problem at all	28	18.7

4.9: Disclosure of incidental findings

Majority (94%) believes that incidental findings should be disclosed , for similar reasons for disclosing general genomic results

4.10: Preferred disclosure process

Third party disclosure of negative results was accepted by 130 (86.7%) of the participants. The recipients of the information accepted by the respondents were shown in table 4.10 and mostly includes the next of kin (30.7%) and spouses (20%). Reasons for accepting third party disclosure include to obtain social support (37.3%) and medical support (22%). The participants also recommended that the physician (68%) , participant himself (20.7%), researcher (16%) and counselor (16.7%) should be all involved as a group in the process of the disclosure of the research results to the third party. of the research results. Most (70.7%) of the participants also want consent of the participant to be obtained before the disclosure

Table 4.10 Preferred disclosure process suggested by the participants

Characteristics	Frequency	Percentage
Recipient of the negative research results (N=130)		
Father	13	8.7
Mother	12	8.0
Siblings	5	3.3
Children	7	4.7
Spouse	30	20.0
Other relatives	12	11.3
Next of kin	46	30.7
Nobody	20	13.3
Reasons for third party disclosure (N=116)		
To obtain social support	56	37.3
To obtain medical support	33	22
To obtain counselling/ advice	12	8.0
Life planning support	10	6.7
Persons that should be involved in the disclosure process (N=148)		
The participant	31	20.7
The researcher	24	16.0
The counselor	25	16.7
The participants physician	68	45.3
Predisclosure consent (N=148)		
Required	106	70.7
Not required	42	28

4.11: Perceptions on regulations for disclosure process

About half of the respondents indicated a preference for regulation of the disclosure process. The scope of the regulation proposed are to include protection of the confidentiality of the research participant's information from unauthorized persons, the kind of personnel who should do the disclosure, the recipient of the information and the type of results to be disclosed.

Table 4.11: Scope of regulations on disclosure

Variable	Frequency	Percentage
Need for regulation		
Yes	77	51.3
No	71	47.3
No response	2	1.4
Scope of regulation		
Confidentiality and privacy	24	31.2
Who should do the disclosure	9	11.6
Recipient of the information	10	13
Type of result to be disclosed	2	2.6
No response	32	41.6

Cultural acceptability of disclosure of results

Overall most of the participants opined that disclosure of genomic research results is culturally acceptable to them. However, a significant percentage (30.7%) preferred that return of genomic research results should be personalized, although a higher percentage (44%) indicated no such personalization. It is also noted that some gave reasons that traditional antecedents of prediction of likelihood of diseases is exists among the Yorubas and so is culturally acceptable.

4.12: Cultural acceptability of disclosure of results

Acceptability	Frequency	Percentage
Yes, but dsiclosure should be personalised	46	30.7
Yes	66	44
Traditional antecedents are present	8	5.3
No	22	14.7
Dont Know	7	4.3

CHAPTER FIVE

DISCUSSION

This study examined the individual participants' awareness of genomic research, expected benefits of the research and preferences for individual return of genomic research results. The study also examined the participants' viewpoint on third party disclosures, its consequences and the process for such disclosures.

5.1 Summary of the findings

The study found out that the participants in this study were aware of genomic identification of diseases, and the prediction of likelihood of genomic diseases. Expected of advantages and disadvantages of genomic research were mainly about clinical utility of the results. The study participants want the findings from the genomic research to be communicated to the individuals involved the research and third parties, however the process of disclosure should be strictly regulated. Participants suggested that regulations and guidelines for the disclosure process should be concerned with confidentiality and privacy issues. The suggested main criteria that should guide the decision to disclose the results are the clinical utility of the research result and health status of the recipient of the disclosure. For third party disclosures, the participants preferred recipients of genomic research information are those who could provide medical and social support.

5.2 Demographic characteristics of the respondents

The respondents interviewed in this study were mostly young, the majority being in the productive age group of 20-39 years. Understanding the perception of this group of persons on genomic research is important for ethics policy making, which may impact on the uptake of preventive services uptake. Some complex diseases transmitted through genomic pathways are

manifests around the fourth decade of life. Hypertension for example begins manifestation in the fourth decade of life, likewise adult onset diabetes and many cancers. Uptake of predictive services in the decades of life preceding manifestation of these diseases provides ample opportunity for utilization of preventive and curative intervention. Furthermore, majority of the participants in this study were married and had children. Since results of genomic research have implications for the reproductive decision making of the participants, modification of reproductive decision and making of choices that are more adapted to the predicted future of the participants and their offsprings health may be warranted. Thus for these reasons it can be safely concluded that the participants age group and other characteristics made them appropriate for the objectives of this study.

5.3 Awareness of genomic research studies among the participants

Majority of participants in this study were aware of genetic transmission of diseases. Common chronic diseases such as hypertension, diabetes and heart diseases are identified as having a genetic mode of inheritance, and being transmitted through familial pathways. Participants aware of genetic transmission are more likely to accept individual results of diseases discovered through genomic research, since such experience had already been anticipated. Furthermore, in this study family experiences of genetic transmission of some chronic diseases were reported and a significant personal experience of such transmission were recorded among the participants. Ormondroyed et al reported that experiential knowledge of cancer in the family, among other factors, tended to improve or enhance adjustments to disclosed results (Ormondroyd E, Moynihan E, Watson M, Foster C, Davolls S, Ardern-Jones A 2007). In this study, the family experiences of diseases transmitted through genetic pathways may mediate the psychological impact of discovery of other genetic diseases and subsequent disclosure of the

findings to the participants. Thus likely psychological trauma may be minimized among this group of participants since such experiences are not altogether uncommon.

Awareness of prediction of genetic diseases through body tissues examination and certainty of the predicted likelihood were very common among the participants. Such certainty may have impact on the willingness to participate in genomic research and the preference for the return of the results. Although this study did not address the hypothetical question of desire to participate in genomic research, those who are certain of likelihood of the prediction may not be willing to participate in genomic research if undesirable results are expected. However the reverse may be the case if desirable results are expected.

5.4 Awareness of possible consequences of disclosure of genomic results

Participants in this study expected varying benefits from disclosure of results of genomic research. The major expected benefits are the awareness of personal health status. Desire to be aware of personal health status may arise from a desire not to be excluded from information about oneself which is available to others, especially the researcher. Shalowitz et al reported that participants in clinical trials research desiring return of results do so for a variety of reasons of which one is the curiosity to know any information possessed by the physician on a participant which they are not yet privy. In other regions of the world, personal desire to know health status had also been found to be a driver of the desire to know research results, indicating that participants consider such awareness as an advantage of disclosure. Also, Wendler and Pentz also indicated that participants in a clinical research may want to know the results out of the desire to know more about themselves (Wendler & Pentz 2007). Such findings reported across diverse cultures and communities, indicates a basic desire in all for self awareness.

Apart from personal awareness of health status, expected benefits of being in a position to make decisions about treatment and preventive decisions as indicted by these participants, may also enhance willingness to receive results of genomic research. This is an indication of clinical utility of the results. Studies in certain settings had shown that participants may not be willing to receive results that are not actionable. In the Matsui study, majority of the respondents wanted results returned only if intervention in the course of the disease is possible. The importance of clinical utility of the results is further emphasized by the opinions of those who would not want the results returned. Despite the reported advantages of disclosing genomic research results, some participants opined that genomic research results should be withheld in certain circumstances, notably nature of the results, participants mental and physical health status and comprehensibility of the results. In this study, disclosure is discouraged when the diseases found are incurable. This indicates clinical utility of the result. The clinical utility of result concern getting prevention or treatment. Murphy et al (2008) had noted that the nature of the result may be an important factor in desiring results.

Concern about the impact of the disclosure on the participants' mental health and physical health indicates the participants interest to minimize the possible harm that may be consequent to knowing the result of the research. However, it should be noted that in this study, only a few participants indicated stigmatization and discrimination may be a reason not to disclose the results to the participants of third parties. Expected consequences of disclosure expressed by the participants focused mainly on the psychological impact of the discovery. Surprising findings in this study is that only a few respondents expected the results of genomic research to impact on their reproductive or social lives.

5.5 Willingness of the participants to accept the disclosure of their genomic result and the recipients of such disclosure

Majority of respondents in this study opined that individual participants results should be communicated to them. This viewpoint had been observed in similar studies in diverse settings in both developed and developing countries. In a review by Shalowitz et al, it was found that a median of 90% want to receive individualised results of the research. Although the review by Shalowitz is not specifically on genomic research, other studies found similar desire for return of individualized results. Matsui documented overwhelming desire for return of results in a Japanese study (Matsui et al. 2008). A high proportion of participants were also willing to receive their results in a study by Koegh et al in Australia.

Participants in this study also showed a high preference for third party disclosures. In this study, next of kin, spouses and parents are recommended as recipients of a participant's genomic research results. The choice of the third party for the disclosure is steeped in the need for support. Participants made their choice based on who they believe will provide the support required to bear the consequences of the result. Spouses and parents are in the position to provide the needed medical and social support required. Furthermore the choice of next of kin may be based on the need to make end of life decisions should the disease discovered become invariably fatal. Thus, choice of third party recipients of participants genomic information should be tailored to the specific needs of the individual.

5.6 Preferences on the mode of disclosure of genomic research results

The process of disclosure of individual result preferred by the participants also reveals a strong interest in ensuring support particularly medical support. Most of the participants want their physician to be the one communicating the genomic research result to them. This may have

arisen from the participants' awareness of the fiduciary relationship between the patient and the physician. The fiduciary relationship between the patient and his physician requires that the interest of the patient be protected above all else and that the physician must do the patient no harm. The choice may also have arisen out of therapeutic misconception in which participants may expect cure from participation in a therapeutic trial. Among our participants, there may be inability to distinguish between a research and a treatment. Thus the choice of the physician may be linked to the misconception that research is not different from therapy. It should be noted that a few wants counselors to disclose the result while the researcher is preferred by a fewer participants. In about one fifth of the participants, self disclosure is preferred.

Recipients also want all aspects of the third party disclosure to be regulated. Most were concerned about who should do the disclosure, confidentiality and privacy and the recipient of the information. These are ethical concerns of any research endeavour and disclosure process.

5.7 Conclusion

Participants in this study were aware of genomic identification of diseases, and the prediction of likelihood of genomic diseases. Expected of advantages and disadvantages of genomic research were mainly about clinical utility of the results. The clinical utility and state of the patient were the main suggested determinants of disclosure. Preferred recipients of genomic research information are those who could provide medical and social support. Participants suggested that regulations and guidelines for the disclosure process should be concerned with confidentiality and privacy issues.

5.8 Limitations of the study

Considerable confusion exists among the participants in distinguishing family history of a disease and the genetic transmission of a disease and genomes. Specific lexicon referring to these

terms are not found in the local languauge, therefore the nearest equivalent or explication of these terms were used in the questionnaire. Thus for the participants, these terminologies perhaps refers to the same concept. The differences in the terminologies were however clarified in the course of the interview. It thus difficult to investigate into details the meanings of such unfamiliar concepts.

Sources of information about genetic inheritance which were provided by the respondents are also not validated. Genetic transmission among the family members is inferred from their biological relationship and not from objective assessments. Assumptions were made that the information provided by the respondents on the genetic transmission of diseases in their family are correct. This may not be accurate and the findings in this regard should be interpreted with caution.

Furthermore the study was carried out among predominantly young participants who have not suffered any chronic illnesses before. In addition none of these are involved in any genetic or genomic research. The responses and preferences of these participants may thus be limited by their experiences and exposures. Thus the findings may have limited generalizability.

5.9 Gaps remaining to be explored

Cultural acceptability of prediction of the future of a person is indicated in this study although it was not fully explored. Further studies needs to be commissioned on the meaning and scope of this concept among the Yoruba who form the majority of the study participants. The implications of this concept for genomic research needs to be explored in order to understand its application to genomic studies among the people.

5.10 Recommendations

The findings from this study suggest that genomic researchers in Nigeria, a developing country should expect their participants to be willing to receive the results of their genomic research. The findings also indicate that process of disclosure of the result would have to be an on-going interactive process beginning from the time of enrolment into the study. Given this finding, therefore, the process of obtaining consent for participation in genomic research should put emphasis on informing the patient about the possible consequences of receiving their research result and obtaining consent on the type of result preferred to be disclosed. The clinical utility of the results would have to be explained during the disclosure process. Participants may be required to indicate the third party to which the result should be provided. The findings from this study also indicates that more education is required to enhance participants appreciation of the roles of genetic counselors in the disclosure process.

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QUESTIONNAIRE ON ETHICAL CHALLENGES IN DISCLOSING GENOMIC TEST RESULTS IN A DEVELOPING COUNTRY

INFORMED CONSENT FORM

I am Dr Magbagbeola David Dairo, a student of Bioethics at the West African Bioethics Training Centre, University of Ibadan. I am studying the ethical challenges in disclosing genomic test results in a developing country. Thus I will need to ask you about your understanding of genomic research and your views about revealing the results to the participants. You may find some of the questions difficult to answer. You are free to decline answers to any questions you find difficult or which you deliberately decide not to answer because ylou are not comfortable with it. The answers given in this study will not be used for any other purpose and the outcome will be used for evidence based decision making in the formulation of health policy and to guide approval of research studies in Nigeria. You will not be victimized for not participating in this study; this study does not involve any invasive procedure that may cause injury to you. Your response will be treated with utmost confidentiality as such will not be disclosed to anyone without your permission. To further ensure your confidentiality, the questionnaire will carry no names or identifiers but serial number for proper data processing.

You are free to refuse to participate in this study and you have right to withdraw at any time you choose to. I will greatly appreciate your help in responding to the survey.

Thanks for your participation.

INFORMED CONSENT

Now that the study has been explained to me and I fully understand the study process, I willing to take part in the research.

Signature/thumbprint of participant……

Date of interview……(dd)/……(mm)/..... (yyyy)

Signature of witness……

QUESTIONNAIRE ON ETHICAL CHALLENGES IN DISCLOSING GENOMIC TEST RESULTS IN A DEVELOPING COUNTRY

Demographic Information

1. Age as at last birthday
2. Sex 1. Male 2. Female
3. Ethnicity 1. Yoruba 2. Hausa 3. Ibo 4. Others Specify
4. Religion 1. Christianity 2. Islam 3. Others (Please Specify)
5. Highest Education level attained

1. Some Primary School 2. Some High School 3 University/Other tertiary school

6. Marital Status

   Single never married Married Divorced Separated

7. Do you have siblings? 1. Yes 2. No
8. How many siblings do you have?
9. Do you have children? 1. Yes 2. No
10. How many children do you have?
11. Employment status

    1. Self employed (small scale business) 2. Not Employed 3. Government worker

12. Average monthly income (Please Indicate in Naira)

Personal and Lifestyle Habits

13. Have ever taken alcohol 1. Yes 2. No
14. Do you currently take alcohol? 1. Yes 2. No
15. If yes, How many bottles of beer do you take per day?
16. Have you ever taken cigarettes 1. Yes 2. No
17. Do you currently smoke cigarettes? 1. Yes 2. No

18. If yes, how many packs of cigarettes do you smoke in a day? ☐

19. Do you take any other stimulants ? 1. Yes 2. No ☐

20. If yes which one do you take (Please specify) _____

Awareness and Family History of diseases transmitted through inheritance

21. Apart from sickle cell disease which of the following diseases are you aware can be transmitted through family line ? ☐

1. Hypertension 2. Diabetes 3. Heart disease of any type 4. Cancer of any type 5. All of the above 6. Any of the above 7. Dont Know

22. Do you know of anyone who had these diseases which he got through family line?

1. Yes 2. No ☐

23. Please indicate your relationship to the person who had the disease ☐

1. Myself 2. Father 3. Mother 4. Sibling 5. Other relatives 5. Friend 6. Acquaintance 7. Not related in any way

24. Please indicate if you have at least one of the following conditions ☐

1. Hypertension 2. Diabetes 3. Heart disease of any type 4. Cancer of any type 5. More than one of the above 6. Dont Know

25. Please indicate if your father have any of the following conditions ☐

1. Hypertension 2. Diabetes 3. Heart disease of any type 4. Cancer of any type 5. More than one of the above 6. Dont Know

26. Please indicate if your mother have any of the following conditions

1. Hypertension 2. Diabetes 3. Heart disease of any type 4. Cancer of any type 5. More than one of the above 6. Dont Know ☐

27. Please indicate if your sibling have any of the following conditions

1. Hypertension 2. Diabetes 3. Heart disease of any type 4. Cancer of any type 5. More than one of the above 6. Dont Know ☐

Awareness of genomic research into diseases

28. Can the possibility of transmission of any disease be detected through the examination of body tissues (such as biopsies and blood)? 1. Yes 2. No ☐
29. Transmission of which one of these diseases can we detect through examination of body tissues?

    1. Hypertension 2. Diabetes 3. Heart disease of any type 4. Cancer of any type 5. All of the above 6. Any of the above 7. Dont Know ☐
30. Can the likelihood of someone developing diseases be made from examination of body tissues? 1. Yes 2. No ☐
31. How certain are you of these likehood which are made?

    1. Very certain 2. Certain 3. Uncertain Very Uncertain ☐
32. Do you think there are benefits to a person submitting himself for tests for the detection or prediction of these diseases that can follow inheritance?

    1. Yes 2. No ☐
33. What are the possible benefits? Please describe them

34. Do you think there are disadvantages to submitting oneself for such kind of test?

    1.Yes 2. No ☐
35. What are the possible disadvantages? Please describe them

Perception of Ethical Problems of Returning the results of genomic research

36. If a person participates in a research study and his body tissues were taken for examination, should the results of the examination be provided to him?

    1. Yes 2 No [ ]

37. Why should the person be given the results of such examination and prediction of likelihood of developing a disease?

38. Why should the person not be given the results of such examination and prediction of likelihood of developing a disease?

39. What problem do you think can arise from knowing or being given a prediction of the kind of diseases that is present in ones blood line?

40. Can you please describe these problems?

41. If in such a study, some other diseases are found apart from the one the participant agreed should be investigated, should the result still be provided to him?

1. Yes 2. No

42. Why should the person be given the results of such examination and prediction of likelihood of developing a disease which he had not agreed to when consenting to participate in the research?

43. Why should the person not be given the results of such examination and prediction of likelihood of developing a disease which he had not agreed to when consenting to participate in the research?

44. Are there kinds of results that should not be told the participants in such kind of research?

1. Yes 2. No

45. Can you kindly describe the kinds of results that should not be disclosed or shared with the participants in such kinds of research?

46. Apart from the person whose tissues were examined, should others also be told of the unexpected result that was found after the examination?

1. Yes 2. No

47. Who should be told? [ ]

1. Father 2. Mother 3. Siblings? 4. Children? 5. Spouse

6. Relatives 7. Employers 8. Nobody 9. Next of kin 10. Dont know

48. Why should the person be told the results?

49. Who should do the telling of results? [ ]

1. The person examined 2. The investigator 3. Counselor 4. Physician

50. Does the investigator need the permission of the person whose tissues were examined before he discloses the results to others

1. Yes 2. No [ ]

51. Are there problem that can arise when other persons know the kind of disease or conditions present on someone elses body line?

1. Yes 2. No [ ]

52. Please describe the problems

53. Should the telling of these kinds of results be regulated law?

1. Yes 2. No [ ]

54. What do we need to regulate about the telling process?

55. Why do we need to regulate the telling process?

56. Please describe how you will want to be told the results of such kind of finding

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_____

57. Is submitting oneself for genomic research and knowing the results acceptable in our cultural setting?

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ILANA IBERE LORI IPENIJA TI A LE BA PADE TI A BA FE SE IFIHAN ESI IWADI NIPA OHUN ISEDA (GENOME) TI O NBE NI ARA ENIYAN NI ORILE EDE TO O SESE N DIDE ILE

IWE IFOHUNSI TI O NI OYE

Emi ni Dokita Magbagbeola David Dairo, ti o je akeko ni eka ikoni ni pa bi a ti n huwa si ohun elemi to o wa ni Unifasiti Ibadan. Mo nse iwadi lori ipenija ti a le ba pade ti a ba fe se ifihan esi iwadi nipa ohun iseda (genome) ti o nbe ni ara eniyan. Nitorinaa, e mi ma beere awon ohun ti o je oye yin ninu oro yi. O le je isoro fun yin lati fun mi ni esi fun die ninu awon ibeere wonyi. Ominira wa fun yin lati ko jale ati se idahun fun awon ibeere ti ko ba yin lara mu. Ko si ijiya kankan fun kiko lati dahun ibere ti e ko fe. A wa fe lati fi awon idahun yin se atunto ilana nipa ifohunsi imo ijinle iwadi ni orile ede Naijiria. E ki yoo deye si yin beenia ko ni gba ohunkohun ninu ara eran yin ninu iwadi yi. Awon dahun yin je oro asiri to awa ko ni fi han enikeni bi ko se wipe e ti fun wa ni ase lati se bee. Lati fi da yin loju, awa ko ni gba oruko yin sile beeni a wa ko ni gba apeere idanimo kankan lowo yin ninu iwadi yi.

Ni asiko to a ba wun yin ni e le da iforowanilenuwo yi duro. Inu mi yoo dun pupo fun iranlowo yin lati dahun awon ibeere wonyi.

E se pupo fun ikopa yin.

IFOHUNSI TI O NI OYE

Niwon igbati a ti fi oye iforowanilenuwo yi ye mi, mo gba lati ko ipa ninu iforowanilenuwo naa.

Ifowosi /iteka olukopa……

Ojo oforowanilenuwo ..…(ojo d-d)/……(osu m-m)/..... (odun y-y-y-y)

Ifowosi eleri……

Ibeere nipa odiwon eniyan

1. Kini iye odun ti e ti gbe ni okee erupe ti a ba ka de ojo ibi yin ti o gbehin?_____
2. Kini eya yin ako tabi abo: 1. Ako 2. Abo
3. Kini irufe ede eya yin: 1. Yoruba 2. Hausa 3. Ibo 4. Omiran (so n

4. Ki ni esin yin:1. Atelekrisit 2. Musulumi 3. Omiran (so ni pato)

5. Ipele wo ni e ka iwe de? ☐

2. Ile iwe alakobere (ipele kinni) 2. Ile iwe giga (ipele keji) 3 Ile iwe ikeko gboye (Unifasiti – tabi ile iwe ipele keta miran)

6. Ipo igbeyawo ☐

1. Nko gbe yawo/loko ri 2. Mo ti gbeyawo/loko 3. Mo ti se ikosile/ipinya

7. N je e ni aburo tabi egbon? 1. Beeeni 2. Beeko ☐

8. Awon aburo ati egbon melo ni e ni ? ☐

9. N je e ti bi omo ? 1. Beeni 2. Beeko ☐

10. Omo melo ni e ti bi? ☐

11. Kini Ipo isise yin? ☐

2. Osise alara eni (alabode) 2. Osise ijoba 3. Emi ko sise rara

12. Kini gbagede owo ti o nwo apo yin losoosu? (soo ni naira) _____

Ibeere nipa awon asa ati ise baraku

13. Nje e maa nmu oti ti ole pani? 1. Beeni 2.Beeko ☐

14. Ti o ba je beeni, igo oti melo ni e maa nmu lojoojumo? ☐

15. Nje e maa nmu siga? 1. Beeni 2. Beeko ☐

16. If Ti o ba je beeni,paali siga melo ni e maa nmu lojoojumo? ☐

17. Nje e maa nmu ohun miran ti o le mu ki oju yin le tabi sana? ☐

1. Beeni 2. Beeko

Ibere nipa Ikiyesi asian ti o n ta tagba ninu ebi

18. Awon aisan wo ninu iwonyi ni o le ta atagba ni iran de iran ninu ebi ? ☐

1. Eje riru 2. Ito sugar 3. Aisan okan 4. Jejere 5. Gbogbo awon tin a la sile wonyi 6.Eyikeyi ninu won 7.Ko daju

19. Nje iwo mo enikeni ti o ni okankan ninu awon aisan ti o nta atagba ni iran de iran ninu ebi? 1. Beeni 2. Beeko

20. Ki ni ibatan re pelu eni naa ti o ni okankan ninu awon aisan ti o nta atagba ni iran de iran ninu ebi?

1. Baba mi ni 2. Iya mi ni 3. Egbon tabi aburo mini 4. Molebi mi miran ni 5. Ore mi ni 6 Ojulumo mi ni 7. Nko moo rara

21. Nje iwo tikarare ni okankan ninu on aisan ti a ka sile wonyi ?

1. Eje riru 2. Ito sugar 3. Aisan okan 4. Jejere 5. Gbogbo awon ti a ka sile wonyi 6.Eyikeyi ninu won 7.Ko daju

22. Nje baba re ni okankan ninu on aisan ti a ka sile wonyi ?

1. Eje riru 2. Ito sugar 3. Aisan okan 4. Jejere 5. Gbogbo awon ti a ka sile wonyi 6.Eyikeyi ninu won 7.Ko daju

23. Nje Iya re ni okankan ninu on aisan ti a ka sile wonyi ?

1. Eje riru 2. Ito sugar 3. Aisan okan 4. Jejere 5. Gbogbo awon ti a ka sile wonyi 6.Eyikeyi ninu won 7.Ko daju

24. Nje aburo tabi egbon re ni okankan ninu on aisan ti a ka sile wonyi ?

1. Eje riru 2. Ito sugar 3. Aisan okan 4. Jejere 5. Gbogbo awon ti a ka sile wonyi 6.Eyikeyi ninu won 7.Ko daju

Ikiyesi iwadi aisan nipa ayewo ohun iseda

25. Nje ti a aba mu die ninu ara eniyan, a le se iwadi nipa ona ti aisan se nse atagba?

1.Beeni 2. Beeko

26. Awon aisan wo ninu eyi ti a ko sile yi ni a le mu die ninu ara eniyan lati fi se iwadi nipa ona ti awon aisan naa ngba se atagba?

1. Eje riru 2. Ito sugar 3. Aisan okan 4. Jejere 5. Gbogbo awon ti a ka sile wonyi 6.Eyikeyi ninu won 7.Ko daju

27. Nje ti a ba ye die ninu ara eniyan wo, a le mo lileribee atagba aisan ni ara awon eniyan naa? 1. Beeni 2. Beeko

28. Kini odiwon lileribbee naa?

2. Dajudaju peregede 2. Dajudaju 3. Ko daju 4. Ko daju rara

29. Nje anfaani kan wa ninu ifi ara eni jin fun ayewo ati isotele aisan ti o nse atagba ninu ebi ? 1. Beeni 2. Beeko

30. Kini awon anfaani naa? Jowo se alaye won

31. Nje ewu kan wa ninu ifi ara eni jin fun ayewo ati isotele aisan ti o nse atagba ninu ebi?

1. Beeni 2. Beeko

32. Kini awon ewu naa? Jowo se alaye won

<u>Ifojusun Awon Isoro Ti O Nje Yo Nigabti A Ba Sipaya Esi Ayewo Ohun Aseda Fun Olukopa</u>

33. Ti olukopa ba fi ninu eya ara re sile fun ayewo ohun iseda, nje o ye ki a fun ni esi ayewo naa? 1. Beeni 2. Beeko

34. Kini idi ti a ni lati fun olukopa ni esi ayewo ati isotele lileribee aisan ti o wa ara re?

35. Kini idi ti a ni lati fi esi ayewo ati isotele lileribee aisan ti o wa ni ara olukopa pamo fun olukopa naa ?

36. Awon isoro wo ni o le jeyo nigbati olukopa ba mo esi ayewo ati isotele aisan ti o wa ni ara re ati ti o sile di atagba ninu iran re?

37. Jowo Se alaye awon isoro naa?

38. Nje ninu awon ayewo ati iwadi ohun iseda, ti a ba ri awon aisan miran lairotele, se o tona lati fi esi naa han olukopa? 1. Beeni 2. Beeko

39. Kini idi naa ti a ni lati fi esi aisan airotele naa han olukopa? Jowo Se alaye

40. Nje ninu awon ayewo ati iwadi ohun iseda, ti a ba ri awon aisan miran lairotele, se o tona lati fi esi naa pamo fun olukopa? 1. Beeni 2. Beeko

41. Nje irufe awon esi iwadi kan wa ti ko ye lati fi han olukopa?

1.Beeni 2. Beeko

42. Jowo se alaye irufe awon esi ayewo iwadi ohun iseda ti ko ye lati fi han olukopa

43. Ayafi eni ti a ye eya ara re wo, nje elomiran wa ti o ye ki o mo esi ayewo naa? nation?

1. Beeni 2. Beeko

44. Tani awon eniyan naa ti o ye ki o mo nipa esi ayewo iwadi naa/ se alabapin imo esi ayewo naa? 1. Baba mi 2. Iya mi 3. Awon egbo ati aburo mi ?

4. Omo mi ? 5. Iyawo/Oko mi 6.Awon molebi mi 7. Afuninise mi

8. Enikeni ko gbodo mo 9. Ko daju

45. Kini idi pataki ti eni naa fi gbodo mo nipa esi ayewo naa/ se alabapin imo nipa esi ayewo naa?

46. Tani eni naa ti o ye lati so fun tabi je alabapin esi naa??

2. Eni ti a yewo 2. Oluyeniwo 3. Oludamoran 4. Onisegun eni ti a yewo

47. Nje oluwadi ni lati gba iyonda lowo eni ti a se ayewo fun ki o to se ibapin esi ayewo naa

1. Beeni 2. Beeko

48. Nje isooro kankan le sele ti awon enikan ba se ibapin esi ayewo ohun iseda AX elomiran? 1. Beeni 2. Beeko

49. Jowo se alaye irufe awon isoro bee

50. Nje o ye ki a fi ofun se itona bi a ti nse alabapin imo nipa ohun iseda?

2. Beeni 2. Beeko

51. Awon Ilana ofin wo ni o ye ki a fi mu le lori ibase alabapin imo ohun iseda?

52. Jowo se alaye bi iwo ti fe ki a se ibapin irufe esi ayewo bayi fun iwo tikarare?

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_____

53. Nje ifi ara eni jin fun ayewo ohun iseda baa asa ati ise awon eniyan wa jo?

E se Pupo