# ETHICS OF DONATION OF FAECES FOR GUT MICROBIOME RESEARCH IN TYPE-2 DIABETES

**BY**

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A dissertation submitted to the Department of Surgery,

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in partial fulfilment for the award of the Masters' Degree in Bioethics

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**JUNE, 2017**

## CERTIFICATION

I hereby certify that the research titled, "**Ethics of Donation of Faeces for Gut Microbiome Research in Type 2 Diabetes**" is being conducted by OGWU-RICHARD, Sandra Olukemi under my supervision.

…….. ……..

**DR. T.O. OGUNDIRAN** **DATE**

**Supervisor**

## DEDICATION

I dedicate this work to God Almighty for his love, mercy and enablement throughout the duration of this research work.

## ABSTRACT

### Ethics of Donation of Faeces for Gut Microbiome Research in Type 2 Diabetes

There is growing realization of the role that microbiome play in health and diseases including diabetes mellitus. Despite this, little is known about the attitude of research participants to the use of their samples for these types of research. This is a qualitative study aimed at assessing the perceptions and attitudes of individuals to donation of faecal samples for gut microbiome research.

In this study, we enrolled participants in an on-going study of the genomics and microbiomics of T2DM in Africans called the Africa America Diabetes Mellitus (AADM) study taking place in Ibadan, South Western Nigeria. A convenience sampling technique was used to recruit 57 participants for this study. The participants were grouped into the following categories: Gender: Male and Female; Health status: Participants with diabetes mellitus (DM) and those without DM. Two FGDs for each of these strata making a total of 8 FGDs, each FGD consist of 6 to 9 individuals making a total of 57 participants. Membership of each FGD group was diversified by age, religion, socio-economic status as much as possible in order to get a broad representation of opinions from these strata.

The categorization based on sex shows that 16(27.6%) of respondents were males while the remaining 42(72.4%) were females. The classification based on ethnic affiliation shows that 56(96.6%) of respondents were Yoruba while the remaining participants 2(3.4%) were others ethnic affiliation. The marital status distribution of the respondents shows that 46(79.3%) of respondents were married, 3(5.2%) were single while 9(15.5%) of respondents were widowed. On religion, half 29 (50%) of the respondents are Muslims and 29(50%) were Christian. The result showed that a large percentage of the participants value and understood faeces as important while very few of the respondents were indifferent. A good number of the respondents were willing to give out their faeces for gut microbiome research for more innovative contributions to knowledge. While those with DM careless on the use of their faecal samples many without DM showed concern on the safekeeping of their information. Also, the result showed that most of the participants wants a fair share of any benefits amass as a result of their donated samples, in other words the participants believed that they still own their faeces despite it is being used for gut microbiome research but a very few of the respondents do not wish to claim ownership of what has been donated. Cultural beliefs were a major factor that

could affect donation of faeces but the respondents claim this does not affect their participation in research that would lead to health benefits.

In conclusion, transparency, confidentiality and complete release of information about microbiome research is highly recommended and also the issue of benefits should be discussed and agreements made before embarking on a microbiome research to promote an ethically balanced research.

**Keywords:** Microbiome, Diabetes Mellitus, Faeces and Donation

**Word count:** 467

## ACKNOWLEDGEMENT

My profound appreciation goes to the West African Bioethics Training Program (WAB) for sponsoring this Master's program through a distinguished man, Professor Clement Adebamowo who dedicated his time and energy into seeing younger generations in Nigeria become formidable in the world of research at international level in which I am a partaker.

I would like to show my gratitude to my mentor and supervisor, Dr. Sally Adebamowo for her thorough supervision and sincere mentorship throughout the process of this work. I also want to say a big thank you to all my delectable and professional lecturers: Dr. Ogundiran, Dr. Afolayan, Dr. Adejumo, Dr Odebunmi, Prof. Ajuwon, Prof. Malomo and Prof. Jegede to mention a few, you all contributed to this achievement.

I will not forget to mention all the staff in WAB center, Mr Segun Adeyemo, Mr. John Ipadeola, Miss Faith Fagbohunlu and Miss Blessing, you all were extremely supportive during my field work and I will not take lightly of your friendliness and corporation.

My sincere appreciation goes to my colleague and friend, Dr. Fakorede Omokehinde for her constant encouragements and support at each level of this work, may God bless you. Also, I want to use this medium to say a big thank you to my parents Dr & Mrs. K.G. Sowande, siblings, my in-laws (Steve Collins & Pastor Debola Ogwu-Joseph) and the immediate past President of the YWCF (TREM) Onikolobo, Sis Bisi Musari for her love and support.

Finally, with a genuine heart of appreciation, I want to appreciate my husband, Mr Ogwu-Richard, Vincent Ifeanyi for his love, understanding, emotional and financial support throughout the duration of this project, likewise my children, Annora, Roanna and Jeremiah may God bless you all abundantly.

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## CHAPTER ONE

## INTRODUCTION

Microbiome research is the study of the totality of microorganisms and their collective genetic material present in or on the human body or in another environment (Turnbaugh et al., 2007). The environments habited by the microorganisms that constitute the microbiome can be characterized as niches which are specific to different parts of the human or animal body parts or in the environment. Microbiome research evolved as a logical extension of the Human Genome Project, which led to the formation of the Human Microbiome Project - an interdisciplinary effort consisting of multiple projects that was launched concurrently worldwide in 2007, focused on studying the microbiome from different parts of the human body (Friedrich, 2008; Turnbaugh et al., 2007). Several projects investigating the role of microbiome in the pathogenesis of various diseases are underway in different parts of the world including Africa (Ameur et al., 2014; Iwai et al., 2014). In Nigeria for example, the African Collaborative Center for Microbiome and Genomics Research (http://h3accme.com/) is researching the vaginal microbiome and has published findings on the association between vaginal microbiome and human papilloma virus (HPV) infection, a risk factor for cervical cancer (Dareng et al., 2016).

Reports from some studies suggest that numerous interactions, some mutually beneficial while others are lethal, occur between humans and their microbiome (Albenberg & Wu, 2014). For example, the microbiome of the lung and gut contribute to the pathogenesis of asthma and allergy, and differences have been found in the lung microbiome of healthy and asthmatics (Riiser, 2015). Likewise, the gut microbiome has been found to be associated with neurodevelopment in infants and psychiatric disorders in adult (Sherman, Zaghouari, & Niklas, 2015). Many of the microorganisms that live symbiotically with humans are un-culturable and

the advent of highly parallel DNA sequencers and high-throughput mass spectrometers with remarkable mass accuracy and sensitivity have been extremely important in the development of microbiome research (Group, 2016). The high-throughput mass spectrometer focuses on the characterization and operations of whole communities of microorganisms and uses metagenomics to characterize the genomes in these communities (McGuire et al., 2012) as well as their corresponding messenger RNA, protein and metabolic products (Chen, He, & Huang, 2014).

Faecal microbiome, also called gut microbiota (Vrieze et al., 2010) is the entirety of the microorganisms, their genes and surrounding environment (complete ecosystem) that exists in the faeces of an individual (Pfefferle & Renz, 2014). The human gut harbors about a trillion microbes, of which bacteria are the most abundant (Upadhyaya & Banerjee, 2016). This population of bacteria are from five phyla: Firmicutes, Bacteriodetes, Actinobacteria, Proteobacteria and Verrucomicrobia (Berlanga, Paster, Grandcolas, & Guerrero, 2011; Dubourg et al., 2013; Seksik, 2010). Although, there is high variability in the composition of these bacteria among different individuals; their distribution along the intestinal tract increases in density from the proximal to the distal gut (Miele et al., 2015). Studies suggest that there are few bacteria in the stomach, duodenum, and jejunum while a higher quantity of bacteria, about $10^7$ cells per gram of faeces are located in the ileum and a much higher quantity, up to $10^{12}$ cells per gram of faeces, in the colon (Miele et al., 2015). The state of the gut microbiota is modified by diet, lifestyle, genetic and environmental factors such as antibiotics use (Kovatcheva-Datchary & Arora, 2013).

The gut microbiome has been demonstrated to play an important role in the body's nutrition and metabolic functions (Yildirim et al., 2010). They contribute to the fermentation of unused energy substrate, training of the immune system, prevention of growth of pathogenic bacteria, development of the gut, production of Vitamins B and K and stimulation of satiety hormone (Upadhyaya & Banerjee, 2016). In addition, some studies have suggested that there is an association between the gut microbiome and Type 2 Diabetes Mellitus (T2DM), a chronic, metabolic disease characterized by high levels of glucose in the blood. Worldwide, in 2015, 415 million adults had diabetes; this is expected to rise to 640 million by 2040 (http://www.diabetesatlas.org/). The risk factors for T2DM include obesity, physical inactivity, increasing age, hypertension and genetic factors (http://www.diabetesatlas.org/). Studies have shown that there is a difference between the specific types of microbiome in diabetics compared with non-diabetic individuals. For instance, diabetics have been shown to have a

lower concentration of *Roseburia intestinalis* and *Faecalibacterium prausnittzii* but a higher concentration of *Lactobacillus gasseri*, *Streptococcus mutans* and Clostridiales (Karlsson et al., 2013; Larsen et al., 2010). These differences may be associated with metabolomics functions that play a role in the development of T2DM.

Faeces or stool is generally considered to be of no value but, it is now finding increasing use in microbiome research. Other uses of faeces in genomics research include its use in detection of colon cancer and germline mutations (Morgan & Huttenhower, 2012). Faeces, referred to as a 'waste product'(Codron et al., 2005) and a direct link to the gut microorganisms , can reveal personal information about the donor (Hawkins & O'Doherty, 2011). Therefore, the use of faeces for research may raise some ethical concerns. The change in the fortune of faeces raises potential ethical questions about the attitude of research participants who donate faecal samples for research and concerns that such donations may lead to possible breach of confidentiality and information misuse. Given the possibility that commercial benefits may accrue from microbiome research, questions about value and ownership of the sample may also become controversial. These and possibly many more are some of the ethical issues arising from use of faeces in microbiome research.

The perception of participants to donation of faecal samples for microbiome research may affect their willingness to participate in such studies. Studies have been conducted on various concepts of perception such as, Paramsothy and his colleagues investigated the perceptions of 52 clinicians towards faecal microbiota transplantation (FMT) and their experiences with FMT. Kerath et. al. 2013 sought to assess the general attitudes towards genetic research and participation in biobanks. The National institute of health (NIH) conducted a study on the use of genome-enabled approaches to study microbial communities and also ethical, legal, and social implications (ELSI) of donation of samples for microbiome research. The study explored the perception and attitude of respondents on donation of samples to this novel research (Group, 2016). but there is dearth information on the perception and attitude of donors to the donation of their faecal samples for gut microbiome research in a developing country such as Nigeria, hence the need for this study.

Nigeria is a multicultural and multi-religious country (Udebunu, 2011) with over 300 tribes and 3 major religions (Christianity, Islam and indigenous/traditional practices). The different cultural and religious beliefs of these people may reflect on their attitude to the use of their faeces in research. Considering the growth of microbiome research throughout the world

including Nigeria, it is important to ascertain the views of potential participants in microbiome research. This study will therefore expose the thoughts and opinions of individuals of diverse cultures and religions to the use of faeces in gut microbiome research, bridging the gap between researchers and their potential participants to promote a more ethical research.

## 1.0 Statement of Problem

Presently, the perception and attitude of Nigerians to the use of the faecal microbiome samples for research are yet unknown. Although, the National Institute of Health conducted a pilot study on the perception and attitude of participants to donation of samples for gut microbiome research; this study was carried out among the Amish in United States (Group, 2016), this is a developed country. It is therefore imminent to explore, the rate at which Nigerians, being a representative of a developing country, are willing to donate faecal samples for gut microbiome research. Considering the genetical information linked with the faecal samples, it is also important to find out the perception of Nigerians on faeces as a waste product or a vital product which is part of them and carries their identity.

Secondly, it will be ethically unbalanced or biased not to find out if the perceptions and attitudes of Nigerians will be affected positively or negatively, should there be any awareness of any financial benefits or therapeutic potentials in the course of the microbiome research considering the ethical implications on ownership of sample. While the negative effect could be potential risks ranging from social sensitivity, justification on recruitments of research participants, modalities on feedbacks and identifiable links to donors (McCormick, Boyce, & Cho, 2009).This study consequently affords the opportunity to fill these gaps and also to know the views of individuals from an African and a developing nation's perspective.

The importance of the socio-cultural characteristics of Nigerians to the use of faecal samples for gut microbiome research is indeed not known presently; and as a result, failure to explore the perception and attitude of Nigerian on the relationship between the donation of faeces and socio-cultural affiliations exposes dearth information in this area. It is germane to therefore, consider the traditions and religious affluence that are associated with faeces in this part of the world. As it is known that Nigeria is multi-ethnic country (Udebunu, 2011), it will not be out

of context to explore the perception and attitude of participants in the region where this study will take place.

**Research Questions**

This study will therefore address the following research questions:

- Do participants consider faeces to be a part of themselves or a waste product?
- How important do participants view faeces?
- What are the perceptions of participants to the use of their faeces for gut microbiome research?
- What will be the perception and attitude of participants to donating their faeces for gut microbiome research, if they are aware of its therapeutic benefits?
- What will be the perception and attitude of participants to donating their faeces for gut microbiome research, if participants are aware that their faeces could yield financial benefits?
- How willing are participants in giving up their faeces for gut microbiome research?
- To what extent can participants give up their faeces?
- Who claims the ownership of the faecal microbiome, the researcher or the one who donates?
- Who owns the faeces after it must have gone out of their body?
- What do participants think about the influence of culture in the use of their faeces for gut microbiome research?
- What can participants say as regards their religious affluence in releasing their faeces for gut microbiome research?

## 1.2 Broad Objective

To assess the perceptions and attitudes of individuals to the donation faecal samples for gut microbiome research with regards to ethical implications.

## 1.3 Specific Objective

- To find out the importance of faeces to participants for a gut microbiome research
- To explore the perception and attitude of participants for donation of faeces for gut microbiome research.
- To identify the factors that influence the perception and attitude of participants to the use of the faecal samples for gut microbiome research

## 1.4 Significance of Study

The outcome of this research knowledge will be useful in designing future research studies, developing patents, guiding policy, ethical considerations etc. Research in Nigeria and other countries will potentially benefit from the findings in this study in promoting ethical and scientific researches. It will create awareness on the sensitivity of microbiome researches and possible considerations of the underlying ethical challenges such as, ownership, feedback, and bases for recruitment, identifiable links. This study will also contribute to the development of a guide in developing policy for conducting microbiome research such that the interest of research participants will be protected and not exploited.

The result of this study will also be useful as template in developing patents such that the participants will be aware of potential benefits. The awareness of the benefits associated with patency will be made exposed to the participants, such that guidelines in protecting these participants are developed and used. Studies have demonstrated participant's willingness to donate some biological samples such as blood, semen, urine, saliva to research (Babatunde et al., 2013). Faeces, which is naturally a waste product is currently being utilized for research purposes in developed and developing countries, though these studies which utilize faeces for microbiome research are not common in Nigeria at the moment, the possibility that it will gain prominence cannot be ignored.

The cultural and religious beliefs of study participants in a developing country like Nigeria may influence their attitude to the donation of their faecal samples for a microbiome research. These cultural and religious beliefs may affect the thoughts, emotions and decision-making capacities of these people, which may ultimately influence their attitude to microbiome research. Failure to explore these concepts may be a costly mistake to the nation because these variables may contribute to further decline in research output from Nigeria.

# CHAPTER TWO

## REVIEW OF LITERATURE

The emergence of genomics and metagenomics has propelled microbiological studies into interesting discoveries(de Vries et al., 2011). These discoveries reflect human body as a world that is inhabited by numerous other organisms of various communities and of different genetic make-up (Vrieze et al., 2010). These organisms are known as microorganisms and are known in the past to be mostly pathogenic and causal agents of most of the deadly communicable and non-communicable diseases that have plagued and endemic the existence of man (Gerritsen, Smidt, Rijkers, & de Vos, 2011). It is in the quest of solving this problem that a good number of these microorganisms in the human body have been eliminated and some others forced into extinction through the production and use of antibiotics (McGuire et al., 2012; M.J. Slashinski et al., 2013) and disinfectants. However, studies have also shown that only few of these microorganisms are pathogenic while majority are of immense benefits to the human host. This is one of the reasons for this study to illuminate the advancement of genomic and microbiological research and the therapeutic potency of these microorganisms (microbiome) in human life. The gut microbiome research is one of the products of Human Microbiome Project (HMP) which is also an offshoot of genomic and microbiological research. Globally, the study is more pronounced in the developed countries like USA, Canada, Asian countries (China), Australia etc., but has not gain much prominence in Africa, although initiatives have begun in this respect, this is still at the embryonic stage. Particularly in Nigeria, as at the time of this study gut microbiome research has not gain prominence as far as the findings of this study.

Subsequently, it is germane to assess the donation of faeces for gut microbiome research (genomic research), considering ethical implication that surrounds this research. The issue of

informed consent; are we certain that the research participants are well informed? What happens to the leftovers of the faeces after use? The issue of confidentiality, will there be any feedback? What about the patent right of the donor – these are the likely ethical issues that should be considered in the course of any microbiome research.

## 2.0 A Brief History on Human Microbiome

To understand the concept of microbiome, it is pertinent to explore the basic foundation of this given concept. These microbes originates from the microorganisms that humans come in contact with at birth, during the passage from the birth canal- the vagina; and some others came into man from the milk sucked from the mother's breast (Hoffman, Fortenberry, & Ravel, 2013; Pfefferle & Renz, 2014). Therefore, as the child grows these microbes takes full form at the age of three. Every individual possess their own unique microbes which is constituted by that individual's genome (Hawkins & O'Doherty, 2011). The microbes do the job of educating the human immunity how to fight against external attack (disease) (Zimmer, 2011). When a child becomes an adult, the microbes becomes the first line of defence, they fight off germs that tries to invade the human body, by protecting the human body(Zimmer, 2011).

The human body serves as a host to the collection of diverse community of microorganisms or microbes and are either commensally or parasitic in their association with the human body (Vrieze et al., 2010). It is also important to note that most of the microbes in the human body are good for protection, defence against diseases by signalling the human immune cells and physiological activities; this they do by regulating the human metabolism, the energy burn and the process and quantity of fat stored (Reid et al., 2014; Melody J Slashinski, McCurdy, Achenbaum, Whitney, & McGuire, 2012). There are also suggestive evidences that microbiome and probiotics could be used as solution because the useful microbes detoxifies the human system and put down the cholesterol level, while a very few population of them are pathogenic as earlier stated (Pfefferle & Renz, 2014; Reid et al., 2014).

Sometimes, these activities may not be efficient due to the kind of food consumed and the intake of antibiotics and the use of some disinfectants. Scientists think that this may also be due to the loss of key role player of microbes in the gut due to C-section and in the pursuit of

cleanliness, humans have unconsciously eradicated these useful microbes and the ones still present have been incapacitated (McGuire et al., 2012; M.J. Slashinski et al., 2013). Various microbes are located at different part of the human body and thereby colonize such areas and perform specific responsibility in those areas of the body. These microbes become recognized and specific to those parts of the body in which they are found (Borody, Paramsothy, & Agrawal, 2013; Carroll, Threadgill, & Threadgill, 2009).

A collection/community of these microbes or a cluster of microbes or microorganisms are referred to as microbiota while "microbiome" is referred to as the entire habitat, including the microorganisms, their genomes (i.e. genes) and the surrounding environmental condition both biotic and abiotic factors of a given or defined environment(Hawkins & O'Doherty, 2011; Vrieze et al., 2010). The human microbiome is therefore the collection of genes and surrounding environmental conditions of all the microbes in the human body. Studies have reported that the genes of the human microbes (microbiome) outnumber the genes of the human body, in ratio hundred to one (Hawkins & O'Doherty, 2011; Zimmer, 2011). It is also interesting to find out that the human microbiome invariably outnumbers the human cells in ratio ten to one; it will therefore not wrong to say that the human body is a "conveying ecosystem" just like the earth of both biotic and abiotic factors.

They inhabits every part of the human body from the mouth to the nose, eyes, skin, guts or intestines and of course the genitals (Velasquez-Manoff, 2015; Vrieze et al., 2010). They could be found in either wet (mouth, nose and armpit) or dry (forearm, back and scalp) places. These microbes are distinguished by their various habitats in the human body; for example the oral microbiota, vaginal microbiota, guts microbiota etc. and so each of these microbes adapt to their habitats (Ley, Peterson, & Gordon, 2006). The most important microbes in the human body seem to be in the gut, they are the most complex, intense and diverse in activities(Borody et al., 2013; Vindigni, Broussard, & Surawicz, 2013). The collection of genes of these microorganisms found in the specific microbiota is referred to as the microbiome of such respective microbiota, for example the "gut microbiome" is found in the faeces that exeunt the gut, which is the focus of this discourse.

Research has revealed that DNA-sequencing tools help us to see this microbiome clearly and their respective functions in the human body (Lee, Lattimer, Stephen, Borum, & Doman, 2016; Vindigni et al., 2013). The microbiome performs life sustaining functions and without them the human body cannot function optimally, leading to the fact that, the human body is more of super-organism than merely human (Hoffman et al., 2013; McGuire et al., 2012). The relationship activities of these human microbes range from symbiotic to commensals and pathogenic (bacteria, fungi and viruses). Due to this realization, science has since developed and has given birth to the advent of prebiotics and probiotics as treatment and remedies for some metabolic disorders and some disease conditions (Gerritsen et al., 2011; Reid et al., 2014), instead of the antibiotics that were formerly used.

In 2013, the International Scientific Association for Probiotics and Prebiotics (ISAPP) organized a meeting re-examining the concept of probiotics, defined probiotics as live organisms that confer healthiness on the individual when it is administered in adequate proportion (Ley et al., 2006). Some bacteria and fungi are considered good and are responsible for keeping the gut healthy (Vindigni et al., 2013). Researchers in their findings revealed that probiotics can be used to replace the good microbes that human host lose to antibiotics, because these probiotics are helpful in the workings of the body by balancing the good and the pathogenic microbes in that system(Gerritsen et al., 2011; Vindigni et al., 2013; Vrieze et al., 2010).

Probiotics are divided into two groups; Lactobacillus and Bifidobacterium (Lederberg, 2000). The former is found in yogurt and other fermented foods. Lactobacillus are useful in the prevention from diarrhoea and aid in the digestion of lactose in milk, while the latter is found in dairy products and is helpful to ease symptoms of irritable bowel syndrome (IBS). Other activities of probiotics is to prevent inflammatory bowel disease (IBD), infectious diarrhoea, antibiotic-related diarrhoea, skin condition (e.g. eczema), urinary and vaginal health, allergies and cold and oral health (Lederberg, 2000). They are also useful in the promotion of healthy digestive system tract, immune system and changes in human behaviour and this according to researchers is the mostly wide benefits. The essence of this review on probiotics is to relate what was in use before the initiation of human microbiome.

### 2.1 The Human Microbiome Project/Research (HMP)

The studies on probiotics influenced the emergence of human microbiome project which is believed to be more reliable and a better approach of treatment of some human diseases (M.J.

Slashinski et al., 2013). The human microbiome project (HMP) helps to study the good microbes in the human body that are responsible for keeping healthy system and to understand their genomic peculiarities and specific functions in the human body (McGuire et al., 2012). The HMP is the National Institute of Health (NIH) USA initiative with the goal of identifying and characterizing the microbes' which are found in association with both health and disease in humans as announced by Francis Collins, the NIH director(Group, 2016; Lederberg, 2000).

This initiative was first launched in 2008, a five years' project with a budget of $115million; and was accompanied by various articles on nature and several journals in public library of science (PLoS) (Lederberg, 2000). Although, the human genomic project (HGP) is regarded as the biggest and the best known large-scale biomedical research project undertaken till date, a more recent big science initiative is the HMP (Hoffman et al., 2013). The HGP possess certain similarities with the HMP as viewed by researchers and this has led to relating HMP as the 2$^{nd}$ generation of HGP. In fact an author refers to HGP as the "warm up exercise" for HMP (Hoffman et al., 2013). Hoffmann further clarified the issue of rating HMP higher than the HGP as too early or premature discourse since there are a lot yet to be discovered about human microbiome and its significance to health and diseases.

Also in 2008, the European Union and China collaborated on a similar expedition called the Metagenomics of the Human Intestinal Tract (MHIT) project and the Asian Microbiome Project (Hoffman et al., 2013). These projects focused on the study of genetic materials of the collection of microbes from a mixed community in the intestinal tract of humans just like the HMP but in this case, it is more specific to gut microbiota which will be extracted from fecal samples of healthy individuals.

Recently, a workshop was organized in Nairobi, Kenya to harnessed microbiome and probiotics in sub-Saharan Africa in which recommendations were made (Reid et al., 2014). One of the aims of this workshop was to discuss human, animal, insect and agricultural microbiome as well as prebiotics/probiotics researches. Researchers with track record of microbiome research were invited across Africa, but were attended by thirty-two participants from ten countries due to logistic reasons and no funding for travel expenses. Discussion was also centered on the possibility of African Microbiome Project (AMP), as obtainable in the developed countries (Reid et al., 2014). Although very few studies were done on the microbial diversity of African humans, except for determination of the association with health and diseases (Reid et al., 2014).

The AMP hopes to determine the taxonomic and functional (metagenomics) diversity of bacteria present in human feces of 10,000 individuals across ten different sites in Africa, a ratio of 1,000 individuals in each site (Reid et al., 2014). According to Reid and his colleagues, the data generated from this study will be of high quality that will be well represented in the different cultures, groups (rural and urban dwellers), religion and traditions of the African microbiome as well as create a platform for future researches using the data generated from this study. The funding of this project was a major concern; attention was therefore focused on this in 2014 by these researchers of multi-national teams and multi-disciplines to source for relevant funding to commence this project (Reid et al., 2014).

Globally, the impact of HMP was to develop parameters to pattern, implement and monitor strategies for intentionally influencing the human microbiota to optimize its activities in the context of an individual's physiology (Hoffman et al., 2013; Melody J Slashinski et al., 2012). This project aimed to be beneficial in terms of understanding of human nutritional requirements (that is, how individual responds to a particular type of diet), which will lead to innovative food productions and distribution strategies and other public health benefits, advancement in generalizable knowledge of areas relevant to microbial transplantation and successful manipulations, forensic tools and pharmacomicrobiomics (Cho & Blaser, 2012; Melody J Slashinski et al., 2012).

The uniqueness of the HMP exposes that while the human genome contains only about 20,000 protein coding genes, the human microbiome is thought to be made up of 8 million unique protein-coding genes or 360 times more microbiome than human genes (Hoffman et al., 2013). Although some authors have suggested that differences in individuals' microbiome can predispose such individual to certain disease conditions, such as cancer, Alzheimer, obesity and this information is similar to that which was generated from HGP in terms of the information given by the human genome as regards likelihood of the onset of some diseases (Hawkins & O'Doherty, 2011; M.J. Slashinski et al., 2013).

Apart from unifying the composition of human microbiome, there is a major question of "core", a subset of community of microbes shared between most individuals (Vindigni et al., 2013); ability to assert this, would determine one of the goals of HMP (Hawkins & O'Doherty, 2011). The variability of the human microbiome in a single individual and different individuals as shown by investigators (Hoffman et al., 2013; Vrieze et al., 2010; Zimmer, 2011), who found out the gut microbiota of individuals are not the same in any way. Mapping of normal microbial

make-up of healthy people using DNA genome sequencing techniques was performed by the HMP. This was used to create a reference database and boundaries for normal microbial variations in human in which various samples from men (15) and women (18) tissues of different body sites such as nose, skin, mouth, gut (feces), and vagina were collected and analyzed. The various microbial genomes were extracted where specific ribosomal 16S r RNA and 81-99% of the genera were identified (McGuire et al., 2012).

With this insight, it will be interesting to explore some perspectives of different authors and researchers on their thoughts and knowledge on the emergence of human microbiome and its relevance to genomics and science as a whole.

## 2.2 Perspectives of Some Scientists on Human Microbiome

According to Martin Blazer, the role of microbiome in human physiology is very important. The gut microbiota helps the pregnant mothers in their metabolism by increasing the nutrients for the offspring. He further said that there is a host-link co-evolution of the microbiota and immune responses because of the initial colonization of the host T-cell population by the microbiota. He concluded that some gut microbiota is detrimental to human health and proposed an advanced monitoring, prevention and curative treatment by regulating the activities of the human microbiota (Blaser, Bork, Fraser, Knight, & Wang, 2013).

Peer Bork was fascinated by the gut-brain microbiota and how the microbiota affects the human behavior, an intensive network between the human and microbial cell which is far beyond immune response. He anticipates more solid proof of principal study and robust statistics that can prove earlier hypothesis to justify the enthusiasm of various emerging trends in microbiomics. He also reflected on the association study linking gut microbiota and Type 2 Diabetes, all these findings is continuously paving way to the use of microbiome for improving human health (Blaser et al., 2013).

Claire Frazer, suggested that most findings on microbiome as a partnership between the microbial genes and human genes. The identification of shared sets of functions across different community types, the significant impact of perturbation such as diet and antibiotics on the extinction of human microbiome; all these suggest that it is time to take a more holistic approach on health and diseases (Blaser et al., 2013).

On the other hand, Rob Knight in his own opinion was illuminating his findings on the microbiome and the nervous system which he said, includes the neurodegenerative disease and

on the human behavior. The transmissibility of changes in the microbiome in pregnancy from humans to their offspring also exists in mice. The most valuable findings to date have been links between the microbiome and drug metabolism including the use of the microbiome its self as a drug target (Blaser et al., 2013).

Jun Wang, an Asian researcher, explores the relationship between the microbiota and the host disruption of the homeostasis; this is known as the dysbiosis. He pointed the important role of the microbiome than that of the human genome in the development of the disease such as IBD, obesity and Type 2 Diabetes. His suggestions pointed to the fact that it would be more practicable to monitor, prevent, or even cure human diseases by regulating the human microbiota. He concluded that the study of gut microbiota will be helpful and important development of personalized healthcare in the future (Blaser et al., 2013).

Abreu et al, 2014 reported that gastrointestinal (GI) microbiota is a complex ecosystem that more than three million genes encoding enzymes that generate metabolites can influence health as well as diseases. The GI can also constrain or facilitate tumor growth by altering immune mechanisms and affecting the metabolism of chemotherapeutic agents. Focus was on gastric, colon and oesophageal malignancies or cancers.

All these contributions point to the necessity and importance of microbiome in the human system, its role in the advancement in science and its potency in the treatment of Diabetes, and other autoimmune diseases. It is therefore germane to explore science and find out the relativity of fecal microbiome in all of these discoveries, its history and advantages in the treatment of some diseases in which diabetes is part of and more importantly its advancement so far in the developed and developing countries.

### 2.3 Gut Microbiome Research

Gut microbiome as the name implies is the entirety of the microorganisms, their genes and surrounding environment (complete ecosystem) that found in the faeces of an individual. These microbes which originally exist in the guts are the normal micro-floral of that part of the human body and are specific to that locality in the human body; in essence the gut microbiome is constituted of the gut microbiota. They are characterized by their role in nutrition, protective and metabolic function in the gut. Some authors refer to the gut microbiota as the most important in all the microbiota that are found in the human body (Borody et al., 2013; Vindigni et al., 2013). It is in this fact that, scientists began to explore the activities of the gut microbiome

in the human body and how it can be used as treatments from a healthy individual to treat a diseased individual whose gut microbiota has been depleted. The depletion could be as a result of major circumstances such as, the constant use of antibiotics and diet which has gradually forced these guts microbiota into extinction (McGuire et al., 2012; Zimmer, 2011).

Borody and his colleagues in their studies on the "Fecal microbiota Transplantation" (FMT), noted that FMT has become generally acceptable therapy that is valuable with biological plausibility. In their findings, it was revealed that the human gut harbour 15,000- 36,000 bacterial specie which just 500- 1500 can only be detected by culture-based technique but detailed sequencing studies have revealed the presence of these other bacteria present in the human gut. Studies have revealed that the most prominent of these microbes belong to the two major phyla- Bacteriodetes and firmicutes. The bacteriodetes consist of the most common genera- bacteroides and prevotella while the phylum Firmicutes which is probably the largest, consist of over 200 genera (Vindigni et al., 2013).

Also, that metagenomics sequencing analysis authenticated a human gut microbiota gene catalogue, detecting 3.3 million active (non-redundant) microbial genes, about 150 times larger than the entire human gene complement (Borody et al., 2013). The microbial populace in the gut and the genetic composition exist in a complex but balanced homeostasis. However, the disruption of the normal genetic composition of these microbes will give rise to various disease states, and such disease conditions are responsive to the therapy with FMT, which can be used as remedy or treatment.

Historically, it has been proven by many authors that, international sites exhibited the validity in the treatment of Clostridium difficile infection (CDI) (Borody et al., 2013; Carroll et al., 2009; Vindigni et al., 2013). In the last few years there has been a remarkable use of FMT but majorly in a few specialized centres globally, although most of which has not been controlled but have all reported success rates of 90% and above. Their studies further exposed that the first randomized controlled trial involving FMT for relapsing CDI was published early 2013 and has upheld the huge efficacy of FMT over the conventional antibiotic therapy. This innovation positioned FMT to the mainstream of medicine which made the American College of Gasteroenterology formally recommend FMT in its guidelines for Relapsing CDI (R-DCI) (Vindigni et al., 2013).

The review of the publication of Vos et al, 2011, focuses on the current knowledge on the composition and diversity of the intestinal microbiota, new molecular methods that have

present new insights towards phylogenetic and functional characterization of the gut microbiota. Also, they explore the recent insights on the interaction between gut microbiota and the human health and finally their study presented an overview of ways to modulate the gut microbiota with specific attention on the use of live microorganisms which when administered in sufficient amount give health benefit to the host. In their study, they made known the findings of some authors, Martin and his colleagues on the metabolic profiling which can be used to demonstrate the interaction between nutrients microbiota by investigating the effects of dietary intervention on the presence of fecal metabolites (Gerritsen et al., 2011). Also, that a number of systemic disease such diabetes and hypertension seem to be controlled by microbial metabolic process in both humans and animals.

Borody and his colleagues gave the detailed process of the collection, storage and transplantation of the fecal sample. In medicine, the FMT is also referred to as transplant material (TM) and is grouped as human tissue gotten from healthy donors who do not exhibits any risks factor that could change the cellular composition or transmissible diseases, most especially in the use of antibiotics. To embark on this treatment, the published international guidelines by the FMT group outline on donor-selection criteria and screening test has to be strictly adhered to. At the onset of this FMT research, patients could identify their donors who were selected members of their families and friends. Successively, some researchers in some institutions suggested the option of "anonymous donor(s)"(Borody et al., 2013).

With this novel idea, the burden of donor identification moved from the patients to their physicians (Borody et al., 2013), thereby provides the availability of tested healthy donors with a history of cure, and also precludes donors with shared genetic or environmental predisposition to the patient or recipient. They further showed that, the donor's faeces is conveyed to the institution within a few hours of passage and then go through three main process of (1) dilution (with normal saline) (2) homogenization (with a blender to achieve a liquid slurry) (3) filtration (to remove the particulate matter) (Borody et al., 2013). Most institutions use fresh feces which compel the collection and use of the fecal sample on the same day planned for the FMT. Although, other authors have adopted another method of utilizing highly filtered human microbiota mixed with a cryoprotectant and then frozen and stored at -80°C until when required for use. (Borody et al., 2013)

Hawkins et al, 2011 raise the question of ownership of data and information resulting from samples collected for gut research purpose. This is because the procedure calls into question

established research ethics norms and accepted practices. Some of the ethical issues such as privacy, informed consent, secondary use of biological samples and information and benefits sharing were highlighted, while these ethical issues remain problematic and unresolved others areas of science are moving ahead rapidly, and have the potential to further complicate matters, more importantly with human microbiome research.

Further findings from Hawkins et al, 2011 reported that human as super-organism with over 100 million microbiota that are essential for nutrition, immunity some are pathogen resistance. While some are harmful majority are beneficial with interaction with human cells in physiological functions and metabolic functions. Research on human microbiome aimed to elucidate the relationship between human health, physiology and behaviour and various microbial communities. Also, the goal of HMP is to characterize the role of microbiota in human health and disease (Hawkins & O'Doherty, 2011). It investigates such basic scientific questions as whether humans share a common core microbiome or whether a particular change in the human microbiome lead to changes in human health and diseases states. Their research was hoped to lead to diverse benefits such as a better understanding of human nutritional requirement (including how individuals will respond to specific diet), resulting in innovative food production and distribution strategies and other public health benefits.

According to these researchers 'privacy' is the ability to protect both the clinical and genetic data stored in biobanks; but this has become a pivotal biobanks discussion since such research was conceived. Due to the potential sensitive nature of samples (faeces) collected, considering the anxiety regarding the possibility of privacy breaches, resulting in personal information being misused. This is particularly relevant in the context of genetic data as access to individuals' biological specimens and DNA may reveal sensitive information such as predispositions to certain disease as well as identity and ethnic background.

These issues raised by Hawkins and her colleagues are not unique to microbiome studies but may manifest rather distinctly this type of research or its applications. An example is a controversial method for treating certain forms of bowel disease involves the use of fecal transplants, in which a slurry of faeces from a healthy donor is transplanted into a patient. This treatment procedure seems rather to be extremely sensitive.

Chen and his colleagues also reported their findings in the diet effects in gut microbiome and obesity that microbiota varies from individuals but studies of microbiome (microbial metagenomics sequences) have demonstrated that the functional gene repertoires exhibit great

similarity among individuals especially adults. They further reported that the composition of gut microbiota within an individual is inherently associated with host genotype and age and moreover presents dynamic which is affected by external factors such as diets, antibiotics, lifestyle and prebiotics which may result in dysbacteriosis (Chen et al., 2014; Miele et al., 2015).

They pointed out further that gut microbes play a crucial vehicle in the host metabolism by improving energy harvested from food. That is, these microbes are able to degrade the polysaccharides that are indigestible to the host. Besides these microbes can improve mucosal immunity, intestinal permeability and modulate the derived compounds (Chen et al., 2014).

This procedure is essentially new in Nigeria at this time, but shall become generally acceptable procedure for collection and storage of fecal samples for genomic and microbiological research when human microbiome project is initiated in Nigeria. Also, it is important to explore the attitude of Nigerians to microbiome research and the plausible response to it. This is mostly relevant in bioethics, to consider the feelings, thought and behavior of research participants and to protect their rights and also from future risks that could be associated with their participation in a microbiome research.

## 2.4 Diabetes Mellitus (Type 2) in Gut Microbiome Research

Second to HIV pandemic and continuous rise in prevalence is the diabetes mellitus (DM) (Semenkovich et al., 2015). Studies have shown an increasing significance at global level, starting that from 2012 to 2014, DM had recorded 1.5 to 4.9 million deaths each year (Wikipedia.org 2014) (Hartstra, Bouter, Backhed, & eiuwdorp, 2015). As at 2014, 387 million people have DM worldwide and estimated prevalence by 2035 is 592 million. Type 2 DM (T2DM) being the most common with a prevalence of 90% compared with the other types of DM – Type 1 and gestational diabetes (Wikipedia.org 2014). In Nigeria, previous studies revealed that Ibadan has the prevalence of 1.5% in a study and 0.8% in another study (Nyenwe, Odia, Ihekwaba, Ojule, & Babatunde, 2003), in Jos, a prevalence of 3.0%, Portharcourt having a prevalence of 7.4% and 3.0% in Umudike in Abia state .

DM is a group of diseases caused by an increase in the level of sugar over a prolong period (Wikipedia.org 2014) (Hartstra et al., 2015). This could be as a result of none secretion of insulin by the pancreas or none utilization of secreted insulin by the body cells (Wikipedia.org 2014). The early symptoms includes frequent urination and increased appetite for food,

however delayed diagnosis could lead to serious complications – diabetic ketoacidosis and nonketonic hyperosmolar coma which could be long term in form of cardiovascular diseases, stroke, foot ulcers, kidney failure and perpetual damage to the eyes (Wikipedia.org 2014). Reports have shown that T2DM is as a result of failure of the body cells in utilizing the available insulin(Karlsson et al., 2013; Nyenwe et al., 2003). It is sometimes referred to the 'Non-Insulin Dependent DM' which is mostly attributed to excessive body weight – termed 'obesity' (Grootaert, Wiele, & Verstraete, 2010; Karlsson et al., 2013; Vrieze et al., 2010).

Gut microbiota has been recently established to have a contributory effect in the development of Type 2 DM (cardio-metabolic disorder) and growing interest has focused on modulates of gut microbiota as a therapeutic strategy in metabolic disorders such as Type 2 DM- a primary public health concern (Miele et al., 2015). Human gut microbiota is complex and mainly composed of more than $10^{14}$ bacteria and archaea as well as by viruses, fungi and protozoa. Bacteria belonging to five phyla dominate the gut such as Firmicutes, Bacteriodetes, Actinobacteria, Proteobacteria and Verrucomicrobia (Miele et al., 2015).

Further investigations revealed that gut microbiota has a peculiar distribution along the intestine as its destination and increases from the proximal to the distal gut; bacteria are scan in the stomach, duodenum and jejunum, while their concentration in the ileum rises up to $10^7$ cells per gram of faeces and in the colon goes up to $10^{12}$ cells per gram of faeces (Miele et al., 2015).

Miele and his colleagues further reported a recent study which was linked to lower polysaccharide plants among Italian children and consumption of polysaccharide plants among African children. The study demonstrated that the microbiota of the Italian children living in town compared to that of the African children living in rural villages had a lower concentration of Bacteriodetes and higher concentration of Enterobacteriacae. In addition to this, human metagenome wide association study showed significant correlation of specific gut microbiota, certain bacterial genes and metabolic pathway in T2DM patients.

In a symposium organized by American Diabetes Association and JDRF research, Semenkovich Clay of Washington University, St Louis, gave a report on the interaction between T2DM and microbiome. In his account, he reflected on the progression and risk factors of T2DM to be influenced not only by genetic variants but also by environmental dynamics which explains its high prevalence. Also, the interaction of the microbiome of the host and the

cells of the host may be a major effect. He related that the gut microbiota has a vital link to the metabolic health of the individual with T2DM.

Using the gnotobiotic mice to illustrate his point and bariatric surgery, there is evidence that the transplant of microbiome of a lean individual can prevent extreme conditions from an obese person, and also, "a complex effect on the microbiome improved and resolved T2DM and in the process decreasing cardiovascular risk even before weight loss is realized" respectively. Consequently, his reports suggest that the manipulation of the microbiome activities could improve the T2DM therapy (Semenkovich et al., 2015).

It is of great importance to take into account the connection between obesity and T2DM (Grootaert et al., 2010; Lee et al., 2016; Raoult, 2008; Vrieze et al., 2010). Studies have shown that the gut microbiota is associated with storage of energy gotten from food and how energy is being expended (Grootaert et al., 2010; Karlsson et al., 2013; Semenkovich et al., 2015). Food intake that is high in calories and not expended will promote body weight and ultimately result into obesity which may lead to T2DM (Raoult, 2008). Another researcher, Micheal Rosenbaum of Columbia University, New York, at the same symposium exposed that the colonization of the gut of germ-free mice through fecal transplant led to weight gain and that the degree of weight gain depends on the donor, that is, the greater the weight of the donor, the greater will be the weight gained by the recipient mice (Semenkovich et al., 2015).

It was also observed that the microbiome in the obese and lean mice responded differently to weight loss (Borody et al., 2013; Pinn, Aronidiasis, & Brandt, 2015). This implies that the gut microbiota of an obese individual is lower in diversity compared to the microbiota of a lean individual. Authors have presented evidence that the microbiome gene count of the gut microbiota of an obese individual is lower and cannot perform essential metabolic activities as those in healthy lean individual (Grootaert et al., 2010; Hartstra et al., 2015). Studies have also shown that the bacterial genera, Bacteriodes has shown to be more in the gut of lean mice while Firmiticus is high in both obese mice and humans (Borody et al., 2013; Grootaert et al., 2010). It is these evidences that birth the fecal microbiome transplant in humans and have shown to be reliable in the treatment of T2DM, because in treating obesity one is also treating T2DM.

All these studies have highlighted the evidence of relationship between obesity and diabetes (T2DM) and the effect of fecal microbiome transplants in its therapeutic process in the developed countries. Conversely, in Africa and most importantly in Nigeria, dearth studies have been done in this area. Thus, more studies are needed in this respect in Africa at regional

level and in Nigeria to find out the possibilities of microbiome research in the treatment of these systemic diseases that are common among us (Hoffman et al., 2013).

## 2.5 Attitude of T2DM Participants to Gut Microbiome Research

Attitude, according to the Encarta Dictionary is an opinion or general feeling about something. It could also mean, a physical posture, either consciously or unconsciously, especially when interacting with people. Following these definitions, attitude is an important concept in the research enterprise that exposes the rate and manner of participation of research participants. It is the embodiment of affective, cognitive, and behavioral components of an individual who is a potential research participant (Wikipedia Psyc 2015). The type of attitude displayed by the research participant explains the interest, knowledge and consent of that participant to the research in question.

It is pertinent to explore the attitude of T2DM individuals to gut microbiome research – a sensitive investigation that may reveal an individual's genetical identity, ethnicity and nationality, where the person has been to in the past and in the recent time, the kind of food the person eats, and so many other personal information that may be divulged as a result of the experiment (Hartstra et al., 2015; Semenkovich et al., 2015). Undermining the study on attitude of participants to gut microbiome research will deny the exhibition of the ethical and social concerns that accompanies the use of faecal samples in gut microbiome research in Nigeria and ultimately in Africa at large. Ethical and social concerns such as privacy, confidentiality, disclosure and feedback, monetary returns and stigmatization etc. may pose as barriers to the participation of the T2DM individuals in a fecal microbiome research.

According to Carl Zimmer in New York Times, he advised transparency in the interaction of researchers with their study participants in genetic research as this will foster a good attitude with the fundamental knowledge of the research and proper agreements on the findings from the research. He quotes Kieran O'Doherty of the University of Guelph outside Toronto, on the role of ethics as the "key to respective interaction", which he believed will enhance responsive attitude of the participants (Hawkins & O'Doherty, 2011; Zimmer, 2011). Also, this interaction will mediate the gap that exists between the research and the general public who do not think like the scientists. Researchers anticipate and perform innovative experiments to bring about curative measure and treatments for these diseases that are so prevalent but fail to consider the attitude of their research participants to this study.

Some publications have raised alarm on the ethical implications of research participants donating their biological samples for genetic research in the USA (Kerath et al., 2013). These scholars disclose their fears in the aftermath of the genetic research. Some of the issues raised were stigmatization, privacy, confidentiality and disclosure (de Vries et al., 2011; Jamal et al., 2014; McGuire et al., 2012). These may affect the participants' family, ethnicity affiliations, even to the extent of identification within a public data, using smaller subsets of their genome. This process may not be easy but with effort and all the resources required by a participant or donor can be identified. These concerns were investigated in these publications and this has helped genomic research in the USA (New York, Baltimore, Pennsylvania etc). But the attitude of individuals to gut microbiome research in Nigeria is yet to be done and that is why this study hopes to fill this gap.

Other studies have intensify on the study of attitude of research participants to only microbiological samples (Tolomeo et al., 2008), which is for the sole purpose of identifying resistant pathogens and to produce antibiotics that these pathogens are sensitive to, in the bid to eliminate them. Some of these studies were done in Africa and even in Nigeria although this may not be conspicuous like studies done in the developed countries, but many studies have been done on attitude of participants to biomedical research and not necessarily on genomic research in Nigeria and some African countries (Babatunde et al., 2013). Babatunde et al, 2013, did a study on the willingness of health workers to research with biological samples but these research participants are those with prior knowledge on genomics but this type of study cannot be said of general public, which is the participant who does not know much about what goes on in genomic research.

In an article by Moises Velasquez-Man off, New York Times on "Should we Bank our Own Stool" there was an encouragement for people to a have good attitude towards banking their stool for future treatment (Velasquez-Manoff, 2015). He emphasized that the benefits of banking or freezing the stool for future use of the donor or any other person like family members surpasses any doubt or issues people may tend to have against fecal donation. Again, this is an opinion paper which has highlighted the importance and benefits of fecal microbiome research to medical advancement and healthier status to the world at large.

Further investigations by some investigators considers the cultural and traditional beliefs of research participants to microbiome research in the Unites States (Kerath et al., 2013) but did not investigate the religious inclinations and disposition of study participants to gut

microbiome research. Hawkins and O'Doherty presented the relevance of culture in determining the attitude of human microbiome research participants and also describes it under two reasons; the dignity of man which is the first, which talks about respecting every individual's body and life of persons while the other enunciated the consequences of the ownership, especially commercial benefits that may be accrued from the individuals' samples (Hawkins & O'Doherty, 2011).

Finally, Jamal and his cohort carried out a study on "Research Participants' Attitude towards Confidentiality in Genomic Sequence Information" and it expresses the significance of informed consent which provides options for flexibility in the procedure of data governance, to either continue or opt-out, new communication strategies for updates on samples, as a means of equating the risks and benefits and also providing user-friendly websites for the research participants to update their knowledge of genomics as it progresses or advances (Jamal et al., 2014). However, being a qualitative design makes the research not generalizable (Jamal et al., 2014) and this gives room for further studies on genomic research such as the attitude of research participants on fecal microbiome research.

## 2.6 Perception of Individuals to Gut Microbiome Research

The perception of participants in microbiome research is germane in reflecting their willingness to participate (Borody et al., 2013; McCormick et al., 2009). Perception is the complex sequence of processes by which we take the information received from our senses and then organize and interpret it, which in turn allows us to see and hear the world around us as meaningful, recognizable objects and events with clear locations in space and time (Pomerantz, 2006). Perception to an issue demonstrates the understanding and the sense knowledge of an individual as regards a particular concept, in this case, the use of faeces for microbiome research. Some international studies have explored the perception of people in their countries to fecal microbiome research. Paramsothy and his colleagues found out in a their study in Australia that, 52% of the population had good perception of the utilization of faecal samples for microbiome research while 6% of the medical institutions in Australia are already conducting microbiome research (Borody et al., 2013). Other authors also found out that public perceptions of the use of faeces for microbiome research suggests these transplants are lucrative, and are becoming essential to peoples' preventive health care regimens (M.J. Slashinski et al., 2013), and consumers generally perceive these products as both safe and effective (Borody et al., 2013; McGuire et al., 2012). The donation and use of faeces appears

not be alien to the general populace in developed countries such as USA, Australia, Canada, China possibly due to the fact that healthy donation of faecal samples for therapeutic uses is a common practice there (Dominianni, Wu, Hayes, & Ahn, 2014; Hoffmann, Fortenberry, & Ravel, 2013; Pfefferle & Renz, 2014; Zimmer, 2011). Considering the possibility of rapid development of research in Nigeria, it is important that the views of potential respondents in genomic research be obtained.

# CHAPTER THREE

# RESEARCH METHODOLOGY

## 3.0 Study Location

This study was conducted in Ibadan, Nigeria. The study recruitment site was Adeoyo General Hospital (AGH), Ibadan, in Oyo State. AGH is a state-owned hospital, secondary healthcare institution, with facilities for medical, surgical and psychiatric care. AGH serves the residents of Ibadan, a city of 3.6 million people who are a representation of Nigerians in the South-Western region (Oyo State, 2010).

## 3.1 Research Design

This was a qualitative research study. Focus group discussions (FGD) were used to explore the perception and attitude of participants to the use of their faeces for microbiome research. The FGD employed a face-to-face approach, which enabled us observe all non-verbal gestures that took place during each session. The sessions were interactive and participants were allowed to freely discuss each question until the point of saturation was reached.

Eligible participants were approached and the study objectives and procedures were discussed with them. Those who were willing to participate in the study signed informed consent forms before enrolment into the study.

## 3.2 Study Population

The study participants were individuals from Ibadan and its environs who were obtaining treatment for various conditions at the AGH, Ibadan. However, some of these patients were also part of a larger study- African American Diabetes Mellitus (AADM) study in which participants (enrolled between August 2015 – July 2016) belonged to either of two groups namely patients with T2DM and patients without T2DM. The inclusion criteria for this index study are that respondents must be part of the AADM study, have a minimum of primary education and must be at least eighteen years old. Patients who met these criteria were recruited from the larger study population through purposive and criterion sampling methods.

### 3.3 Sample Size

Purposive sampling and criterion sampling method was used to select participants into groups for FGD.

The participants were grouped into the following four categories, with six to ten members expected in each group:

(a) Men with T2DM

(b) Men without T2DM

(c) Women with T2DM

(d) Women without T2DM

**Table 1 shows the expected number and distribution of participants in the study**

| Group Name | Group Category | No of members |
|---|---|---|
| **A** | Men with T2DM | 6-10 |
| **B** | Men with T2DM | 6-10 |
| **C** | Men without T2DM | 6-10 |
| **D** | Men without T2DM | 6-10 |
| **E** | Women with T2DM | 6-10 |
| **F** | Women with T2DM | 6-10 |
| **G** | Women without T2DM | 6-10 |
| **H** | Women without T2DM | 6-10 |
| **TOTAL** | | **48-80** |

However, we were unable to enroll the equal number of men and women for the present study because most men approached to participate refused to provide consent. Table 3.2 shows the total number and distribution of participants enrolled.

In total, eight FGDs were conducted with six FGDs consisting of both males and females while the remaining two FGDs were made up of females only (Table 3.2). Of these eight groups, four groups were made up of individuals with T2DM and the remaining four groups consisted of healthy individuals.

**Table 2 Actual number of participants enrolled at study site**

| Group Name | Group Category | No of members |
|---|---|---|
| **A** | Women with T2DM | 8 |
| **B** | Men & Women with T2DM | 9 |
| **C** | Men & Women without T2DM | 6 |
| **D** | Men & Women without T2DM | 9 |
| **E** | Men & Women with T2DM | 7 |
| **F** | Women without T2DM | 6 |
| **G** | Men & Women with T2DM | 6 |
| **H** | Men & Women without T2DM | 6 |
| **Total** | | **57** |

### 3.4 Inclusion and Exclusion Criteria

The inclusion criteria were being a participant in the AADM study, at least eighteen years of age with a minimum of primary level of education. Consented individuals were recruited for the study.

However, individuals who fulfilled the above criteria but did not give consent to participate in the study were excluded.

### 3.5 Description of Study Instruments

#### 3.5.1 Focus Group Guide

A focus group guide (Appendix 4) was developed for the purpose of this study. The questions in the guide were open-ended and were structured in a way to allow free flow of ideas and opinions which gave participants the opportunity to respond in their own words. It gave room for expression of various views about the study topic and did not accommodate a 'yes' or 'no' response. The research interview guide utilized in this study focused on the following:

- Perception of participants in giving up their faeces for gut microbiome research
- The level of importance that participants ascribed to their fecal samples
- Participants' views on the ownership of the faeces after donation for microbiome research.
- The factors that influenced the attitude of participants in donating their faeces for gut microbiome research

- The attitude of participants to donating their faeces if aware of the potential financial benefits that may be gotten from gut microbiome research
- The religious and cultural influence on the donation of faecal samples for the use of gut microbiome research.
- Anticipated feedbacks from the gut microbiome research.

### 3.6 The FGD Interview

Focus Group Discussions were conducted with research participants in various groups at the study site. The researcher introduced herself to the participants and subsequently asked the questions that stimulated the views of the participant on the research topics. The focus group guide that was used tailored the discussion and ensured that all important issues were covered. Probing questions were also asked when necessary. The responses to the questions were recorded (audio) by a voice recorder and transcribed later. Relevant points mentioned during the discussion was documented and non-verbal communication, interferences, gestures and background events that occurred in the course of the interview were also recorded and noted by the researcher.

The duration for each discussion lasted for 40 to 45 minutes. Participants were reimbursed for their transportation expenses. The phone numbers and e-mail addresses of the participants were obtained and noted (as a separate document and not on the questionnaire) for possible future clarifications.

### 3.7 Data Management

The audio- recordings were transcribed shortly after the discussions have taken place in order to avoid the risk of loss of information. These transcripts were further classified into separate files with an appropriate file naming system (site/participant's category/type of document/sequential number/date). For instance, the transcript of the Group A FGD with eight participants ( 1$^{st}$, 2$^{nd}$ & 3$^{rd}$ participant labeled as P1, P2, P3) that was done on the 12$^{th}$ day of October, 2016 who also fell in the category of individuals with diabetes in AADM study, at Adeoyo were saved as *AGH/GRPA/trans/ACASE/121016*, while *AGH/GRPA/P2/audio/121016* meant the "audio recordings of the 2$^{nd}$ member of group A1, who fell under the group of men and women with diabetes in AADM study which was conducted on the 12$^{th}$ of October, 2016 at the State General Hospital, Adeoyo Ibadan. All the discussions were saved in their

corresponding folders: *ALL/FGD/AUDIO/121016* and *ALL/FGD/TRANS/211016* meaning the "audio recordings of all the focus group discussion collated on the 12th day of October, 2016" and the "transcripts of all the participants' discussions collated on the 21st day of October, 2016" respectively. A similar approach was employed for the notes taken during the discussion sessions.

The notes taken, audio tapes used and the transcripts obtained in the study was kept by the researcher in a secure location dedicated for research purpose away from the public to guarantee the reliability of the data obtained.

Confidentiality of the data obtained was ensured throughout the study by conducting the discussions in a quiet and private venue within the State General Hospital, Adeoyo. This also helped to reduce interferences from third parties during the discussions. In addition, each research participant was given a code other than the real name for identification, which was an alphanumeric code containing alphabet and number. At the beginning of the interview, each research participant was addressed with the codes and not by the real name. The reason was also to protect the identity of the participants both in the audio-taped recordings as well as the transcribed records. For example, an identification tag of P1 and P2 meant 1st and 2nd participants respectively. The notes that were taken during the interviews also bore the codes (and not the name) of the participant.

### 3.8 Data Analysis Procedure

The raw notes taken during the discussion were transformed into expanded field notes to capture all observations made shortly after the discussions. The audio recordings of the discussions were also transcribed thereafter.

Descriptive, content and thematic analyses were employed in the analysis of data obtained in the study. The expanded field notes and interview transcript were read through to familiarize with their contents. The expanded field notes and the transcripts were then tallied based on the categories of the FGDs in order to codify the contents into meaningful themes. The meaningful themes are formed based on the words of the participants. Also, the recurring themes or themes with similar focus in them were identified and integrated. All the text and other data that have associated thematic ideas were examined together and then different cases were compared in that respect.

The audio recordings were transcribed and all the transcripts were carefully reviewed. The transcripts were entered into the ATLAS ti software, major themes and their supporting quotations were identified. Sub-themes (such as participants' view on faeces) within the major themes were further identified and aggregated into categories. The recurring themes were noted and their relationship with the research questions were documented. Overall, these encoded themes were grouped into the relevant study objectives.

### 3.9 Expected Outcomes

This study was expected to identify the attitude and perception of individuals in donating fecal samples for microbiome research.

### 3.10 Ethical Consideration

Eligible potential participants were approached to participate in the study. The purpose, procedure, risks and benefits of the study were discussed with potential participants. Voluntary participation of the respondents was ensured by informing them of their right and choice of participation or withdrawal at any time during the study. Ethical approval for this study was obtained from the University of Ibadan/University College Hospital Health Research Ethics Committee (Appendix 1). Consent was obtained using the consent form in Appendix 2 and signed informed consent forms were obtained from individuals who agreed to participate in the study.

Confidentiality of the identities of the respondents was maintained from the commencement of interview to the completion of the study. Alphanumeric identity was given to participants' and the data obtained in this study was kept in a secure location dedicated for this purpose, away from the public and was not be tampered with in anyway.

# CHAPTER FOUR

# RESULT

## 4.0 Socio-Demographic characteristics of respondents

A total of fifty-seven participants were enrolled in this study. About half (52.6%) of the respondents had T2DM (Figure 1) and the female gender (74.0%) was more represented (Figure 2). Table 3 shows that most of the respondents were of the Yoruba tribe (96.5%), and ages ranged between 21years to 80years with a mean of 54.2years and were mainly within the 41-60 age bracket (61.4%). Both predominant religions had almost equal representations; about three-quarters were married (78.9%) and 22.8% had only tertiary level of education completed (Table 1).

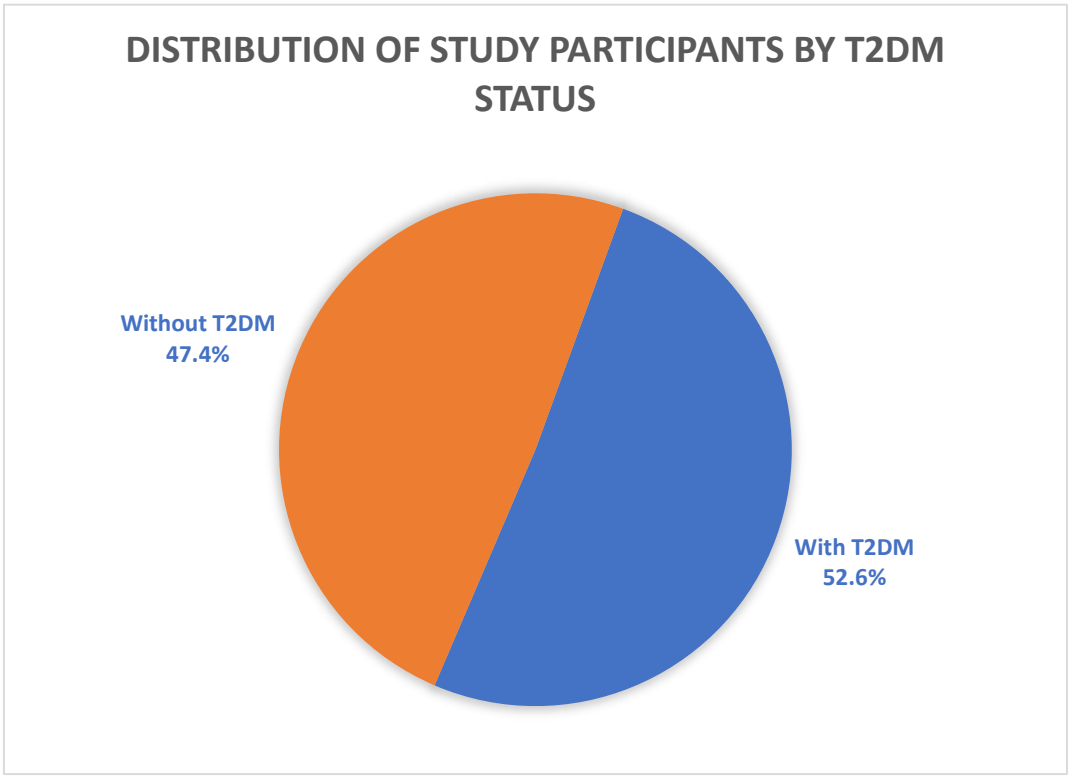


**Figure 1: Distribution of study participants by T2DM status**

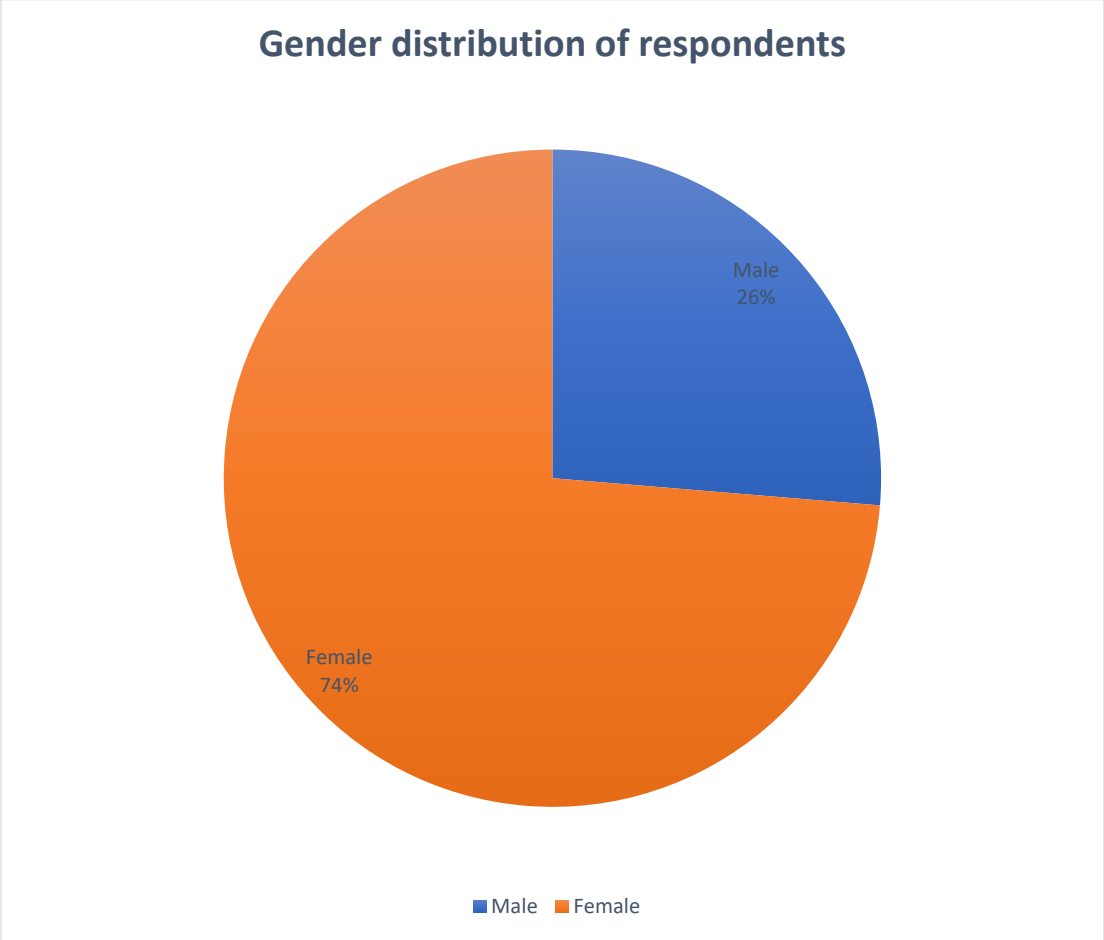


**Figure 2: Gender distribution of respondents**

**Table 3: Showing the socio-demographic characteristics of the participants**

| **Sociodemographic characteristics** | **Frequency (n=57)** | **Percentage (%)** |
|---|---|---|
| **Tribe** | | |
| Yoruba | 55 | 96.5 |
| Others | 2 | 3.5 |
| **Age(years)** | | |
| 21-40 | 7 | 12.3 |
| 41-60 | 35 | 61.4 |
| 61-80 | 15 | 26.3 |
| **Religion** | | |
| Muslim | 29 | 50.9 |
| Christianity | 28 | 49.1 |
| **Marital status** | | |
| Married | 45 | 78.9 |
| Not Married | 12 | 21.1 |
| **Highest level of education Completed** | | |
| Primary | 21 | 36.8 |
| Secondary | 23 | 20.4 |

| | | |
|---|---|---|
| Tertiary | 13 | 22.8 |

### 4.1 Participants' views on importance of faeces

Participants had different views on the significance of faeces. Some saw it as a waste product of the body's metabolic process that must be expelled in order to have sound health and even survival. In fact, some respondents expressed worries over the financial implications of eliminating faeces in the event of constipation. These are some excerpts in support:

*"Faeces is a waste product in any food that we eat. Faeces is something important, if one eats and excrete faeces, his/her body would be light and experience sound health condition"* **(Female 55 years old, with T2DM)**

*"Inability to excrete faeces may cause bad health……; Faeces has value for real because if one is unable to excrete he/she would not be able to sleep……faeces is very important, it is useful because if you don't defecate one would not live" (***Female 55 years old, With T2DM)**

*"If one eats and not excrete, he/she would not feel good……. Inability to excrete faeces may cause bad health"* **(Female 46years old, Without T2DM)**

*"If one is unable to excrete faeces, it may lead to surgical operation and it costs money"* **(Female 43 years old, with T2DM)**

Though some participants described the repelling nature of faeces:

"*Faeces is something irritating……"* ***(Male, 78 years old, With T2DM)***
*"It is a dirty thing, it smells"* ***(Female, 50 years old, With T2DM)***;
its role in detecting possible medical condition when subjected to analysis was also emphasized:

*"That we give our faeces for checkup enables you to find out what is wrong in our body system. Faeces is something irritating but it is more effective than urine and blood test"* **(Female 52years old, With T2DM)**

*"Faeces are something bad in the body, a waste product of the body. It helps us to know the state of health condition"* **(Female 43years old, Without T2DM)**

Two respondents with T2DM also expressed the economic importance of human faeces. They noted the usefulness of human excreta as farm manure which helps to boost agricultural yield:
*"It is also useful for fertilizing our plants" (***Female 55 years old, With T2DM)**

*"Faeces have value; it is manure that has benefit for planting"* **(Male 78years old, With T2DM)**

## 4.2 Perception towards ownership of faeces for microbiome research

Respondents had varying views as regards the ownership of their faeces after expulsion. Some respondents believed that even after expulsion, their faeces were still theirs and this view was held by both individuals with T2DM and those without:

"*I own it. It is still mine." (**Female, 56years old, With T2DM**)*

*"There is nothing concerning me again, it is no longer my own."*
***(Male, 35years old, Without T2DM)***

In the event of discontinuation from gut microbiome research for any reason, majority of the respondents opined that the withdrawal of consent to the use of the faeces earlier donated was unnecessary:

*"There is no reason to withdraw it. We are still alive and would still need medical attention".* ***(Male, 56 years old, With T2DM)***

*"There is no need that I should withdraw it, it means nothing to me."*
***(Female, 50 years old, Without T2DM)***

### 4.3 Attitude towards donation of faeces for microbiome research

Pertaining to donation of faeces for microbiome research, respondents with T2DM said they would donate their faeces:

*"I know that the blood-sugar (DM) that is wrong with us will be found and treated in our faeces, and maybe some other things. That is why I'm willing to donate my faeces"* ***(Female 59 years old, With T2DM)***

*"I am willing to give it particularly because it is useful for others"* ***(Male, 60 years old, With T2DM)***

However, most of these respondents stated categorically that they will only donate their faeces to researchers or medical personnel and not traditional doctors:

*"It is okay for us to donate our faeces because you are civilized researchers. We know that you are taking it, and it is meant strictly for research".* ***(Male, 66 years old, With T2DM)***

*"You (researcher) are taking these faeces from us so as to give us medical treatment. It is only the native doctor that one cannot give".* ***(Male, 76 years old, With T2DM)***

*"We are happy about it because you are not one of traditional herbal people who would tell someone to bring faeces that one would be fearful of what they would want to do with it. In fact, I don't see anything you require from me that I will not be willing to give".* ***(Female, 39 years old, With T2DM)***

On the contrary, it was observed that most of the respondents without T2DM agreed to donate their faeces only if they would be compensated:

*"If you make money from it, I also want a fair share of the profit"* ***(Female, 60 years old, Without T2DM)***

*"We will have to negotiate the compensation plan with my lawyer"* ***(Male, 52 years old, Without T2DM)***

Also, majority of the respondents did not consider the act of faecal donation as being overtly different from the donation of other samples:

*"They are same. We see it as similar. We have been donating blood sample before now. So, donating faeces is as well giving out something from your body."* ***(Male, 52 years old, Without T2DM)***

*"We can give any of them. There is absolutely no difference in the donation of faeces and other biological samples"* ***(Female, 60 years old Without T2DM)***

### 4.4 Factors influencing donation of faeces for gut microbiome research

All the respondents who were of the Yoruba tribe opined that the donation of faeces for use by another is a taboo due to potential diabolic implications while the two non-Yoruba participants had contrary beliefs.

*"Yoruba culture doesn't permit it."* ***(Female, 48 years old, With T2DM)***

*"…according to Yoruba culture, there is nothing they can't do with faeces in a wicked way. Yoruba culture doesn't permit giving faeces for any reason. In fact, when we excrete faeces in the farm we are advised to cover it with sand."*
***(Male, 52 years old, Without T2DM)***

*"Yoruba people are wicked. Yoruba culture doesn't permit it. There is a belief that faeces can be used to harm people and for money rituals if eaten with bread"* ***(Female, 44 years old, Without T2DM)***

A native of Kabba tribe (from Kogi) asserted that:

*"…our culture doesn't debar us from giving our faeces."*
***(Male, 60 years old, With T2DM)***

While the Ishan (in Edo *State*) participant noted:

*"I don't think that any culture is against it, because my culture is not against it".*
***(Male 39 years old, Without T2DM)***

Respondents (both Christians and Muslims) opined that their religion was not in opposition to the donation of their faeces in any way:

*"My religion doesn't stop me from giving out faeces or anything."* ***(Female 54 years old, Christians, With T2DM)***

*"My religion does not go against it."*
***(Female, 59years old, Moslem, With T2DM)***

Protection of participant's identity and dissemination of research findings also emerged as determinants of respondent's donation of faeces. Members of both study groups had different views about these. Pertaining to participant's identity, some of the excerpts were:
*"It is not good leaking someone's information".*
***(Female 56years old, With T2DM)***

*"… It would not be alright to link such to the people. The information should be kept secret."*
***(Male 27years, Without T2DM)***

*"My secret is secret with you (researcher)."*
***(Female 66 years old, Without T2DM)***

While in regards to results disseminations, respondents opined that:
*"It should not be personal because the researchers should be able to release it to the public, for them to benefit from it."*
***(Female, 64 years old, Without T2DM)***
***"****There should be a form of dissemination. In fact, we need feedbacks"* ***(Male, 66 years old, without T2DM)***

Discussants had divergent opinions on the issue of the monetary gains that may accrue from faeces donated for gut microbiome research. Majority of the participants with T2DM said they would freely donate their faeces as a form of humanitarian service and would not expect any benefit. Common responses given by these set of discussants were:

*"I will simply see it as my contribution to humanity"*
***(Female, 75 years old, With T2DM)***

*God says we should help our neighbors. I will help others with it freely."* ***(Male, 46 years old With T2DM)***

Some others without T2DM however believe they should gain from such benefits and should even have equal or greater share from such proceeds:

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*"If you make money from it, I also want a fair share of the profit; I have a share in it. If they come too often, I will like to have a share of the profit"*
***(Female, 58years, Without T2DM)***

*"It is my right but I won't be selfish. We would share it equally."*
***(Female 32years, Without T2DM)***

*"I will have a share. It is my own. They should take permission from me before they take any step on it. I need to be notified. This thing is market and I should have my fair share. I will take 90% and give them 10%."* ***(Female, 52years, Without T2DM)***

# CHAPTER FIVE

# DISCUSSION

This study revealed various opinions by the participants on the importance of faeces. A major finding of this study was that participants had varying knowledge about faeces and its importance to wellbeing. In line with other research findings, nearly all the participants agreed that faeces is a waste product which may be useless (Codron et al., 2005) and failure to excrete faeces in time may lead to great discomfort (van Baal, Leguit, & Brummelkamp, 1984).

Though the participants in this study were aware of the use of faecal samples for diagnostic purposes, they were largely uninformed about its role in gut microbiome research. The unawareness may not be surprising as similar observations were reported by Morgan & Hutterhower (2012) in a study conducted among gastroenterologists in Australia. A possible reason may be the general low level of research awareness (Morgan & Huttenhower, 2012; Taiwo & Kass, 2009) which is even worse among Nigerian patients than their counterparts (Marshall et al., 2006). As suggested by some participants, non-medical uses of faeces also exist but only one usefulness was identified – agriculture. Many authors have also highlighted the importance of faecal matter in agriculture (D et al., 2005; Wlasiuk & Vercelli, 2012) which in turn will boost a nation's economy (Ogen, 2007).

The participants' major ethical concern was the safe keeping of information obtained from the data generated in such studies. While some respondents remained indifferent as long as they had access to the results obtained, a large percentage of the participants wanted an assurance of confidentiality if they were to partake in such studies. Similar concerns had also been raised

among various groups in previous studies (Consortium et al., 2009; Heeney, Hawkins, De Vries, Boddington, & Kaye, 2010; Hoeyer, Olofsson, Mjörndal, & Lynöe, 2004).

The concept of ownership of biological samples donated for research has been a controversial topic (Hawkins & O'Doherty, 2011). While some studies showed that most donors of biological samples believe they own those samples (Moodley, Sibanda, February, & Rossouw, 2014), others found that the ownership has been transferred to the researcher during the process of giving informed consent (Lecky, Hawking, & McNulty, 2014). In the present study, both views- donors who believed they still own donated samples and those who believed that ownership have been transferred to researchers, were largely represented among the respondents in this study. Similar views were obtained from the studies carried out by Haga & Bekow (2008) and Vermeulen et al. (2009). This may be explained with the concept of right of property in which it is believed that a chip of an entity is still part of the entity whether it breaks off or not (Mahomed, Nothling-Slabbert, & Pepper, 2013). The concept of ownership is further engrained by the scientific knowledge that specific and unique data about a person can only be obtained from the cells, tissues or organs of such individuals (Mahomed et al., 2013). These explain why some individuals strongly believe in the ownership of whatever leaves their body including faeces, whether processed or not.

In the present study, the views of withdrawal of consent or demand for retrieval of faecal samples in the event of reversal of decision by donors were explored. We found that individuals who believed they own their donated samples also think that earlier donated samples should be returned to them if they were no longer interested in such research. Though in an earlier work published by Emanuel et al. (2000) on what makes a research ethical, it was noted that return of such earlier donated samples may be impossible as it may have had undergone irreversible transformation. However, Mahomed and his colleagues (2013) insisted that such participants retain the right to withdraw their consent at any time. The latter also supports Nuremberg Code and Council of International Organisations of Medical Sciences (CIOMS) guidelines on withdrawal of consent in the conduct of ethical research.

In this study, participants with T2DM were willing to donate their samples more readily and even without recourse to compensation. This may portray a desperate need by this group for a definitive cure. A similar observation had been noted among patients with various chronic conditions in six hospitals in the US (Kerath et al., 2013). However, the rising spate of research misconduct (Ana, Koehlmoos, Smith, & Yan, 2013; Sox & Rennie, 2006) may explain why

this study participants insist on donating their faeces to researchers or orthodox medical practitioners.

That respondents without T2DM insisted on financial compensation as a pre-requisite for the donation of their faeces for research may be explained with the social contract theory between resources' "providers" and "users" (Coleman, 1986; Gough, 1938). With this theory, parties in agreement believe that mutual benefits should exist between them (Gough, 1938). Though various studies have shown that research participants see the donation of different biological samples as having peculiar challenges (Kettis-Lindblad, Ring, Viberth, & Hansson, 2006; Wang, Fridinger, Sheedy, & Khoury, 2001), majority of the respondents in this study were largely indifferent. Some of the reasons adduced by the former include pain from needle pricks in blood sample donation, fear of manipulation of some samples over others and easy loss of donor's control (Grady et al., 2015). However, the latter may believe that all the different biological samples emanate from the same body (Group, 2016) and the ultimate goal of taking any is likely for diagnostic or therapeutic purpose.

Various tribes have cultural underpinnings for their beliefs and behavior (Rim-Rukeh, Irerhievwie, & Agbozu, 2013). Most African culture, especially the Yoruba tribe, generally believe that supernatural forces have a role to play in the health and survival of human beings (Jegede, 2002; Mackenzie, Rajagopal, Meilbohm, & Lavizzo-Mourey, 2000). They also believe that these diabolical powers can attack man through direct contact with human body and substances obtained from it (Jegede, 2002). This may explain why the Yoruba respondents may be aversive to the release of their faeces for whatever purpose.

Adherents generally opined that these two religions are not aversive to donation of their faecal samples for research. Though there have not been relevant studies to compare the latter finding with, this observation may be a pointer to the fact that the development of microbiome research in Nigeria may not experience a religion-based opposition.

Protection of donor's identity was a major ethical concern raised by most of the respondents in this study. Previous works on related topics revealed that the use of faeces in research raised similar ethical concerns- breach of confidentiality, information misuse, privacy, disclosure and stigmatization- among various study groups (de Vries et al., 2011; Jamal et al., 2014; McGuire et al., 2012)

Dissemination of research findings by authors from developing nations, including Nigeria, is one major aspect of research that has undergone significant improvement (Chan & Costa, 2005; Ezema, 2011) as this aspect is just gaining increased attention (Ezema, 2013). Specifically, respondents in this study emphasized the importance of one-on-one feedbacks to them and this may have stemmed from their previous experience with researchers who do not return to inform them of the research results. Christian (2009) however adduced this to the fact that respondents may no longer be traceable at the time of results' dissemination.

While majority of respondents with T2DM considered the donation of their faeces for microbiome research as a humanitarian service, a greater percentage of those without T2DM wanted a fair share of any commercial gain that may accrue from such. The desire to donate towards a research without expecting compensation may be due to innate tendencies to "give" while the latter may perceive their involvement in the research from a contractual standpoint. Given the possibility that commercial benefits may actually accrue from microbiome research (Hawkins & O'Doherty, 2011; Slashinski, McCurdy, Achenbaum, Whitney, & McGuire, 2012), ethical questions about the value and ownership of the faecal sample becomes controversial.

**Limitations of the study**

One of the major limitations of this study was the inability to determine the role of gender in relation to the research objectives. This was largely due to the over-representation of female gender in the AADM study population (M: F = 147:503) and the finding of more non-consenting males (M: F=21:2) at the study site. However, other variables were adequately explored.

Secondly, most participants were of the Yoruba tribe and this may be because the study was conducted in a hospital in southwest Nigeria, the latter being largely dominated by the Yorubas. These findings may not be generalized to patients in all hospitals due to different peculiarities, patients with T2DM or research participants for any study in general. This is because of the qualitative nature of the study which includes the small-sized study sample, open ended nature and the difference in the quality and quantity of information obtained from respondents and arriving at non-consistent conclusion.

# CHAPTER SIX

# CONCLUSION AND RECOMMENDATIONS

## CONCLUSION

In spite of the limitations noted above, this work appears to be the first in Nigeria and Africa to explore the ethics of donation of fecal samples for gut microbiome research.

Though the participants were largely ignorant about microbiome research and the use of faeces for such research, they readily identified the role faeces as a human waste-product which if not eliminated, poses a great danger to wellbeing and survival.

Views on ownership of faecal samples as well as retrieval of such sample in the event of withdrawal from research were largely divergent. Culture and religion appeared to be favourable factors to donation of faecal samples for microbiome research. However, privacy, protection of participant's identity, one-on-one feedback to donors and compensation were the recurring ethical concerns expressed by willing donors.

## RECOMMENDATIONS

Microbiome research is novel in Nigeria and the findings from this study may be significant in ensuring its success. This form the basis for the following recommendations:

- Researchers should be willing to share all necessary information on the research with the potential participants before the commencement of the study.
- The consent form should contain a clause on the sharing formula for potential benefits between research stakeholders.
- Consent forms should also specify various feedback strategies that researchers would employ to ensure participants are informed of the results of the research. The most acceptable and achievable one-on-one feedback option should be identified by the participant on the consent form.
- Various strategies to increase awareness on the conduct of ethically sound researches with much emphasis on the rights of participants should be employed across various institutions and organisations.
- Utmost confidentiality should be maintained in the conduct of microbiome research and other ethical concerns such as stigmatization and misuse of information should be avoided.
- Erring researchers should be penalized by the relevant Health Research Ethics Committees.

- More caution and close monitoring is encouraged on the part of the ethics committees that grants approval for microbiome researches so as to ensure proper feedbacks
- The result of this study should serve as a template for further ethical policy formulations as regards microbiome research and other researches.

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**INSTITUTE FOR ADVANCED MEDICAL RESEARCH AND TRAINING (IAMRAT)**
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UI/UCH EC Registration Number: **NHREC/05/01/2008a**

**NOTICE OF FULL APPROVAL AFTER FULL COMMITTEE REVIEW**

**Re: Ethics of Donation of Faeces for Gut Microbiome Research in Type-2 Diabetes**

UI/UCH Ethics Committee assigned number: UI/EC/16/0246

Name of Principal Investigator: **Ogwu-Richard Sandra O.**

Address of Principal Investigator: Department of Surgery,
College of Medicine,
University of Ibadan, Ibadan

Date of receipt of valid application: 01/08/2016

Date of meeting when final determination on ethical approval was made: **29/09/2015**

This is to inform you that the research described in the submitted protocol, the consent forms, and other participant information materials have been reviewed and *given full approval by the UI/UCH Ethics Committee.*

This approval dates from **29/09/2016 to 28/09/2017.** Note that no participant accrual or activity related to this research may be conducted outside of these dates. *All informed consent forms used in this study must carry the* UI/UCH EC *assigned number and duration of* UI/UCH EC *approval of the study.* It is expected that you submit your annual report as well as an annual request for the project renewal to the UI/UCH EC at least four weeks before the expiration of this approval in order to avoid disruption of your research.

*The National Code for Health Research Ethics requires you to comply with all institutional guidelines, rules and regulations and with the tenets of the Code including ensuring that all adverse events are reported promptly to the* UI/UCH EC. *No changes are permitted in the research without prior approval by the* UI/UCH EC *except in circumstances outlined in the Code. The* UI/UCH EC *reserves the right to conduct compliance visit to your research site without previous notification.*


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**Professor Catherine O. Falade**
Director, IAMRAT
Chairperson, UI/UCH Ethics Committee
E-mail: uiuchec@gmail.com

## APPENDIX 2

## INFORMED CONSENT FORM

IRB Research approval number: UI/EC/16/0246

This approval will elapse on: 29/09/2016

**Title of the research:** Ethics Donation of Faeces for Gut Microbiome Research in Type 2 Diabetics

**Name(s) and affiliation(s) of researcher(s) of applicant(s):** This study is being conducted by Ogwu-Richard, Sandra Olukemi of the Department of Surgery, University of Ibadan.

**Sponsor(s) of research:** West African Bioethics Training Programme

**Purpose(s) of research:**

As part of the requirements for the award of the masters' degree in Bioethics at the University of Ibadan, I will be conducting focus group discussion (FGD) to identify the perceptions and attitude of individuals to the use of their faeces for a gut microbiome research. The purpose of this research is to identify the ethical issues associated with the use of faecal samples for gut microbiome research.

**Procedure of the research, what shall be required of each participant and approximate total number of participants that would be involved in the research:**

A total of 48 to 80 participants will be recruited into the study. Each FGD will be engaged in a discussion with questions that bothers on ethics of donation of faeces for gut microbiome research. The discussions will be conducted at the State General Hospital, Adeoyo (the study site).

**Expected duration of research and of participant(s)' involvement:**

Each FGD would be conducted once and the duration of the discussion would not exceed an hour

**Costs to the participants, if any, of joining the research:**

I will be taking some of your time out of your busy schedule to participate in this discussion.
**Benefit(s):**

Participating in this study is an opportunity to represent the Nigerian populace in providing researchers with better approach in recruiting participants for microbiome researches. Findings from this study will facilitate a better and ethical approach in recruiting participants and promote a better procedure in conducting faecal microbiome research in Nigeria. This study will also serve as a template for subsequent studies on microbiome researches which will be beneficial to the entire Nigerian populace.

**Confidentiality:**

All information collected in this study will be kept by the researcher in secure location dedicated for purpose of this study and no name or any personal identifying information will be recorded. This cannot be linked to you in anyway and your name or any identifier will not be used in any publication or reports from this study. As part of my responsibility to conduct this research properly, officials from West African Bioethics Training Programme and National Health Research Ethics Committee may have access to these records.

**Voluntariness:**

Your participation in this research is entirely voluntary and if you choose to withdraw this will not affect your care and treatments in anyway.

**Alternatives to participation:**

If you choose not to participate, this will not affect your person, treatments, or status in any way.

**Due inducement(s):**

As a token to appreciate your participation; I will be giving you light refreshment but you will not be paid any fees for participating in this research.

**Consequences of participants' decision to withdraw from research and procedure for orderly termination of participation:**

You can also choose to withdraw from the research at any time. Please note that some of the information that has been obtained about you before you chose to withdraw may have been modified or used in reports and publications. These cannot be removed anymore. However, the researcher promises to make effort in good faith to comply with your wishes as much as is practicable.

**What happens to research participants and communities when the research is over:**

The researcher will inform you of the outcome of the research by giving you the details of the article when the result of the research is published.

**Any apparent or potential conflict of interest:** None.

**Statement of person obtaining informed consent:**

I have fully explained this research to _____ and have given sufficient information, including about risks and benefits, to make an informed decision.

DATE: _____SIGNATURE: _____

NAME: _____

**Statement of person giving consent:**

I have read the description of the research and have had it translated into language I understand. I have also discussed with the doctor to my satisfaction. I understand that my participation is voluntary. I know enough about the purpose, methods, risks and benefits of the research study to judge that I want to take part in it. I understand that I may freely stop being part of this study at any time. I have received a copy of this consent form and additional information sheet to keep for myself.

DATE: _____SIGNATURE: _____

NAME: _____

WITNESS' SIGNATURE (if applicable): _____

WITNESS' NAME (if applicable): _____

**Detailed contact information including contact address, telephone, fax, e-mail and any other contact information of researcher(s), institutional HREC and head of the institution:**

This research has been approved by the Ethics Committee of the University of Ibadan and the Chairman of this Committee can be contacted at Biode Building, Room 210, 2nd Floor, Institute for Advanced Medical Research and Training, College of Medicine, University of Ibadan, E-mail: **uiuchirc@yahoo.com** and **uiuchec@gmail.com**

In addition, if you have any question about your participation in this research, you can contact the principal investigator, Name: OGWU-RICHARD Sandra Olukemi

Department: Surgery Phone: 08033357004, 08030766687

Email: ksandemy@yahoo.com

PLEASE KEEP A COPY OF THE SIGNED INFORMED CONSENT.

## APPENDIX 3

### Demographic Survey

PARTICIPANT ID …….

### ETHICS OF DONATION OF FAECES FOR GUT MICROBIOME RESEARCH IN TYPE-2 DIABETES

INTERVIEWER'S NAME: …… DATE OF INTERVIEW: DD/MM/YR

STUDY SITE: …….....

SURNAME: ……..... FIRST NAME: ……

PHONE NUMBERS: …….

Tick '√' to answer the next sets of questions

**A.SEX:** 1. Male⬭ 2. Female⬭

**B. AGE**: **Date of birth:** DD/MM/YR

**C. ETHNICITY: (Please, tick)**

What tribe do you belong to? 1.Yoruba 2. Igbo 3. Hausa 4. Others, please specify: _____

**D. MARITAL STATUS:**

Are you married, widowed, separated, divorced, or have never been married?

1. Married⬭ 2. Widowed ⬭ 3. Separated ⬭ 4. Never been married ⬭

**E. RELIGION:**

1. Christian ⬭ 2. Moslem⬭ 3. Traditional⬭ 4. Others, please specify: _____

**F. EDUCATION:**

What is the highest grade that you completed?
1. Never attended ⬭ 2. 6 years of education or less ⬭ 3. 6 to 12 years of education ⬭

4. More than 12 years of education ⬭

## APPENDIX 4

## FOCUS GROUP GUIDE FOR DISCUSSION

**Brief information on faecal microbiome research**

*Gut microbiome research is a research in which we identify bacteria present in faeces by using advanced techniques to classify them based on their genetic materials. Recent research has shown that the knowledge derived from such research can explain a wide range of disease and health states including obesity, several types of cancer, diabetes mellitus. Because this research is new, uses genomics techniques and relies on biological samples, researchers throughout the world are keen to know the attitude of research participants to this type of research. The information derived from this research will guide the design and implementation of similar research projects in future.*

*Thank you.*

**Question 1**

What do you think or feel about faeces? Why do you think or feel this way?

Prompt: Do participants think it is valuable or it is a waste product of no value?

**Question 2**

If an individual feel that his /her faeces have value, what value does it have and how can that value be extracted or transformed?

Prompt: Is the value economic, religious, medical etc.?

**Question 3**

If you are asked to provide a faecal sample for gut microbiome research, will you be willing to?

**Probing question**: Why?

**Question 4**

Prompt: Describe genetic research?

Do you see donation of faecal samples for gut microbiome research and donation of other genetic materials similarly or do you think they are different?

**Probing question**: Why do you feel so?

**Question 5**

Would your preference be any different if you were donating what you might consider to be more sensitive samples e.g. blood, sperm or ovum?

**Brief Information**

*Institutions such as the government and ethics review committees make decisions about what research can and can't be done on human samples. Ethics review committees are usually made up of different experts such as of doctors, scientists, ethics experts and lay person*

**Question 10**
How does your religion or culture influence your donation of faecal sample for a microbiome research? Kindly explain based on the injunctions of your religion.

**Brief Information**
*Researchers often need to have access to the donor's medical records in order to be able to meaningfully interpret the results of the microbiome research. However, information, such as names or addresses are always removed and not included with the sample. This is so that the person who donated the sample cannot be identified by the scientist conducting the research or anyone analysing the results of the research. However, the sample may have a code so that someone not involved in the research can identify the individual if necessary.*

**Question 11**
Would you be happy with your medical records being linked to your faecal sample or would you have concerns?
**Probing question**: Why?

**Brief Information**
*Sometimes it can also be helpful for the researcher to have certain information about the lifestyle of the person who donated the faecal sample, for example whether they smoked, drank alcohol, how often they exercised etc. This information might help them to better understand the particular condition they are investigating.*

**Question 12**
Would you be happy for this information to be made available or would you have concerns about your lifestyle information being associated with your sample?
**Probing question**: Why?

***(Ownership of faecal sample)***

**Question 13**
If you decide to withdraw consent would you be happy for researchers to use the data that had already been generated up to that point using your faecal sample?

**Question 14**
What significance do you attach to your faecal sample once it has been removed from your body? Do you still see it as yours or part of you in some way?

Thank you so much for your time and comments, your various contributions shall promote a better procedure for microbiome research.
Discussion ends at…….