A pilot study of how individuals with Inherited Retinal Degenerative Disorders perceived being part of a genetic research programme.

by

Frieda Basson

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Supervisor: Assoc. Prof. J Greenberg **Co-supervisor:** Dr. M Futter

Division of Human Genetics

Department of Clinical Laboratory Sciences

University of Cape Town

DECLARATION

I, Frieda Basson, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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ABSTRACT

The successes of molecular genetic research studies depend on participants' willingness to donate blood specimens. It is thus important to explore the attitudes of individuals that participate in such studies to ensure that molecular genetic research studies are complemented by the participants' input.

This study used a qualitative research framework to explore how four individuals with inherited retinal degenerative disorders (RDD) in the Cape Town Metropolitan area perceived the experience of participating in the "Molecular Genetics of RDD in South Africa" research programme. Individual semi-structured interviews were conducted by the researcher as a means of better understanding the experience of the individuals' decision to participate in the research programme, their expectations of the research programme, the result-giving process and what the effect of knowing that a causative mutation had been detected had had on these individuals and their families. Qualitative thematic analysis was performed.

Overall, the study revealed that all the participants had positive attitudes towards participating in the research programme. The major motivations to participate were the hope of it leading to a cure for themselves and for future generations. The participants were all satisfied with the way in which they had been managed by the Division of Human Genetics. However the participants also recommended that an ophthalmologist as well as a genetic counsellor should be present at the result-giving session. There should be greater consistency in the correspondence from the Division of Human Genetics to each of the participants and improved communication between the Division of Human Genetics and the ophthalmologists who were managing them clinically. This study showed that the result of finding the RDD causative mutation does not necessarily have a profound impact on the family, since it does not change their situation significantly, as there is no treatment available. Although presymptomatic and prenatal testing is possible following the detection of the mutation, none of the families in this study had chosen to explore these options.

This was the first time that a genetic research programme in South Africa has been evaluated from the users' perspective. The findings of this study will help healthcare providers involved in the "Molecular Genetics of RDD in South Africa" research programme to become more insightful in meeting families' needs. The knowledge gained will lead to a better understanding of the motivation, concerns, and expectations of individuals and families regarding the research programme. This could potentially lead to improved and more appropriate genetic services and genetic counselling for individuals with RDD and their family members throughout South Africa.

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DEFINITION OF TERMS

Carrier testing The use of tests to determine whether a person is heterozygous for a recessive gene. Males or females are at risk of being carriers for autosomal recessive disorders, while only women are at risk of being carriers for X-linked recessive disorders

Genotype The genetic constitution of an individual (Mueller and Young 2001).

Heterozygous The state of having different alleles at a locus on homologous chromosomes (Mueller and Young 2001).

Macula The central area of the retina.

"Molecular Genetic of RDD in South Africa" research programme
The overall molecular genetic research programme conducted by the Division of Human Genetics at the University of Cape Town.

Multifactorial Influenced by many genes and the effects of the environment.

Phenotype The appearance (physical, biochemical and physiological) of an individual which results from the environment and the genotype (Mueller and Young 2001).

Photopic vision Daylight vision.

Prenatal testing The use of tests during a pregnancy to determine whether an unborn child is affected with a particular disorder (Mueller and Young 2001).

Presymptomatic testing The use of tests to determine whether a person has inherited a gene for a disorder before he/she has any symptoms or signs (Mueller and Young 2001).

Proband The first individual of each family to become part of the Molecular Genetics of RDD research programme.

This study This qualitative study of how individuals with Inherited Retinal Degenerative Disorders perceived being part of the "Molecular Genetic of RDD in South Africa" research programme.

LIST OF ABBREVIATIONS

CINAHL	Cumulative Index Literature of Nursing and Allied Health Literature
RDD	Retinal Degenerative Disorders
RP	Retinitis Pigmentosa
UCT	University of Cape Town
UK	United Kingdom
USA	United States of America

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Chapter 1

INTRODUCTION

1.1 INTRODUCTION

"Disabled individuals will have different views on genetics, depending on their own experiences and outlooks: some will welcome screening, because of the suffering they have personally experienced. Others will oppose screening, because it is very difficult to support a practice which would have prevented one's own existence. It is important... to develop rational arguments about the value of disabled people's lives and their views, which are likely to be varied and reflective." (Shakespeare 1998:674)

In this introductory chapter the researcher outlines the issues at the time of the study regarding research and testing for inherited Retinal Degenerative Disorders (RDD). The chapter concludes with the motivations for the study, the aim and the objectives.

1.2 RDD RESEARCH IN SOUTH AFRICA

The "Molecular Genetics of RDD in South Africa" research programme was initiated by the Division of Human Genetics at the University of Cape Town (UCT) in 1990 and continues to carry out research, investigating various forms of genetic blindness (Greenberg and Ziskind 2001). The short-term objective of the research programme was to define the genetic profile of subjects with RDD in South Africa. The long-term objective was to establish a genetic registry of individuals with RDD which contained comprehensive information relating to phenotype and genotype. This was in preparation for possible future treatments and was aimed at improving the management of individuals affected with any of these conditions as well as at-risk family members (Greenberg and Ziskind 2001). The Division of Human Genetics developed a protocol (Appendix I) for both the delivery of genetic results and the management of individuals who are at risk of RDD. Incremental changes were made to the protocol in 2004 (Appendix II) to include the involvement of genetic counsellors in this genetic service that forms part of the "Molecular Genetics of RDD" research programme.

Retina South Africa is a foundation that represents conditions including: Retinitis Pigmentosa, Macular Degeneration, Usher Syndrome and more than 200 other rare conditions. The foundation has played a crucial role in the financial as well as patient support for this research programme, offering support, education and counselling to affected people and their families.

The Department of Human Genetics at the UCT has done groundbreaking research on RDD. Two novel gene loci were localised (RP13 in 1994 and RP17 in 1995) and the corresponding genes causing these two forms of autosomal dominant RP were later identified (McKie *et al.* 2001; Rebello *et al.* 2004). These findings confirm that this research programme had been beneficial to science by improving the understanding of the causes of these forms of inherited blindness. Testing for RDD was not a fully developed diagnostic service at the time of this study, but an evolving genetic service that formed part of the research programme.

If the causative mutation in a family was found during the research programme, testing could subsequently be offered to the rest of the family in the form of confirmation of diagnosis, presymptomatic, prenatal or carrier testing (Greenberg and Ziskind 2001). "Presymptomatic testing is the use of tests to determine whether a person has inherited a gene for a disorder before he/she has any symptoms or signs." ... "Prenatal testing is the use of tests during a pregnancy to determine whether an unborn child is affected with a particular disorder" (Mueller and Young 2001:356). Carrier testing is the use of tests to determine whether a person is heterozygous for a recessive gene. Males or females are at risk of being carriers for autosomal recessive disorders, while only women are at risk of being carriers for X-linked recessive disorders (Mueller and Young 2001).

The proband (first individual of each family to become part of the Molecular Genetics of RDD research programme) was contacted and was informed that the causative mutation in the family had been found. The result was given to the proband either by the registered genetic counsellor in the Division or by the ophthalmologist managing the individual. The probands were expected to convey

the information they had received to the rest of their families. Other family members could then approach the Division of Human Genetics to be informed of these results and pursue genetic testing should they choose to do so.

At the time of this study the genetic database of the "Molecular Genetics of RDD in South Africa" research programme consisted of DNA from 2705 individuals from 1028 families (as at 27 July 2005). UCT was the only centre where RDD mutation detection was conducted in South Africa, thus these figures reflected the entire population of individuals with RDD that had participated in the research programme in South Africa. Since the initiation of the programme in 1990, the causative genetic mutations had been identified for 37 families. At the time of this study only 13 families throughout South Africa had received their results. The reasons for this small number were limited resources; the fact that some family members did not respond to letters indicating that their mutation detection results were available; difficulties in tracking families due to relocation; and deceased family members. There was a limited number of staff involved in the research programme that were able to counsel individuals and to deliver their results. A registered genetic nurse and the co-principal investigator of the research programme (who is a genetic counsellor) were involved in delivering results but no other genetic counsellors formed part of this programme. At the time of this study 4 families in the Cape Town Metropolitan area had received their results.

1.3 MOTIVATIONS FOR THE STUDY

Scientific publications arising from the RDD research proved that the "Molecular Genetics of RDD in South Africa" research programme had been beneficial to science (McKie *et al.* 2001; Rebello *et al.* 2004). However, the purpose of this current study was to investigate whether it had been beneficial to the individuals and families involved, and thus to complement the scientific research by assessing the attitudes of the participants towards the research programme.

This study will help healthcare providers involved in the "Molecular Genetics of RDD in South Africa" research programme to become more aware of and insightful

in meeting the families' needs. It is anticipated that the knowledge gained will lead to a better understanding of the motivation, concerns, and expectations of individuals and families regarding the research programme. This could potentially lead to improved and more appropriate genetic services and genetic counselling for individuals with RDD and their family members throughout South Africa.

1.4 AIM

The aim of this study was to explore how individuals in the Cape Town Metropolitan area with inherited RDD perceived being participants in the "Molecular Genetics of RDD in South Africa" research programme.

1.5 OBJECTIVES

1. To explore the motivations and concerns of the individuals when deciding to participate in the RDD research.
2. To explore their expectations of the research programme related to the causative family mutation and their personal contribution to science.
3. To investigate how the individuals perceived the experience of participating in the molecular genetics research project and the rest of the family being offered testing after the identification of the mutation in the family.
4. To investigate the impact that the detection of the causative genetic mutation has had on the individual and other family members.
5. To determine how participants perceived the way in which they were managed, counselled and supported by the research team and health care providers.
6. To inform and counsel the participants, where needed, and to provide a therapeutic platform for them to discuss their experiences relating to RDD.

1.6 ORGANISATION OF THIS DISSERTATION

Chapter 2 consists of a literature review of the clinical aspects of RDD; genetic counselling of RDD; and public attitudes towards genetic testing and research. Chapter 3 describes the methodology and the research process of the study. The findings and discussion are presented in chapter 4. The conclusion is presented in chapter 5 and recommendations in chapter 6.

Chapter 2

LITERATURE REVIEW

2.1 INTRODUCTION

This chapter includes literature reviews of the clinical aspects of RDD, the genetic counselling of RDD and public attitudes towards genetic testing and genetic research in general. Literature searches were performed using PubMed, CINAHL (Cumulative Index Literature of Nursing and Allied Health Literature), EBSCOhose and Google Scholar research databases. Search terms used were "research participants attitudes", "subjects' attitudes towards research participation", "genetic counselling", "retinal degenerative disorders", "inherited retinal degeneration", "retinitis pigmentosa", "macular dystrophy" and "management". There was a limited amount of literature available on genetic counselling related to RDD, while that of counselling associated with other disorders (such as Huntington disease and familial breast cancer) was more prolific, but not relevant to this study. The literature discussed in this chapter mostly refers to research conducted in developed countries, such as the UK and USA. The remainder of the literature was from outside Africa, except for some articles from the Division of Human Genetics at UCT, South Africa. Therefore, most of the literature discussed does not directly relate to South Africa. In addition, a hand search through the UCT, Faculty of Health Science Medical library was performed in an attempt to obtain non-published literature on RDD.

2.2 CLINICAL ASPECTS OF RDD

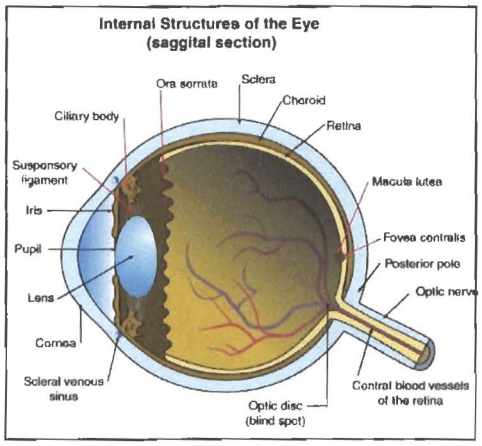


Figure 1: A diagram to illustrate the anatomy of the eye (http://www.mscd.edu/).

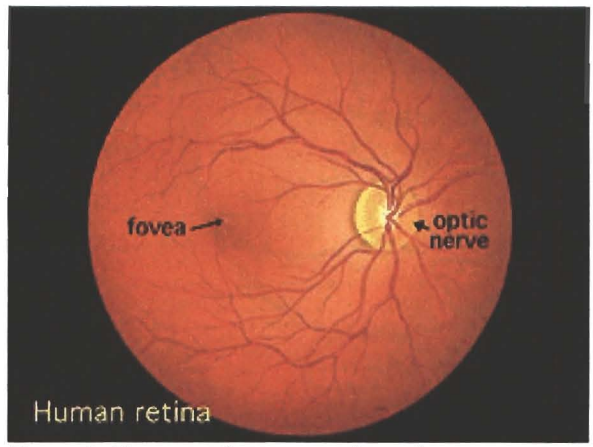


Figure 2: Human retina as seen through an ophthalmoscope (http://webvision.med.utah.edu/).

"Approximately one third of all human inherited diseases include defects of the eye" (Hims *et al.* 2003:120). This might be due partly to the non-lethal nature of eye defects and the obvious presentation of retinal disorders (Hims *et al.* 2003). RDD are a heterogeneous group of diseases that cause visual loss due to premature death of rod and cone photoreceptor cells. Inherited RDD affect approximately 1 in 2000 individuals worldwide (Sohocki *et al.* 2001). The pathogenesis of retinal degeneration is complicated. The involvement of the genetic aspects is well established, but there is increasing evidence that environmental factors may also play a role (Yu and Cringle 2005). The types of inherited RDD relevant to this study are retinitis pigmentosa, macular degeneration and Sorsby fundus dystrophy. Although there are numerous other disorders that form part of the RDD group of diseases, they are beyond the scope of this study.

Retinitis Pigmentosa

Retinitis pigmentosa (RP) is the most common RDD that is clearly hereditary (Rivolta *et al.* 2002). It is a leading cause of blindness with a worldwide prevalence of 1:3000 to 1:5000 (Kalloniatis and Fletcher 2004). The primary causes of RP include defects in the visual pigment, defects in the proteins important for photoreceptor function and defective enzymes involved in visual transduction. The proposed pathway of cell death is through apoptosis, a form of programmed cell death (Kalloniatis and Fletcher 2004). Initially the rod cells are lost and individuals

present with night blindness and this is followed by a progressive loss of cone cells. Symptoms include elevated dark adaptation thresholds and loss of peripheral vision with progressive constriction of the visual field, which eventually leads to blindness after several decades (Hamel 2003). The death of the photoreceptor cells is usually accompanied by changes in the retina such as the abnormal accumulation of pigment, attenuation of the blood vessels and pallor of the optic disc (Greenberg and Peters 1995).

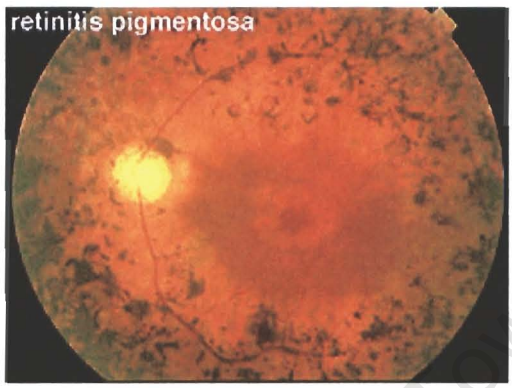


Figure 3: Photograph of the retina of a patient with Retinitis Pigmentosa (http://webvision.med.utah.edu/).

Macular Degeneration

Another form of RDD is macular degeneration. The macula of the eye is a cone-rich area which lies in the visual axis and plays a major role in daylight (photopic) vision (Greenberg and Peters 1995). Individuals with macular degeneration lose the rods and cones of the macula (central retina), while the photoreceptor cells in the retinal periphery are spared (Rivolta *et al.* 2002). Cell death in this relatively small region causes severe deterioration of visual acuity and photopic vision, being maximal in the central visual field. The majority of macular degeneration cases are age-related or associated with diabetes mellitus. However, about 10% are due to genetic causes, thus contributing significantly to familial blindness (Greenberg and Peters 1995).

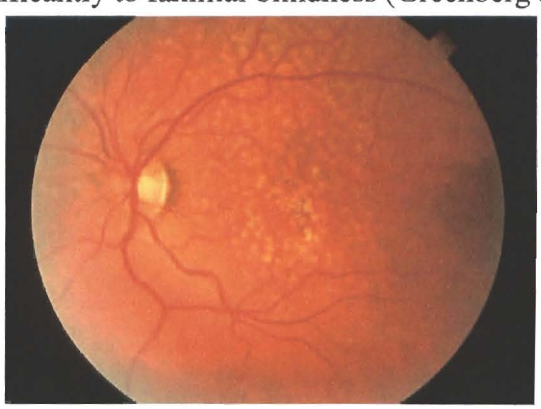


Figure 4: Photograph of the retina of a patient with Macular Degeneration (http://www.ohiovalleyeye.com/).

Sorsby Fundus Dystrophy

Sorsby fundus dystrophy is a rare autosomal dominant form of macular degeneration. Individuals with this disorder report night blindness in young adulthood and later experience sudden decreased vision loss associated with sub-retinal neovascularisation and haemorrhage. Progressive peripheral vision loss can occur at later stages (Berson 1999, Peters and Greenberg 1995).

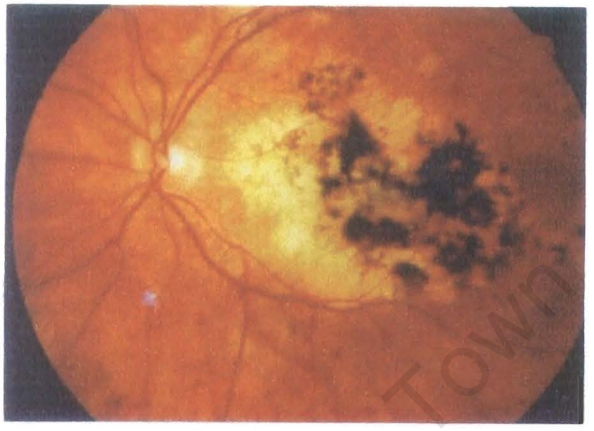


Figure 5: Photograph of the retina of a patient with Sorsby Fundus Dystrophy (Peters and Greenberg 1995).

The management of individuals with RDD is complex due to the following reasons:

Broad usage of the term RDD:

"Inherited retinal degeneration" is a very broad term used to describe a number of categories of RDD. The term encompasses inherited forms of visual impairment that affect the peripheral retina such as retinitis pigmentosa and congenital stationary night blindness; disorders that affect the central retina such as macular degeneration; and others in which the pattern of degeneration is complex such as choroideremia (Greenberg *et al.* 1999). The boundaries separating some of the diagnostic categories are also not distinct (Rivolta *et al.* 2002).

Heterogeneity:

The extent of the heterogeneity seen in inherited RDD has hampered molecular diagnosis (Hamel 2003) and has the following clinical implications:

"Genetic heterogeneity – mutations in different genes may cause the same retinal disease;

Allelic heterogeneity – many different disease-causing mutations are found in most RDD genes;

Phenotype heterogeneity – different mutations within the same gene may produce different clinical phenotypes; and

Clinical heterogeneity - the same mutation in different individuals, even within the same family causing different clinical symptoms."

(Daiger 2004:19).

Different patterns of inheritance:

RP can follow any of the classical inheritance patterns. It can thus exhibit an autosomal dominant, autosomal recessive, X-linked recessive or mitochondrial inheritance pattern in a specific family. However, some families with RP may even have more complex inheritance patterns, but this is beyond the scope of this study. Many forms of macular degeneration are also monogenic and have classical inheritance patterns, but the most common form, age-related macular degeneration, is multifactorial. A small portion of individuals with inherited RDD are considered to have syndromic disorders due to the association with other extraocular manifestations, for example, RP associated with hearing loss in Usher syndrome (Rivolta *et al.* 2002).

Variable age of onset and rate of progression:

RDD display marked variation in the age of onset and progression of the disease. Traditionally it has been thought that the progression of visual dysfunction is slowest in those with autosomal dominant RP, followed by recessive RP and that it is fastest in those with X-linked recessive RP. Molecular genetic techniques have subsequently both proved and disproved this clinical view (Kalloniatis and Fletcher 2004).

Absence of any efficient treatment:

Retinal degeneration is currently incurable and there are no established treatments proven to slow down the degenerative process (Yu and Cringle 2005). The management is restricted to sunlight protection, vitamin A supplementation and management of the complications of cataract and macular oedema (Kalloniatis and Fletcher 2004, Berson 1999).

The present data concerning the effects and safety of vitamin A intake supports the idea that, at least in some forms of RP, the development of the disease can be positively influenced with vitamin A supplementation, without side effects (Berson *et al.* 2004). However, there has been much debate around the effectiveness of vitamin A supplementation.

Medical intervention for Sorsby fundus dystrophy using argon laser treatment (Holtz *et al.* 1994), photodynamic therapy (Wong *et al.* 2003) and steroid therapy (Atan *et al.*

2004) have all evolved over the past 10 years and appear to have been effective. Due to the above mentioned advances, early investigation and management is the key to delaying the onset of the serious blinding complications of this disease.

Therapeutic strategies are in the process of being intensively researched; these include gene-based therapy, neuroprotection and retinal prosthesis (Kalloniatis and Fletcher 2004).

Psychosocial management of RDD patients

Health care providers are confronted with patients with RDD to whom they can offer no therapy. These patients have to adjust and adapt continuously to their visual loss which means constantly giving up everyday activities which they are no longer capable of performing. Individuals with RDD and their families face a lifetime of coming to terms with the disease and coping. Management of these individuals should include assistance, advice and support from health care providers according to the symptoms that develop during the disease (Guignard 1990).

2.3 THE PSYCHOSOCIAL IMPACT OF RDD

As mentioned in the previous section (section 2.2), there is variation in the age of onset, severity and rate of disease progression in the different types of RDD, which makes accurate prognosis challenging. However, all RDD involve some degree of visual impairment which leads to various degrees of disability. A disability, whether mild or severe, can significantly impact a person's day-to-day living and most individuals need to adapt alternate ways to function in every day life. It has been said that blindness is one of the most severe disabilities to affect an individual, his or her family and society (Brezin *et al.* 2005).

Loss of sight has a major impact on the emotional well-being of individuals and their families. The progressive loss of vision which is experienced by individuals with RDD leads to grieving for loss of the previous function, which causes frustration, sadness and depression. The progressive nature of this group of disorders causes ongoing loss and bereavement throughout the lives of these individuals and their families. Psychological counselling is beneficial to facilitate individuals in dealing with their emotions and adapting to their continuously changing lives within their occupational, family and community environments (Lloyd 1994).

Hayeems *et al.* (2005) reported that individuals with RP experience functional and psychological challenges as they adjust to progressive loss of visual function. These challenges are related to education, employment, mobility, socialisation, psychosocial

development, use of assistive technology and mental health. They also reported that adjusting to RP entails a certain degree of suffering. Such suffering may manifest as denial, anger, fear or depression.

Brezin *et al.* (2005) evaluated the social consequences of blindness in France through a national survey. Their findings showed that individuals with visual impairment needed more assistance with daily activities and house modifications than individuals with no visual problems. Individuals with blindness or low vision had fewer paid activities, lower monthly household incomes and many of them were registered for social allowances.

The secondary effects of vision loss include depression, functional limitations, lower quality of life, psychological distress and disability. Severe vision loss is associated with high levels of emotional distress and reduced quality of life, primarily through its disabling effects on the ability of individuals to perform activities of daily living. Even in those patients without clinical depression, the psychological impact of vision loss is profound. Finding suitable employment can also be a problem for visually impaired individuals who desire to work. Vision loss is thus a multifaceted problem affecting many aspects in the affected individuals' lives as well as that of their families (Gieser 2004).

The genetic nature of RDD may impose several challenges for families. Individuals with a genetic disorder and their families may experience ostracism and isolation from their family members and their communities. Parents may experience feelings of guilt, shame and remorse at the possibility of having passed on a serious condition to their children (Knebel and Hudgings 2002).

Parents may also have concerns about future reproductive decisions. Even though prenatal testing for RDD is technically possible, prenatal testing for any disorder which is not life threatening is controversial. Tessitore *et al.* (2002) were the first to perform prenatal diagnosis for RP. They primarily reported on the technique that was used, but commented that this technique may provide earlier diagnosis and in association with proper genetic counselling, may support families in making critical decisions about possible termination of pregnancy.

There is no treatment available for RDD before or after birth. Thus, a positive prenatal test result creates decisions for parents including the possibility of terminating the pregnancy. This may cause an ethical dilemma for a couple, who may not want to make such decisions and may not choose to pursue prenatal testing (Lea *et al.* 2005).

Even though it is the role of the genetic counsellor to inform parents of the benefits, risks and limitations of their options in order for them to make informed decisions, studies have also shown that prenatal testing decisions are often based on facts other than those presented during counselling (Hunt *et al.* 2005). These factors include the meaning of the pregnancy for the parents, their personal attitudes towards abortion and disability and their spiritual beliefs. It is thus important to take into account the individual perceptions, moral values and circumstances of each patient (Tercyak *et al.* 2001).

Predictive testing for RDD is a controversial issue. Three clinical ophthalmic geneticists provided opinions on the problems of predictive testing in an ophthalmic setting of Autosomal Dominant RP to debate this issue in the British Journal of Opthalmology. The controversial issues include the fact that there is currently no treatment for RP, the unpredictability of the phenotype and predictive testing of children. Further research is needed to clarify the penetrance and expressivity of the different mutations due to the extent of heterogeneity seen in inherited RDD (Mackey *et al.* 2003).

2.4 GENETIC COUNSELLING OF RDD

Genetic counselling is to educate, manage and counsel individuals and families diagnosed with, or at risk of, genetic diseases and how they affect the psychological, medical, financial and social aspects of one's life (Bennett *et al.* 2003).

The main elements of genetic counselling are:

- Documentation of family and pedigree information;
- Diagnostic and clinical aspects;
- Recognition of inheritance patterns and risk estimation;
- Communication and empathy with those seen;
- Information on available options and future measures; and
- Support in decision-making and for decisions made (Harper 2004).

Genetic counselling of RDD is complicated by the complex genetic characteristics of this group of diseases, as mentioned previously (section 2.2).

Emery and Smith (1970) established that only a minority of individuals at high risk for transmitting a serious disease received genetic counselling at the time. In response to this Bundey and Crews (1982) evaluated the perceptions and attitudes towards genetic counselling of individuals with RP. Their results showed that the majority of individuals with RP wished to receive genetic counselling in spite of the variable severity of the condition. The authors

recommended that genetic counselling should form part of the routine management of individuals with RP.

In a nationwide survey of individuals affected with RP and their relatives conducted in the USA, data were generated on the patient's perceptions of the clinical aspects of the disease, family history and the understanding of the disorder (Baughman and Caldwell 1982). The authors emphasised the importance of genetic counsellors understanding the limitations of the diagnostic evaluation. They encouraged co-operation between counsellors and ophthalmologic diagnosticians and claimed that, due to the lack of available treatment, genetic counselling and supportive follow-up should be viewed as an essential service.

A qualitative research study on "The lived experience of Retinitis Pigmentosa" conducted in Cape Town, South Africa described how the life of an individual with RP was one of continual challenge. The themes identified in this study included the physical, psycho-emotional, spiritual and socio-economic impact of living with RP, negative experiences on seeking medical help and the supportive role of the family. This study emphasised the importance of psychological and vocational counselling (Lloyd 1994).

Jay and Evans (1996) discussed the increasing need for informed genetic counselling in ophthalmic practice due to increased patient demand, improved diagnostic techniques allowing improved prognostication and the availability of molecular genetic information. They reported that the increasing need for ophthalmic genetic counselling was beyond the scope of the general ophthalmologist. They described ophthalmic genetic counselling as a time-consuming, potentially emotive undertaking, requiring detailed knowledge which could have profound effects on the futures of patients. They recommended the interdisciplinary team involvement of ophthalmologists, an obstetric unit, molecular genetic laboratory and high quality psycho-social support.

In an online review of RP on the Orphanet Encyclopaedia (updated July 2003), Hamel included sections on the management of blind individuals, genetic counselling and antenatal diagnosis. He advocated that psychological help is often necessary when reaching milestones in the course of the disease such as diagnosis of the disease, occurrence of mobility difficulties and loss of reading. This support could be provided by both professionals and support groups. Since all genetic forms can be encountered in RP, Hamel advised that all patients with RP receive genetic counselling. Antenatal diagnosis of RP was recognised as an ethical issue as RP is a non life-threatening disease and the justification of the investigative risks associated with amniocentesis is, therefore, questionable (Hamel 2003).

In a recent review of the presentation, mechanisms and management of RP by Kalloniatis and Fletcher (2004), genetic counselling was recommended for all patients with RP. However, they recognised that the complexity underlying the different RP phenotypes may necessitate expert genetic and ophthalmic counselling (Kalloniatis and Fletcher 2004).

Rebello *et al.* (2003) emphasised the implications for the rest of the family when a diagnosis of RP was made in an individual and the causative mutation found. Pre-symptomatic and/or diagnostic testing could be offered to individuals. However, should the individuals not have had any prior exposure to the idea of inherited risk for RP, genetic counselling should be provided.

Greenberg *et al.* (2003) described a particular case of a patient with RP that highlighted some of the problems associated with genetic testing in general and how they attempted to address some of the difficult universal issues. They suggested that the ethical issues regarding genetic testing had not been addressed in the context of RDD. Ethical issues included the extent to which testing of potential carriers should be pursued, whether and how to inform family members of molecular findings and the testing of children. The authors regarded ophthalmic genetic counselling as extremely important. They argued that people's misconceptions and misinformation could cause fear of modern technology resulting in them declining genetic testing. They, therefore, recommended that a detailed description of the consequences of different phenotypes, modes of inheritance and molecular genetic information should be carefully explained by genetic counsellors to the individuals concerned. They stated that a defined structured approach is essential to manage the delivery of genetic testing results and have developed a protocol (Appendix I) for both the delivery of genetic results and the subsequent management of individuals who are at risk of genetic disease.

2.5 PUBLIC ATTITUDES TOWARDS GENETIC TESTING & RESEARCH

The researcher found limited literature available detailing how individuals with a genetic disorder and their family members perceive being part of a genetic research project and their attitudes towards the counselling and testing services that are offered. In this section the researcher outlines the research that has been done on the attitudes of the general public towards genetic research in general as well as one study on individuals' willingness and motivating factors to participate in a genetic research study of Hereditary Pancreatitis as a point of reference.

The mapping and sequencing of the human genome has resulted in the rapid development of genetics and genomics (Burke and Emery 2002). Through genetic research clearer understanding of the pathogenesis of a variety of genetic conditions has been developed (Begleiter 2002). Knowledge of the genetics of common and complex diseases is growing at an unprecedented rate and, as a result, opportunities for genetic testing are increasing and other applications of genetic technology, such as pharmacogenetics and gene-based therapies are being actively investigated (Burke and Emery 2002). These profound technological advances have potential implications on a variety of societal values and institutions (Singer *et al.* 1999).

The rapid progress being made in the area of genetic testing provides an opportunity to study the relationship between technological and social change. A variety of social changes precipitated by technology include effects on the institution of the family, medical care as well as life and health insurance (Singer 1991). As new genetic tests are introduced into public health and medical practice there are many medical, scientific, ethical, legal and social concerns that should be considered. Predictive genetic testing for adult-onset diseases raises concerns about screening in the absence of effective interventions, the ethical acceptability of screening children and the prospect of complicated decision making and counselling (Gollust *et al.* 2005).

Several studies have investigated public attitudes towards genetic testing and genetic research. Singer (1991) reported the results of a telephone survey designed as a measure of attitudes towards genetic testing of a sample of the adult US population. Their findings included the following:

- Attitudes towards prenatal testing for genetic defects were overwhelmingly favourable;
- Information about genetic testing was not yet widely dispersed in society;
- Belief in the accuracy of the technology was one of the strongest predictors of favourable attitudes towards testing;
- Attitudes towards testing for genetic defects in the foetus and the attitudes towards abortion if the tests are positive appeared to be distinct;
- Testing for foetal sex was clearly not seen as acceptable practice; and
- The image that came to mind when asked about serious genetic defects were primarily that of Down syndrome and other disorders that involve intellectual disability, while physical disabilities were mentioned less frequently.

Shaw and Bassi (2001) reported on lay attitudes towards genetic testing for susceptibility to inherited diseases. Their questionnaire was designed to assess the general public's attitudes towards many of the personal and societal issues surrounding genetic testing. Their results

demonstrated that people's attitudes towards genetic testing for inherited diseases are complex constructs that cannot be captured in one or two questions. Respondents were generally optimistic about the potential benefits of genetic tests and attitudes were associated with personal interest in being tested. Respondents' interest in being tested was affected positively by the high predictive value of the test and the availability of a cure, whereas respondents were least likely to undergo testing for a severe disease with no cure. Their results demonstrated that controllability and predictability are two distinct motivations for engaging in genetic testing. This study showed that respondents were wary of granting access to genetic testing results to anyone other than doctors and family members and did not want the government, religious leaders or the courts involved in regulating genetic testing.

Wang *et al.* (2001) assessed the public attitudes regarding the donation and storage of blood specimens for genetic research. The American Healthstyles Survey (1998) of health attitudes and behaviour included four questions regarding blood donation and storage for genetic research. Forty three percent (1122/2621) were in favour of both blood donation and long-term storage; 37% (943/2621) were in favour of either donation or storage, but not both; and 21% (556/2621) were not willing to donate blood or have it stored for genetic research. Their results showed that respondents with a positive attitude towards donation and storage of blood for genetic research included persons who favour participation in government research in general, persons who believe that genetic research would prevent disease in the future and those believing that genes are more determinant of a person's health than behaviour or environment. Their findings demonstrated that attitudes towards blood donation/storage for genetic research were indirectly associated with demographics, including education, race and positive family history of a genetic disorder.

In the light of future population-based studies to determine gene variants across ethnic groups that would lead to a better understanding of disease causation, Wong *et al.* (2004) explored and compared individuals' concerns of participation in genetic research across three ethnic groups in Singapore. Focus groups among 98 participants revealed that concerns were diverse, with all ethnic groups expressing anxiety about breach of confidentiality, finding out that they have a disease and misuse of research for cloning. The Malay-Muslim ethnic group were generally concerned about potential racial discrimination, the selection process and religious beliefs regarding blood storage. The Chinese and Indian ethnic groups were concerned about giving blood to strangers and being inconvenienced by participating. Their qualitative investigation provided greater insights on ethnic-specific concerns that should be addressed before planning campaigns to encourage community participation in genetic research.

Gollust *et al.* (2005) researched community involvement in developing policies for genetic testing. They proposed that individuals affected with genetic conditions should have a role in policy decisions about genetic testing. They considered different mechanisms for promoting participation including membership on advisory committees, community dialogues and surveys that provide evidence for supporting practice guidelines. Their recommendations included that future research of affected communities' interests should be pursued so that underrepresented voices of affected individuals could be included.

Bates *et al.* (2005) conducted a focus group study in the USA of public understandings of genetics. They outlined the warrants or publicly accepted "good reasons" for accepting some aspects of genetic technology and for rejecting other aspects. The warrants presented by the participants indicated that the public has a complex, informed understanding of genetic research, although not a technical understanding. The concerns that were raised as well as the benefits stated by participants during the focus groups regarding genetic research are listed below.

Concerns:

- Genetic discrimination in employment.
- Genetic discrimination in insurance.
- Privacy concerns.
- Generalised cloning.
- Racial discrimination.
- Changes in familial expectations /designer babies.
- Creation of "master race".
- Unequal economic access to benefits.
- Government or corporate exploitation.
- Offence to religion.
- "Playing God".
- Side effects/accidents.
- Other.

Benefits:

- Prevention and treatment of genetically linked disease.
- African Americans benefit from inclusive research protocols.
- Other.

Applebaum-Shapiro *et al.* (2001) determined that the major motivating factors behind individuals' willingness to participate in a Hereditary Pancreatitis genetic research study were to obtain genetic testing and to help other family members and future generations. However, a major concern of those participating was the perceived possibility of insurance companies discriminating against them on the grounds of the research findings. They also demonstrated

that genetic testing has an impact not only on the patient, but also on his or her extended family.

In an ethical review of research into rare genetic disorders by Parker *et al.* (2004) they discuss the distinction between clinical practice and research. They underlined the necessity of conducting research into the attitudes of families with inherited disorders regarding key ethical values.

The literature reviewed above highlights the importance of evaluating the attitudes of affected individuals and families involved in genetic testing programmes. However, the limited amount of literature exploring the attitudes of individuals participating in genetic research stimulated the researcher to conduct this study.

Chapter 3

RESEARCH METHODOLOGY

3.1 INTRODUCTION

This study aimed to explore the attitudes of individuals that had been involved in the "Molecular Genetics of Retinal Degenerative Disorders in South Africa" research programme. In this chapter the methodological process is described and issues pertaining to the research conducted are discussed. The reasons for having selected particular methodologies are provided, potential sources of bias are identified and attempts made to minimise these biases are described in the relevant sections.

3.2 RESEARCH DESIGN

This qualitative research project was designed as a prospective cross-sectional descriptive study conducted in partial fulfilment of the MSc Genetic Counselling course.

3.2.1 Qualitative Approach

A qualitative approach was selected as it attempts to describe, interpret and understand the research topic through the views and meanings ascribed to it by the sample population (Mason 2002). The knowledge gained through qualitative research can contribute to theory, practice and policy (McMillan and Schumacher 2001). The results of this study were intended to contribute to the practice and policies of the RDD molecular genetic service at the University of Cape Town and the rest of the country.

In contrast to quantitative research, qualitative research is based on the premise that people have different views on reality and that as a result there are multiple realities. In qualitative research both participants and the researcher actively participate in creating meaning in a situation (Smith *et al.* 1995).

In this cross-sectional study data were collected by means of interviews conducted with the participants. This method is less costly and simpler than longitudinal

research, but the disadvantage is that it does not capture social processes or change over a period of time (Neuman 1999).

A descriptive study design is concerned with the current or past status of some phenomenon. This type of study describes the attitudes, behaviours, achievement or other characteristics of a group of subjects (McMillan and Schumacher 2001). Descriptive research provides valuable data, particularly when first investigating an area (McMillan and Schumacher 2001). The attitudes of individuals with inherited RDD who had been part of a molecular genetic research programme were thus described in this study. As this was a pilot study investigating the RDD molecular genetic service from the user's point of view, a descriptive design was an appropriate method.

3.3 SAMPLE

3.3.1 Population

The population consisted of the 13 families in South Africa who had received the information that their RDD causative mutations had been identified by the "Molecular Genetics of RDD in South Africa" research programme. The Division of Human Genetics at UCT is the only centre where RDD mutation screening is conducted in South Africa.

Currently the genetic database of the RDD programme comprises 1028 families consisting of 2705 individuals from different areas in the country. Since the initiation of the research programme in 1990, results have been obtained by mutation screening for 38 families. To date only 13 families have received their results, 4 of whom reside in the Cape Town Metropolitan area.

3.3.2 Sampling Method

Both convenience and purposeful sampling were used as sampling methods. Convenience sampling is when participants are selected on the basis of being

accessible (McMillan and Schumacher 2001). Only participants in the Cape Town Metropolitan area were interviewed in this study as they were accessible to the researcher with respect to time and cost constraints. Purposeful sampling (also known as purposive sampling) is when participants are selected to provide the best information to address the purpose of the research (McMillan and Schumacher 2001). Purposeful sampling is appropriate when it is used to select unique cases that are especially informative and to identify particular types of in-depth investigations. This sampling method is designed to gain a deeper understanding rather than to generalise to a larger population (Neuman 1999). The inclusion criteria of this study were designed to include individuals that had had several interactions with the service because they had received their mutation detection results. These individuals were thus regarded as the experts and were asked to give their opinions of the service. The proband of each of the four families in the Cape Town Metropolitan area who had received the research results on behalf of the family was interviewed. Thus the research sample comprised of four participants.

3.3.3 Inclusion and Exclusion Criteria

Participants were included in the study if:

- the RDD causative mutation had been identified as part of the "Molecular Genetics of RDD" research programme and the family had been informed of their test results;
- the individual was living in the Cape Town Metropolitan area;
- the individual was over the age of 18 (since the Division of Human Genetics at UCT offers molecular genetic testing to individuals over the age of 18 years);
- the individual could be contacted by means of the details in the Divisional patient files; and
- the individual agreed to be interviewed and audio-taped by the researcher following a phone call from the genetic nurse associated with the "Molecular Genetics of RDD" research programme.

Participants were excluded from the study if:

- the individual was contacted three times and did not respond;
- the individual was not willing to participate in the study; and
- the individual was not willing to participate if the interview was audio-taped.

3.4 STUDY METHODS AND MEASURING INSTRUMENTS

Semi-structured interviews, designed by the researcher, were used in order to gain a comprehensive understanding of the participants' beliefs, perceptions and accounts of being part of the RDD research programme. This method gives both the researcher and the participants more flexibility than a structured interview. A semi-structured interview enables the researcher to follow up on particularly interesting topics that emerge during the interview and permits the participant to provide a more comprehensive description of his/her personal experience (Smith *et al.* 1995).

3.4.1 Data Collection

i) Files:

Data collection from the patient files of participants took place in the Division of Human Genetics at UCT. The data collected included the gender, date of birth, marital status, number of children, age at testing, age upon receiving results, a *priori* risk, known family history, type of RDD, details of family members affected as well as past and present clinical management.

ii) Interviews

Semi-structured individual interviews using open-ended questions were used to gather data. This data collection method was chosen as opposed to using structured interviews with closed-ended questions as important data can be lost when participants' beliefs and feelings are forced into several fixed categories created by the researcher (Neuman 1999). Open-ended questions were used in order to allow the researcher to probe in depth the attitudes of the participants and to determine which aspects of the RDD programme were important to them (Neuman 1999). The

interviewer followed up on the clues about specific topics that the participant provided and explored certain aspects in depth if the required content was not covered by the initial response (Rossouw 2003).

As the researcher is fluent in English and Afrikaans the interviews were conducted in the language of the participants' choice. Obsequious bias (when participants systematically alter questionnaire responses in the direction they perceive to be desired by the investigator) was minimised by the fact that the researcher was unknown to the participants and had previously not been involved with the RDD programme (Sacket 1979). Ensuring that the questions and the information sheets (Appendix III, Appendix IV) were made available to the participants at least a week prior to the scheduled interviews allowed participants time to consider the topics to be discussed. By doing this the researcher minimised rumination bias (when participants have never previously considered the question being asked) (Sacket 1979).

3.4.2 Research Setting

Interviews were conducted at a private venue of the participants' choice, either at their homes or at their workplaces. Individuals were most likely to be more comfortable in their home environment when responding to some of the questions which they might consider sensitive (Smith *et al.* 1995). This approach also took into consideration that some of the participants were visually impaired and that mobility might be a problem for them.

3.5 PROCEDURE

3.5.1 Design of Questions

The questions (Appendix III) were constructed to explore the attitudes of the participant regarding the different stages of interaction between the participants and healthcare providers associated with the "Molecular Genetics of Retinal Degenerative Disorders in South Africa" research programme.

The questions were designed to be neutral rather than loaded or leading. The researcher avoided using jargon during the interviews and attempted to frame the questions in a way that would be familiar to the participants. Open-ended questions allowed the participants the opportunity to state their own points of view without being led by the researcher (Smith *et al.* 1995).

In preparation for the interviews the researcher constructed probes for some of the questions. A probe is a neutral request to clarify an ambiguous answer or to complete an incomplete answer (Neuman 1999). Probes were used during the interview to prompt for more information from the participant when required.

3.5.2 Pilot Interviews

Pilot interviews were conducted with two colleagues who were familiar with RDD to refine the structure of the questions and to give the researcher practice in posing the questions, listening and responding appropriately in an interview situation and to familiarise the researcher with the practicalities of the recording equipment.

3.5.3 Recruitment

A genetic nurse telephoned each of the prospective participants and explained the purpose of the research, but she did not use any form of persuasion to encourage the individuals to participate. She asked permission for the researcher to contact them. She informed the participants that the interview would be conducted by a researcher who had not previously been part of the RDD genetic team and that the interview would be audio-taped. If the individual did not wish to participate in the study the genetic sister asked to be given a reason. She reassured each participant that:

- All information provided to the researcher during the interview would be kept confidential apart from publication of the findings in a scientific journal where names would not be used;
- The information would not be discussed with extended family members; and

- Enrolment was completely voluntary and they may choose not to participate or withdraw from the study at any time without jeopardising their access to the medical and genetic services to which they were entitled.

3.5.4 Consent

Full written consent was given by each participant prior to the interview being conducted. Written consent was also obtained for each interview to be audio-taped. Before each interview, a few minutes were spent re-introducing the main aim and reason for the project and issues of confidentiality. The participant information sheet and consent form were read to each of the participants and they were given an opportunity to discuss any issues relating to the project. Following this, the consent form (Appendix V) was signed.

3.5.5 Interviews

All the interviews were conducted by the researcher personally. The interviews were audio-taped to avoid unnecessary writing of notes by the researcher. Audio-taping allows a more complete record than hand-written notes taken during the interview and it enables the researcher to concentrate on how the interview is proceeding (Smith *et al.* 1995). The interviews were later transcribed from the audiotapes by the researcher.

Following the interviews the researcher allowed the participants to share their feelings and ask questions about the RDD in their family. If necessary and the participant agreed to it, a second interview was arranged to address the issues raised by the participant. If the researcher was unable to answer certain questions, the participant was referred to an expert who would be able to address those particular issues. The participants were asked their opinion of the interview and thanked for their time. Throughout the process of the interviews, the questions were reviewed and revised by the researcher.

Some of the questions posed may have been sensitive to the individual and could have caused emotional reactions. The researcher monitored the effect of the interview on the participants by observing non-verbal behaviour and the way in which participants replied to the questions (Smith *et al.* 1995).

3.6 ETHICAL CONSIDERATIONS

3.6.1 Ethical Approval

This study was granted approval without reservations by the Medical Research Ethics Committee of the University of Cape Town (Reference number 394/2004) (Appendix VI).

3.6.2 Consent

Full written consent was obtained from each of the participants (Appendix V). The procedure of obtaining consent is discussed above in section 3.5.4.

3.6.3 Confidentiality

As confidentiality is of central concern, audio-taped recordings were transcribed as soon as possible after the interviews. The audio-tapes and transcriptions were kept in a safe in the Division of Human Genetics and audio-tapes and transcriptions were destroyed once the study was completed. The participants were assigned numerical codes and their names did not appear anywhere on the transcribed interviews.

3.6.4 Risk

There was minimal risk involved in participating in the study and no insurance was deemed necessary.

3.7 ANALYSIS

Content analysis was used in this qualitative study to capture the richness of the themes emerging from the conversation, rather than reducing the participants'

responses to quantitative categories, as is obtained in structured interviews and questionnaires (Smith *et al.* 1995).

The data obtained from the interviews was transcribed and organised into themes and categories through content analysis of the actual words used by the participants and not the researcher's preconceived hypothesis (Smith *et al.* 1995). Although content analysis is often seen as a quantitative method, it can be used in qualitative research to analyse a small number of texts where the aim is to understand the participants' categories (Silverman 2003). The data was grouped into data sets or clusters according to the shared experience of the four participants.

3.8 RELIABILITY

The questions and probes were reviewed prior to the commencement of the project by two independent members of the RDD programme who are experts in the field. This was done to ensure that the questions were relevant, comprehensive and would be understood easily by the participants.

In order to ensure that the information was an unbiased, fair representation of the participants' views, the researcher discussed the responses of the participants with her neutral supervisors to ensure that they agreed on the analysis and categorisation of the data, thus ensuring inter-rater reliability (Cutliffe and McKenna 1999).

3.9 TRUSTWORTHINESS AND VALIDITY OF THE STUDY

Trustworthiness was increased by using verbatim language of the participants, mechanically recorded data and the physical presence of the researcher (McMillan and Schumacher 2001).

Validity in field research is the confidence placed in the researcher's analysis as well as the data being accurately representative of the social world in the field (Neuman 1999). This was enhanced by the supervisors and experts in RDD checking the

interview schedule. They also reviewed the transcripts and agreed on the categorisation of the data into the various clusters (McMillan and Schumacher 2001). Reproducibility in field research is not a criterion, as it is virtually impossible to replicate such research. Validity can be increased by describing the natural history of how a project was conducted (Neuman 1999). The researcher attempted to maintain transparency of the research method by fully describing the study procedure.

3.10 LIMITATIONS AND STRENGTHS OF THE STUDY

3.10.1 Limitations of the study

- Due to the small sample size, the findings can not be generalised;
- It was not possible to select the sample randomly, due to the small number of families available to participate in the study. There could thus have been selection bias;
- The study did not include those who declined to receive the result that the causative mutation had been found. Their perspective of the RDD programme might have been different;
- Due to the small sample size of 4 individuals from 4 families, subjects from all the ethnic groups in South Africa and different socio-economic status could not be included. There were 3 Caucasian families and 1 Mixed Ancestry family, but no Black or Indian families. All the participants were of a high educational level and had sufficient finances to support a comfortable lifestyle;
- A limited amount of literature on counselling of RDD and specifically related to South African conditions was available at the time of the study;

- There are limitations associated with any method that is dependant on self-reported data by participants. Even though attempts were made to minimise rumination and obsequies bias, the study was still vulnerable to such bias;

- As this was a cross-sectional study, it did not capture social processes or change over a period of time; and

- The researcher has had relatively little interviewing experience and may not have had the necessary skills to identify all the verbal and non-verbal cues from the participants' responses. Thus optimal probing of the responses might not have occurred.

3.10.2 Strengths of the study

- The entire study population (according to the inclusion and exclusion criteria of the study) in the Cape Town Metropolitan area were interviewed;

- The researcher conducted all the interviews personally;

- All the interviews were transcribed by the researcher;

- Obsequious bias was minimised by the fact that the researcher was unknown to the participants and had previously not been involved with the RDD programme; and

- Rumination bias was minimised by ensuring that the questions and the information sheets were made available to the participants at least a week prior to the scheduled interviews. This allowed participants time to consider the topics to be discussed.

Chapter 4

FINDINGS AND DISCUSSION

4.1 INTRODUCTION

This study aimed to explore the attitudes, thoughts and feelings of the participants regarding their participation in the "Molecular Genetics of RDD in South Africa" research programme. The findings and discussion of this study will be presented in this chapter. Firstly, the participants' background information will be provided after which the clusters identified from the interviews will be presented and discussed.

4.2 PERSONAL DETAILS OF PARTICIPANTS

A summary of the personal details of the participants is presented in Table 1 (page 38) at the end of this section.

Participant 1

Participant 1 (P1) is a 42 year old male affected with X-linked recessive RP. The age of onset of the disorder was 5 years. He is the director of his own company and is independent and mobile with the assistance of a helper.

The pedigree (see Table 1, page 38) of this family shows that there are 2 affected individuals, P1 and his older half-brother. P1 is married and has a son and a daughter. Due to the X-linked recessive inheritance pattern in this family, it was not possible for P1's son to have inherited the mutation and he is thus unaffected. His daughter is also unaffected, but is an obligate carrier. This family has been described in an article by Vorster *et al.* (2004) where the causative mutation and possible germ line mosaicism were described.

P1 consented to donate blood for research in 1986, this was four years before the onset of the research programme. The causative mutation in his family was found in 2002. The result was given to him by a genetic counsellor from the Division of Human Genetics in 2004.

Participant 2

Participant 2 (P2) is a 47 year old male. He has been affected with X-linked recessive macular degeneration since the age of 25 years. He works as an administrator for the provincial government and is able to use public transport independently.

P2 is the only affected member of his immediate family (pedigree in Table 1 on page 38). However, he does have male cousins that are affected. P2 is married and has a son and a daughter. Due to the X-linked recessive inheritance pattern in this family, it was not possible for P2's son to have inherited the mutation and he is thus unaffected. His daughter is also unaffected, but is an obligate carrier of X-linked recessive macular degeneration. This family has been described by Rebello *et al.* (2003), where they emphasised the implications for the rest of the family when a diagnosis of RP was made in an individual and the causative mutation found.

P2 consented to donate blood for research in 2001. The causative mutation in his family was found in 2001. The result was given to him in 2004 by his ophthalmologist.

Participant 3

Participant 3 (P3) is a 77 year old female affected with sectoral autosomal dominant RP. In this condition only a part of the eye is initially affected. The age of onset in her case was 22 years. She is retired and is independent and mobile with the assistance of a helper.

The pedigree (see Table 1, page 38) of the family shows a typical autosomal dominant inheritance pattern, with P3's mother, brother and two of her three children (a son and a daughter) being affected. This family has been described in an article by Goliath *et al.* (1997) where the causative mutation was described.

P3 was first recruited to participate in the research programme in 1992 and she consented to donate blood for research. The causative mutation in her family was found in 1995. Soon after the detection, the result was given to her by her ophthalmologist.

Participant 4

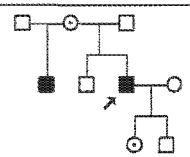
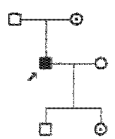
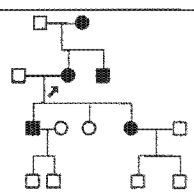
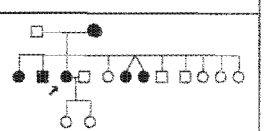
Participant 4 (P4) is a 52 year old female affected with Sorsby fundus dystrophy, a rare autosomal dominant form of macular degeneration with sudden decreased vision associated with subretinal haemorrhage. The age of onset of the disorder in this participant was 38 years. Following the loss of her sight she is no longer able to manage her small business. She has to depend on her family for transport and daily activities outside of her home.

The pedigree of her family shows an autosomal dominant inheritance pattern, with her mother, brother and three of her sisters being affected. The pedigree shown in Table 1 (page 38) represents the first-degree relatives of P4, however, this family consists of many affected family members represented by a large pedigree. This family has been described in an article by Peters and Greenberg (1995) where the variable expressivity of the phenotype and the molecular genetics of the family were described.

P4 was first recruited to participate in the research programme in 1993 and she consented to donate blood for research. The causative mutation in her family was found in 1995. Soon after the detection, she was notified by her ophthalmologist that the causative mutation had been found. Subsequently this result was explained to her by a genetic counsellor from the Division of Human Genetics in 2005.

A summary of the personal details of the participants is presented below in Table 1.

Table 1: A summary of the personal details of the participants.

Participant	Age (years)	Type of RDD	Age of onset (years)	Recruitment (date)	Mutation detected (date)	Result given (By whom; date)	Pedigree
1	42	X-linked recessive RP	5	1986	2002	Division of Human Genetics; 2004	
2	47	X-linked Macular degeneration	25	2001	2001	Ophthalmologist; 2004	
3	77	Sectoral autosomal dominant RP	22	1992	1995	Ophthalmologist; 1995	
4	52	Sorsby fundus dystrophy	38	1993	1995	Ophthalmologist; 1995/ Division of Human Genetics; 2005	

4.3 INTERVIEW PROCEDURE

The proband of each of the four families in the Cape Town Metropolitan area who had received the research results on behalf of the family was interviewed. None of the participants interviewed had other family members that met the criteria of this study. One family member of P3 had been counselled by the RDD service following his request to be informed about the mutation that had been identified in his family, however he did not meet the inclusion criteria as he was not available to be interviewed as he was working in another province at the time of the study.

All of the interviews took less than one and a half hours to complete. None of the participants expressed the need to have a second interview. Two of the participants had questions about their conditions, but asked that the researcher e-mail them with the information. Three of the interviews were conducted at the participants' homes and one at the participant's place of work, as this was his preference.

According to the researcher's observations, during the interviews at their homes and places of work, all of the participants were of a high educational level and had sufficient finances to support a comfortable lifestyle. Three of the participants were Caucasian and one participant was of mixed ancestry. As mentioned in Chapter 2, Wang *et al.* (2001) reported that individuals' attitudes towards blood donation and storage for generic research were indirectly associated with demographics, including education, race and a positive family history of a genetic disorder. This could not be compared in this study due to the small sample size and the lack of diverse educational and socio-economic backgrounds in the sample.

4.4 CLUSTERS IDENTIFIED

The responses of the participants, which were obtained from the open-ended questions asked during the semi-structured interviews, were categorised into clusters. The clusters are presented below according to the items listed in the interview schedule.

The researcher has included direct quotes of the participants' responses in order to provide the reader with insight into their thinking. Repeated words or hesitation were omitted and are indicated with (…) and names were replaced with ### to maintain confidentiality.

A summary of the clusters identified in this study is presented in Table 2 (page 55) at the end of this section.

4.4.1 Reasons for participating

Cure:

All four (4/4) of the participants said that one of the reasons for participating in the research programme was that they were hoping that the research would lead to therapy or a cure for the disorder from which they were suffering. These findings are similar to those of Merz *et al.* (2002) and Wang *et al.* (2001), in which they found that the hope that genetic research would lead to a cure was one of the main reasons for individuals deciding to participate in genetic research.

At first, P1 indicated that this was not one of the reasons for his participation.

"There was certainly no indication to a potential cure (...) so it was more (...) of an interest." (P1)

However, at a later stage in the interview he did state that he had hoped for a cure.

"I guess it's given us (...) and me particularly (...) a hope, a glimmer of hope of some sort of a resolution or a cure or management down the line, but as I say, I'm pragmatic and I don't (...) have the time to sort of dwell on that kind of potential..." (P1)

Two of the participants (2/4) (P1 and P2) made it clear that although they were hoping for a cure, they felt that they were realistic, pragmatic and cautious about the potential for a cure.

The participants had different interpretations of what the cure would be. One thought of it as something that would stop the degeneration (P4); two of the participants were hoping for something that would stop the degeneration and reverse the damage (P2 and

P3). Two of the participants thought that stem cell research would be the approach that would lead to a cure (P3 and P4).

For future generations and family members:

Three participants (3/4) (P2, P3 and P4) indicated that they thought it would take a long time before a cure would become available. They all expressed that they had participated in the research programme with the hope that a cure would be found for other family members and future generations. This is similar to the findings of Merz *et al.* (2002), who found that individuals often feel morally obligated to participate in research for the sake of their families and the findings of Applebaum-Shapiro *et al.* (2001) who reported that the major motivating factors for participation in genetic research in their participants included to help family members and future generations.

"I hoped that within a few years there would be a breakthrough. I didn't feel very hopeful it would be for me, but I hoped that for my children and grandchildren it would come in time to do something." (P3)

Interest/Curiosity:

Two of the participants (2/4) (P1 and P2) responded that one of the reasons for participating in the "Molecular Genetics of RDD in South Africa" research programme was "interest" or "curiosity". These findings differ from those of Merz *et al.* (2002) who found that, in their study participants, "intellectual curiosity" was not one of the reasons given for participating in genetic research.

To help science in general:

Two of the participants (2/4) (P1 and P2) said that another reason for participating was to help science in general. This concurs with the findings by Merz *et al.* (2002) who stated that altruism is one of the main reasons why participants agree to partake in research.

"...some discovery (...) and also curiosity and also to help science in general, I think those were the three main reasons why I sort of opted, or was willing to donate blood and will always be willing to do so." (P2)

Discussion of participants' reasons for participating:

During the interviews, participants were questioned regarding their decision to participate in the Molecular Genetics of RDD research programme. Their motivations for participating included the hope that the research would lead to a cure. The motive here was self-interest in a treatment or cure for their disorder. However, the participants' responses also revealed that they participated in the Molecular Genetics of RDD research programme because of altruism and duty towards their families and future generations. These motivating factors were similar to those identified by Merz *et al.* (2002) who reported that the reasons for participating included financial reward, therapy, self-esteem, intellectual curiosity, altruism and duty.

None of the participants (0/4) mentioned any fears regarding their participation. In other studies the following were reported as the major concerns regarding the participation in genetic research: breach of confidentiality, misuse for cloning, racial discrimination, and discrimination in insurance and employment (Applebaum-Shapiro *et al.* 2001; Wong *et al.* 2004; Bates *et al.* 2005). One could speculate that the general public in South Africa were less aware of these concerns at the time when the participants were enrolled in the Molecular Genetics of RDD research programme (4 to 19 years ago); or that the general public in South Africa is still less aware of such concerns than those in countries such as the USA and Singapore.

4.4.2 Attitudes towards management

Division of Human Genetics

- **Satisfaction with management of the process**

  All (4/4) of the participants reported to be satisfied with the way in which they were managed by the Division of Human Genetics. Two of the four participants (P1 and P4) (2/4) received their results and counselling from the Division of Human Genetics. These participants were pleased with the way in which this was done. (2/4)

"...when we did (go) it was very interesting, it was great, so I was very impressed (...) of them saying, listen come and make an appointment and lets talk about it." (P1)

- **Satisfaction with research programme**

All (4/4) of the participants were satisfied with the research that had been done as part of the "Molecular Genetics of RDD in South Africa" research programme by the Division of Human Genetics at UCT. All four of the participants were grateful for the work that had been done.

"I think they are comparable to anywhere in the world. And we've got a lot to thank them for. They've brought us, you know, to the point we are now. And I think some of the breakthroughs they've had have been equal to anywhere." (P3)

- **Communication**

One participant (1/4) (P1) thought that there had been very little correspondence from the time that he donated blood to the time when he was informed about the detection of the causative mutation in his family. This finding might have been related to the amount of time that had passed between these events in his case (18 years), compared to the other participants (P2 within 1 year, P3 3 years, P4 2 years, see Table 1 page 38). (1/4)

Another participant's view (1/4) (P2) was also that there hadn't been a great deal of communication from the Division of Human Genetics. However, he didn't see the need for more communication. (1/4)

P3 (1/4) was satisfied with the amount of correspondence that had taken place; she felt that she had always been informed about the progress that the research programme had made. (1/4)

P4 (1/4) did not discuss the communication from the Division of Human Genetics, since most of the communication was through the ophthalmologist that was managing her. (1/4)

The different responses from the participants about the amount of communication might indicate that each participant had different needs or that the amount of correspondence from the Division of Human Genetics differed between the participants or both. From the self-reported descriptions, obtained during the interviews, of the nature and extent of communication events (written correspondence, lectures, telephone conversations or home visits) it appeared that the participants had been managed differently. Some of the information regarding the progress that had been made by the "Molecular Genetics of RDD in South Africa" research programme was related to participants through Retina South Africa. Such correspondence should complement the communication from the Division of Human Genetics, but this should not serve as a substitute, as some participants might not wish to join the foundation.

Ophthalmology

- **Attitudes towards management**

Regarding the attitudes of participants towards the management they received from their ophthalmologists, one participant (1/4) was dissatisfied, two participants were satisfied (2/4) and one participant did not comment on this issue (1/4).

P1 was extremely dissatisfied with the way in which he was managed by the Ophthalmology Department at UCT Academic Hospital. The following two quotes illustrate his opinion.

" and there I can actually say (...) with a large degree of assertion, that the Ophthalmology Department dealt with us in a particular difficult way, which wasn't nice. But that's not a reflection on Genetics, at all. In fact it was, ja, we didn't enjoy that in the slightest." (P1)

"I thought it was nicely done (referring to the counselling session at the Division of Human Genetics*), I mean the whole atmosphere was (...) was congenial and*

respectful and thoughtful. Everything that the Ophthalmology Department (...) weren't. (P1)

P2 was pleased with the way in which he had been managed by his private ophthalmologists. He did not find them particularly supportive, but he did not perceive this as part of their role. Since it is the role of genetic counsellors to provide psychosocial support, in the researcher's opinion, P2 might have benefited from receiving his result and support from a genetic counsellor.

"They'll just tell you it is unfortunate, it is sad, that it has to be there, but there's not much, they are not trained pastors or trained comforters or nurses. They are just medical experts and they give you the information and they do it to the best of their ability. And I don't expect anything from them, as far as that is concerned, so I'm happy with the way they treated it..." (P2)

P4 was very satisfied with the way in which she had been managed by her ophthalmologist at University of Stellenbosch Academic Hospital. She felt that he contacted her frequently and kept her up to date with issues concerning RDD.

During the interview, P3 did not state whether she was satisfied or dissatisfied with the way in which she had been managed by her ophthalmologist. She did however state that she didn't think that most ophthalmologists were very informed about RDD.

- **Ophthalmologists' knowledge and understanding of RDD**

Three of the four participants (P1, P3 and P4) felt that most ophthalmologists did not know much about RDD. P3 felt that, due to the fact that RDD are rare, ophthalmologists did not know much about these disorders and were not very interested in them. She felt that it would be useful if one ophthalmologist specialised in RDD so that all those affected with these disorders could then be managed by that person. P1 felt that most ophthalmologists did not understand the genetics of RDD in particular. This finding concurs with the statement by Jay

and Evans (1996) that ophthalmic genetic counselling was beyond the scope of the general ophthalmologists.

Result received from a genetic counsellor compared to an ophthalmologists

Three of the four participants recommended that both a genetic counsellor and an ophthalmologist should be present at the result-giving session. The fourth participant (P2) did not understand the result he had been given, thus indicating that he might have benefited from the management of a genetic counsellor.

P1 received his result from the Division of Human Genetics. His opinion was that an ophthalmologist should also be involved with the result-giving consultation since it would provide more clinical context. He said that ophthalmologists could give the results on their own, providing that they had sufficient knowledge of the disorder and the genetics involved.

P2 received his result from his ophthalmologist. However, during the interview it became clear that P2 wasn't sure whether the RDD causative mutation in his family specifically had been identified. He wasn't sure whether his ophthalmologist meant that they had found it in another family with X-linked recessive macular degeneration or in his own. This uncertainty might be due to the inability of the ophthalmologist to explain the result and its implications adequately or it might be due to P2's lack of interest in these findings.

P3 was under the impression that only genetic counsellors were giving results to families at the time of this study. She felt that if the ophthalmologist gave these results that he/she would take more of an interest in RDD and that individuals would receive more personal attention from their ophthalmologists. She also thought that ophthalmologists were more accessible than genetic counsellors to those in rural areas, as genetic counsellors are mostly only accessible in major cities.

P4 thought that the way she was given her result first by the ophthalmologist that was managing her and then by the genetic counsellor from the Division of Human Genetics worked very well.

The participants' responses indicated that they perceived the research process which involved giving them their research results and their ophthalmic management as two separate issues. Taking into account the responses of all four of the participants, it seems that it would be optimal to have a genetic counsellor from the Division of Human Genetics and an ophthalmologist present at the result-giving session. P1 and P3's responses indicated that the input from the genetic counsellor lacked clinical context, while P2's response indicated that the ophthalmologist who gave his result did not succeed in explaining the result and the implications. This finding thus supports the recommendations by Boughman and Caldwell (1982) that there should be co-operation between counsellors and ophthalmologists and by Jay and Evans (1996) that an interdisciplinary team should be involved in ophthalmic genetic counselling.

The first protocol developed (Appendix I) for both the delivery of genetic results of the "Molecular Genetics of RDD in South Africa" research programme and the management of individuals who are at risk of RDD relied on the managing ophthalmologist or general practitioner of the individual to deliver the causative mutation detection result. However, the need for more support for the ophthalmologist or general practitioner from the "Molecular Genetics of RDD in South Africa" research programme and more support for the individual and family involved was identified. Incremental changes were made to the protocol in 2004 (Appendix II) to include the involvement of genetic counsellors. The new protocol encourages the attending physicians to refer the individual and family to a genetic counsellor for post-result follow-up if they deem it necessary. However, the findings of this study show that the participants would benefit from the involvement of both an ophthalmologist and a genetic counsellor in the result-giving process; optimally both should be present when the result is given. By implementing this approach, the participants might have a better understanding of how the result of the causative mutation detection could influence the way their families are managed. Both misinformation and misunderstanding could immediately be addressed. Since it was the participants' opinions that receiving the

result from a genetic counsellor did not provide information of how this affected their clinical management and information regarding the clinical course and progression of the disease, they felt that an ophthalmologist should be involved. The participants responses that the ophthalmologists that managed them had a poor understanding of RDD and especially the genetics thereof, demonstrated the need for a genetic counsellor to be involved. A genetic counsellor can provide genetic expertise, risk estimation for other family members, information regarding testing options, psychosocial support and follow-up support. The ophthalmologist can provide clinical context to the result, clinical information and clinical management of other family members. This was not the researcher's opinion, but the perception of the participants, who have experienced being part of research programme.

Discussion of participants' attitudes towards management:

Even though all of the participants appeared satisfied with the way they were managed while participating in the "Molecular Genetics of RDD" research programme, it was evident that the participants were each managed differently. They were managed by different ophthalmologists and the results of the research programme were given by different individuals (an ophthalmologist or a genetic counsellor). The participants had different responses regarding the amount of support they received. This might also be a consequence of them being managed by different professionals. The time span during which the participants were involved in the research programme were different (including the duration of time they waited for a result) and they participated in the research programme during different stages of their life-span. Even though a protocol exists for the delivery of research results and the management of participants, the findings of this study indicate that there was little consistency in the way the participants were managed. The participants' responses regarding the amount and type of correspondence from the research programme also highlighted the inconsistencies in management.

The participants' perspectives that the knowledge of RDD and the genetics thereof of the ophthalmologists that managed them were poor might well be a misunderstanding since this was only evaluated from the participants' perspectives. However, the fact remains that the participants experienced it as such. The fact that RDD are rare

conditions with clinical overlap and complex genetics makes it a difficult condition to manage. The findings of this study were thus similar to Jay and Evans (1996) who reported that ophthalmic genetic counselling was beyond the scope of the general ophthalmologist. They described ophthalmic genetic counselling as a time-consuming, potentially emotive undertaking, requiring detailed knowledge which could have profound effects on the futures of patients. They recommended the interdisciplinary team involvement of ophthalmologists, an obstetric unit, molecular genetic laboratory and high quality psycho-social support. If both an ophthalmologist and a genetic counsellor are present when the research result is given, any misunderstanding and misinformation could immediately be addressed.

4.4.3 Communication between Genetics and Ophthalmology

Three of the participants mentioned that there was not sufficient communication between the Division of Human Genetics and both the Department of Ophthalmology at UCT Academic Hospital and ophthalmologists in private practice. P1 said that if there were such communication, he was not aware of it. P2 suggested that there should be more interaction in order for both parties to enrich each other.

"I don't know what the relationship is between the genetics people and the Ophthalmologists at the Universities and research institutes and the practicing surgeons, you know what is the level of contact and how do they enrich each other to see that these things are taken up also seriously." (P2)

P3 felt that since the head of UCT Academic Hospital's Ophthalmology Department had ceased to see private patients, there was no longer a link between the Division of Human Genetics and the ophthalmologists.

The researcher did not ask the participants what they thought of the communication between the Division of Human Genetics and the ophthalmologists. However this issue was raised by 3 of the participants. This had not been predicted by the researcher. Such a novel issue can be most valuable, precisely because it has come unprompted from the participants and is, therefore, likely to be of particular importance to them (Smith *et al.* 1995).

Open and comprehensive communication between ophthalmologists and genetic counsellors, scientists, and clinical staff from the Division of Human Genetics and is of great importance to ensure that individuals with RDD are optimally managed. Sufficient communication between all the parties involved, including the ophthalmologists, Division of Human Genetics and individuals with RDD, could potentially ensure that they are all adequately informed about the clinical, genetic, management and counselling issues regarding RDD.

4.4.4 Attitudes towards causative mutation detection result

Difficulty in understanding

All four (4/4) of the participants found it difficult to comprehend the information and implications regarding the detection of the causative mutation in their families. Two of the participants (P1 and P3) reinforced this statement by saying that they found the information regarding the genetics very technical. This finding is similar to the findings of Bates *et al.* (2005) who found that the public's understanding of genetics is complex, but not technical.

"It was great, but it still there is a lot of techno babble, which I don't get (...) as much as they try very much to explain it..." (P1)

As mentioned before, P2 was uncertain whether the causative mutation in his family had been found.

"...I don't know whether the gene or the specific decoding. Was the discovery on our family? I don't know"

Effect on individuals and families

All of the participants (4/4) responded that the detection of the causative mutation in their families did not have a profound effect on them or their families. The participants felt that they had no choice, but to carry on with their lives and that they didn't want to think about it since it didn't really change anything. P1 said that another reason for this result not having an effect on him or his family was because of their family structure.

"Well in my family it's just ### and I and two small children. (...) one is twelve and she is a, she will be a carrier. (...) She doesn't even know about the results really. And the other one is too young." (P1)

P4 said that the detection of the causative mutation in her family had had an insignificant effect compared to the effect on her and her adult children of seeing close relatives lose their sight.

P2 saw the effect of the detection of the mutation in his family as complex and had mixed feelings regarding this result. He saw the confirmation that it was a genetic disorder running in his family in a negative light, while at the same time he saw it as a breakthrough that could facilitate in developing treatment for the RDD from which he was suffering.

"There's a down side that it can run from family to family, that's also bad news because one would think your eyes get weak or something goes wrong with your eyes for other reasons, so the confirmation is good and its bad news on both sides. Depending on how you look at it. But once you discover something then hopefully with modern technology and science they might within the next ten, five or twenty years come up with something that can either stop it or eliminate it." (P2)

Attitudes towards presymptomatic and prenatal testing

Theoretically, it would be possible to offer presymptomatic and prenatal testing to these families in which the causative mutation had been detected by the "Molecular Genetics of RDD in South Africa" research programme. However, presymptomatic and especially prenatal testing for late onset disorders without effective treatment, such as RDD, raise ethical concerns (Hamel 2003).

The issues of presymptomatic or prenatal testing were discussed in three of the interviews (3/4). One participant (P1) talked about prenatal testing, while the other two (P2 and P4) discussed presymptomatic testing.

P1 discussed prenatal testing, but not presymptomatic testing. The reason for this might have been due to the early onset of RDD in his case (5 years, see Table 1, page 38), which might have lead to him thinking that presymptomatic testing was not an option. P1 did not see the relevance for prenatal testing in his family since they were not planning to have more children. However, he had considered the morality of prenatal testing and he was against the option of terminating a pregnancy following such testing. (1/4)

"It matters not in our personal lives, because we're not planning to have any more children. I always was rather cynical about the concept of being able to, um, identify the gene in utero." (P1)

P2 was in favour of presymptomatic testing. (1/4) He argued that one should know your genetic status and thus your risk of developing a RDD. The following quote depicts his argument.

"I would still (...) go about convincing (family members), because there is no way of trying to run away from something that might exist. You see, so I would always believe that every person in the family should be convinced to go, to know what he or she is in for. Because it can only help, because there is no sense in not knowing and to plead ignorance then 15 years down the line when the child is there, then certain things could have been done or certain things, their mental make-up could have been different also, because that is also important." (P2)

P4 was not against presymptomatic testing, but she would not have chosen to undergo such testing if she had had the opportunity before she became affected. She had shared the information that presymptomatic testing was possible with her adult children and said that she would support them regardless of their decision to be tested or not.

"If I had the opportunity to know or not to know, my preference would be not to know and let it just happen when it happens. Not sit and think for years and years that it is going to happen, because I don't think that even if you prepare yourself, I don't think anything can prepare you for that." (P4)

The different responses by the participants regarding presymptomatic and prenatal testing highlights the already-known ethical issues regarding these aspects and the diverse opinions of individuals in general, as discussed by Hamel (2003) and Gollust *et al.* (2005).

As mentioned before in section 4.2 (personal details of participants, page 35), two of the participants were affected with autosomal dominant RDD (P3 and P4) and two were affected with X-linked recessive RDD (P1 and P2).

The participants with autosomal dominant RDD were both aware of their family members' risks of developing RDD. Two of P3's children were already affected and P4 said in her interview that she had informed her children of their risks.

The two participants with X-linked recessive RDD were both aware and stated in their respective interviews that their daughters are obligate carriers. Carrier testing was thus not necessary for their daughters. One can speculate that P1 and P2 did not discuss carrier testing because it was not relevant to their children. However, the rest of the females in these families (their sisters and female cousins) are at risk of being unaffected X-linked recessive carriers and might benefit from carrier testing. Neither P1 nor P2 stated in their respective interviews whether they had informed female family members of their risks and the option of carrier testing.

Discussion of participants' attitudes towards causative mutation detection results:

The participants found it difficult to comprehend the information and implications regarding the detection of the causative mutation in their families. They also reported that the detection of the causative mutation did not have a profound effect on them or their families. One could speculate that it did not have a huge impact because the participants did not understand the implication. However because all of the participants of this study had already had their children and were not planning to have more children, the implications of prenatal and predictive testing were not applicable. The participants did mention that it confirmed the genetic nature of the disorder, which had emotional consequences for them, but it did not change their day-to-day activities of

living and coping with visual impairment. The emotions associated with the confirmation of a genetic disorder could include guilt, shame and remorse at the possibility of having passed on a serious condition to their children (Knebel and Hudgings 2002).

Prenatal diagnosis for RDD has the same impact as testing for any genetic disorder that runs in a family. It could be argued that testing for RDD prenatally can be more difficult for parents due to the unpredictable severity of the disorder and the fact that it is not life-threatening. In this study the ages of the participants made it difficult to assess their views on prenatal diagnosis or on termination of pregnancy. All of the participants of this study had already had their children and were not planning to have more children at the time of the interviews. Some gave their opinions regarding these issues; however, their opinions were purely hypothetical since none of the participants had experienced predictive or prenatal testing. As illustrated by the quote by Shakespeare in the introduction, people have different views on prenatal testing depending on their own experiences and outlooks. Some will welcome testing, because of the suffering that they have personally experienced. Others will oppose screening, because it is very difficult to support a practice which would have prevented one's own existence.

A summary of the clusters identified in this study is presented below in Table 2.

Table 2: A summary of the clusters identified in this study.

Clusters:	Participant 1	Participant 2	Participant 3	Participant 4
Reasons for participating:				
Cure	✓	✓	✓	✓
For future generations	-	✓	✓	✓
Interest/Curiosity	✓	✓	-	-
Help science in general	✓	✓	-	-
Attitudes toward management:				
Division of Human Genetics				
Satisfaction with management	Very impressed	Happy	Good	Fantastic
Satisfaction with research	Very impressed	Satisfied, grateful	Impressed, grateful	Brilliant
Communication	Too little	Sufficient	Always kept in touch.	-
Ophthalmology				
Management	Very dissatisfied	Impressed	-	Very satisfied
Ophthalmologists' knowledge and understanding of RDD	Poor, especially genetics	-	Very poor	Poor
Result-giving process:				
Comparing genetic counsellors and ophthalmologists	Recommended that both be involved, ophthalmologist would provide more context.	Did not understand the result given by ophthalmologist.	Recommended that both be involved, ophthalmologists would take more of an interest.	Satisfied with both being involved
Communication between Division of Human Genetics and Ophthalmology	Unaware of any	They should inform and enrich each other.	Poor, there needs to be a link.	-
Attitudes toward mutation detection result:				
Difficulty in understanding	Difficult, too technical	Did not understand result.	Difficult, too technical	Difficult
Effect on individuals and families	No profound effect, not relevant to his family situation.	No profound effect, but mixed (positive and negative) feelings.	No profound effect, you just get on with your life.	No profound effect compared to seeing relatives losing sight
Attitudes toward presymptomatic and prenatal testing	Against prenatal testing, but not relevant to him and his family.	In favour of presymptomatic testing	-	Not against presymptomatic testing, but retrospectively wouldn't have wanted to know.

Key: ✓= Participant gave this factor as one of the reasons for participating
- = Participant did not discuss this topic

Chapter 5

CONCLUSION

5.1 CONCLUSION

In the previous chapter the researcher presented and discussed the findings of this exploratory study of how individuals in the Cape Town Metropolitan area with inherited RDD perceived the experience of participating in the "Molecular Genetics of RDD in South Africa" research programme. A qualitative approach facilitated an in-depth exploration of the participants' decision making and perceptions.

Qualitative research is based on the premise that people have different views on reality and that, as a result, there are multiple realities. Descriptive research provides valuable data, particularly when first investigating a topic of interest (McMillan and Schumacher 2001). This was the first exploratory, pilot study investigating the RDD molecular genetic service from the user's point of view.

Biomedical researchers often appear to assume that participants contribute to research solely for altruistic purposes (Merz *et al.* 2002). Others claim that there are obvious benefits to participation in genetic research, including the development of "accurate diagnosis, prognosis and counselling." (Hims *et al.* 2003:121). However, very few studies have explored these issues from the participants' perspectives. Merz *et al.* (2002) found that hope for a cure for a disorder and altruism were the main reasons for individuals deciding to participate in genetic research and that individuals often felt morally obligated to participate in research for the sake of their families. However, in their study, "intellectual curiosity" was not one of the reasons cited for participating in genetic research.

This South African pilot study provided a unique insight to understanding aspects of research that affect participants both psychologically and behaviourally. The study identified the factors that were most important to the participants when deciding to participate in the "Molecular Genetics of

RDD" research programme. The findings showed that individuals participated in the research study with the hope of it leading to a cure for themselves, for other family members and for future generations.

The participants were all satisfied with the way in which they had been managed by the Division of Human Genetics. However, it appeared that there was a lack of consistency in the correspondence from the Division of Human Genetics to each of the participants.

As the participants were all managed by different ophthalmologists, the degree of satisfaction was varied, but three of the participants commented on the lack of knowledge and understanding of their ophthalmologists regarding RDD. The findings of this study suggested that there is a need to educate medical professionals about RDD, genetic counselling and the implications that genetic testing can have on the individual, the family, family planning and personal relationships.

All the participants indicated that an ophthalmologist and a genetic counsellor should be present at the result-giving session, unless or until ophthalmologists become more informed about the genetics of RDD. The participants did not think that there was sufficient communication between the Division of Human Genetics and the ophthalmologists who were managing them clinically. Improved communication between all those involved in the management of individuals with RDD would potentially lead to improved management of these individuals.

The detection of the causative mutation in a family is an important breakthrough from a scientific perspective. However, it is essential to realise that it does not necessarily have a profound impact on the family, since it does not change their situation with regard to their management. This was indicated by all the participants in this study. Although presymptomatic and

prenatal testing is possible following the detection of the mutation, none of the families in this study had chosen to explore these options. The participants had different opinions regarding the justification and morality of such testing.

Overall the participants in this study had positive attitudes towards participating in the "Molecular Genetics of RDD in South Africa" research programme. Two of the participants (2/4) volunteered, without any probing, that they would be willing to participate in further research. This could be interpreted as another indication that they had a positive experience with participating in the research programme and were satisfied with the way in which they had been managed.

This was the first time that a genetic research programme in South Africa has been evaluated from the users' perspective. The recommendations that evolved from the assessment of the research programme in this study are presented in Chapter 6.

Chapter 6

RECOMMENDATIONS

6.1 INTRODUCTION

As this study explored the attitudes of individuals with inherited RDD towards the "Molecular Genetics of RDD in South Africa" research programme, several recommendations were made by participants during the interviews. This chapter will present the recommendations made by the participants and the researcher with the intent to improve the way individuals and families are managed when participating in the "Molecular Genetics of RDD in South Africa" research programme and for future research.

6.2 RECOMMENDATIONS

6.2.1 Recommendations by participants

- The "Molecular Genetics of RDD in South Africa" research programme should have a protocol regarding correspondence with participants to ensure that the amount and type of communication with participants are relatively consistent. Such a protocol should include annual correspondence with updates on the research being conducted on each family. Correspondence from Retina South Africa should complement the communication from the Division of Human Genetics, but this should not serve as a substitute, as some participants might not wish to join the foundation.

- Communication between the "Molecular Genetics of RDD in South Africa" research programme and ophthalmologists managing individuals with inherited RDD need to be improved. Improved communication will potentially enhance the understanding and knowledge of ophthalmologists regarding RDD and the genetics thereof as well as the knowledge of genetic counsellors and other staff from the Division of Human Genetics regarding the clinical and management issues of RDD.

- The "Molecular Genetics of RDD in South Africa" research programme could encourage certain ophthalmologists to develop a special interest in RDD. Individuals affected with RDD could then be managed by these specialists.
- It would be optimal to have a genetic counsellor and an ophthalmologist present at the result-giving session. The first protocol developed by the "Molecular Genetics of RDD in South Africa" research programme relied on the managing ophthalmologist or general practitioner to deliver the result without the input or the Division of Human Genetics. The second protocol designed in 2004 recommends that the physician delivering this result should refer individuals affected with RDD to a genetic counsellor if he deems it necessary. However, the findings of this study

have shown that both an ophthalmologist and a genetic counsellor should be present at the result-giving session according to the participants' perspectives. The genetic counsellor can provide the individual and family with genetic information and support, including follow-up support, while the ophthalmologist can explain the clinical context of the result.

It is the researcher's opinion based on experience in genetic clinics that in some cases it might not always be possible to have both a genetic counsellor and an ophthalmologist present, especially in more rural areas of the country. However, in such a case the professionals involved should consult with others to ensure that the individuals are informed and supported adequately.

6.2.2 Recommendations by the researcher

- Further research is required to increase our understanding of the complexities of decision making in the context of participating in genetic research programmes. The need for increased understanding of individuals' attitudes towards participating in genetic research is pressing; as such research continues to expand rapidly.

- Future research should explore the reasons for some individuals not responding to letters indicating that their mutation detection results were available.

- Future research should include a nationwide study to explore the attitudes of all the individuals in South Africa that have been involved in the "Molecular Genetics of RDD in South Africa" research programme. This could provide a larger and possibly more demographically diverse sample.

- Health care providers who are involved in the "Molecular Genetics of RDD in South Africa" research programme should be made aware of the findings of this study as it might provide insight into participants' needs and they may wish to alter their management style based on these findings.

REFERENCES

REFERENCES

Applebaum-Shapiro S, Peter J, O'Connell J, Aston C, Whitcomb D (2001) Motivations and concerns of individuals with access to genetic testing for Hereditary Pancreatitis. American Journal of Gastroenterology 96:1610-1617.

Atan D, Gregory Evans C, Louis D, Downes S (2004) Sorsby's Fundus Dystrophy presenting with choroidal neovascularisation showing good response to steroid treatment. British Journal of Ophthalmology 88 (3) 440-1.

Bates B, Lynch J, Bevan J, Condit C (2005) Warranted concerns, warranted outlooks: a focus group study of public understandings of genetic research. Social Science & Medicine 60:331-344.

Baughman J and Caldwell R (1982) Assessment of clinical variables and counseling needs in patients with retinitis pigmentosa. American Journal of Medical Genetics 12:185-193.

Begleiter ML (2002) Training for genetic counsellors. Nature Reviews Genetics 3:557-561.

Bennet R, Hampel H, Mandell J, Marks J (2003) Genetic counselors: translating genomic science into clinical practice. Journal of Clinical Investigations 112(9):1274-1279.

Berson E (1999) Nutrition and retinal degenerations. In: Shils M, Olson J, Shike M, Ross A (eds) Modern nutrition in health and disease. Williams & Wilkins. Baltimore. 1491-1501.

Berson E, Rosner B, Sandberg M, Weigel-DiFranco C, Moser A, Brockhurst R, Hayes K, Johnson C *et al.* (2004) Clinical trial of docosahexaenoic acid in patients with retinitis pigmentosa receiving vitamin A treatment. Archives of Ophthalmology 122(9):1297-305.

Brezin A, Lafuma A, Fagnani F, Mesbah M, Berdeaux G (2005) Prevalence and burden on self-reported blindness, low vision, and visual impairment in the French community. Archives of Ophthalmology 123:1117-1124.

Bundey S and Crews S (1982) Wishes of patients with retinitis pigmentosa concerning genetic counselling. Journal of Medical Genetics 19(4):317-318.

Burke W, Emery J (2002) Genetics education for primary-care providers. Nature Reviews Genetics 3:561-566.

Cutliffe J and McKenna H (1999) Establishing the credibility of qualitative research findings: the plot thickens. Journal of Advances Nursing 30(2):374-380.

Daiger S (2004) Identifying retinal disease genes: how far have we come, how far do we have to go? In: Retinal dystrophies: functional genomics to gene therapy. Wiley. Chester. (Novartis Foundation Symposium 225) 37-50.

Emery A and Smith C (1970) Ascertainment and prevention of genetic disease. British Medical Journal 3:636-637.

Gieser J (2004) When treatment fails: Caring for patients with visual disability. Archives of Ophthalmology 122:1208-1209.

Goliath R, Bardien S, September A, Martin R, Ramesar R, Greenberg J (1997) Rhodopsin Mutation G109R in a Family with Autosomal Dominant Retinitis Pigmentosa. Human Mutation supplement 1:S40-41.

Gollust S, Apse K, Fuller B, Miller P, Biesecker B (2005) Community involvement in developing policies for genetic testing: Assessing the interests and experiences of individuals affected by genetic conditions. American Journal of Public Health 95(1):35-41.

Greenberg J and Peters A (1995) Genetic Blindness – macular dystrophies and retinitis pigmentosa. South African Medical Journal 85(6):492-493.

Greenberg J, Rebello G, Ramesar R (1999) Ophthalmic genetics: a review of the molecular genetics of familial retinal dystrophies in Southern Africa. Specialist Medicine XXI(2):108-112.

Greenberg J and Ziskind A (2001) An ophthalmic genetics handbook: for Ophthalmologists in South Africa. Retina South Africa. Johannesburg.

Greenberg J, Roberts L, Ramesar R (2003) A rare homozygous rhodopsin splice-site mutation: the issue of when and whether to offer presymptomatic testing. Ophthalmic Genetics 24(4):225-232.

Guignard E (1990) Psychosocial management of retinitis pigmentosa from the viewpoint of the physician and the patient. Klinische Monatsblätter für Augenheilkunde 196(5):436-437.

Hamel C (2003) Retinitis Pigmentosa. Orphanet Encyclopedia, created July 2003. http://www.orpha.net/data/patho/GB/uk-RetinitisPigmentosa.pdf, retrieved 18 February 2005.

Harper P (2004) Practical Genetic Counselling. 6th Edition. Arnold. London.

Hayeems R, Geller G, Finkelstein D, Faden R (2005) How patients experience progressive loss of visual function: a model of adjustment using qualitative methods. British Journal of Ophthalmology 89:615-620.

Hims M, Daiger S, Inglehearn C (2003) Retinitis pigmentosa: genes, proteins and prospects. Developments in Ophthalmology 37: 109-125.

http://webvision.med.utah.edu/

http://www.mscd.edu/

http://www.ohiovalleyeye.com/

Holtz F, Haimovici R, Wagner D, Bird A (1994) Recurrent choroidal neovascularisation after laser photocoagulation in Sorsby's Fundus Dystrophy. Retina 1994 ; 14 (4) 329-34.

Hunt L, Voogd K, Castaneda H (2005) The routine and the traumatic in prenatal genetic diagnosis: Does clinical information inform patient decision-making? Patient education and Counseling 56:302-312.

Jay M and Evans K (1996) Retinal dystrophies and genetic counselling. Acta Opthalmologica Scandinavica 74:5-7.

Kalloniatis M and Fletcher E (2004) Retinitis pigmentosa: Understanding the clinical presentation, mechanisms and treatment options. Clinical and Experimental Optometry 87(2):65-80.

Knebel A and Hudgings C (2002) End-of-life issues in genetic disorders: Literature and research directions. Genetics in medicine 4:366-372.

Lea D, Williams J, Donahue M (2005) Ethical issues in genetic testing. Journal of Midwifery & Women's Health 50(3):234-240.

Lloyd P (1994) The lived experience of retinitis pigmentosa. B.Sc Nursing dissertation, Department of Nursing, University of Cape Town, Cape Town.

Mackey D, Heon E, Webster A (2003) Predictive testing in ophthalmology. British Journal of Ophthalmology 87:633-638.

Mason J (2002) Qualitative researching. 2nd Edition. Sage. London.

McKie A, McHale J, Keen T, Tarttelin E, Goliath R, Lith-Verhoeven J, Greenberg J, Ramesar R *et al.* (2001) Mutations in the pre-mRNA splicing factor gene PRPC8 in autosomal dominant retinitis pigmentosa (RP13). Human Molecular Genetics 10(15):1555-1562.

McMillan James H and Schumacher S (2001) Research in education: a conceptual introduction. 5th Edition. Longman. New York.

Merz J, magnus D, Cho M, Caplan A (2002) Protecting subjects' interests in genetic research. American Journal of Human Genetics 70:965-971.

Mueller and Young (2001) Emery's Elements of Medical Genetics. 11th Edition. Churchill Livingstone. Edinburgh.

Neuman WL (1999) Social Research Methods: Qualitative and Quantitative Approaches, 4th Edition. Allyn and Bacon. Massachusetts.

Parker M, Ashcroft R, Wilkie A, Kent A (2004) Ethical review of research into rare genetic disorders. Brittisch Medical Journal 329:288-289.

Peters A and Greenberg J (1995) Sorsby's fundus dystrophy: A South African family with a point mutation on the tissue inhibitor of metalloproteinases-3 gene on chromosome 22. Retina 15(6):480-485.

Rebello G, Voster A, Greenberg J, Coutts N, Roberts L, Ehrenreich L, Gama D, Ramesar R (2003) Analysis of RPGR in a South African family with X-linked retinitis pigmentosa: Research and Diagnostic Implications. Clinical Genetics 64: 137-141.

Rebello G, Ramesar R, Voster A, Roberts L, Ehrenreich L, Oppon E, Gama D, Bardien S *et al.* (2004) Apoptosis-inducing signal sequence mutation in carbonic anhydrase IV identified in patients with the RP17 form of retinitis pigmentosa. Proceedings of the National Academy of Sciences of the United States of America 101(17):6617-6622.

Rivolta C, Sharon D, DeAngelis M, Dryja T (2002) Retinitis pigmentosa and allied diseases: numerous diseases, genes, and inheritance patters. Human Molecular Genetics 11(10):1219-1227.

Rossouw D (2003) Intellectual Tools: Skills for the human sciences. 2nd Edition. Van Schaik. Pretoria.

Sacket DL (1979) Bias in analytical research. Journal of Chronic Disease 32:51-63.

Shakespeare T (1998) Choices and rights: eugenics, genetics and disability equality. Disability & Society 13:665-681.

Shaw J and Bassi K (2001) Lay attitudes toward genetic testing for susceptibility to inherited diseases. Journal of Health Psychology 6(4):405-423.

Silverman D (2003) Interpreting Qualitative Data. 2nd Edition. Sage. London.

Singer E (1991) Public attitudes toward genetic testing. Population research and Policy Review 10:235-255.

Singer E, Corning A, Antonucci T (1999) Attitudes toward genetic testing and fetal diagnosis. Journal of Health and Social Behaviour 40:429-445.

Smith J, Harrer R, Van Langenhove L (1995) Rethinking methods in psychology. Butterworth- Heinemann. Oxford.

Sohocki M, Daiger S, Bowne S, Rodriquez J, Northrup H, Heckenlively J, Birch D, Mintz-Hittner H *et al.*(2001) Prevalence of mutations causing retinitis pigmentosa and other inherited retinopathies. Human Mutation 17:42-51.

Tercyak K, Bennet Johnson S, Roberts S, Cruz A (2001) Psychological response to prenatal genetic counselling and amniocentesis. Patient Education and Counseling 43:73-84.

Tessitore A, Toniato E, Gulino A, Frati L, Ricevuto E, Vadala M, Vingolo E, Martinotti S (2002) Prenatal Diagnosis of a rhodopsin mutation using chemical cleavage of the mismatch. Prenatal Diagnosis 22:380-384.

Vorster A, Rebello M, Coutts N, Ehrenreich L, Gama A, Roberts L, Goliath R, Ramesar R *et al.* (2004) Arg120stop nonsense mutation in the RP2 gene: mutation hotspot and germ line mosaicism? Clinical Genetics 65:7-10.

Wang S, Fridinger F, Sheedy K, Khoury M (2001) Public attitudes regarding the donation and storage of blood specimens for genetic research. Community Genetics 4:18-26.

Wong M, Chia K, Wee S, Chia S, Lee J, Koh W, Shen H, Thumboo J, Sofjan D (2004) Concerns over participation in genetic research among Malay-muslims, Chinese and Indians in Singapore: A focus group study. Community Genetics 7:44-54.

Wong S, Fong C, Lee N, Gregory-Evans C, Gregory-Evans K (2003) Successful photodynamic therapy for subretinal neovascularisation due to Sorsby's fundus dystrophy: 1 year follow up. British Journal of Ophthalmology. 87(6): 796-7.

Yu and Cringle (2005) Retinal degeneration and local oxygen metabolism. Experimental Eye Research 80:745-751.

THE GENETICS OF RETINAL DEGENERATIVE DISORDERS IN SOUTHERN AFRICA

Principal Investigators

Raj Ramesar Ph.D.
Professor : Human Genetics
rr@cormack.uct.ac.za

Jacquie Greenberg Ph.D.
Associate Professor & Genetic Counsellor
jg@cormack.uct.ac.za

Department of Human Genetics
University of Cape Town Medical School

Clinical Research Co-ordinator
Lecia Bartmann Srn.Srm.

Protocol for the delivery of genetic results arising from the research study of
The Genetics of Retinal Degenerative Disorders in Southern Africa.

Informed consent has been obtained from all individuals from whom DNA has been isolated and on whom mutation screening or linkage analysis has been undertaken. An information sheet is given to the individual and then a follow-up letter is sent to participants, explaining that no information will be available until there are significant results.

Once a genetic mutation has been identified and confirmed in a subject/family with a history of RDD it is proposed that :

1. Sister Bartmann will contact either the referring clinician or ophthalmologist who is documented as treating the individual or principal family member for their RDD and confirm that they are still in contact with the patient. Sister Bartmann will then inform them that a written report will follow with the molecular diagnosis.

2. Professor Greenberg will send a detailed report to the clinician on the molecular results, together with references, where applicable.

3. The clinician will decide what to do with this information. Professor Greenberg will follow-up with the clinician within a month of sending the report to ascertain what has been planned. The individual or principal family member will be contacted by the clinician and given the genetic result. The decision of who else in the family will and should be told. will be discussed with the individual and decided upon by the family member, in consultation with the clinician. The individual retains the right at all times to either receive or refuse the results.

4. Should there be any need to study additional family members, this will be discussed with the clinician and a course of action will be decided upon as to who makes the contact and what the family is told.

5. Should there not be a referring clinician, Sister Bartmann will send a letter to the participant/s telling them that there has been a significant molecular genetic finding and asking them to contact her. A form will be sent with the letter asking them to give their permission to release their results to a clinician, whom they nominate. This form has to be signed and returned to Sister Bartmann and then we will follow the procedure as stated in points 1, 2, 3, and 4.

6. Should the individual not have a clinician of choice, we will invoke a course of action involving a genetic counsellor or a local retinal specialist.

7. All costs involved in this process of informing subjects of their molecular results ought to be borne by the participants.

8. All genetic information is regarded as strictly confidential. Only information relating to the potential genetic cause of the inherited retinal degenerative disorder will be released to the individual concerned, personally. No other genetic information or family information produced by this study will be released to any one else, including other family members. At this stage, it needs to be stressed and understood that no additional treatments will be available as a result of these test results.

9. Participants need to be informed that there is no financial compensation, commercial benefits or other rewards for participation in this programme. There may be no direct benefit as a participant other than the possible medical advances and greater understanding of the genetic condition in the family that may result if causative genes are found.

10. Individuals will be informed and assured that other qualified research investigators may study their DNA samples, if necessary, but only for the purpose of further investigations of genetic factors causing genetic eye disease.

THE GENETICS OF RETINAL DEGENERATIVE DISORDERS IN SOUTHERN AFRICA

Division of Human Genetics, Wernher & Beit North - Level 3

Faculty of Health Sciences, University of Cape Town,

PRINCIPAL INVESTIGATORS

Professor Raj Ramesar Ph.D. rr@cormack.uct.ac.za

Professor Jacquie Greenberg Ph.D. jg@cormack.uct.ac.za

Clinical Research Co-ordinator

Lecia Bartmann SRN/SRM.

lb@cormack.uct.ac.za

Protocol for the delivery of genetic results arising from the research study of

"The Genetics of Retinal Degenerative Disorders (RDD) in Southern Africa."

Informed consent has to be obtained from all individuals from whom DNA has been isolated and on whom mutation screening or linkage analysis has been undertaken. Once a genetic mutation has been identified and confirmed in a subject/family with a history of RDD, the delivery of results will be as follows:

Sister Bartmann will contact the family (individual or principal family member) by telephone, followed by a letter, informing them that the disease-causing mutation has been found in their family. Included with this letter will be the option to receive their detailed results. Their signature on a consent form will be required along with details of the clinician/ophthalmologist of their choice who they wish to have deliver their results to them. The patient thereby gives us consent to release their molecular diagnostic results to the clinician/ophthalmologist/genetic counsellor as stated on the form.

Professor Greenberg will contact the professional of the individual's choice and send the results to her/him. Attached to this will be a letter of recommendation regarding the delivery of the genetic test results, counsellor information for post-result follow-up, together with references, where applicable. Should there be any need to study additional family members, this will be discussed with the clinician and a course of action will be decided upon as to who makes the contact and what the family is told.

The individual or principal family member will be contacted by their managing clinician and personally given the genetic result. Thereafter, the family members who would like to receive their results need to contact this division or their doctor. Sister Bartmann will follow-up within a month of the sending the report to ascertain what has transpired. A plan of action as to how the results are delivered and whether predictive counselling is required will depend on the nature of the results and also the decision of who else in the family will and should be told. This will be discussed with the individual and decided upon, in consultation with the clinician/counsellor.

The individual retains the right at all times to either receive or refuse the results.

All costs involved in this process of informing subjects of their molecular results ought to be borne by the participants.

All genetic information is regarded as strictly confidential. Only information relating to the potential genetic cause of the inherited RDD will be released to the individual concerned, personally. No other genetic information or family information produced by this study will be released to any one else, including other family members. At this stage, it needs to be stressed and understood that no additional treatments will be available as a result of these test results.

Participants need to be informed that there is no financial compensation, commercial benefits or other rewards for participation in this programme. There may be no direct benefit as a participant other than the possible medical advances and greater understanding of the genetic condition in the family that may result if causative genes are found.

Individuals will be informed and assured that only other qualified research investigators may study their DNA samples, if necessary, but only for the purpose of further investigations of genetic factors causing inherited retinal eye disease.

1/11/2004

Questions:

1. What lead up to you having your blood taken for research?

2. What did you think would happen when you gave your blood?

3. During the waiting period, how did it affect you? and your family?

4. Who gave you the result?
   How did you feel the information was conveyed to you?

5. The genetic lab identified the mutation (change in the gene/DNA) causing RDD in your family:
   How did the test result affect you and your family?

6. In conclusion: What would you say about the RDD programme as a whole?

THE GENETICS OF RETINAL DEGENERATIVE DISORDERS IN SOUTHERN AFRICA
Division of Human Genetics, Faculty of Health Sciences
University of Cape Town

PRINCIPAL INVESTIGATORS

Professor Raj Ramesar Ph.D. Professor Jacquie Greenberg Ph.D.
Clinical Research Co-ordinator: Lecia Bartmann SRN/SRM.
Telephone: 021 406 6467 Fax: 021 4480906 E-mail: lb@cormack.uct.ac.za

M.Sc. in Genetic Counselling Research Project
Entitled:

A pilot study of how individuals with Inherited Retinal Degenerative Disorders perceive being part of a genetic research programme.

Participant Information Sheet:

Thank you for agreeing to participate in the above-mentioned study.

The Genetics of Retinal Degenerative Disorders (RDD) in South Africa research programme was initiated by the Division of Human Genetics at the University of Cape Town in 1990 and continues to carry out research, looking at various forms of genetic blindness. This present study is being conducted to explore how participants and their family members who have participated in the RDD research programme have perceived their involvement and feel about the experience.

By participating in this study you will be potentially helping us to become more insightful in meeting families' needs. It is hoped that the knowledge gained will lead to a better understanding of the motivation and concerns, as well as the expectations of patients and families regarding this research. The gained knowledge could potentially lead to better and more appropriate genetic counselling for RDD patients and other family members. This could assist in determining whether this research project has been beneficial, not only to science, but also to all members of the families involved in the RDD research programme.

An interview will be conducted which could take up to two hours. The interview will be recorded so that the researcher will be able to document and analyse the interview accurately. A second interview might be necessary.

Your privacy will be maintained as all the information obtained during the interview will remain confidential and all identifiable data will be removed. A coding method will be used to identify the different families and only the principal investigator will have access to the code. After the tapes have been transcribed, they will be destroyed.

Participation in this study is entirely voluntary. You, the participant, have the right to withdraw from the study at any stage without this having any effect on your future management or treatment.

Should you have any queries regarding any aspect of this study, please do not hesitate to contact me at the following number: 021 406 6425.

Thank you for your participation.

Frieda Basson
M.Sc. Genetic Counselling student (2nd year of registration)
Division of Human Genetics, University of Cape Town

THE GENETICS OF RETINAL DEGENERATIVE DISORDERS IN SOUTHERN AFRICA
Division of Human Genetics, Faculty of Health Sciences
University of Cape Town,

PRINCIPAL INVESTIGATORS

Professor Raj Ramesar Ph.D. rr@cormack.uct.ac.za

Professor Jacquie Greenberg Ph.D. jg@cormack.uct.ac.za

Clinical Research Co-ordinator
Lecia Bartmann SRN/SRM.
Telephone: 021 406 6467 Fax: 021 4480906 E-mail: lb@cormack.uct.ac.za

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M.Sc. in Genetic Counselling Research Project
Entitled:

A pilot study of how individuals with Inherited Retinal Degenerative Disorders perceive being part of a genetic research programme.

Participant consent form

I, the undersigned, have read the attached participant information sheet.

I understand that my privacy will be maintained at all times and that all the information obtained during this study will remain confidential. I am aware that I, the participant, have the right to withdraw from the study at any stage without this having any effect on my future management or treatment. I understand that the interviews will be audiotaped and transcribed.

I understand the purpose and nature of the study and I voluntarily agree to take part.

Participant:		**Witness:**	
Name:	_____	Name:	_____
Date:	_____	Date:	_____
Signature:	_____	Signature:	_____
Place:	_____	Place:	_____

UNIVERSITY OF CAPE TOWN

Research Ethics Committee
E53 Room 44.1, Old Main Building Groote
Schuur Hospital, Observatory, 7925
Queries : Xolile Fula
Tel : (021) 406-6492 Fax: 406-6411
E-mail : Xfula@curie.uct.ac.za

02 December 2004

REC REF: 394/2004

Prof. J. Greenberg
Human Genetics

Dear Prof. Greenberg

HOW INDIVIDUALS AND FAMILIES WITH INHERITED RETINAL DEGENERATIVE DISORDERS PERCIEVE BEING PART OF A GENETIC RESEARCH PROGRAMME

Thank you for submitting your study to the Research Ethics Committee for review

Date Considered: 26 November 2004

Decision: Approved

Please find attached the attendance register of member.

Please quote the REC. REF in all your correspondence

Yours sincerely

PROF. T. ZABOW
CHAIRPERSON