An investigation into the reasons for non-uptake of carrier testing in a family affected by Alpha Thalassaemia X-Linked Mental Retardation (ATR-X) syndrome

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ABSTRACT

Alpha thalassaemia X-linked mental retardation (ATR-X) syndrome is a rare, X-linked intellectual disability syndrome with an estimated prevalence in the range of 1-9/1 000 000. The prevalence in South Africa (SA) is unknown; however in Cape Town there is one extended family with seven males who were clinically, and later molecularly, diagnosed with this condition. Due to the identification of the mutation in this family, carrier and prenatal testing is available. However, since the announcement in 2007 that testing is available, no individuals have presented themselves for their carrier status to be determined. The aim of this study was to investigate the reasons why females in this family have not presented for carrier testing.

A phenomenological qualitative approach was used in this study as it aims to understand social phenomena from the participants' perspective, therefore enriching the data. Following a pilot study with 2 female subjects, eleven semi-structured interviews were performed with female relatives of a male with ATR-X syndrome. The participants were recruited by convenience and snowball sampling and did not have an affected son themselves. Thematic analysis was used to analyse the data.

The majority of the participants in this study knew that ATR-X syndrome was inherited and that they were at risk of being carriers. Their perception of this risk, however, may have been low as no one in the generation interviewed has yet experienced the birth of an affected son. The level of knowledge was linked to the participant's socio-economic status and the amount of involvement with the extended family. None of the participants viewed their affected relatives negatively; they felt they were normal and accepted their disabilities as personal characteristics, rather than abnormalities. This was closely tied to a religious framework. A limited number of participants were aware of the available carrier testing, with the majority wanting testing. Prenatal diagnosis views were varied; however, none of the participants felt they would terminate an affected pregnancy. There was generally a lack of communication and dissemination of genetic knowledge in this family. This was linked to underlying family tensions, feelings of guilt and the responsibility for dissemination of information mainly falling on one individual.

Although qualitative research has previously been conducted to investigate the level of knowledge and dissemination of information about genetic conditions, the current study was the first to investigate the reasons why individuals in families affected by an X-linked condition have not presented for carrier testing in SA. The findings of this study will help to inform researchers involved in family studies that informed consent should include addressing the expectations of the family regarding the research outcomes. It will also help health care professionals to understand some of the barriers to the dissemination of information within families and highlight the necessity of developing tools to facilitate this process.

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LIST OF TERMS AND ABBREVIATIONS

Anticholinergic	A substance that opposes or blocks the action of acetylcholine
Aspiration	The accidental inhalation of food or fluid into the lungs
ATRX	ATRX protein
ATRX	ATRX gene
ATR-X syndrome	Alpha thalassaemia X-linked mental retardation syndrome
bp	Base pairs
Botulinum toxin	A neurotoxin that is produced by the bacterium Clostridium botulinum and causes muscle paralysis
CF	Cystic fibrosis
Choreoathetotic movements	Twitching or jerking movements not associated with purposeful movement
CVS	Chorionic villus sampling
DMD	Duchenne muscular dystrophy
DNA	Deoxyribonucleic acid
DNA methyltransferase	An enzyme that attaches methyl groups to a DNA molecule
DS	Down syndrome
FXS	Fragile-X syndrome
GP	General practitioner

Gr	Grade
GSH	Groote Schuur hospital
HD	Huntington disease
HBOC	Hereditary breast and ovarian cancer
Hydronephrosis	The swelling of the kidneys when urine flow is obstructed in any of part of the urinary tract
Hypoplasia	Incomplete development or underdevelopment of an organ or tissue
ID	Intellectual disability
IQ	Intellectual quotient
mRNA	Messenger RNA
No	Number
P	Participant
Patent ductus arteriosus	A condition in which a blood vessel called the ductus arteriosus fails to close normally in an infant soon after birth
R	Rand (South African currency)
RCWCH	Red Cross War Memorial Children's Hospital
RNA	Ribonucleic acid
SA	South Africa
SNF	Sucrose Non Fermentation
Spastic paraplegia	Paraplegia is an impairment in motor or sensory function of the lower extremities

Stats SA	Statistics South Africa
Stenosis	A constriction or narrowing of a duct or passage
TOP	Termination of pregnancy
USA	United States of America
WC	Western Cape
XLMR	X-linked mental retardation

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CHAPTER 1:

INTRODUCTION

1.1 INTRODUCTION

Alpha thalassaemia X-linked mental retardation (ATR-X) syndrome is a rare, X-linked condition in which 95% of individuals are moderately to profoundly intellectually disabled. According to Stevenson (2009), approximately 200 cases have been identified worldwide, resulting in an estimated prevalence in the range of 1-9/1 000 000 (Gibbons, 2006). The prevalence of ATR-X syndrome is unknown in South Africa; however, in Cape Town, there is a large extended family (spanning three generations and comprising approximately 100 people), Family X, well known to the Division of Human Genetics, University of Cape Town (UCT). Family X has seven males diagnosed with ATR-X syndrome. The diagnosis of ATR-X syndrome was initially suspected due to the clinical phenotype, but was later confirmed by molecular diagnosis made possible by a PhD student in the Division of Human Genetics, UCT, who identified the disease-causing mutation in the *ATRX* gene for this particular family (Carvill, 2010).

With the identification of the mutation in this family, it became possible to molecularly identify carriers of the mutation in unaffected females and thus offer carrier testing and prenatal diagnosis. However, since the announcement in 2007 that testing is available, no individuals have presented to determine their carrier status, despite this information being available to the family.

There are many possible explanations for the failure to take up the opportunity of carrier testing. These include an individual's personal experience of the condition, their reproductive life stage, psychological factors such as denial, socio-economic factors, education level and inadequate communication, either within families or by the health professionals dealing with affected members of the family (Anido *et al.*, 2005; Beeson &

Golbus, 1985; Eggers *et al.*, 1999; Gallo *et al.*, 2005; Kay & Kingston, 2002; Kessler, 1989).

It is important for genetic counsellors and other health professionals dealing with genetic conditions to determine and understand the reasons for the non-uptake of carrier testing in a South African context so that they may determine how genetic counselling services may be improved for this family and for others affected by other X-linked conditions, such as Fragile-X syndrome (FXS), where there is a similar poor uptake of carrier testing services.

1.2 AIMS

The aim of this study was to investigate why females in Family X, who have relatives with ATR-X syndrome, have not approached the Division of Human Genetics, UCT, for carrier testing.

1.3 OBJECTIVES

- To compile a socio-demographic profile of the participants.
- To measure the participants' level of genetic knowledge of ATR-X syndrome.
- To investigate the participants' perception of their recurrence risk.
- To identify socio-economic factors preventing family members from undergoing carrier status testing or receiving their results.
- To investigate previous experiences and the impact of having family members affected with ATR-X syndrome.

- To investigate the communication networks of sharing and transmission of information in Family X.
- To determine if participants are aware of the testing and counselling services offered.
- To determine the opinions of members of Family X regarding genetic testing.
- To improve participants' level of knowledge about ATR-X syndrome and access to genetic testing.

1.4 ORGANISATION OF THE STUDY

A literature review of ATR-X syndrome and relevant aspects of genetic counselling is presented in Chapter Two. Chapter Three describes the methodological approach used in this study. This includes an explanation of the research process, the sample, how participants were recruited, a description of the measurement instruments and their validity/trustworthiness, ethical considerations together with a brief explanation of the data gathering and analysis procedures. Due to the nature of qualitative research, the results of the research and the discussion of the findings are customarily presented together and intermixed in Chapter Four (Hansen, 2006; McMillan & Schumacher, 2001). A summary of the main findings of this study are provided in a conclusion in Chapter Five, while Chapter Six contains recommendations based on the findings of the research.

CHAPTER 2:

LITERATURE REVIEW

2.1 INTRODUCTION

This chapter includes a review of literature on the clinical description of ATR-X syndrome; the genetics of the condition; the impact of disability on a family and reproductive decisions; factors influencing level of knowledge of genetics and uptake of carrier testing; and communication within families. Due to the paucity of literature on ATR-X syndrome, literature regarding related conditions or that has similarities in terms of testing and communication will be discussed.

Due to the aims of the research outlined in Chapter One, literature concerning the impact of a genetic disorder, or disability, on the family will mainly be discussed in terms of the impact on siblings and extended family members, rather than on parents.

2.2 CLINICAL ASPECTS OF ATR-X SYNDROME

2.2.1 Clinical description

Phenotypic features

The majority (>90%) of individuals with ATR-X syndrome will have facial dysmorphism and hypotonia. An example of the appearance of an individual with ATR-X syndrome is presented in Figure 2.1 (Gibbons *et al.*, 1995a).

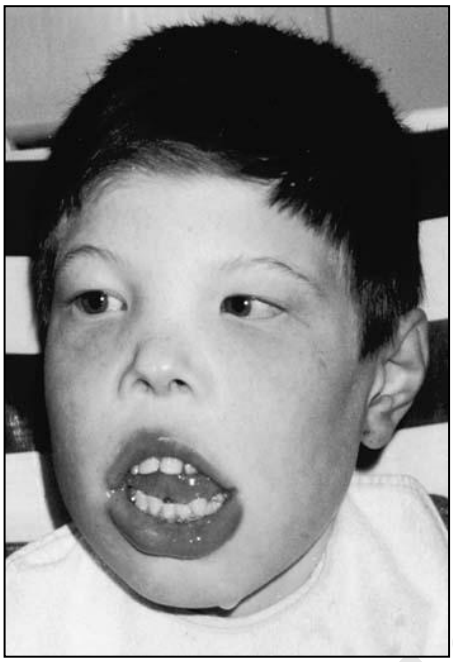

Figure 2.1 Typical facial appearance of a 13 year old boy with ATR-X syndrome (Gibbons *et al.*, 1995a).

Genital abnormalities occur in approximately 80% of cases. The abnormalities range in severity from undescended testes, to a micropenis, to ambiguous external genitalia. A delay in puberty is frequently noted and in some cases it may even be arrested (Gibbons & Higgs, 2000; Gibbons, 2006; Stevenson, 2009).

Other abnormalities reported in individuals with ATR-X syndrome include recurrent vomiting or regurgitation, excessive drooling and constipation. Aspiration has been implicated as a common cause of death in early childhood. Seizures occur in about one third of cases and spasticity can occur with increasing age. Post-natal microcephaly (occurring in 75% of cases), skeletal abnormalities (90%), short stature (65%), cardiac abnormalities (20%) (For example: septal defects, pulmonary stenosis, aortic stenosis, and patent ductus arteriosus), as well as renal abnormalities (15%) (For example: hydronephrosis, renal hypoplasia, and polycystic kidney) associated with recurrent urinary tract infections, may also be present (Gibbons & Higgs, 2000; Gibbons, 2006; Stevenson, 2009). Clinical variability, even within the same family, has been reported in ATR-X syndrome (Pavone *et al.*, 2010).

When ATR-X syndrome was first described, the presence of alpha thalassemia was a key defining element. However, it has now been observed that the haematological manifestations that can be associated with mutations in the *ATRX* gene are highly varied. Although 90% of affected individuals have alpha thalassemia, it is no longer viewed as a defining factor in the syndrome. This is due to the fact that, in a number of families, some or all family members affected with ATR-X syndrome may have no clinical signs of it. If alpha thalassemia is present, individuals are usually mildly affected by the haemoglobinopathy, as opposed to the classical form of alpha thalassemia which has a different aetiology (Gibbons & Higgs, 2000; Gibbons, 2006).

Neurodevelopmental features

Intellectual disability (ID) is a key feature of ATR-X syndrome and is found in 95% of individuals with this condition (Gibbons & Higgs, 2000; Gibbons, 2006). ID is relatively common and is said to occur in approximately 2–3% of the general population in developed countries (Johnson & Walker, 2006; Ropers & Hamel, 2005). The prevalence of ID in South Africa (SA) is unknown, although a study by Christianson *et al.* (2002) showed that the prevalence of ID in a sample of rural SA children was approximately 3.5%. The criteria for a diagnosis of ID involves: (a) significant sub-average general intellectual functioning; (b) inadequate adaptive functioning in at least two of the following skill areas: communication, social and interpersonal skills, decision making, ability to live independently, use of community/public resources, self-care, health, safety, work, functional academic skills and leisure activities; (c) onset before the age of 18 years (Raymond, 2006; Ropers & Hamel, 2005). Intellectual functioning is defined by the intellectual quotient (IQ), with an IQ of below 70 being classified as an intellectual disability. The different categories of ID are mild (IQ = 50–70), moderate (IQ = 35–49), severe (IQ = 20–34) and profound (IQ < 20) (Raymond, 2006). The categories of ID can also be classified according to the abilities of an individual and this is shown in Table 2.1 taken from Katz and Lazcano-Ponce (2008).

Table 2.1 Classification of ID stratified by three age groups (Katz & Lazcano-Ponce, 2008).

0 to 5 years *Maturation and development*	*6 to 20 years* *Training and education*	*21 years and older* *Social and vocational adequacy*
Degree: Mild (IQ 50–70) Generally develop communicative and social skills. May not be distinguishable until starting school.	Can learn up to 4th/5th primary school grade skills when reaching the ages of 18 or 19 years. Can be integrated into society.	Is capable of acquiring social and work skills for integration into the work force at a minimum wage.
Degree: Moderate (IQ 35–49) Can speak or learn to communicate. Some difficulties with motor skills.	Difficulty meeting 2nd primary school grade academic objectives.	May be able to partially maintain oneself economically in manual work under protected conditions.
Degree: Severe (IQ 20–34) Marked limitations in motor skills. Minimal language ability.	Can speak or learn to communicate. Can learn elementary self-care and health habits.	Can partially contribute to maintaining oneself economically, under total supervision.
Degree: Profound (IQ <20) Significant delay and minimal functional ability in sensorimotor areas. Requires basic care.		Some motor and language development. Can learn very limited personal care skills.

In ATR-X syndrome affected individuals have moderate to profound ID. There is usually global developmental delay with an emphasis on limitation of expressive language. Most affected children will have no speech, however there are a number of cases reported in which a few words or signs are used in communication. All developmental milestones are delayed in early childhood. In the most severe cases, children may never walk, or may only walk later in childhood. Most children affected with ATR-X syndrome are dependent on others for assistance in daily tasks and activities, although it has generally been observed that new skills can be acquired. (Gibbons & Higgs, 2000; Gibbons, 2006).

Behaviourally, children affected with ATR-X syndrome have generally been described as having a happy nature. However, reports of emotional outbursts involving sustained laughing or crying have been made, together with reports of autistic-like behaviour and intense emotional fluctuations between states of excitement, and withdrawal and depression. Individuals may be restless with choreoathetotic movements, and may exhibit self-mutilating behaviour such as biting and hitting themselves. Induction of vomiting may also frequently occur in affected individuals (Gibbons, 2006).

2.2.2 Prevalence of ATR-X syndrome

ATR-X syndrome is rare with only about 200 cases being described worldwide, resulting in an estimated prevalence in the range of 1–9/1 000 000 (Gibbons, 2006; Gibbons *et al.*, 2008; Stevenson, 2009). However, there is clinical heterogeneity regarding the phenotype in individuals with *ATRX* mutations. This heterogeneity complicates a clinical diagnosis and therefore some individuals may not be recognised as having ATR-X syndrome. Consequently, there may be a greater number of individuals with ATR-X syndrome than was originally estimated (Gibbons *et al.*, 2008; Stevenson, 2009).

2.2.3 Management of ATR-X syndrome

According to Johnson & Walker (2006), there are four main areas of caring for children with ID. These include health; developmental, behavioural and educational interventions; socialisation and community integration; and considerations during the transition into adolescence and adulthood.

A diagnosis of ATR-X syndrome is important at a young age so that the appropriate intervention and management are in place. It is important that developmental interventions are introduced early so as to ensure optimisation of the affected individual's capabilities. This may include infant stimulation, special education and one-to-one therapy to improve socialisation. Appropriate behavioural interventions may also be prescribed (Gibbons, 2006). As affected individuals get older, respite care and placement in a home or institution may be considered (Johnson & Walker, 2006).

Specific health management for ATR-X syndrome may include a calorie-dense formula due to feeding difficulties and physiotherapy for hypotonia. Constipation may be improved or prevented with adequate hydration, together with a bulky diet, to ensure it does not become a serious management problem. In the event of excessive drooling, speech therapy, anticholinergic treatments to reduce saliva production, botulinum toxin type A injections or surgery may be considered. Recurrent vomiting, gastro-oesophageal reflux and food refusal should be carefully evaluated for the underlying cause, for example peptic ulceration. Treatment of other complications, such as seizures, should be treated according to standard therapy (Gibbons, 2006; Stevenson, 2009).

2.3 GENETICS OF ATR-X SYNDROME

2.3.1 Introduction

The causative gene for this form of ID was first identified by Gibbons *et al.* in 1995(b). The gene, *ATRX*, located at Xp13.3, encodes the ATRX protein that has been hypothesised to be involved in the regulation of gene expression. This hypothesis is based on two observations; firstly because ATRX belongs to the SNF2 family of proteins, which is involved in chromatin remodelling, and secondly that the protein contains a zinc finger domain highly related to that of the DNMT3 family of *de novo* DNA methyltransferases. The observation of alpha thalassemia in some patients with ATR-X syndrome has aided in the understanding of ATRX's putative function as this clinical feature is caused by the reduced expression of the alpha globin genes (Gibbons *et al.*, 1995; Gibbons, 2006; Gibbons *et al.*, 2008).

A number of phenotypically overlapping conditions, caused by allelic mutations in the *ATRX* gene, have also been described such as Carpenter-Waziri syndrome, Juberg-Marsidi syndrome, Holmes-Gang syndrome, Smith-Fineman-Myers syndrome, Chudley-Lowry syndrome and X-linked mental retardation (XLMR) with spastic paraplegia (Gibbons *et al.*, 2008).

ATR-X syndrome follows an X-linked recessive pattern of inheritance. Therefore the chance of a female carrier passing the disease allele to a child is 50% in each pregnancy. However, as only male children are affected by this condition, there is a 25% risk of having a child affected by ATR-X syndrome with each pregnancy. There have been reports of female carriers showing signs of alpha thalassemia, however they are not otherwise phenotypically affected (Gibbons, 2006; Gibbons *et al.*, 2008).

The molecular diagnosis of ATR-X syndrome in the study family was recently made possible by a PhD student in the Division of Human Genetics, UCT, who identified the

disease causing mutation in the *ATRX* gene. The mutation was found to be a novel deletion of 24 base pairs (bp) in exon 26 of the genomic DNA (Carvill, 2010). This corresponds to a larger deletion of 66bp from the messenger RNA (mRNA) transcript which has been previously described in two separate cases (Gibbons & Higgs, 2000; Gibbons *et al.*, 2008), but which were caused by different genomic mutations.

2.3.2 Carrier testing

Carrier testing involves identifying individuals who are not affected by the genetic condition, but who carry the disease-causing gene in a heterozygous state and who are therefore at risk of having an affected child. This testing is most important in the case of X-linked recessive conditions as females have a high risk of having an affected male child independent of their partner, which is in contrast to autosomal recessive conditions where both parents carry the disease-causing gene (Harper, 2001).

In general, close relatives of an affected individual are offered carrier testing first; more distant relatives are then offered testing based on the results. This is termed 'cascade screening' and it essentially involves starting with an affected individual and radiating outwards to identify family members who are at risk of being carriers. Those individuals who test positive form the base to identify more possible carriers, who are then offered testing. In this manner entire extended families may be systematically tested (Super *et al.*, 1994). Carrier testing is usually postponed until an individual is of child-bearing age and is able to give proper informed consent, therefore the testing of minors (younger than 18 years) is generally not recommended (Borry *et al.*, 2006; McConkie-Rosell *et al.*, 2005).

2.3.3 Preventive strategies for ATR-X syndrome

Knowledge of carrier status for X-linked conditions enables at risk women to make informed choices regarding reproduction, such as the decision whether or not to have biological children, and to allow prenatal diagnosis to be offered (Kay & Kingston, 2002). The decision to have a prenatal diagnosis should ideally be planned before a pregnancy as otherwise the procedures involved may need to be hurried, and rushing through the decision-making process may result in decisions that are not objective or fully thought through (Harper, 2001). Certain criteria regarding prenatal diagnosis need to be considered to justify the procedure and these include: the accuracy of the prenatal diagnostic test, a significant risk that the foetus may have the disorder, the severity of the disorder, if termination will be offered, whether termination of pregnancy (TOP) is acceptable to the couple, and what treatment is available for the disorder (Harper, 2001).

Previously, the only option available to pregnant women known to be carriers or at a high risk of being a carrier for an X-linked condition was foetal sexing. If the investigation showed a male foetus, termination may have been considered by a couple. This decision was based on risk alone and not on certainty of whether the male foetus was affected or not. Therefore molecular prenatal diagnosis of at-risk pregnancies can give an expectant couple better information on which to base their decisions. With the knowledge of a specific disease-causing mutation, molecular diagnosis of a disorder can be easily and accurately made (Harper, 2001).

In order to perform molecular diagnosis on a foetus, an invasive procedure such as amniocentesis or chorionic villus sampling (CVS) is necessary to obtain foetal cells from which DNA can be extracted, and molecular testing performed (Wilson *et al.*, 2005). Based on these results, the option of terminating an affected pregnancy can be offered and discussed (Kay & Kingston, 2002). The invasive procedures do however have a risk of causing a miscarriage; these are normally in the range of 0.5–1% for amniocentesis and 1–2% for CVS (Wilson *et al.*, 2005). Due to the complexity of carrier and prenatal testing, along with the difficult decisions that need to be made if an affected

foetus is identified, it is recommended that testing be accompanied by genetic counselling (McConkie-Rosell *et al.*, 2005).

2.3.4 Genetic counselling

Genetic counselling is a communication process whereby individuals and their families affected by, or at risk of, a hereditary condition are provided with information and support regarding the condition, its consequences and its inheritance (Resta, 2006). It is important for individuals to have a thorough understanding of what implications the disease will have on the family, the appropriate management options and the recurrence risk for the individual and other family members. This knowledge allows individuals to make informed decisions regarding reproductive choices (Baker, Schuette & Uhlmann, 1998; Resta, 2006). Genetic counselling can also aid in informing individuals of available genetic testing and assist families in understanding the results and dealing with the consequences of this knowledge (Harper, 2001; Resta, 2006).

Genetic counselling for ATR-X syndrome should follow guidelines recommended for X-linked disorders such as FXS, which include:

- A targeted enquiry of family history and drawing of a three- to four-generation pedigree.
- Identifying female relatives who are at risk of being carriers.
- Discussing the clinical presentation of the condition.
- Exploring the impact the condition has had, or is having, on the individual and family.
- Informing them about X-linked recessive inheritance and offering genetic testing (carrier, prenatal and diagnostic in the case of suspected affected males).
- Assessing and discussing support structures and community resources.
- Addressing any psychological issues such as guilt or anxiety.

- Encouraging them to inform at-risk family members of their potential risk and the availability of genetic counselling and testing services.
  (Bennett *et al.*, 2002; McConkie-Rosell *et al.*, 2005; McIntosh *et al.*, 2000)

When working with extended families, it may be useful to utilise the family network to facilitate informing relatives of their genetic risk; whereby at-risk family members are initially informed by a relative known to them and then followed up by a genetic counsellor. However, when utilising this approach, genetic counsellors should reassure family members that the provision of in-depth counselling, or ensuring that others pursue testing, is not their responsibility (McConkie-Rosell *et al.*, 2005). In studies with families with FXS, it has been found that it is useful, when informing other family members, to have a summary letter or similar document which contains details of the condition and the genetic counsellor's contact details (McConkie-Rosell *et al.*, 2005). Claes *et al.* (2003) also emphasised the importance of developing these tools to help family members inform relatives. It should also be mentioned that, when working with extended families, genetic counsellors should ensure that they do not breach the confidentiality of others in the family (McConkie-Rosell *et al.*, 2005).

2.4 MODELS OF DISABILITY

There are different models that have been used to describe disability and two that are of importance are the medical model and the social model. The medical model views disability as a negative condition and emphasises the need for treatment, rehabilitation or cure so that the individual achieves or returns to 'normality'. Conversely, the social model views disability as being caused by society and their stigmatisation of disability, resulting in physical and social barriers to individuals fully participating in society. Furthermore, in line with the social model, an 'affirmation model' of disability has been suggested where disability is viewed as a 'normal form of human diversity' (Seligman & Darling 2007: pg 5).

2.5 IMPACT OF DISABILITY ON THE FAMILY

According to the family systems theory, a family operates as an interactive unit whereby an effect on one individual will affect all other members of the family (Seligman & Darling, 2007). Therefore, the presence of a genetic condition or disability in one individual will have an impact on all members of a family; however this impact may be both positive and/or negative (Rodger & Tooth, 2004; Ross & Deverell, 2004; Seligman & Darling, 2007).

The diagnosis of a genetic condition in a family has psychosocial implications for parents, the affected child, unaffected siblings and grandparents or other members of the extended family. This, together with the knowledge of genetic risk, impacts on family relationships, individual psyche and family identity (Lehmann, Speight & Kerzin-Storrar, 2011; Ross & Deverell, 2004).

2.5.1 Impact on siblings

The impact on siblings may manifest in various ways. Siblings share the emotions that their parents may experience with the diagnosis of a disability in their sibling, such as grief, pain and fear. The amount of time that parents may have to spend in caring for their disabled child may result in the non-disabled siblings feeling angry, resentful and bitter as there is limited attention given to them. This may also result in guilt related to the negative feelings towards their siblings. 'Survivor guilt' may also be experienced by siblings as they, in contrast to their disabled siblings, are in good health or can go on to lead normal lives (Ross & Deverell, 2004; Seligman & Darling, 2007).

Due to the considerable amount of stress and time needed to look after a disabled child, many siblings may experience a sense of responsibility and may be forced into 'precocious responsibility' or taking on parental roles at an early age (Benderix &

Sivberg, 2007; Seligman & Darling, 2007). The danger of this is that siblings may lose their childhood in the process of helping their parents look after their disabled siblings. The gender of non-disabled siblings may influence the level of caregiving responsibilities undertaken, with female siblings often being given more of these responsibilities and burdens. Siblings may also feel burdened and pressured to achieve and compensate for their parents disappointment and unfulfilled hopes concerning their affected sibling (Ross & Deverell, 2004; Seligman & Darling, 2007). Embarrassment can become an issue as siblings reach adolescence and they may experience difficulty in bringing friends home because of their disabled sibling's behaviour or because of parental stress and lack of time to support and interact with them and their friends (Benderix & Sivberg, 2007; Rodger & Tooth, 2004; Ross & Deverell, 2004). Unaffected siblings may also experience anxiety concerning being a carrier and thus experience anxiety regarding the risk of having disabled children themselves (Ross & Deverell, 2004).

Despite these negative impacts described, there are many studies that mention the positive impact that disabled individuals have on their siblings, family and community. Disability in a family may offer the non-disabled siblings the opportunity for growth and maturation. Siblings also report greater understanding of others, tolerance, compassion, sensitivity regarding discrimination and stronger family relationships. Despite reports that siblings may feel guilty about their own health, an appreciation of their own good health and abilities is also reported. A sibling's disability may also lead to greater clarity regarding future and career goals of the unaffected sibling, as well as setting priorities and improving their sense of purpose (Eisenberg, Baker & Blacher, 1998; Rodger & Tooth, 2004; Ross & Deverell, 2004; Stainton & Besser, 1998).

Furthermore, a study by Griffiths and Unger (1994) showed that over half of the individuals interviewed who had a brother with ID did not want their disabled sibling to be placed in an institution or home, but rather wanted their siblings to remain in their family home. They also found that just under half of the non-disabled siblings were

willing to look after their affected sibling should their parents die. This suggests that the care of disabled siblings may not always be viewed as a major burden as previously portrayed.

Positive acceptance of a sibling and their disability may also be influenced by religion, which provides a framework for providing a sense of meaning for their situation and purpose in life (Michie & Skinner, 2010; Poston & Turnbull, 2004; Rodger & Tooth, 2004). Michie and Skinner (2010) examined how religion influenced the illness narratives of mothers of children affected by FXS; their finding was that 62% of mothers indicated that religion played a significant part in their daily lives by providing them with support, source of meaning and encouragement. Furthermore, 52% said that they felt closer to their faith as a result of having FXS in their family. Poston and Turnbull (2004) also found that individuals who had a child affected with a disability gained meaning and purpose in life through their faith. They found that individuals gained strength from their spiritual beliefs and participation in religious activities, and that this strength acted as a resource for families in facing the challenges and difficulties of everyday life.

2.5.2 Impact on extended family

With the exception of grandparents, there is a paucity of literature regarding the impact of an individual with a disability on the extended family such as aunts, uncles, cousins, nieces and nephews. Literature regarding grandparents has shown that, especially in the case where a child's disability originated from one side of the family, there may be a great sense of guilt (Seligman & Darling, 2007). This is especially evident in X-linked conditions, where 'grandmother guilt' has been described (Anido *et al.*, 2005; Lehmann, Speight & Kerzin-Storrar, 2011). Grandparents may also face a sense of loss of a 'normal' grandchild and the loss of their dream for their own child to have a 'normal' life, free of burden. How grandparents react to this situation and the amount of support

offered, can influence family functioning, especially at the time of diagnosis (Seligman & Darling, 2007).

2.5.3 Community impact and reactions

Stainton and Besser (1998) reported that families with a child with ID indicated that their child had had a positive impact on their community as they taught others to be more accepting of differences, and others discovered what the potential of people with disabilities were.

Despite the potential positive impact on the community, people with a disability still experience negative reactions and stigma. Individuals with a disability deviate from the norms of society regarding physical or mental ideals; the extent to which they deviate from these ideals influences the degree to which they are shunned, avoided, mocked, ostracised and discriminated against. Stigma is therefore socially constructed and depends on the visibility of the disability, its perceived controllability and its perceived danger (Seligman & Darling, 2007). From this, it is apparent that individuals with ATR-X syndrome could be stigmatised due to the fact that their disability is visibly apparent due to the characteristic dysmorphic features. However, ID may not be viewed as being under one's control, although the aggression of some individuals with ATR-X syndrome could be perceived as dangerous. A qualitative study in Australia, investigating the impact of caring for a school-aged child with a disability, found that the four mothers interviewed experienced negative reactions from the community, which were upsetting and led to social isolation (Bourke-Taylor, Howie & Law, 2010).

A factor that may influence attitudes towards ID is social class, with individuals from middle- to upper-class backgrounds often perceiving mild ID as being a devastating condition. Conversely, individuals from lower-class backgrounds may not consider mild ID to be a disability at all. This is consistent with the finding that middle- and higher-

class parents tend to have higher educational and career aspirations for their children and tend to also expect achievement and independent behaviour. Parents from lower-class families tend to be less achievement-oriented and more accepting of disability (Seligman & Darling, 2007).

2.5.4 Social support

The way in which a family views disability is influenced by a number of factors, such as how illness in general is dealt with in the family, its severity and the amount of social support (Seligman & Darling, 2007).

Social support is an important factor that influences how an individual or family copes in a stressful situation (Seligman & Darling, 2007; Ziolko, 1991). Social support networks have been reported to increase an individual's well-being and feeling of competence, while the absence of it may result in isolation, depression and doubts (Seligman & Darling, 2007). Families with children with ID should ideally receive multiple levels of support, namely from their family and friends, support groups and from professionals amongst others, which can help with coping, adaptation, reducing stress, positive family functioning and maintaining a sense of normalcy (Johnson & Walker, 2006; Seligman & Darling, 2007). Social support from the nuclear and extended family, together with friends, is crucial, with feelings of togetherness, or cohesion and co-operation in the family being important factors in the family's ability to cope (Seligman & Darling, 2007; Taanila *et al.*, 2002). Families may also find that sharing their experiences with other families who are in a similar situation as particularly rewarding and helpful (Taanila *et al.*, 2002).

2.6 REPRODUCTIVE IMPLICATIONS

Personal experiences with a condition may influence or have an impact on reproductive decisions made by family members (Beeson & Golbus, 1985; Kay & Kingston, 2002; Peterson, 2005). Beeson and Golbus (1985) investigated the decision-making process in couples at risk of having a child with an X-linked condition, and found that, out of 11 couples at-risk of having a child with Duchenne Muscular dystrophy (DMD), the three couples willing to take the risk of having an affected child were those with no exposure to the advanced stages of DMD. This finding shows that the personal experience of being exposed to the later stages of the illness influenced the willingness of the other couples to risk the birth of a child with the same condition. Kay and Kingston (2002) also investigated what influenced reproductive decisions in women known to be carriers for an X-linked condition. They found that the women who had personal experience with the condition (lived with an affected relative) were more certain of and concrete in their decision to avoid having an affected child, while those without personal experience were less certain of the decision to avoid having an affected child. Furthermore they also found that 13 of the 14 individuals interviewed, intended, or had already decided, to have prenatal diagnosis and termination of an affected foetus in order to avoid having a child with the condition.

A study by McConkie-Rosell *et al.* (1997), investigating attitudes and opinions of obligate carriers for FXS towards genetic testing and the impact of the condition, showed that 67% of them felt that their plans for having more children changed as a result of their child being diagnosed with FXS. Furthermore 89% indicated that if they had known they were a carrier for FXS before having children, they would have either reduced the number of children that they had, or not had any biological children. Eighty-two percent also indicated that they would have opted for prenatal diagnosis, if they had known of it before, to avoid having an affected child or to be prepared for it. The reproductive decisions that parents make have been found to be heavily centred around

social meaning and perceived social consequences that are subjective and are dependent on the life experiences of a couple (Beeson & Golbus, 1985).

Further understanding on how parents may view the implications of an affected child is shown by research involving cystic fibrosis (CF). De Braekeleer, Rault and Bellis (2004) found that 76.2% of couples who had a previous child with CF would have an abortion after positive prenatal diagnosis. This is in contrast to an earlier study by Wertz *et al.* (1992), where only 20% of couples with a child with CF were willing to abort a pregnancy due to CF. This inconsistency probably reflects that there are various factors that may influence abortion attitudes, such as education, religion, opinions of others and risk interpretation (De Braekeleer, Rault & Bellis, 2004; Wertz *et al*., 1992). In addition, Beeson and Golbus (1985) found that variables influencing an individual's willingness to take the risk of having a child affected with an X-linked condition were level of education, income and career commitments. A higher level of each of these factors independently related to less willingness to take the risk.

De Pina-Neto and Petean (1999) found that the recurrence risk for a genetic condition or disability was an important factor in a couple's decision to have more children as couples with a high recurrence risk were more likely to decide not to have children than those with a lower risk. There was also a correlation between the motivation to avoid having more children and understanding the recurrence risk, showing that level of understanding has important implications for reproductive decisions. In respect of TOP, significantly more high risk couples (57.1%) indicated that they would accept TOP, if the foetus was shown to have a severe disease via prenatal diagnosis, than low risk couples (39.6%). This is despite the fact that 71% of the individuals felt that their religion was opposed to TOP, therefore emphasising that recurrence risk and the original impact of the condition may be more important than religious views.

Bryant, Green and Hewison (2010), investigated whether attitudes toward individuals with a condition would predict prenatal decisions and found that unfavourable attitudes towards people with Down syndrome (DS) were predictors of the intention to terminate a pregnancy. They also found that individuals who felt that their religion influenced their decisions considerably, were significantly less likely to use screening, prenatal diagnosis or termination of a pregnancy for DS, which is contrary to the findings of De Pina-Neto and Petean above.

Klitzman (2010) found that misunderstandings concerning a genetic condition may influence an at-risk individual's decisions surrounding marriage or having children. Some individuals may also perceive themselves to be carriers of a genetic condition in order to reduce their anxiety related to the uncertainty of not knowing their carrier status (Klitzman, 2010).

2.7 ATTITUDES TOWARDS GENETIC TESTING

An important factor influencing the decision to undergo carrier testing may be a woman's personal experience of the disease. Family members who were unaware of, or distant to, an affected relative may not have the same feelings regarding the desire to know their status when compared to a close sibling of an affected individual. This may be related to their perceived risk of being a carrier and the perceived value of the knowledge of carrier status (Anido *et al.*, 2005; Archibald *et al.*, 2009; Beeson & Golbus, 1985; Kay & Kingston, 2002; Peterson, 2005; Varekamp *et al.*, 1990). Beeson and Golbus (1985) observed that perceptions of individuals who had not lived with a child affected by a genetic condition were vague and abstract, while those who had, were clear and concrete. Those living with an affected individual were more aware of the daily challenges faced by both the family and the affected individual (Beeson & Golbus, 1985).

Varekamp *et al*. (1990) investigated the attitudes towards genetic carrier and prenatal testing for haemophilia in 549 potential and obligate carriers. They found that only 27% of nieces and 19% of cousins of an affected individual had carrier testing, versus 62% of sisters, indicating that uptake of carrier testing is influenced by one's relationship to an affected relative and experience with the condition. Distant relatives are not part of the nuclear family of an affected individual and may be less socially and psychologically involved, therefore knowing less about the consequences of the disease on the affected individual and their immediate family. This may result in them being less inclined to have carrier testing (Varekamp *et al.*, 1990). They also found associations between the uptake of carrier testing and both the severity of haemophilia in their relatives and whether women had previous children.

The reproductive life stage of a woman may also influence her decision regarding the uptake of carrier and prenatal testing. Carrier testing may be viewed as unnecessary by individuals not planning to have a family in the near future or women who feel that their family is already complete (Anido *et al.*, 2005; Archibald *et al.*, 2009). De Braekeleer, Rault and Bellis (2004) found that 70.7% of couples in their study did not intend to use prenatal diagnosis for CF. However, the motivation for 93% of these couples was because that they did not intend to have more children.

The decision to undergo carrier testing may also be influenced by whether a woman considers abortion as an option. In a study investigating attitudes towards carrier testing in FXS, one woman's advice to others was to consider whether they would abort a pregnancy if their child were disabled. She felt that if a woman would not be able to abort and would be happy to raise a child with a disability there was no reason to do carrier testing and suggested "*Why not just assume everything is wonderful and then deal with whatever you get?*" For other women in the study, carrier testing was viewed as providing them with a choice of whether to have children with the condition or not, while others did not want to know their status as it removed their confidence in having a 'normal' child (Anido *et al.*, 2005).

In line with the findings by Anido *et al.* (2005), Archibald *et al.* (2009) also found that certain individuals felt that knowledge of their carrier status would create unnecessary anxiety during the pregnancy in their study investigating opinions concerning carrier testing for FXS in the general population. Women may also not want to undergo carrier testing as a form of denial and avoidance of the threatening knowledge of being a carrier and difficult decisions that come with that knowledge (Kay & Kingston, 2002; Shiloh & Ilan, 2005).

Anido *et al.* (2005) and Archibald *et al.* (2009) both found that within the general population, many individuals would want carrier testing out of curiosity. However, when there was a family history of FXS, motivation to have carrier testing was related more to providing the information to their children or extended family, so that they could make informed reproductive choices in the future (Anido *et al.*, 2005). The desire to help family members know more about their own genetic risk was also acknowledged as a strong motivator for seeking genetic testing in a literature review by Peterson (2005).

The decision to undergo carrier testing may be influenced by practical and socio-economic reasons. In a study by Archibald *et al.* (2009), the need to return to the clinic to take a blood sample was reported as a barrier for testing; with one woman reporting that she "*couldn't be bothered organising the appointment*" despite the fact that she wouldn't mind having the carrier test done.

Eggers *et al.* (1999) investigated the impact of genetic counselling on women, who were potential carriers for DMD, regarding their opinions on testing and reproductive decisions. One of their findings was that genetic tests (both carrier and prenatal) were more often requested by women who had a higher educational level and who were not against the idea of abortion. Similarly to carrier testing and TOP attitudes, the intention to use prenatal testing may be influenced by factors such as religion, education, family income, size of the family and the willingness to abort an affected child (De Braekeleer,

Rault & Bellis, 2004; Wertz *et al.*, 1992). The desire for prenatal testing may not be exclusively related to the intention to terminate an affected pregnancy, but may also be desired for preparation purposes (Bryant, Green & Hewison, 2010; McConkie-Rosell *et al.*, 1997).

An important factor that may influence the uptake of genetic testing is the level of understanding of how the condition is inherited and the risk of recurrence in a family (Sivell *et al.*, 2008). It was previously assumed that accurate recall of recurrence risks and diagnostic information was necessary for decision making (Austin, 2010; Kessler, 1989). However, an individual's perception of their risk, and the meanings that they attribute to it, may be more important in this process (Sivell *et al.*, 2008). In a literature review by Sivell *et al.* (2008), it was reported that one's perception of genetic risk may be based on many factors including previous experiences, environmental factors, occupation, diet, stress and anxiety, physical appearance or resemblance to an affected relative and family history. The perception of being either at high or low risk, due to family history, was shown to influence the uptake of carrier testing by Archibald *et al.* (2009).

The uptake of carrier testing may also be influenced by individuals in the family being unaware of the availability of testing. This may be due to poor communication between counsellors and the family or within the family. Varekamp *et al.* (1990) found that 25% of women who had not been tested for their carrier status were unaware of the availability of testing and were only made aware of this availability through the research. Ignorance of the available testing was associated with a more distant relationship to an affected relative. Binedell, Soldan and Haper (1998), similarly found that approximately 25% of individuals who had not presented for testing for Huntington's disease (HD), were not aware of the available testing prior to receiving the letter inviting them to participate in the research. However, simply being aware of carrier testing may not always influence uptake of testing as seen by Claes *et al.* (2003). They found that in 40% of participants who had informed relatives of the available

testing for hereditary breast and ovarian cancer (HBOC) due to a known mutation, not a single relative presented for testing; thus indicating no association between informing relatives and testing uptake.

2.8 LEVEL OF KNOWLEDGE OF GENETICS

Genetic concepts and terminology are complex and confusing and are often poorly understood by the public who do not know the basics of human biology or genetics (Chapple, Campion & May, 1997; Klitzman, 2010). Delivery of factual information is the most frequent form of interaction between genetic counsellors and clients (Michie, Marteau & Bobrow, 1997). However it has been observed that client recall of information is selective and is influenced by personal meaning attached to the information given and by the expectations of the client regarding the appointment (Davey *et al.*, 2005). There may be numerous factors that influence an individual's level of understanding of genetics or their perception of genetic risk.

De Pina-Neto and Petean (1999) found that there was a predominantly inadequate level of understanding amongst the parents interviewed after initial genetic counselling for their child with a genetic condition or disability. Parents' knowledge was seen to be dependent on the amount of time that had lapsed between genetic counselling and the research interview, with the amount of knowledge decreasing over time. Furthermore, it was clear that the major factor influencing the parents' level of understanding was related to the family's socio-economic and cultural level; with a reduced level of understanding relating to lower socio-economic-cultural status. Henley and Hill (1990) found a similar finding with the level of parental knowledge on CF being related to social class. This study was the only study of its kind published in SA and they suggested that the reason for the finding could be that individuals from a lower social class are less likely to ask for more information from health professionals. They also

found that the level of genetic knowledge of patients and siblings of patients was approximately 20% less than that of their parents. Siblings also had the least amount of knowledge about CF overall.

In the study by Eggers *et al.* (1999) regarding views of women at risk of being carriers for DMD, they found that the level of understanding of participants was associated with their educational level, where a good comprehension of genetic counselling issues was significantly associated with a higher socio-educational level. This view is supported by Klitzman (2010) who found there were fewer misunderstandings amongst individuals who had some education in science (high school or college). In addition, Molster *et al.* (2009) found that higher levels of education and income were significantly associated with greater genetic knowledge amongst participants from the Australian public. They propose that fewer years of education result in individuals being less exposed to genetic information in the school biology curriculum and having fewer skills to search for information. They also suggested that individuals from a lower socio-economic class may be less motivated to acquire genetic information as it may be viewed as complex or undervalued (Molster *et al.*, 2009).

A study by James *et al.* (2006), in the United States of America (USA), found that the level of understanding of one's reproductive risk was independently associated with a higher level of education and mode of inheritance of the condition in the family. They found that the knowledge of individuals who were from a family affected with an X-linked condition was better than that of individuals from families where a family member had an autosomal recessive condition. Family members from an X-linked family were able to answer questions regarding the mode of inheritance between 57–79% correctly, while that for autosomal recessive family members was between 18–75% correct.

Many individuals may not understand numerical risk values and may instead dichotomise risk, in other words, they think that they will either get the condition or mutation or not, and thus may refer to a 50/50 chance (Hallowell, Statham & Murton, 1998; Sivell *et al.*, 2008). This observation was also made by Klitzman (2010) who investigated misunderstandings concerning genetics. Alternative views regarding the cause of genetic conditions may also be present due to cultural or religious beliefs, for example that a genetic condition is present as a result of punishment from God for some wrong-doing (Klitzman, 2010). In further support of the idea that individuals may not understand numerical risk figures, Varekamp *et al*. (1990), also found that 40% of obligate and potential carriers for haemophilia did not report their risk of being a carrier in percentages.

The acquisition of genetic knowledge may also be due to inadequacies of the counsellor such as unclear explanations and inadequate educational methods (Kessler, 1989). The acquisition of risk information may also be inadvertently interfered with by the provision of a considerable amount of other information during a counselling session (Kessler, 1989) or the emotional impact of hearing a diagnosis and trying to interpret what it all means.

Furthermore, as many individuals who have a family history of a genetic condition may not have access to genetic services, they may be more reliant on other primary health care providers for genetic information. In a study by Baars, Henneman & ten Kate (2005) in the Netherlands, the level of knowledge of genetics among gynaecologists, paediatricians and general practitioners (GPs) in particular was too low to ensure that they would be able to adequately answer patient's questions regarding genetics and genetic tests. The authors concluded that the lack of genetic knowledge by non-genetic physicians may be a global problem.

2.9 FAMILY COMMUNICATION

Communication within families is vitally important in genetics as genetic conditions are a family matter. Knowledge of one's individual risk for a genetic condition invariably provides risk information about other biological relatives which has implications for their own or their offspring's future (Sorenson, Jennings-Grant & Newman, 2003). Adequate family communication is vital to disseminate this information accurately, and the lack of communication of these risks potentially denies others the right to make informed decisions regarding health and reproduction (Forrest *et al.*, 2003; Peterson, 2005; Wilson *et al.*, 2004). Family communication plays a major role in how well a family manages stress and tension, and how they adjust and adapt to situations (McConkie-Rosell, Heise & Spiridigliozzi, 2009). Communication styles within a family may be varied (McConkie-Rosell, Heise & Spiridigliozzi, 2009; McConkie-Rosell, Del Giorno & Heise, 2011), however a meta-analysis of literature concerning family communication about genetic conditions between children and their parents, reported that open communication within a family had the ability to promote trust, increase support and resilience, reduce stress and improve family functioning (Metcalfe *et al.*, 2008).

Information sharing between parents and children is often complicated and parents views vary on when and how to disclose information (Gallo *et al.*, 2005; McConkie-Rosell *et al.*, 1997). Informing relatives about genetic information should rather be viewed as a process than as an act (Forrest *et al.*, 2003). Literature concerning informing daughters of their risk of being carriers for FXS, also emphasises the need for individuals to be informed in stages (McConkie-Rosell, Heise & Spiridigliozzi, 2009; McConkie-Rosell, Del Giorno & Heise, 2011; Wehbe *et al.*, 2009). It was suggested that the first stage of informing children should be to inform them that the condition in the family is inherited; the second stage would be to inform them of their risk of being a carrier and the third stage to inform them of their actual carrier status (McConkie-Rosell, Del Giorno & Heise, 2011; Wehbe *et al.*, 2009). The manner in which information is

disclosed can also influence how individuals cope and how they disclose information in the future (Forrest *et al.*, 2003; Wilson *et al.*, 2004).

Opinions on when to tell children about genetic information are also varied. Forrest *et al.* (2003), found that parents with a family history of HD felt that their children should be informed in time for making their first key life decision where HD could have an impact, such as marriage or having children, as they also felt the need to protect them for as long as possible. The age of a child also has an influence on when a parent may disclose information, as children of a younger age may still be too young to understand the information concerning genetics or the implications thereof (Forrest *et al.*, 2003; Gallo *et al.*, 2005). However, a study concerning the opinions of adolescents and young adults from FXS families, showed that the majority of the participants felt that children should learn about the inherited nature of the condition before 10 years, their risk of being a carrier between 11–13 years and be offered carrier testing between 14–18 years of age, which is younger than that typically endorsed (Wehbe *et al.*, 2009).

The responsibility to inform relatives about potential genetic risk was felt to be the responsibility of the family by the majority of participants with a family history of HD, seen by Forrest *et al.* (2003). There was, however, less consensus as to whether the health professional or family should inform relatives in the case of HBOC, which was related to the uncertainty of risk information in the condition. Support by the health professional may be needed in these cases (Forrest *et al.*, 2003). McConkie-Rosell *et al.* (1997) agreed that families should be informed of their risk for FXS by a relative known to them first, with follow-up by a genetic counsellor afterwards.

Sorenson, Jennings-Grant & Newman (2003), reported that 60% of patients with haemophilia had discussed carrier testing with relatives in the past, and 70% felt an obligation to inform family members about the genetic testing available through the research. Furthermore potential carrier females discussed carrier risk information with

other relatives showing that communication was relatively open in this family. However, communication was selective within the family, with females being more likely to be informed than males, due to the gender lines involved in X-linked inheritance.

There may be more barriers to informing more distant relatives, with van Rijn *et al.* (1997) showing that despite 100% of first degree relatives being informed of their genetic risk for FXS, only 59%, 39% and 3% of second, third and fourth degree relatives were informed respectively. Claes *et al.* (2003) reported similar findings that dissemination of information to distant relatives was more problematic, with 40% of participants with a known HBOC mutation indicating that they did not inform distant relatives as they thought another relative would pass on the information. Barriers to informing distant relatives include lack of contact, lack of emotional connection, belief that the information was not relevant to them, and not being personally known to the patient (Claes *et al.*, 2003; Forrest *et al.*, 2003; Wilson *et al.*, 2004).

There may be many other barriers to communicating genetic information and these may include feelings of not wanting to be the bearer of bad news, denial, blame and guilt, together with a wish to protect relatives from distress (Claes *et al.*, 2003; Davey, Newson & O'Leary, 2006; Forrest *et al.*, 2003; van Rijn *et al.*, 1997; Wilson *et al.*, 2004). Individuals may also feel ill-equipped to disseminate genetic information as they do not understand the information fully and do not know how to explain the condition or its inheritance and the implications thereof (Claes *et al.*, 2003; Gallo *et al.*, 2005; McConkie-Rosell, Heise & Spiridigliozzi, 2009; Wilson *et al.*, 2004). An understanding of the condition and its risks, is vital to the dissemination of knowledge in genetics as a lack of understanding can result in information being inaccurately or selectively passed on to others, which may perpetuate further misconceptions (Claes *et al.*, 2003). Family conflict and tension acts as a further barrier to communication within families (Claes *et al.*, 2003; Davey, Newson & O'Leary, 2006; Fransen, Meertens & Schrander-Stumpel, 2006; Wilson *et al.*, 2004).

As can be seen in this literature review, there are many factors that can influence an individual's experiences and decisions regarding disability and genetic conditions, and it is important to keep this in mind when performing research.

CHAPTER 3:

METHODOLOGY

3.1 INTRODUCTION

The research design, participant recruitment and the measurement instruments utilised in the research are presented in this chapter. An explanation of the data gathering procedure and analysis is also provided. The reasons for having chosen the relevant methodology are provided and potential sources of bias are described together with strategies employed in an attempt to minimise this.

3.2 RESEARCH DESIGN

A qualitative approach, utilising a phenomenological, cross-sectional design, was used for this research. Qualitative research is concerned with the way in which individuals interpret and make sense of their experiences and therefore aims to understand social phenomena from the participants' perspective (Holloway, 1997; McMillan & Schumacher, 2001). This understanding is acquired by the many contexts of the participant and by the narration of the participants' meanings for these situations and events. Their meanings include their feelings, beliefs, ideas, thoughts and actions (McMillan & Schumacher, 2001). Qualitative research, in contrast to quantitative research, takes into account that individuals may have different views about the same situation and therefore multiple, or alternative realities exist (Denscombe, 2008; McMillan & Schumacher, 2001).

In qualitative research, it is assumed that participants are contextually bound, namely, that an individual's thoughts, feelings and actions are influenced and interpreted within a certain context. This context is influenced by locality, time and history, and broadly includes the economic, political and cultural framework of the individual. For this

reason, a researcher needs to become immersed in, and familiar with, the world of the participant in order to understand the participants' interpretations of their life experiences. This is different to quantitative research which requires the researcher to remain detached from the study to avoid bias and ensure that the findings are objective (Holloway, 1997; McMillan & Schumacher, 2001).

Qualitative research is based on the assumption that individuals are best placed to describe situations, phenomena and feelings in their own words, and as a result, rich, thick data is obtained (Hansen, 2006; Holloway, 1997). As phenomenology is concerned with the lived experience and describing of phenomenon, which are not affected by prior assumptions of the researcher (Denscombe, 2008), this mode of enquiry was the most suitable for this study.

As the study investigated participants at a single, specific point of time, a cross-sectional design was used. This is in comparison to a longitudinal study which investigates the same participants and phenomena at different points of time. A cross-sectional study is disadvantaged because the circumstances of an individual's life may change and that kind of data are not captured (Brink, 2006), however a longitudinal study was not possible due to the time constraints of a minor dissertation.

3.3 STUDY POPULATION AND SAMPLE

3.3.1 Population and sample size

For the purpose of this study, the participants were recruited from an extended family (Family X) that comprises approximately 100 individuals, spans three generations and has several relatives diagnosed with ATR-X syndrome.

As the purpose of qualitative research is to obtain in-depth information and it is less concerned with generalisability, a small, information-rich, sample was selected (Holloway, 1997). The researcher recruited 11 female participants from the selected family, who met the eligibility criteria. The nature of a minor dissertation, time and cost constraints prevented the recruitment of a larger sample size.

3.3.2 Eligibility criteria

i) Inclusion criteria

- potential carrier females who had previously had blood taken for research but who did not know their carrier status;
- individuals who lived in the greater Cape Town area;
- females who were 18 years or older;
- individuals who consented to be interviewed and to have the interview audio-taped by the researcher.

ii) Exclusion criteria

- obligate carriers;
- individuals who did not respond after being contacted three times by the researcher.

3.3.3 Sampling method and recruitment

The sample was selected by purposive and snowball sampling techniques. Purposive sampling involves selecting cases that are knowledgeable and likely to provide in-depth

information regarding the specific phenomenon being investigated (McMillan & Schumacher, 2001). On the other hand, snowball sampling is where study participants already recruited recommended other individuals to participate in the research as they had been through a similar experience and were able to provide similar in-depth information (Holloway, 1997).

The first family member was contacted by one of the genetic nurses from the Division of Human Genetics, to inform her of the objectives and the method of the proposed study. This family member was an obligate carrier of ATR-X syndrome, and therefore excluded from the research. Following initial contact, the family member contacted other family members within her nuclear and extended family to inform them of the aim, objectives and method of the research. Those individuals willing to participate in the research were then contacted by the researcher, with their permission, in order to clarify the purpose and method of the study and to arrange an interview date, time and venue of their choice.

Participants were also informed that the interview should be private and that no family members should be present at the time of the interview. If this was not possible, an alternative venue of the participants' choice was arranged. Participant recruitment and interviews took place between July 2010 and February 2011.

3.4 METHODS AND MEASUREMENT INSTRUMENTS

For the purpose of this qualitative research, a semi-structured interview schedule, designed by the researcher, was used to collect the data (Appendix I). Semi-structured interviews allowed individuals to describe their experiences in their own words, and enabled the participants' thoughts, feelings, beliefs and attitudes to be explored (Holloway, 1997). This type of interview did not require questions to be asked in a

particular order which allowed specific topics of interest to be discussed with the flexibility of pursuing other emergent issues (Kvale, 1996; Patton, 2002). Furthermore, face-to-face interviews enabled the researcher to note verbal and nonverbal behaviour. As the interview technique was flexible and adaptable, it also allowed the researcher to follow up, clarify and elaborate on participant responses in order to achieve specific accurate information (McMillan & Schumacher, 2001).

The interview schedule comprised of both closed- and open-ended questions. Closed-ended questions were those that only required a 'yes' or 'no' answer, or those that did not require any elaboration. These types of questions were typically used to obtain socio-demographic information. Open-ended questions were questions that allowed the participants to respond freely, using their own words, thoughts and insights to answer the questions (Patton, 2002). The absence of preset categories enabled the participants to express themselves more accurately and in greater depth. Neutral probes, or prompt questions, were used in order to clarify or elaborate on incomplete responses or if a response was not understood, or to gain deeper insight. These questions also aided in guiding the interview and increased the richness and depth of responses (Patton, 2002), therefore allowing for the maximal amount of information to be collected during the interview. Although the family tree, or pedigree, of the participants was known, a brief family history was taken and pedigree drawn at the beginning of the session. This was done to determine if there were any changes to the family tree (unknown to the clinical service), to allow for the development of mutual trust between the researcher and the participant and for exploration of family relationships and feelings surrounding the condition in the family (Harper, 2001; Weil, 2000).

The questions in the interview schedule were constructed by the researcher from information obtained from literature and after evaluating interview schedules utilised in previous research dissertations in the field of genetic counselling (Schoeman, 2007; Loggenberg, 2006). The interview schedule comprised of 49 questions in total, which were divided into five sections: sociodemographic information, level of understanding of

genetics, impact and experiences of having family members affected by ATR-X syndrome, current opinions regarding genetic testing and communication within the family.

In order to ensure the validity of the interview schedule, it was critically reviewed by two independent supervisors to certify that all necessary and relevant questions were included and sequenced in an appropriate manner. The interview schedule (Appendix I) and the informed consent forms with information sheets (Appendix II) were all available in both English and Afrikaans, depending on the preference of the participant. The interview was also conducted in the participants' language of choice.

All interviews were audio-taped in order to record the actual words of the participant and to avoid unnecessary note-taking during the interview, which further allowed the researcher to engage uninterruptedly with the participant and make observations (Patton, 2002). The interviews took approximately one hour to complete, but if additional time was required, further interviews were arranged at a time and place that suited the participant.

3.5 TRUSTWORTHINESS/VALIDITY

Validity is a concept that refers to the truth and authenticity of research; in qualitative research it is measured by trustworthiness. If the reality, together with the thoughts and ideas, of the participants are reflected accurately in qualitative research, it qualifies as trustworthy. Authenticity refers to the appropriate use of strategies to truly report participant's thoughts and ideas. The concept of trustworthiness was first reported by Lincoln and Guba in 1985, and it was stated to include credibility, transferability, dependability and confirmability (Holloway, 1997).

Credibility can be likened to the concept of internal validity that is used in quantitative research. Credibility refers to the extent to which the results of the study represent the reality of the participants (Holloway, 1997; McMillan & Schumacher, 2001). Therefore, the researcher's findings need to be compatible with the perceptions of the individuals interviewed in the study, and the researcher needs to describe the individuals and their context accurately (Holloway, 1997).

Transferability refers to the generalisability of the study, which is the equivalent of external validity in quantitative research. Therefore it refers to the extent to which the research findings in a particular context can be transferred to a comparable situation or participants. In order for the study to be transferable, thick, accurate and detailed descriptions of the data, in context, is necessary to ensure that a clear and comprehensive picture of how the research was conducted can be obtained and replicated (Holloway, 1997).

A dependable study is one which is consistent and accurate. Dependability is also termed reliability and is discussed separately in Section 3.6 below. Confirmability, which is the equivalent of objectivity, means that possible bias and subjectivity by the researcher has not affected the findings of the research. To achieve this, as above, detailed descriptions of the decision-making process were provided (Holloway, 1997).

3.5.1 Validity of instrumentation in study

As previously stated, validity refers to the degree to which research findings are true and accurate, or otherwise, the degree to which the explanation of a phenomenon correlates to the reality of it (Holloway, 1997; McMillan & Schumacher, 2001). To increase the validity in the present study, verbatim accounts of the mechanically recorded interview data (audio-taped) were used in order to obtain an accurate and complete record of the

spoken information in the interview (McMillan & Schumacher, 2001). Credibility was improved in this study by using the technique of peer-debriefing; whereby the researcher regularly met with her supervisor to ensure that the data obtained during the interviews was accurately recorded and transcribed. The interpretation and categorisation of the results were also monitored to ensure that the correct conclusions were reached; this was incorporated with feedback on the validity of the interview schedule and the pilot study. Member checking during the interview was utilised (McMillan & Schumacher, 2001), whereby the researcher reflected the participant's experiences back to the participant to ensure that the information given was accurately interpreted.

3.6 RELIABILITY

Reliability refers to the consistency of the findings obtained (Kvale, 1996). It requires a complete and detailed description of the decision-making process to ensure that others may follow the same procedures (Holloway, 1997). To ensure consistent results were obtained, all interviews were conducted by the same person, the researcher, and all initial questions were asked in the same way. In addition, the classification or categorisation of responses by participants was agreed upon by the researcher and supervisors to ensure 'coder reliability' (Kvale, 1996).

3.7 PROCEDURE

3.7.1 Piloting

A pilot study was conducted on two female individuals, purposively selected, prior to the commencement of the interviews with the actual research participants, in order to test the designed interview schedule. The individuals recruited for a pilot study need to have characteristics similar to those of the study sample (McMillan & Schumacher, 2001) and as there was only one known family that was affected by ATR-X syndrome in

the Western Cape, the individuals recruited for the pilot study were from families affected by FXS, a similar condition that is also characterised by X-linked intellectual disability. These individuals, who were at risk to be carriers for FXS, were recruited from the genetic clinic at Red Cross War Memorial Children's Hospital (RCWCH) and were contacted by the researcher to explain the purpose of the study. All procedures implemented during the pilot study were identical to those implemented during the study. A pilot study is important to determine if the questions are understandable, to ensure questions are not ambiguous, to help the researchers develop their interviewing skills and to establish how much time will need to be allotted for the interview (Holloway, 2008; McMillan & Schumacher, 2001). The checking of questions also helped to improve the reliability of the interview schedule (Neuman, 2006).

Following two pilot interviews, it was clear that the participants' responses did not actually add value to determining whether the interview schedule needed adjustments as the individuals were not aware of the diagnosis in the family and so could not answer many questions. It was decided that, although this may be the same situation in the study sample, it would be beneficial to conduct a third pilot interview with a more informed participant so as to assess all the questions in the interview schedule comprehensively. Following the pilot interviews, adjustments to the interview schedule were made. Data from these interviews were not included in the results of this study.

3.7.2 Research setting

Interviews were conducted in the participants' homes as it was more likely that they would feel more comfortable and less inconvenienced when discussing sensitive issues, compared to a clinical setting. However, if participants did not wish to have the interview at their home, a private venue, chosen by the participant, was arranged.

There is a potential benefit to observing participants in their home environment, as more information is available than that which can be obtained from a clinical setting (Smith, Harrer & Van Langenhowe, 1995). The researcher may be able to observe the interactions between family members, the home circumstances and environment in which they live, supportive structures, together with natural reactions to questions unbiased by a clinical setting, where perceptions of expected behaviour may be an influence.

3.7.3 Data collection and management

At the beginning of each interview, the researcher went through the informed consent form with the participant, informing them of the objectives of the study and reassuring them of confidentiality.

The participants were also informed that the researcher did not know their carrier status results based on previous research. All the interviews were conducted by the researcher personally, and the data generated during the semi-structured interview process were audio-taped and transcribed verbatim. Interview recordings and transcriptions were stored in a safe to ensure that the confidentiality of the participants was maintained. Only the participant's code, not their name, was presented on the interview schedules, transcripts and in data in this dissertation.

Due to the sensitive nature of the questions in the interview, the participants were informed that should the questions upset them in any way, a follow-up appointment with a genetic counsellor would be arranged if they wished and, if indicated, appropriate referral for psychological support would be made.

Following the interview, the participants were given time to ask questions regarding the condition and about the testing procedure. Contact details of the researcher and course convenor were provided should the participant want additional information regarding the research, genetic counselling or testing. When requested by the participant, appointments were arranged for the participant to see a genetic counsellor (not involved in the research) as a patient in the clinical setting and testing was facilitated.

3.8 DATA ANALYSIS

The data generated during the interview process were raw and had no meaning on their own. To be able to make sense of the data and for it to be meaningful, the data needed to be organised and interpreted so that important findings could be identified (Hansen, 2006; McMillan & Schumacher, 2001). In this study, thematic analysis was used to explore the data, whereby underlying themes were identified. In contrast to quantitative data analyses that aim to quantify data, qualitative data analyses, and therefore thematic analysis, aims to describe data (Neuman, 2006).

The process of thematic analysis involved sifting through the data to identify categories and patterns that were similar and then grouping these together to identify themes (Hansen, 2006; Holloway, 2008). In the present study, the researcher searched through the data to identify recurrent ideas or issues in the observations and quotations. The data was then reread in order to structure and group the ideas into categories and later re-organised into themes (Holloway, 1997; Patton, 1987). From this, meaning was inferred, which is illustrated by quotations from the raw data (Holloway, 1997). In order to avoid bias and ensure the correct categories and themes emerged, the interpretation of the data was validated by the research supervisors.

Although the aim of qualitative research was to describe phenomena, counting the occurrence of certain types of data, e.g. socio-demographic data, was sometimes useful to provide a summary of these aspects of the analysis (Hansen, 2006). Therefore, responses to certain portions of the interview schedule were analysed using descriptive statistics such as percentages, measures of central tendency, ranges and other frequency data.

3.9 ETHICAL CONSIDERATIONS

3.9.1 Ethical approval

Ethical approval for this study was granted without reservation by the Medical Research Ethics Committee of the University of Cape Town (HREC/REF: 291/2010, Appendix III).

3.9.2 Consent

Individuals were contacted by the researcher to explain the purpose of the study to be conducted and to see if they would be interested in participating in the research. No form of persuasion or coercion was used to encourage individuals to participate. Participants were informed that they would not benefit medically or financially from the study, and that there would be no additional costs to them. Reassurance was given that:

- All information provided during the interview (which would be audio-taped) would be kept confidential, and if the data resulted in a publication in a scientific journal, no names would be used.
- The data would be anonymised and destroyed once the research was complete.
- Information provided would not be discussed with other family members.

- Participation was voluntary. Individuals had the right to withdraw from the study at any stage should they no longer wish to participate. This would not jeopardise the medical care that they were entitled to receive in any way.

The researcher obtained written informed consent before the interviews were conducted and this included consent for the interview to be recorded by means of audio-taping (Appendix II).

3.9.3 Confidentiality

Confidentiality was a primary concern and therefore the audio-taped recordings of the interviews were transcribed as soon as possible following the interview. Both the audio-tapes and transcripts were kept in a locked cabinet in the Division of Human Genetics to which only the researcher had access. Once the research was completed and had been written up, these were destroyed. As anonymity was also of primary importance, no names were used and participants were provided with numerical codes which appear on the interview schedule, transcripts, spreadsheets and the dissertation.

3.9.4 Risks/benefit to subjects

The researcher ensured that confidentiality and anonymity was maintained during the research process. Risks to the participants included the discussion of sensitive information and stressful experiences that may have stirred up emotions. The researcher was sensitive to the emotional state of the participant during the research process and ensured that participants were made aware that they had the opportunity of having a second session with the researcher where any questions that the participant had would be answered and where any emotional issues evoked during the initial interview would be discussed. In the case where the researcher was unable to help with emotional issues that

arose, the participant was offered counselling by a qualified genetic counsellor and/or mental health professional.

As information about ATR-X syndrome was provided after the interview if the participant wished, participants benefited from a greater level of understanding and knowledge about the condition in the family. They also benefited from the opportunity to ask questions and the provision of contact details for further information or testing. Despite possibly evoking emotional issues, there is also a potential therapeutic benefit surrounding discussing one's experiences and this may have been experienced by the participants.

The long term benefit of the investigation was to utilise the findings of this study to, if necessary, improve the genetic counselling process and services provided, specifically concerning the uptake of carrier testing in X-linked conditions.

3.10 ASSUMPTIONS

A major underlying assumption in this study is that the participants provided an honest and accurate reflection of their lives and their feelings associated with their experiences.

3.11 LIMITATIONS OF STUDY

3.11.1 Limitations of the study

- A major limitation of this study was the small sample size which was due to availability and time constraints. This means that the results obtained would not be able to be generalised to a larger population, and would only be valid under similar circumstances in which this sample was obtained. Furthermore, the

participants were from the same family and therefore the data acquired may not be representative of other individuals or families who have different values or belief systems.

- It is important to consider that participants may not have responded truthfully and may have provided answers that they deemed were socially desirable. Moreover, participants may have reacted differently to how they would usually behave as a direct result of being involved in the research.
- Responders and non-responders may have differed significantly regarding their view, experiences or understanding of the condition, and therefore there may be important factors involved in these processes that could not be identified. Furthermore, there is a bias to including participants who are similar to each other in terms of their beliefs due to the use of snowball sampling, as estranged family members are less likely to be recruited via this method.
- The data obtained is based on the participant's subjective experiences and no formal measures of psychological impact were utilised in this study.
- Another limitation is that information and research concerning ATR-X syndrome is rare worldwide. Where possible, information gathered in other countries regarding similar issues and conditions was used, but caution would need to be exercised regarding generalising information.
- The researcher was also aware that her counselling and interview skills and experience may not have been adequate to facilitate the building of sufficient rapport with the participants, and therefore sensitive information may not have been fully disclosed, or certain areas not explored fully.

3.11.2 Strengths of the study

- All interviews were conducted in person and by the same researcher.

- Open-ended questions were utilised, which allowed participants to respond openly and express themselves fully without being bound by pre-set categories.
- As most of the interviews were conducted in participants or other family members' homes, the participants were more likely to feel relaxed and comfortable to discuss personal and emotional issues as compared to the clinical environment.
- Audio-taping of the interviews allowed for a more complete record than would have been possible by handwritten notes by the researcher
- The researcher was new to the clinical team at the Division of Human Genetics and so the participants did not know the researcher and vice versa. The researcher thus had no prior agenda or vested interest and the participants could talk freely regarding their feelings and experiences of the condition and the original genetic research conducted.

CHAPTER 4:

ANALYSIS, RESULTS AND DISCUSSION

4.1 INTRODUCTION

The sample description, data analysis and research findings are presented in this chapter. The majority of the data is presented in table format, followed by a discussion. Direct quotations from the raw data are also included in the discussion in order to provide the reader with greater insight into the perceptions of the participants and hence the meaning of the data. Where applicable, reference to other literature is made, with the intention of demonstrating similarities and differences with existing data on disability (intellectual, mental or physical) or other genetic conditions, as research on ATR-X syndrome is limited. However, it has to be acknowledged that comparisons with other studies are problematic due to the small number of participants in this study.

4.2 INTERVIEWS AND PEDIGREES OF PARTICIPANTS

To ensure confidentiality, the participants were assigned an alpha-numerical code and this will be used to identify them throughout this chapter. Eleven interviews were conducted in total. Of these interviews, five were conducted with siblings of male relatives diagnosed with ATR-X syndrome (P001–P005). Of the remaining six interviews, one was conducted with an aunt (P011), one with a niece (P006), and four with cousins of the affected males (P007–P010). One participant (P010) has a son who was in the process of being investigated for developmental delay, but who had not been diagnosed with ATR-X syndrome.

Of the eleven interviews, three were conducted in the participant's home (P001, P004 and P006), while five participants (P002, P003, P007, P008 and P009) chose to have the interview conducted at another participant's home. This may have to do with the fact that the two participants whose homes were used for the interviews (P001 and P004), were integral in helping recruit others into this study. Of the remaining three interviews,

one was conducted in a private room at the participant's workplace (P005) and two participants (P010 and P011) chose to have the interview conducted in a private office at the researcher's place of work. With the exception of one, which required two appointments to complete, all interviews lasted approximately an hour.

In order to clarify extended family relationships, the families of the participants were separated into nuclear families A, B, C and D (Figure 4.1). Figure 4.2 illustrates the pedigree of extended Family X.

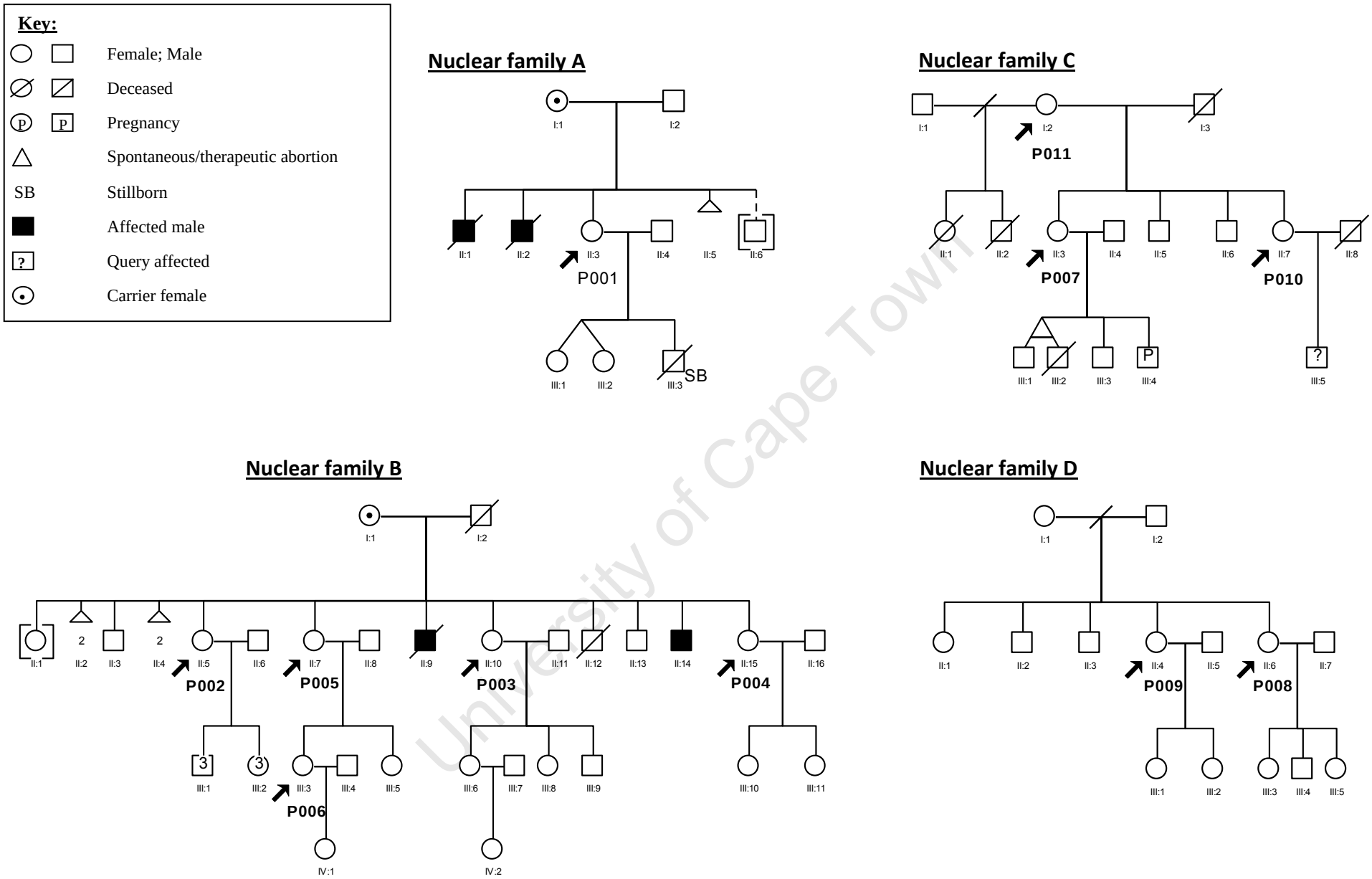

Figure 4.1 Pedigrees illustrating each participant's nuclear family (A–D). Each participant is denoted by their participant number (P001–P011) and with an arrow.

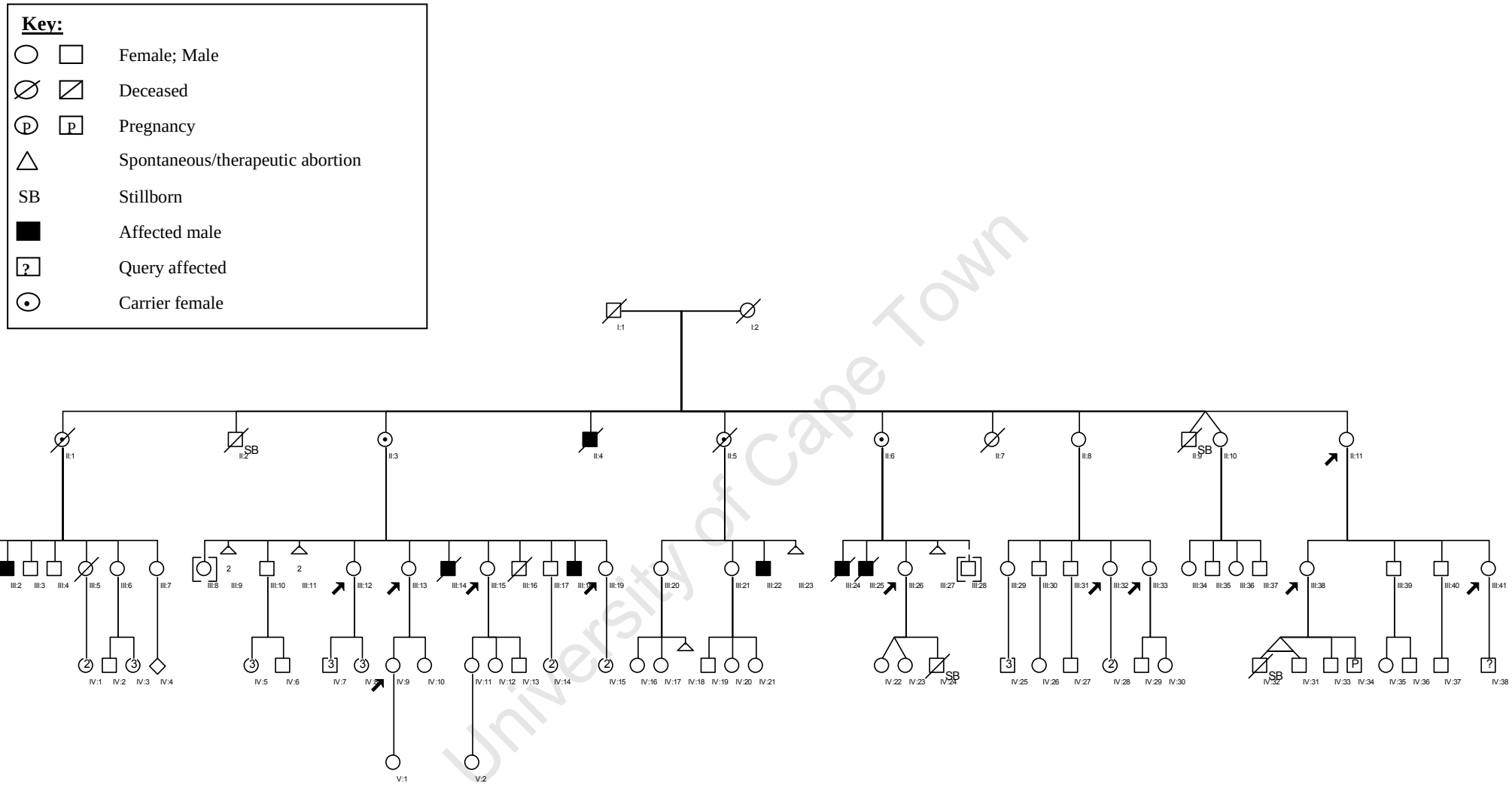

Figure 4.2 Pedigree illustrating extended Family X. Each participant is denoted with an arrow.

4.3 SOCIO-DEMOGRAPHIC INFORMATION OF PARTICIPANTS

A summary of the socio-demographic data of the participants is presented in Table 4.1. All the participants were from the mixed ancestry population group and lower to middle socio-economic income levels. The average age of the participants was 36 years, with a range of 25–57 years old.

Of the 11 participants, four were unemployed, one individual was self-employed and one individual was on unpaid leave at the time of the interview. Due to the high rate of unemployment in SA, many people are dependent on small state grants. In this study, five participants received state grants in addition to other income that they received, with this often being the sole source of income for P005 and P006. P011 was the only participant who received a disability grant due to her own health concerns.

Table 4.1 Summary of participant socio-demographic information.

P	Age	Marital status	No. of Children	Level of education		Employment status	Current occupation	Household income per month (indicated by income bracket)	Grants contributing to income	Residence	Transport
				School	Tertiary						
001	34	Married	2	Gr 12	Short courses	Permanent, full time	Administration	R8001-R11000	-	Own house	Family car
002	46	Married	6	Gr 11	Gr 12/ Short courses	Unemployed	Housewife/ volunteer	R3501-R4500	Child support & disability	Own house	Family car
003	42	Married	3	Gr 7	-	Self-employed	Sewing	R3501-R4500	-	Own house	Train & taxi
004	31	Married	2	Gr 12	Short courses	Permanent, full time	Personal assistant	R16001-R30000	-	Own house	Family car
005	45	Single	2	Gr 9	Short course	Unemployed	Casual work/ volunteer	Irregular and unspecified	Child support, disability & 2 pensions	Living with parent	Train
006	18	Single	1	Gr 9	-	Casual/ contract	Cleaning	Irregular	Child support	Irregular	Train
007	32	Married	2†	Gr 9	-	Contract/ unpaid leave	Driver (maternity leave)	R2501-R3500	-	Own house	Family car
008	34	Married	3	Gr 10	-	Unemployed	Casual/ housewife	R501-R1000	-	Living with parent- separate area	Taxi
009	35	Married	2	Gr 10	-	Permanent, full time	Chef	R6001- R8000	-	Living with parent- separate area	Taxi
010	25	Single	1	Gr 12	-	Full time (did not specify permanent/ contract)	Waitress	R2501-R3500	Child support & disability	Living with parent	Lift club/ Taxi
011	57	Widowed	6	Gr 9	-	Unemployed	Retired/ disabled	R2501-R3500	Disability & child support	Own house	Taxi

† Participant was pregnant at time of interview

Figure 4.3 shows the numbers of participants in each monthly income range, as specified by the 2001 census data presented in the primary tables by Statistics South Africa (Stats SA) (2005).

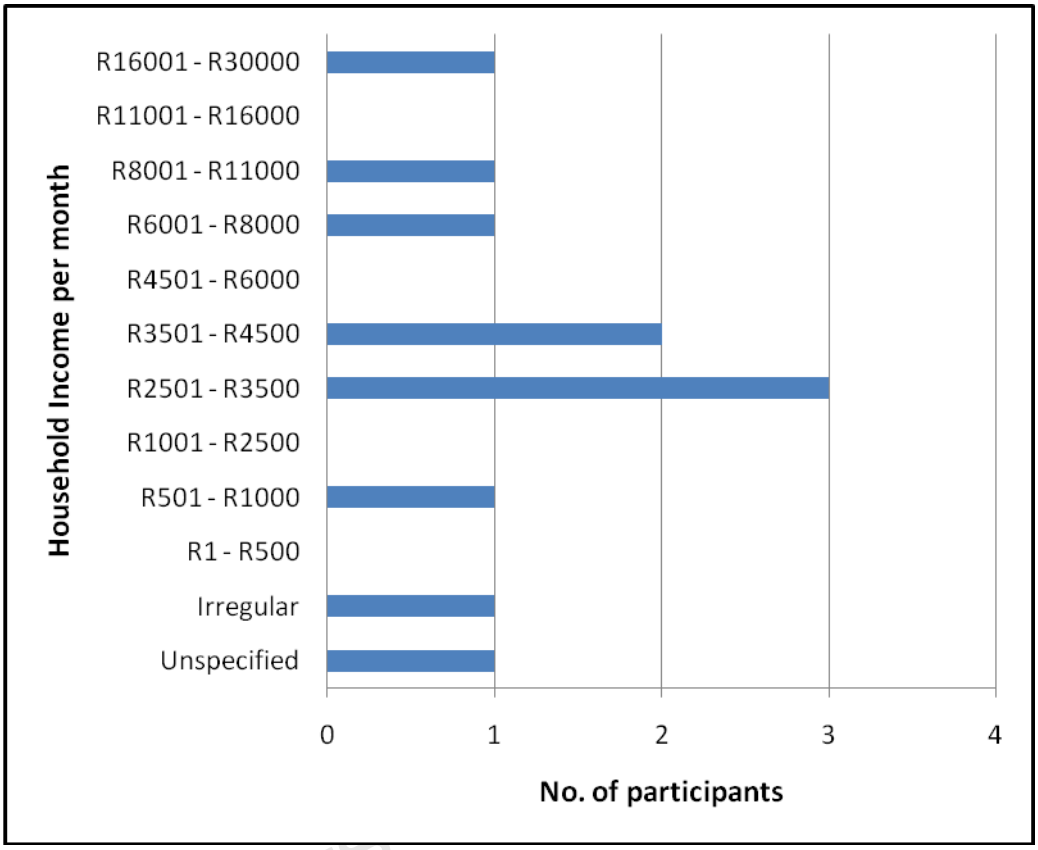

Figure 4.3 Household income range per month (n=11). Income brackets/categories provided by Stats SA (2005).

According to Stats SA (2002), the latest data from 2000 showed that the average annual income per household in South Africa was R45 000 (R3750 per month). However, the individual data per province showed that the Western Cape (WC) had the highest average annual income per household of R74 000 (R6170 per month), with the mixed ancestry population in particular earning R55 000 per household per annum (R4580 per month).

As can be seen in Figure 4.3, the majority of the participants in this study had a current household income less than the average monthly income for their population group in the WC, as determined a decade ago. It is not certain how the national income figures have changed since 2000, but it is possible that, due to inflation, the disparity could be even greater between the participants and the general population. In general, the communities in which these participants lived were poor socio-economic areas. The two participants' homes used for the interviews with certain participants were those of the participants with the highest monthly household income (P001 and P004).

The majority (eight) of the participants did not complete high school. None of the participants completed a tertiary degree or diploma, but four individuals had completed short certificate courses after school, with P002 also completing her high school education at a later stage. The educational level attained by the participants during school is shown in Figure 4.4.

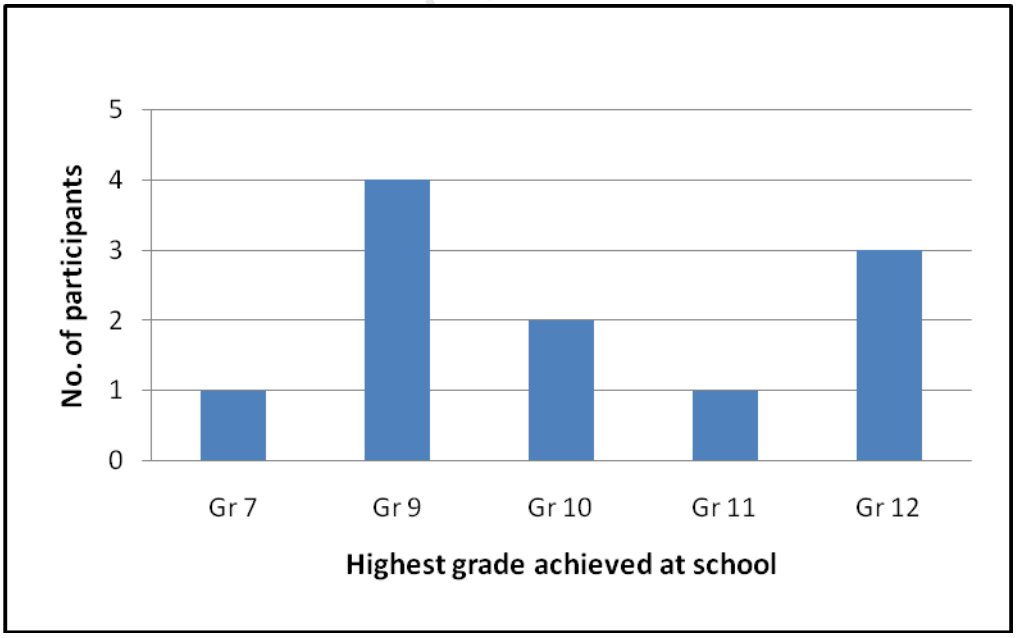

Figure 4.4 Participants highest grade achieved in school (n=11).

Beeson and Golbus (1985), who investigated factors involved in making decisions in X-linked inherited conditions, found that a higher educational level, higher income and stronger career commitments resulted in a reduced willingness to take the risk of having an affected child. As the majority of the participants did not complete high school and had a lower than average household income, their willingness to take the risk of having an affected child was not influenced by this. Eggers *et al.* (1999) found that those with a lower socio-educational level requested DNA tests for DMD significantly less frequently than those from a higher socio-educational level. Therefore, the non-uptake of carrier testing by the participants in the current study may be related to the fact that the majority of the participants did not finish high school.

4.4 LEVEL OF GENETIC KNOWLEDGE

The level of understanding of the inheritance of a genetic condition or the perception of recurrence risks in a family may be a factor that could contribute to the uptake of genetic testing in an affected family (Sivell *et al.*, 2008). In order to investigate whether this was a factor in Family X, various questions relating to genetic knowledge were investigated; a summary of selected data is presented in Table 4.2.

Before discussing the findings with regards to the level of genetic knowledge, it is important to indicate that none of the participants interviewed had received individualised or formal genetic counselling. A number of the participants were present at one or two of the family conferences organised with the genetic services to discuss the original research to determine the genetic cause of the condition in their family. At these conferences, and especially the last meeting, the diagnosis was named, the inheritance of the condition explained, and risks given. The family was informed of the availability of carrier testing as a diagnostic service for the family. The family was encouraged to share the information with other members of the family not present at the meetings, or those

not old enough to receive the information at the time. The assumption that family members will communicate test results, or the availability of testing, if requested, is common in clinical genetic practice (Sorenson, Jennings-Grant & Newman, 2003).

In order to objectify the findings, the level of knowledge for each participant was assessed by correct and incorrect answers to the categories presented in Table 4.2 below. It should however be noted that many answers reflected a partial understanding of the information so the final score may not be a true reflection of the participants knowledge. If the participant knew that there was a risk of being a carrier, having a child with ATR-X syndrome, or that their children could be carriers, they were considered correct, even if they could not provide an absolute risk number. In order to substantiate individual scores, selected participant explanations to the questions are presented in Table 4.3.

Table 4.2 Participants' level of knowledge scores.

P	Cause	Inheritance	Gender affected	Carrier	Risk carrier	Risk of child with ATR-X	Unaffected children carriers	Total score (/7) (%)
001	✓	✓	×	✓	✓	✓	✓	**6 (85%)**
002	✓	✓	×	✓	✓	✓	×	5 (71%)
003	✓	×	×	✓	✓	✓	×	4 (57%)
004	✓	✓	×	✓	✓	✓	✓	**6 (85%)**
005	✓	×	×	✓	✓	×	×	3 (43%)
006	✓	✓	×	✓	✓	×	✓	5 (71%)
007	×	×	×	×	×	✓	×	**1 (14%)**
008	✓	×	×	✓	✓	×	✓	4 (57%)
009	✓	×	×	✓	✓	×	✓	4 (57%)
010	✓	✓	✓	✓	×	✓	×	5 (71%)
011	✓	×	✓	×	×	×	✓	3 (43%)

Table 4.3 Participants' knowledge of the genetics of ATR-X syndrome.

P	Cause of ATR-X	Inheritance	Boys and girls affected	What is a carrier?	Risk carrier	Risk of child with ATR-X	Unaffected children carriers
001	"It's a chromosome problem" "I know it's passed on"	"It depends on what X I'm giving, which will make it either abnormal or normal boy."	"Only boys now, she said maybe it might be in the girls."	"They have got it in their genes and that is why they have these retarded boys."	"It could be possible seeing that my mom was a carrier."	"50/50 because I never know when it will happen."	"If I'm not the carrier then they could be."
002	"It was an extra chromosome that they have, that we don't have as normal people."	"They told us that girls are the carriers and boys are affected."	"I don't know if in the next generation if it's going to be switched, or, so I don't know."	"A carrier means that you have the germ, but you wont, you are not affected."	"I was told that I am a carrier."	"I thought one of them would be affected but they not."	"In my heart of hearts I hope it's not."
003	"I think if it is maybe in your blood you will get it."	"It is in my parent's blood, in my mother's side."	"I say boys mostly affected." (girls could be)	"If we are a carrier, we're not infected but our children are infected."	"I think it's a low chance."	"Um…maybe 50/50."	"I don't know"
004	"It is the chromosomes."	Explanation of X-linked inheritance.	Only boys in our family (thinks it may be girls in next generation).	"I knew that I could have a baby who was affected."	"I actually haven't thought about that."	"our family is complete now"	"I suppose there could be."
005	"Its about chromosomes."	"I can't really say."	"I don't know what to expect."	"That I most likely will have a child like that."	"50/50 maybe."	"I don't really know."	"I left it up to the Lord to decide."
006	"Ours is a family thing, it goes through the blood."	Explanation of X-linked inheritance.	Thinks girls could be affected	"If she was a carrier, then maybe her son would be retarded."	"I think I'm a carrier, but its life."	Didn't answer	"Yes"
007	"I understand that they were born that way."	"maybe skip a generation"	"A girl hasn't had it yet."	Hadn't heard of word before	Didn't know	"There can be a chance."	Didn't know
008	"It is in the family."	Didn't answer	"It can maybe affect both but in our family its only boys."	"I can have it in my cells and I can carry it over to my child."	"Yes"	"It's something that God gives you."	"Yes"
009	"I think its inherited."	"Pattern in our family is that it's only in the boys."	Thinks both can get it	"You can be a carrier of something but you don't necessarily have it."	"Yes, there can be a chance."	Didn't answer	"Yes"
010	"It's in our family. It comes from my mom's mom."	"Boys only have one of those but women have two of those (that means they won't get it)."	Only boys affected	"My mom's mom was the carrier. They can't be affected."	6/10	"There is a chance."	No other children
011	"I don't know."	"It's inherited but its our children's children that will inherit it."	"It's only boys"	"It's about when they get pregnant, they carry the baby."	Didn't answer	Family complete	Yes

As can be seen in Tables 4.2 and 4.3, none of the participants were able to answer all of the questions about genetic inheritance and risks correctly. However, ten of the eleven participants knew that the condition in the family was inherited.

P001 and P004 had the highest, and P007 the lowest, level of knowledge about the condition. P007 expressed uncertainty about the cause of the condition in the family: *"I don't know if it's something that happens in the pregnancy, if it's something that's in the family, or if do something wrong in the pregnancy. There's just not an answer for it."* This participant was not present at any of the family conferences and said that no one in the family had discussed the condition with her. Nevertheless, she felt that there could be a chance that she could have a baby that was affected, as she felt that *"It can happen to anyone."* P007 was pregnant at the time of the interview and had recently been counselled about an increased risk of her baby to have DS. This may have contributed to her confusion and it was not clear to the researcher during the interview whether she was referring to ATR-X syndrome or DS in the preceding comment.

Five of the participants were able to provide a description of X-linked inheritance, with P001, P004 and P006 providing the most detailed and accurate explanations. Despite P001 and P002 knowing that the condition was inherited and the inheritance pattern, they had a misconception regarding the genetic mechanism; they thought it was caused by extra genetic material:

P001: *"There is an extra . . . can I say link or . . . to the X for the boys, which is for the males, it is just something extra on it in the case of our family."*

P002: *"It was an extra chromosome that they have, that we don't have as normal people."*

When asked about the cause of the condition, some of the participants found it difficult to differentiate between ATR-X syndrome in the family and other causes of ID. P003, P005, P007 and P011 all mentioned other causes for ID, such as alcohol and drug use,

but then added that this was not the case in their family. P005 also discussed that she had originally wondered, *"Could it be a curse that was on the four of them?"* but she had spoken with a genetic doctor at one of the family conferences and later said, *"I know he said it's not a curse, I take it that it's just something that happens."*

There was also a misconception as to whether only boys could be affected with ATR-X syndrome, or whether girls could be as well, with only two participants definitively answering that only boys could be affected. Five of the remaining nine participants said that there were only affected boys in the family but when probed, indicated that they believed girls could possibly be affected as well. This indicates uncertainty and lack of understanding of the underlying mechanism causing the condition. P005 and P006 were uncertain if there was a gender difference, as they were aware of a female cousin who had a daughter who was born with a problem. They were uncertain, however, whether it was the same problem as that of the males with ATR-X syndrome.

A recurring idea of the condition 'skipping a generation' was evident throughout this line of questioning, with seven participants mentioning it. P006 gave the clearest explanation: *"I heard that it's in every second generation. Like my granny has retarded children, then her children won't have any retarded children, then us cousins, we will have retarded children, and then my children won't have, so it's like every second."* Information regarding the condition 'skipping a generation', seems to have been provided by the older generation to emphasise the importance of knowing about the condition, as future generations could still be affected. However, it seems that this message may have been misunderstood, with participants literally thinking that only every second generation would be affected. P001 described how she originally thought that the condition had stopped at her mother's generation: *"I just thought that I'm not a carrier you know, that it stopped by my mother. That's really what I thought at first, but then after having a discussion with the Sister (genetic nurse), she said that it can go further onto the family because it's like, cancer . . . But I didn't think of it in that way, I just thought that it would stop right there because nobody else ever had it now, in my*

generation, nobody else had a child like that." This belief may have been held by more participants even though it was not voiced.

Experiences influence perception of risk, behaviour and reproductive decisions (Beeson & Golbus, 1985; Kay & Kingston, 2002). The fact that no individuals in the generation interviewed have had an affected son may therefore have led individuals to believe that they are not at risk. Combined with the belief that the condition 'skips a generation', the perception could have arisen that carrier testing was not necessary. Klitzman (2010) found that it is important to identify misconceptions, as they may result in individuals avoiding testing. As can be seen from the above, misconceptions may be a factor in the current study. Similarly, regarding the perception that the condition 'skips a generation', six of the participants knew that there was a chance that their children could be carriers although no actual numerical probability was given.

Nine of the participants had a clear understanding of what a carrier was; however, when asked about their own risk of being a carrier, only one participant provided the correct answer numerically. Despite giving the correct answer, she did not seem confident about it. Nonetheless, the majority (eight) felt that there could be a chance that they were a carrier, although they were not able to give a number.

P010 said her risk of being a carrier was 6/10; when probed as to whether this was information that had been given to her, she said: *"It's how I feel because it can be that it is because it's in the family, and he is a boy"*. The latter response seemed to indicate that P010 was referring to the chances of her son being affected with ATR-X syndrome, not to her chances of being a carrier. (Note: P010's son was being investigated for developmental delay.) In order to determine if that was what she was referring to, she was then asked what the chances were of her having an affected son; she provided a different response, leaving a level of uncertainty regarding which risk she was originally referring to.

Strong religious convictions were a factor in many explanations and played a role in understanding risk. For example, P005 and P006 expressed that they were concerned that they were carriers for religious reasons. P005 mentioned that she had prayed to God to ask that she not have affected children and said: "*So most probably that's why He gave me girls. I would say rather two girls than a boy and then to find out the boy is retarded."* P006 recently had a baby girl and, when asked what she thought her chances were of being a carrier, she said: *"I'm not sure, I'm a little bit worried because my mother doesn't have boys, she only has girls and when I was pregnant I thought I wanted a boy, and I prayed and I asked if I can have a boy, but if my boy is going to be retarded then it's best that I have a girl. So ja, maybe I think I'm a carrier, but it's life."*

Klitzman (2010) found that individuals may describe themselves as carriers to decrease their anxiety related to the uncertainty of not knowing their carrier status. Similarly, the above descriptions by P005 and P006, describing themselves as potentially being carriers, may also be a defence mechanism employed to decrease their anxiety.

Unlike the other participants, P002 said that she was informed by her parents that she was a carrier, this is despite research results on carrier status not being delivered to any family member. As a consequence, she thought that one of her children would be affected with ATR-X syndrome. Communication within the family seems to be an issue and it is possible that she or her parents had misunderstood the condition and its inheritance. As she was the eldest daughter in her nuclear family, and the first to come to child-bearing age, they may have felt a more urgent need to inform her that she could also have affected children.

Regarding the participants understanding of their risk of having a son with ATR-X syndrome, P001 and P003 were the only two participants to provide the accurate 50/50 risk figure. However, it did seem as though P003 was not sure and was instead referring to the risk in a binary fashion (whether it could happen or not) and also said, *"Maybe I'm lucky, maybe I'm not."*

Although it is thought that accurate recall of objective numerical risk information is important for decision making (Austin, 2010; Kessler, 1989), researchers have become increasingly aware that an individual's perception of risk and the meanings attributed to their risk are more important. Accurate recall of risk may also not demonstrate that individuals understand their risk (Hallowell, Statham & Murton, 1998; Sivell *et al.*, 2008). An example of how individuals may differ in the meanings they attribute to risk is provided by P004, when describing her risk of being a carrier: *"I actually don't think about it often, because even if I'm not a carrier, the chances are still there that any other abnormality could be possible still (in general), so I don't think about it often."*

The finding that individuals in this study referred to risk in a dichotomous or more absolute manner is compatible with findings by Hallowell, Statham and Murton (1998) and Klitzman (2010). Varekamp *et al*. (1990) found that approximately 40% of potential and obligate carriers for haemophilia did not give a risk estimate of carriership in percentages. The finding that very few of the participants in this study gave numerical values regarding their risk of being a carrier or having a child affected with ATR-X syndrome is in keeping with this. Hallowell, Statham and Murton (1998) also found that there was inaccurate recall of numerical risk figures given to patients with HBOC. As it is unclear whether the participants in the current study had been given numerical risk figures previously, it is difficult to compare this finding. As the majority of the participants perceived themselves to have some chance of being a carrier, and yet have not presented for carrier testing, it suggests that their perceived risk of being a carrier had not influenced their decision regarding the uptake of these services. This is in agreement with Binedell, Soldan and Harper (1998) who investigated the uptake of predictive testing in Huntington's disease (HD) and found no association between uptake of testing and perceived risk. However, there are inconsistencies in the literature regarding the relationship between perceived risk and the uptake of genetic testing with much of the research in this area focusing on individuals with hereditary cancer syndromes (Sivell *et al.*, 2008), which by its nature may have different implications.

The overall level of understanding of the genetics of ATR-X syndrome was 59% for all of the participants together. However, the level of understanding amongst the participants was varied, with P001 and P004 having the highest level of understanding and P007 the lowest, as previously mentioned. The level of knowledge in the current study was similar to that found by James *et al*. (2006), who found that individual's knowledge of X-linked inheritance ranged from 57–79% in families from the USA. James *et al*. (2006), Klitzman (2010) and Molster *et al.* (2009) all found an association between higher levels of education and greater levels of understanding.

However, the variation in the current sample's level of knowledge may not only be explained by educational level; despite P001, P004, P002 and P010 all having completed high school, there were discrepancies in their levels of knowledge (P001 and P004 had a high level of understanding and P002 and P010 had a lower level of understanding). In addition, P007 had the lowest level of understanding of the condition, but did not have the lowest level of education.

The level of understanding was not clearly influenced by family relationship to an affected male family member, unlike that seen by Varekamp *et al.* (1990), who found that those more distant to a male relative with haemophilia were less likely to be aware of the issues surrounding the condition. In the current study, one of the individuals with the second lowest level of knowledge was P005, who was a sister and lived with her affected brother, while those with the second highest level of knowledge were cousins of affected relatives.

It seems that income may, however, have had an influence on the level of understanding, as P001 and P004, who had the highest level of understanding, also had the highest level of income. This is in accordance with Molster *et al*. (2009), Henley and Hill (1990) and De Pina-Neto and Petean (1999), who showed that those with a higher income level and socio-economic status had a greater level of knowledge. However, the individual with

the lowest level of knowledge, P007, did not have the lowest level of income; therefore the income level is unlikely to completely answer the discrepancy in knowledge between the participants in this small sample.

On the other hand, P007's limited level of participation and engagement, with both family and genetic services, is likely to explain her low level of knowledge because, as mentioned previously P007 did not attend any of the family conferences. In contrast, P001 and P004 showed a higher level of engagement with the process than the other participants, and they were vital in recruiting other participants to the study. Moreover, P005, one of the participants with the second lowest level of knowledge, depicted herself as being the *"black sheep of the family"* and also mentioned that she did not attend the last family conference, further supporting level of involvement as a contributing factor in level of understanding. This finding suggests that it is important to have genetic counselling sessions with individual family members

Participants were also asked to indicate their sources of information about the condition in the family; this is presented in Figure 4.5. None of the participants had any other source of information besides their family and the genetic staff at family meetings. No association was found between information source and level of knowledge.

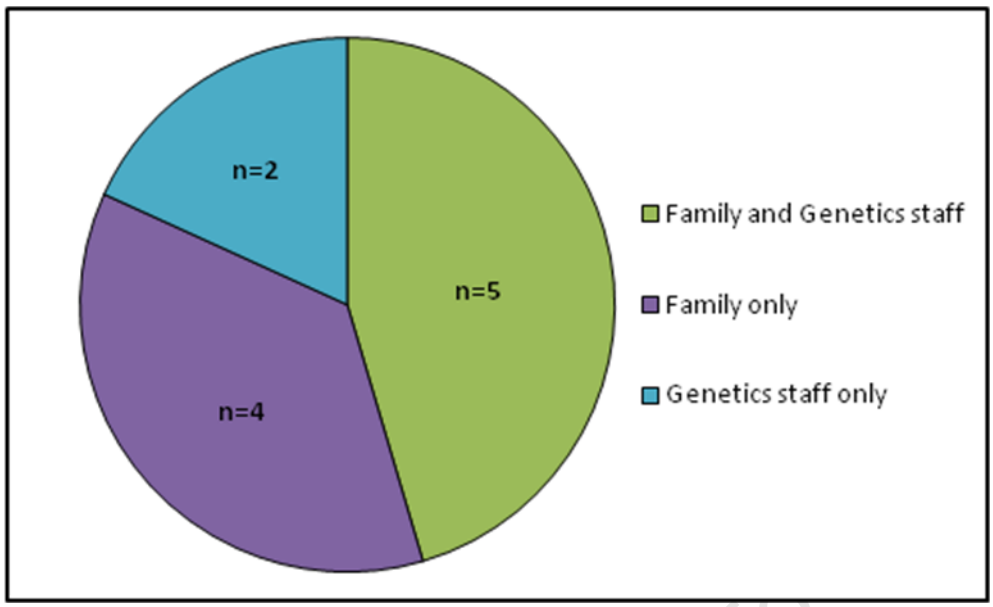

Figure 4.5 Participants' sources of information about ATR-X syndrome (n=11).

An interesting finding was that none of the participants in this study referred to the condition in the family by its name, ATR-X syndrome, implying that they were not aware of the name even though it was on the consent forms. Two participants admitted to not knowing the name of the condition with P004 saying, *"I actually don't know what the condition is called."* P001 said she was aware that it was a long name.

Four participants (P001, P002, P003, and P006) used the word *"infected"* and, P002 referred to the genetic mutation as a *"germ"*, therefore relating ATR-X syndrome to an infectious disease. A similar finding was found by Klitzman (2010), who found that some participants used metaphors of infection as these were understood more concretely than the genetic basis of the disease.

An important misconception was also evident amongst certain participants regarding the purpose of previous genetic research. Disappointment and dissatisfaction were expressed about not having received carrier results from the researchers. P009 indicated that they received no feedback from the researchers and, due to this, they were reluctant to attend

further family meetings: *"They did ask us to come to another session but my mom said no, she isn't interested, because they didn't come back to us that first time with results."* P005 was quite emotional when discussing her risk for an affected child and that with her first pregnancy she was very worried saying, *"Because I wasn't told my results I didn't know what I was going to have . . . I was really scared."* P002 also expressed dissatisfaction with the research, saying, *"We don't know really what's happening and if there are new things that's been discovered or anything like that so . . . it just stopped at a point"* and *"They didn't call us for results or anything."*

Although these three individuals were not present at the last family meeting informing the family of the results of the research and offering diagnostic carrier testing services, these comments have implications for research in the clinical setting, namely that better informed consent of the research may be needed, perhaps with re-informing family members who were young when blood was originally taken. Although research does not typically deliver results, if the results are to be disseminated to the family, it is important that it is done in a more concrete way rather than relying on family members to inform those not present. An example of this would be a letter given to each participant with the outcome of the research and contact details. This finding also raises questions on how to proceed with further genetic research involving families; can family based studies be performed with greater measures in place to ensure that the family understands that they may not benefit from the research, or is it more appropriate to approach each individual in a family separately?

4.5 IMPACT AND EXPERIENCES OF HAVING FAMILY MEMBERS AFFECTED WITH ATR-X SYNDROME

It has previously been shown that the personal experiences of a woman with a particular condition may influence her decision to undergo carrier testing (Anido *et al.*, 2005; Archibald *et al.*, 2009; Beeson & Golbus, 1985; Peterson, 2005; Varekamp *et al.*, 1990). In order to determine if this was a factor in the current study, the participants were asked to elaborate on their experiences of having an affected family member and on the effect this had had on their lives. Family support and community reactions were also explored, as this may influence the impact of the condition on a particular individual. Due to the large amount of information provided by the participants, this section will be discussed in various subsections.

In order to contextualize the information, the characteristics of the individuals affected with ATR-X syndrome in the family are provided as described by Carvill (2010). Out of the seven males clinically and molecularly diagnosed with ATR-X syndrome, four had severe ID and three had moderate ID (See Section 2.2.1 and Table 2.1). One individual was able to communicate in short sentences, whereas the other affected males either communicated using single words or had absent speech. Three of these males were reported to have aggressive and disruptive behaviour. At the time of submission, three of the seven affected individuals, were deceased. Two of these deaths were related to accidents and the third individual died at an age of 38 years due to pneumonia that had progressed from recurrent chest infections and unexplained weight loss. The four affected males who were still alive ranged from 33 and 42 years of age (Carvill, 2010). Out of these four individuals still alive, three were living with family at home and one was in an institution.

4.5.1 Experiences and contact with affected relatives

Participants were asked to comment on how often they had contact with their closest affected family member and to comment on their experiences with them. The researcher also probed to determine if having a family member with ATR-X syndrome affected various aspects of their life, including schooling, childhood, youth, lifestyle and entry into employment. A summary of the participants' comments is presented in Table 4.4.

Table 4.4 Summary of participants' experiences and contact with relatives with ATR-X syndrome.

P	Personal experiences with relative with ATR-X syndrome			
	Level of care	**Description of basic experience/ contact with affected relative**	**Affected childhood/youth?**	**Affected Lifestyle?**
001	Lived with and helped care for brother.	Not primary caregiver but would help. "I would just be on standby. "	"When I was small, it didn't bother me."	"You want to go out but you can't because your mom's not here."
002	Lived with and helped care for brother.	Shared responsibility for helping with affected brothers between siblings. "It wasn't a problem."	"It also affected the friendships that you had."	"You always had to consider them and the situation of the family before you could do things for yourself." Pregnancy-related anxiety major factor.
003	Lived with and helped care for brother.	"It was fine, he wasn't like he was now."	Sometimes had to explain to friends but otherwise fine.	"After my father died it affected my lifestyle a bit as we had to help my mother with him but it was awkward as we have our own family."
004	Lived with and helped care for brother.	"Growing up with him was fine, it was pretty ok." "We would always do things together."	"I never hid it, I still don't hide it away from anybody."	Not really but need to help mom out a bit more now as he can get quite aggressive.
005	Currently lives with and helps care for brother.	"He was our brother, so I didn't find any difficulty growing up with (*) . . . but now in a ways it's hectic."	"When I had my first steady boyfriend I couldn't really go out."	"There's frustration that comes because we don't get as much support from the other children."
006	Currently lives with and helps care for uncle.	"Never knew that it was like a condition, because to me it was like normal growing up with my uncle."	"There's certain people I don't invite over."	"I love babysitting because then it's the only time that I am at home alone."

007	Contact with cousins	“We didn’t grow up in the house with them, we just visited them, we were young so we didn’t have to look after them, the elder people did that.”	No	More accepting of others
008	Contact with cousins	"Mixed with them, we played with them, accepting them as family, and became used to them."	"We were a bit scared of them because we were small and didn’t understand them, we weren’t used to them."	No
009	Contact with cousins	"It wasn’t a problem for us, especially not for me" "they weren’t in my way; they didn’t tease me or anything like that." "It was normal for me."	No	No
010	Contact with cousins	"We aren’t actually very close with them but I am just familiar with one because they visited us often."	"I was scared of them, because they would pinch and grab."	No
011	Helped care for nephews	"It was lovely to be able to help them, because they couldn’t do anything for themselves and I liked to be able to help them."	No	“It didn’t affect me, I just accept.”

As can be seen in Table 4.4, there were a variety of responses regarding what the participants experiences were, with the majority of the responses being positive. There seemed to be a difference between participants who lived with an affected brother or relative, and participants who only had intermittent contact with the relative (cousins), with the former describing the realities of day-to-day living with a family member affected with ATR-X syndrome. This finding is in agreement with Beeson and Golbus (1985), who found that women who lived with a child affected with an X-linked condition had clear and concrete perceptions of the reality of the situation, while the perceptions of those women who had not lived with an affected child were vague and abstract.

P001 described her experience with her brother wearing a nappy: *"So I had to change him and see that he's dry, like a baby actually. Which was also sometimes difficult, because as a woman, I couldn't handle it (laughing) . . . a baby is fine but he was big you know, he was a man, so it was a bit difficult for me."* Interestingly, P007 was aware of the differences between being in contact with a disabled child versus living with a disabled child saying: *"But maybe it's also because we are not 24/7 with them so we don't know about the stress and the amount of time needed to spend time with them, and I don't know how those people feel who spend the whole day with them. Maybe if you spend the entire day or a week with them you will really understand what it's like to have a disabled child. It's different if it's your own child; you need a lot of patience."*

Rodger and Tooth (2004) performed a qualitative study with five siblings to investigate their experiences of family life with a sibling with cerebral palsy. They found that all the siblings described needing to help friends adjust to their sibling with cerebral palsy, and the difficulty in bringing friends home. Similarly, the current study found that a few of the participants from nuclear family B (Figure 4.1) indicated that it affected friendships or that they would need to prepare people who visited, with P002 saying: *"You would always prepare the person or you would be sure that this person would be able to understand the situation at home, so you wouldn't bring just anybody."* The comment

above also seems to describe a fear of judgement by others, or that outsiders to the family may be frightened by the family member affected with ATR-X. Some family members even admitted to being frightened of their affected cousins (P008 and P010). There seems to be an underlying theme of initial fear during early childhood which improved with greater familiarity with affected relatives. Six participants commented on this, with the comments being directed at one particular male relative who had ATR-X syndrome. This is the individual with whom most of the family had contact, as some of the other affected males had passed away and others were in homes or institutions. P005 described the situation: *"When the child is two to three years, in the toddler age, then they tend to be scared of (*), but then there's always somebody that tells them, 'no,' that '(*) wants to play with you.' We try to explain to them what he is trying to do and say."*

P005 also described being worried about her daughter: *"I think my children are having a bit of an effect of having an uncle like that because (daughter) mentioned that she can't have her friends coming over to play at our place because (*) will always bother them and worry them."*

P002 experienced extreme anxiety during her pregnancies as she was concerned about her children being affected, having been told she was a carrier. She indicated that this was the only way in which the condition in the family had really affected her as she had also not known who to approach for more information. She tearfully described that it was still a major stressor for her, as she was now concerned for her eldest daughter: *"I know how it affected me, being 17 and getting that news, I don't know how to tell her so that it doesn't affect her that much, that she doesn't have to grow up with, or go into her life being worried like I was. I want to give her that reassurance and information where she could go to, that's more important to me, that she's not alone, like I was, that's the deepest worry that I have. You know because you can't do anything about it, its there, but to have that person that could give you answers, that's what I want, just so that she can have that."*

This description of her experience also points to poor communication within the family, which will be discussed in further detail in Section 4.7.

P002, P003 and P004 all commented that, although having an affected brother did not really affect them, they felt that their mother was starting to need their help to care for their brother again, with potential implications for their lifestyle. P003: *"We had to help my mother with him but it's awkward. We got our children, and we must see to them, and my mommy wants us to be there to help him with that, she wants to go out and, yes, it was a bit hectic. Now it's a bit better but my mother asked me recently to move in there by her but we still have to think about it."*

As new needs arise, circumstances change; and with this the impact of a condition will change. For example, the worsening situation with their brother's aggression at home seemed to be worrying the above-mentioned participants, with P002 commenting that she felt guilty and P003 saying: *"If we are around him we know he's safe, if we are not around we wonder what he is doing, what he is doing to mommy, because he kicks her a lot hey, he's strong, he's very strong."* This situation also seemed to be causing tension between P005 (currently living with her mother and brother) and her sisters as she felt that *"There's frustration that comes because we don't get as much support from the other children. The thing is, they take it that because I am there with mommy, they don't have to give their support."* She went further to say, *"It's almost like they're waiting for me to do something, if I do something then they will do something, almost like to show me 'if you can do it I can also do it' but now, why wait for me?"* It was clear from the interviews that P005 had conflict with her siblings, particularly around family responsibilities, although other underlying tensions also existed.

None of the participants indicated that having an affected brother or relative affected their schooling or that it was a factor influencing them to enter employment at an earlier stage to help the family, with P001 saying specifically that *"My parents really tried to not let that happen."*

4.5.2 Feelings towards family members with ATR-X syndrome

The majority of the participants described positive feelings and acceptance towards their affected family members, despite difficult experiences described previously. When analysing the data, the following themes emerged: normality and acceptance; love and positivity; and religious convictions. P010 was the only participant to admit to being embarrassed by her affected cousins and said, *"I didn't want to be around them; I was afraid of them."* These feelings may have significant future impact for P010, as her son was being investigated for developmental delay and may have ATR-X syndrome.

Normality and acceptance

All of the participants, besides P010, described their affected male relatives as normal and indicated acceptance of the situation, with P008 saying: *"To us, they are normal people."* The comments made by P007: *"They were normal for me because it was family. Maybe if it was someone else, maybe I would have felt different but they were my cousins, they were part of the family,"* and similarly by P009: *"It was normal for me. We must accept them, they are family,"* also showed acceptance, but implied that they may have felt differently if the affected individuals were not family members.

Participants acknowledged that their affected relatives were different but indicated it was normal for them, *"That is family life to us, so that is what we used to, that is what we used to at home"* (P004), or that there were aspects of normality, *"They might be abnormal but there is normal parts in them, they've got the mood swings, everything"* (P001).

P004 articulated the situation best saying: *"Normal can mean different things to different people, and he was him and that was normal to us. He was part of our family and that was normal, that was our normal, so yes, he has a disability but there were never problems with that."* This participant was also the most expressive in terms of

acceptance of her brother saying: *"Yes, there's something wrong with him but he's my brother, so, ya, he has a disability but that's fine.*" This finding may be related to the fact that P004 was the youngest in her nuclear family and was close to her affected brother, the second youngest child. She described that they *". . . would always do things together."* Growing up with her brother's disability was all she knew, unlike her siblings who were older when their brother was born. P002 was less persuasive in her description of her acceptance of her brother and the situation: *"We knew that when my parents were not available, then one of us should take the responsibility, and it was fine, it was accepted that it was like that,"* and *"Now, it's ok, I understand him and I sit with him."* The finding of a slight difference in the experience of normality due to birth order was similarly described by Rodger and Tooth (2004).

Acceptance of disability may be dependent on family relationships. Siblings had to accept living and growing up with a disabled sibling, while more distant family members merely had to accept the existence of a disabled family member with whom they had contact. P007 said: *"It wasn't bad when I was younger, it wasn't an issue for me to be in contact with them, because I got used to the idea that they were that way."*

P011 was generally very accepting and loving saying: *"It didn't affect me, I just accept them. They just are that way and I didn't ask why or anything, I just accepted it."* Throughout the interview, P011 did not have anything negative to say about the situation in her family. This may be due to her personality or her relationship to the affected boys in this family, as they were her nephews. P006 also indicated that relationships differed depending on how individuals were related: *"I take it like he's my uncle; I must still have respect for him even though he's retarded."*

Social class may also influence the acceptance of an individual with a disability by their family, with families of a lower class generally tending to be more accepting than middle- to upper-class families (Seligman & Darling, 2007). This may have played a

factor in the current study, as the majority of the participants lived in poor socio-economic areas and had a below-average level of household income. However, there was no difference in acceptance between those participants currently with a higher level of income and those with a lower level, reflecting that other factors may play a more important role, such as upbringing and religion.

Love and positivity

Tied in closely with acceptance of affected family members was the expression of love and positive feelings towards them, with P004 and P011 directly saying that they love them. P011 stated: *"I must say that I loved their children very much, I still love them."* P011 again demonstrated her particularly positive attitude saying: *"I didn't have any strange feelings, or angry feelings or bad feelings that they are that way. They were just too lovely; it was too lovely to have them around you. It was lovely to be able to help them, because they couldn't do anything for themselves and I liked to be able to help them."* The latter comment indicated that P011's feelings may have been connected to her own love of helping people.

P001 seemed awestruck with her brother's health saying, *"The doctors said he's not going to live long but I mean he reached the age of 38, which is amazing."* She also indicated that, although there were times when she felt he was a burden, that *"I feel that I can actually now encourage the next person to be more patient with their kids because once they're gone you do miss them."* P004 also described that, when P001's brother was sick, they *". . . would go into the room, sit with him a bit and he would know we were there,"* showing their support for him.

A protective stance towards relatives with ATR-X syndrome was also expressed, with P009 describing how she felt regarding outsiders' judgements: *"If he was my brother, he's my brother, I can't wish him away. God put him there; he's just a person like me.*

It's just that he is disabled, he can't talk and there's certain things he can't do for himself but that's it."

P004 became extremely upset when discussing a previous situation where someone suggested putting her brother into a home saying, *"I got very upset because he was my brother and how could they take him away?"* This situation seemed to be arising in her family again as her mother was no longer coping with her brother and was considering putting him in a home or getting respite care more often. However, P004 was completely against this saying: *"We realise that my mom won't be around forever so we know that one of us will have to take him so we are open to that . . . if nobody wanted to take him in, I will."* This finding is in line with the literature showing that siblings of individuals with ID felt strongly that their sibling should remain in the care of the family and not be placed in an institution or home (Eisenberg, Baker & Blacher, 1998; Griffiths & Unger, 1994)

These descriptions showing loving, positive and protective feelings, together with those of acceptance and the normality of the situation, suggest that, despite the potential for disabled relatives to cause dysfunction in, or a negative impact on a family, the participants' experiences in this family were mainly positive. Other studies (Ali & Sarullah, 2010; Eisenberg, Baker & Blacher, 1998; Michie & Skinner, 2010; Rodger & Tooth, 2004; Stainton & Besser, 1998) have had similar findings.

The positive effect in this family was further illustrated by P001: *"We actually feel more blessed than anything else to have children like this because it just keeps you focused, you know, on life and . . . it made me appreciate the little things."* Empathy towards the disabled relatives was also conveyed in the interviews by P007 and P009:
P007: *"Sometimes I feel sad because, look, they can't lead a normal life like we can."*
P009: *"Even if they were strangers, it's hard and sad to see a child like that."*
The comments noted above show that, in spite of the difficulties and stress experienced due to having a disabled relative, the family can also experience positive effects.

Religious convictions

Religion was a strong undercurrent throughout the interviews, with the majority of participants discussing God and religion at some point in the interviews. Religious beliefs were intertwined with the participants' views of disability, namely that it was accepted and normal in their family. Religious beliefs and spirituality can provide a framework in which families and individuals make meaning of a disability or illness and can often lead to positive acceptance of a disability as was seen in the current study (Michie & Skinner, 2010; Poston & Turnbull, 2004).

Participants' comments regarding religion were mostly regarding having faith and attributing meaning to disability. P005 was the participant who spoke the most about religion and said that, *"Having children like (*) also brings you close to God."* Believing that there is a higher power or having faith in God and that He will do what is best for an individual was expressed by P006: *"God wouldn't give you something if he knew you couldn't handle it,"* and P007: *"I pray every day that it's not like that but it doesn't depend on me, it depends on the Man above, it's His decision, if He wants to give us a child like that, then we must accept it."*

Poston and Turnbull (2004) interviewed families who had a relative affected with a disability to determine how religious and spiritual beliefs influence family quality of life. They found that many of the participants discussed having faith, and that for some, this involved a reliance on God, or crediting God for positive outcomes in their lives. Similarly, P005 also described that she received support from God, relied on God to give her direction and gave credit to God when her daughter was not affected with ATR-X syndrome: *"When she was born and she was normal, I really did praise the Lord and thank Him."* Individuals may gain strength from spiritual beliefs and this can act as an important resource for facing challenges and difficulties, as seen by Poston and Turnbull (2004).

The majority of the participants who discussed religion, attributed meaning to the condition by viewing disability as a gift from God, as a blessing or as a test of their faith, as described by P008: *"It's something that God gives you, and they say it's a gift if He gives you a child like that."* This finding is in agreement with previous literature (Michie & Skinner, 2010; Poston & Turnbull, 2004). Furthermore, P004 described that God must have felt that her family was special, saying: *"We a pretty Christian family and we have accepted all of it as a gift from God and we have realised that these kids aren't given to everybody, you know, so I suppose we a pretty special family to have all of them."*

When asked about their chances were of having a child affected with ATR-X syndrome (see Section 4.4) participants also used a religious framework to make sense of the condition. Although participants indicated that the genetic condition was a gift from God, or 'divinely given', it did not negate their understanding that the condition was inherited, showing that differing scientific and spiritual causal attributions need not be in opposition to one another, and that an individual can believe in both, such as in the current study and as described by Biesecker & Erby (2008), Klitzman (2010) and Michie & Skinner (2010).

4.5.3 Family support

The impact of a condition on an individual or family may be influenced by the amount of social support received from one's family (Seligman & Darling, 2007). Participants were asked to comment on the type of support (financial, psychological and/or child care) they received from their family and how often they saw their nuclear and extended family. A graph describing the type of support received is presented in Figure 4.6.

Only two participants, namely P001 and P010, felt that they received support in all three areas if it was needed. Seven participants indicated that they received psychological support of some kind from their family, with P002, P003 and P004 indicating that this

was the only support they received. This psychological support was also mainly between each other. P002, however, indicated that she could only talk about certain things to certain people and said, *"I feel with me being the eldest I can't share everything because they might not understand, they might not be at that same level. But we speak a lot and we speak about most of our things. We don't have secrets, if something bothers us we know we can go to one another and share."* P004 specifically indicated that she was not close to her mother or her one particular sister, implying that underlying difficulties in relationships could impede communication.

Two participants, P006 and P009, indicated that their only form of support was help from their family with childcare. P006 said that she did not talk to anyone and that *"I bottle up everything. Sometimes there's times when you really want someone to talk to, but most of the time if I bottle up everything and I can't keep it in anymore, I lock myself in the bathroom and I just cry for like an hour and then afterwards I feel better."*

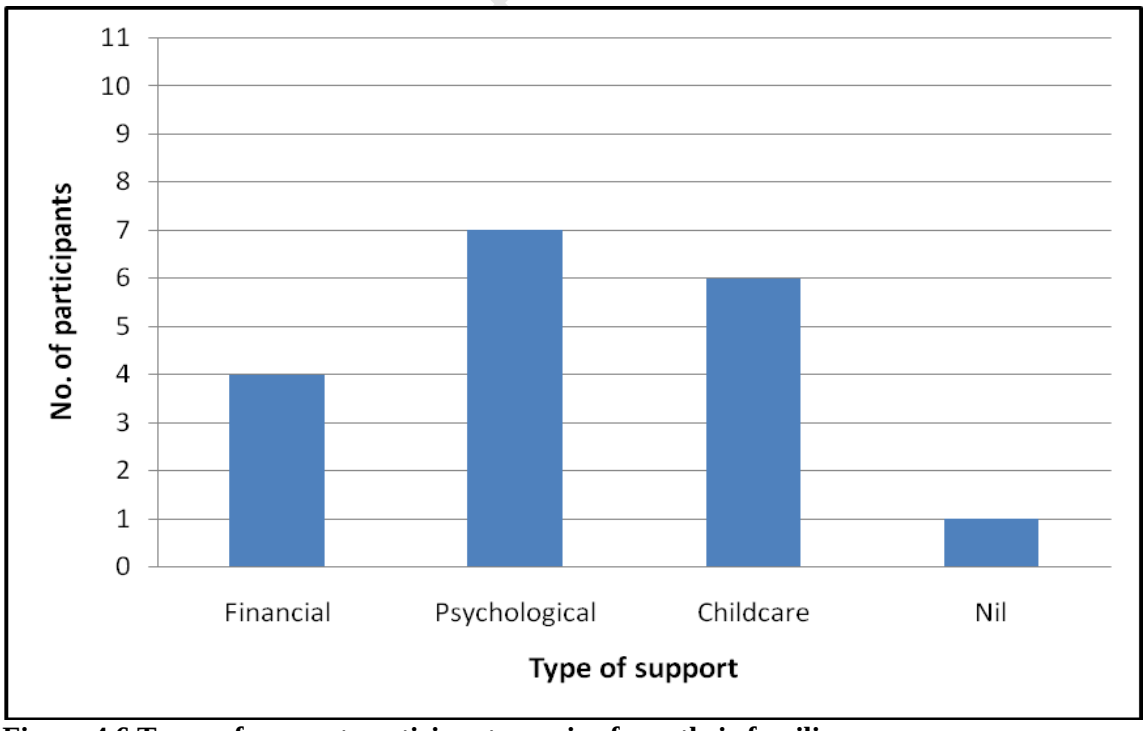

Figure 4.6 Types of support participants receive from their families.

P005 was the only participant to say that she did not receive any support from her family and that, besides her children, the only family member with whom she frequently had contact was her mother, with whom she lived.

The majority of the other participants indicated that they saw their immediate family frequently but that they only really saw their distant family members (e.g. cousins and aunts) on special occasions. P011 was the only participant to quantify frequency and indicated that she only saw her sisters three to four times a year, but that the bond was always there. P008 and P009 lived on the same property, so they saw each other everyday. P007, P010 and P011 all described a close family relationship, with P007 stating: *"We have lots of support and myself, P010 and my brothers are all very close. We see each other every day. I ride to them or they ride to me. They are very supportive with the baby now. We are actually more supportive with P010 now because she is alone and it's hard for her now so we are trying to spend more time with her and (her son). We talk about everything."* Only two participants, P001 and P004, reported frequently speaking to family members outside of their nuclear family, although this was mostly with each other.

As mentioned previously, social support within families is important; when families have a sense of togetherness, co-operate and are cohesive, their ability to cope is enhanced (Seligman & Darling, 2007; Taanila *et al.*, 2002). From the above findings, it can be seen that, although the majority of the participants received psychological support, there were still certain participants who did not seek social support, which could affect their coping ability. Furthermore, the findings provide a clue that there may be differences in what is communicated within nuclear families and extended Family X; this was explored further in Section 4.7.

4.5.4 Community reactions

Participants were asked to comment on how the community reacted to their affected relatives to determine how this influenced the participant and the family with an affected male. A summary of the findings is provided in Table 4.5.

The majority of the participants described negative reactions from the community, mainly involving staring and people being judgmental. However, the majority of the participants indicated that they did not let this bother them. P004 described specific incidents of what had happened with other people, namely that a child in the neighbourhood had poured a liquid over her brothers head and *"Also the person who my mom is now staying next door to, he also has a problem with (*), he's actually an adult, which I think is very sad and I actually see now that the house is for sale . . . because of (*)."* These incidents indicate that stigma towards people with disabilities may be present, but P004 tended to think that these were isolated incidents and that the majority of people were friendly towards her brother.

Table 4.5 Community reactions to individuals with ATR-X syndrome as experienced by the participants.

P	Community reaction
001	"They would pity him." (severely affected brother) "Everybody loved him." (higher functioning brother)
002	"People would be judgmental."
003	"They would stare at him, but we would just ignore them."
004	Described specific incidents but feels people are normally friendly towards him.
005	"We get lots of wrong judgments from the community." "Staring."
006	"Some of them are very scared of him." Described people also being rude and judgmental.
007	"Some people stare, or speak softly but you can see that they are discussing them."
008	"Yes, they reacted, but we didn't let it bother us, I was not bothered by them."
009	"They stand and stare at them and they wonder of course, but further it doesn't worry me."
010	Community would laugh at them and watch them.
011	Didn't answer.

P005 said that she felt that her brother was judged a great deal by his appearance and characteristics but said that she told the people that, *"It's not something that you people make, it's something that God's created and I would tell them that if they are spiritual enough they wouldn't stare,"* again attributing meaning to the situation as being God's will.

Bourke-Taylor, Howie and Law (2010), who investigated the impact of disability in school-aged children in Australia, found that mothers experienced negative reactions and stigma. This is in line with the current findings, where participants mainly reported negative community reactions. Children with ID can have a positive impact on the community by teaching others to be more accepting of differences (Stainton and Besser, 1998). However, none of the participants discussed the impact their affected relative had on the community in a broader sense.

4.5.5 Effect on reproductive choices

Personal experiences, the severity of the condition in a family and perceptions of risk have been identified to influence reproductive decisions (Beeson & Golbus, 1985; Kay & Kingston, 2002; Klitzman, 2010; Peterson, 2005). The participants in this study were specifically asked if their experiences with their affected relatives had affected their reproductive choices in any way. Only one of the participants (P005) indicated that it had. Participants were also asked to imagine how they would feel if they were to have a child affected with ATR-X syndrome. A summary of the findings for each participant is presented in Table 4.6.

Table 4.6 Effects on the reproductive choices of participants and summary of perceived feelings towards having an affected child.

P	Influenced reproductive choices?		How would they feel if they have child with ATRX?
	Yes/No	How and why	
001	No	Didn't think it would continue to her generation when younger.	"I don't know if I will have the strength or be able to handle it."
002	No	"My husband had an influence in that section."	Didn't answer question.
003	No	Would accept a child like that.	"I think I will feel sad sometimes and sometimes not."
004	No	Family complete but nothing to do with affected brothers.	"We would just accept it, that we were chosen to have the baby, and just make the best of the situation."
005	Yes	Affected her decision to get married as thought that if she were to marry she would have a child that was affected.	"I could maybe handle it because now I know that I was able to handle (*)." "I would accept it if it was God's plan."
006	No		"I wouldn't worry about if my child's retarded or if he's normal. I would be worried about his father, how his father would react."
007	No		"Maybe it will be difficult because it's the first time but it will always be your child."
008	No	"I must just accept it."	"I will feel very sad. But I will not reject him, I won't be able to do that, I will just need to build up the strength."
009	No	"It didn't cross my mind."	"I just accepted that if it comes to that I will make peace with it."
010	No	"I didn't know at that stage that I could also get a child like that."	"I will just have to accept it."
011	No		"I will raise a child like that anytime."

When discussing how having a brother with ATR-X syndrome had affected her reproductive choices, P005 indicated that it had affected her interest in men as she was too afraid to get married for fear that she would have an affected child. She indicated that this fear was mostly due to not knowing her carrier status saying: *"Maybe if they told me I was a carrier then I wouldn't have wanted to be married totally, because then I would have been scared, but the mere fact that they didn't tell me anything, I didn't know what to expect or what to do with my life. I think because I did not know my results back then, it made me a even more reluctant to be a married person because I didn't know anything about myself, all the others knew but I didn't know, I wasn't sure. Maybe I could have been married by now, if I had known before."* P005 did not describe any negative experiences of growing up with her brothers with ATR-X syndrome, yet she expressed a strong desire to not have an affected child, as she knew what it was like to grow up with her brother. This suggests that there may be underlying negative experiences and feelings that she did not feel she could discuss with the researcher. The avoidance of marriage by P005 due to her genetic risk was similarly seen by Klitzman (2010), who found that risk for a genetic disease can influence decisions to get married or have children. In addition, the comment by P005 that ". . . all the others knew" implies a sense of conspiracy, again pointing towards underlying relationship difficulties and feuds.

The fact that the reproductive choices of the other ten participants were not affected by their relatives with ATR-X syndrome, and the fact that the majority described that they would accept a child who is affected, may be due to the positive light in which the participants viewed their relatives and their religiosity, as discussed previously in Section 4.5.2. Although the majority of the participants theoretically knew that they were at risk of having an affected child, their reproductive choices may also have been influenced by a perception that the risk was reduced. This perception could have arisen from the discussion surrounding the condition 'skipping a generation', and the fact that none of the individuals in the current generation had an affected child (Section 4.4).

4.6 CURRENT OPINIONS REGARDING TESTING

Despite the family being informed about the availability of carrier testing, it was postulated that lack of this knowledge, due to lack of dissemination of information, may have influenced the uptake of testing. In line with this, participants were asked if they would like to have carrier testing and what had prevented them from coming for testing previously if they did want testing. Their views regarding prenatal testing and TOP were also discussed. Participants' responses are presented in Table 4.7.

Five of the 11 participants were aware that carrier testing was available. Of these five, one participant only recently became aware of testing, as she was pregnant (P006), and P009 seemed to be unsure, or confused it with other testing, although this is not certain. Three of the participants who knew about the testing were sisters of affected men, while those who were unaware of testing were more likely to be distant relatives. These findings are in accordance with Varekamp *et al.* (1990) who similarly found a large proportion of potential haemophilia carriers were unaware of testing and that the lack of knowledge was associated with a more distant relation to an affected individual. Binedell, Soldan and Harper (1998) also found that 25% of the individuals who hadn't requested testing for HD were unaware of the availability of testing until they received the research letter. However, Claes *et al.* (2003), in their study investigating HBOC syndrome, showed that there was no association between the uptake of predictive genetic testing and whether relatives were informed or not, indicating other factors were involved.

Besides P003, participants had no hesitation in stating that they wanted carrier testing, although there were various reasons provided. Lack of hesitation in indicating the desire for testing, and various motivations surrounding this, was similarly found by Anido *et al.* (2005), who investigated opinions related to FXS carrier testing in the general population and those with a family history.

Table 4.7 Participants' opinions regarding carrier testing, prenatal testing and termination of pregnancy (TOP).

P	Aware testing available	Want to know if carrier	Reasons	Reasons for not coming earlier	Test pregnancy	Reasons	TOP	Reasons
001	Yes	Yes	"We would want to know that we are safe or not safe."	"Because I just didn't get there."	Yes	To be prepared	No	"That's not my beliefs."
002	No	Told she is a carrier	N/A	N/A (Also didn't know who to go to)	Yes	To be prepared	No	Didn't answer
003	Yes	No	"I won't have children anymore so that's why it doesn't bother me anymore."	"Not an issue for me."	No	"Just wait and see." (else will worry)	No	"I don't believe in that."
004	Yes	Yes	"Because I know that the tests were done, just for interests sake." "And also just so I can know if I carried it on to my daughters, I suppose."	Not a concern/ knew it should be done but was not urgent for her.	Yes	To be prepared	No	"I don't believe in killing another human being."
005	Unsure	Yes	"I don't know what God has got in store for me, I'm not that old so it would be fine if I could get the test done now."	Didn't know who to contact/ too scared if she had to pay as didn't have money.	Unsure	"I will cross the bridge when I come to it."	Unsure	"It's something I would have to pray about."
006	Yes	Yes	To be prepared/ to know what to expect.	Never had the opportunity/ knew about it before.	No	Would feel pressurised by others to have an abortion if knew before.	No	"I don't like abortions, for me it's like murder."
007	Unaware until recruited	Yes	To be prepared/ to know what to expect.	Not aware	No	Risk of miscarriage (but would want to know)	No	Religious reasons
008	No	Yes	"I want to know just to know." (and for children)	Not aware	Yes	To be prepared	No	"Don't believe in it."
009	Yes	Yes	"Just to know." (and for children)	Thought researchers would come back to them with results.	Yes	To be prepared	No	"That child is your luck, it's what God gave you."
010	No	Yes	To "know if I can have another baby like that again."	Told disability extremely unlikely during pregnancy.	No	Risk of miscarriage (but would want to know)	No	"It's murder."
011	Confused with other test	Yes	"I think it will help for the next person, to inform them."	Didn't think her blood had been taken/ Not aware of who to contact.	Yes	To be prepared	No	"That's in my religion."

Four participants indicated that they would want to know their carrier status in order to be prepared or to know whether they could have a baby that was affected with ATR-X syndrome. This is illustrated by comments from P001 and P007, who wanted to be able to prepare themselves in different ways:

P001: *"My parents never had this opportunity, to have known before the time, to maybe cry their hearts out before the child is born and be strong when the child is there you know, and accept it. So I think it would help for anybody to know before the time."*

P007: *"They always say you can't prepare for something like that, but you can maybe think forward about how it will be to have a child like that. Will you be able to handle it? Will you know how to handle the child? Will you know how to raise them? Will there be a lot of help for you? There must be changes in your life, maybe giving up your job because you will have to look after your child yourself, the income won't be the same as before . . . so there's a lot of things that you must think about."*

The four participants who indicated that they wanted to know in order to be prepared were unsure of whether they had completed their families yet, whereas P003, who was not interested in carrier testing, indicated that she had completed her family and therefore did not see the benefit of testing. The reproductive life stage of a woman was similarly found to influence the uptake of carrier testing for FXS by Archibald *et al.* (2009). However, additional factors also influence testing decisions, as indicated by the fact that there were four other participants who wanted to have carrier testing despite having completed their families. Their reasons for wanting to know their carrier status were mostly for their children or future generations, although there was also an element of curiosity expressed by three participants, which was similarly seen in previous literature (Anido *et al.*, 2005; Archibald *et al.*, 2009). P004 also said that *"If this hadn't come along since an earlier age, I'm not sure if I would have gone out to find out about it,"* indicating that it wasn't much of a concern for her. This ties in with the previous

data that she accepted the condition and that she believed her family was gifted by God with her affected relatives.

P001 felt that there is a lack of interest from her extended family about knowing one's carrier status, saying *"When we were younger, we were more involved, more of the family, but now that everyone is married and they've got their own kids, they are not really worried to actually know, because maybe it's not us. But maybe my kids will have it one day. They (family) should also know that, but they are not interested. And now we more smaller, because previously we used to use a whole clinic to get the whole family there, but now it's just us, the chosen ones."*

P001 also indicated that her relatives may not have understood that carrier testing was private and individualized and rather thought that the family would have their results delivered collectively as a result of previous experiences at family gatherings:
"Maybe they thought that we all sitting together and we say 'You, you and you' and maybe they thought it was that and that's why they don't want to go, but I want to tell them that it's individual. You go on your own and it's your thing, it's like going for a test, and the doctor can only tell you and nobody else. But I would like them to actually know. I want to give them the option and tell that it's more private, and then if they don't budge then no fine, then I accept it." She went further to say: *"It's their choice though, I can't force them to have it, although I would want to, because if they know, it's like an open cloud, but it's their choice."*

Interestingly, although having had her blood taken on two separate occasions, P011 did not remember that she had had her blood drawn at all and said that: *"I'm not 100% sure about that day that they drew blood; I believe that they didn't take my blood for the test."*

Only one participant, P005, indicated socio-economic reasons for not taking up carrier testing services, along with not knowing who to contact. Ignorance of who to contact regarding the condition was mentioned by two other participants. In relation to this, six participants (P002, P003, P005, P006, P007 and P010) described experiences of approaching doctors about the condition when they were pregnant. From the experiences described, participants' concerns were either shrugged off or they were reassured, as the participants themselves could not name the condition running in the family and doctors sometimes assumed that they were referring to something else, like Down syndrome. P002 describes her experience: *"I would ask them to test for it and they would question why I would want that specific test to be done and all that, and I couldn't explain because I didn't know who was in charge or who I could refer the doctors to, then they would normally brush it aside. One doctor said to me 'No, it's only when you're after 37 years of age that they would do that and they would only test on certain people'. . . There was like no, even if I tried, there was no way you were referred somewhere, to take anything further."*

These comments and experiences seem to reflect a poor level of knowledge and awareness of genetics at the primary health care level. An inadequate level of genetic knowledge amongst GPs and other non-genetic health professionals has been found elsewhere, such as the Netherlands, a developed country (Baars, Henneman & ten Kate, 2005). In an example of their findings, Baars, Henneman & ten Kate (2005) found that 47% GPs, 41% of gynaecologists and 15% of paediatricians could not recognise an autosomal dominant inheritance pattern in a pedigree. They also suggested that low levels of genetic knowledge amongst non-genetic health professionals may be a global problem, which may have greater implications for SA which is a developing country with competing health needs.

There seemed to be a lack of communication in the family regarding who could be contacted if they would like further information. To ensure that the family had had all the necessary information, it would have been useful for the family members to have

been given a written letter informing them of the condition in their family, the inheritance, recurrence risks and who to contact should they require further information. This could be an important tool in helping to inform further family members as they become of child-bearing age and for doctors who are not aware of the condition running in the family (Claes *et al.*, 2003; McConkie-Rosell *et al*., 2005)

In comparison to carrier testing, where 10 individuals indicated they would want testing, there was less consensus about prenatal testing, with six participants indicating that they would consider testing a pregnancy, and four that they would not. Explanations for not wanting prenatal testing included the risk of miscarriage associated with an amniocentesis, and the concern of causing unnecessary anxiety during the pregnancy (P003). This finding was also seen by Archibald *et al.* (2009), who investigated the factors surrounding uptake of carrier testing for FXS among woman from the general population. The intention to use prenatal testing has also been shown to be influenced by many factors, such as religion, family income and the willingness to terminate an affected foetus (De Braekeleer, Rault & Bellis, 2004; Wertz *et al*., 1992). In line with this, P006 indicated that she did not want prenatal diagnosis as she would be unwilling to terminate a pregnancy. Despite high levels of religious beliefs and strong views against TOP, there were a significant number of participants who would consider prenatal diagnosis for preparation purposes, which is in agreement with the literature (McConkie-Rosell *et al*., 1997; Bryant, Green & Hewison, 2010).

In contrast to Kay and Kingston (2002), where 13 of the 14 participants at-risk of having a child with an X-linked disorder intended to have prenatal testing and TOP to avoid the birth of an affected child, this study found that only one participant was open to the discussion of TOP, while the rest were completely against it. This was explained by strong religious beliefs against TOP. P009 described her view against TOP as follows: *"I will not stop the pregnancy, that child is your luck, it's what God gave you, and to remove that child just because he is disabled, how is that going to benefit you?. You will wonder, 'How would my child have been?' It's your luck. That's how we were brought*

up, that's how I see it, and that is how my belief sees it, your family is your luck. I don't care if they are disabled or normal, it's your luck." P005, who would consider TOP, however also cited that religion would play a part in her decision saying that *"It's something I would have to pray about also to ask God to give me direction and then what to do and decide."* Attitudes towards termination may also be related to attitudes towards the individuals affected with the condition (Bryant, Green & Hewison, 2010); as the majority of the participants viewed their affected relative in a positive light, this may, in combination with religiosity, account for the strong view against abortion in the current study.

De Pina-Neto and Petean (1999) found that, despite the majority of their sample perceiving that their religion is against abortion, they felt that they would accept a TOP if a subsequent pregnancy was to show an affected foetus, thus highlighting the importance of the lived experience of the participants and the avoidance of recurrence. The low level of consideration of TOP in the current study may therefore be related to the fact that none of the participants had an affected child. In Family X (Figure 4.2), there were some women in an older generation (generation II), who had affected sons and decided to abort a male foetus due to the risk of the baby also being affected; this further supports the above finding. Only two of the participants, P011 and P005, indicated that they knew about this happening in the family.

4.7 COMMUNICATION IN THE FAMILY

Communication within families is a central concept in terms of a functional family system, but it is also vitally important in terms of genetic conditions and testing. Adequate communication is important to accurately disseminate information to family members about a genetic condition and its risk for others in the family. Communication or lack thereof has the potential to lead to emotional distress. Non-disclosure specifically

has the potential to deny individuals the right to autonomous decision making regarding their own health and reproductive decisions (Forrest *et al.*, 2003; Peterson, 2005; Wilson *et al.*, 2004).

4.7.1 Communication about ATR-X syndrome in the family

Due to the reasons cited above, communication within Family X was investigated to determine if there were underlying communication problems that were influencing the uptake of carrier testing in the participants interviewed. Participants were asked to comment on how information regarding the condition in the family was explained to them and also what information they had passed on to their children. This is presented in Table 4.8. A discussion regarding disclosure of information to others, the extent to which genetic information is discussed in the family and beliefs regarding who should inform others in the family follows.

Six participants were informed about the condition by one or both parents, and one by her sisters. The remaining four individuals indicated that they had heard about it mostly from the genetics staff; however, it is likely that some information was explained by the family as well. The finding that the majority of the participants knew that the condition which affected males was in the family or inherited (also shown in Tables 4.2 and 4.3), may indicate that information regarding the condition was openly discussed. This can relate to a feeling of having 'always known' (McConkie-Rosell, Heise & Spiridigliozzi, 2009), although other information regarding risk figures, or details of the inheritance may have been less openly discussed or selectively provided (Wilson *et al.*, 2004).

Table 4.8 Results of communication regarding dissemination of information of ATR-X syndrome to participants and their children.

P	How was it explained to them	What is their children's understanding
001	Started with simple explanation and got more detailed as got older and attended family meetings.	"But they accepted him for who he was and his ways." "But I never explained to them yet in detail, I'll wait until they are a little bit bigger."
002	Poorly explained and didn't explain much or give contact names/numbers.	"It's like a germ that's in the family, that's in our blood and I just stop short of saying that it will carry on."
003	Explained that she could have a child that is affected.	"We just told her that if you try to have children one day, they must just remember, it can be, it's 50:50, it can be or it can be not (that they have a child like that)."
004	"I don't remember if anything was explained but, it was never a problem to us so it was never as if he set aside as somebody special."	Nothing explained yet as too young.
005	Didn't answer.	"Edwina is young still to understand (that could also have affected children). Pauline, I think she has it in her head now that she might be that's why she also wants a test now."
006	Heard about it from the genetic staff recently for the first time. Felt family is very secretive.	N/A (Daughter <1 year)
007	Spoke about condition being in the family and that grandchildren could get it. "She never spoke to us in detail about what it really means to have a child like that."	"All that we could explain to him was that 'they are sick, we can't say that they normal like you'."
008	Heard about it from the genetic staff when blood was taken to do research on carrier status.	Has not discussed with daughter that it's in the family.
009	"I can't say because nothing was explained. Look, we were still young so our parents got those answers but my mom said that nothing has come back from that."	"That he is not normal, and he won't hurt her and she mustn't be scared of him."
010	"I knew there were children like that in the family, and there were people that took blood, I think they were from Pretoria, and they told us a little about the condition in the family."	N/A (Son <2 years)
011	"And they said that it's in family from mother's side and that it can be passed on to our children's children. They didn't explain much but when my children started getting pregnant then she gave me information."	"They don't know much about the condition" but they apparently know that they could have children like that.

Table 4.8 also shows a difference in the way in which information was given to P001 and P002, with profound emotional consequences for P002. P001 reported being given information in stages, which is consistent with literature that telling relatives should be seen more as a process than as an act (Forrest *et al.*, 2003). Research by Wehbe *et al.* (2009) also found that adolescents and young adults recommended being told in stages about the condition in the family and then the risk of being a carrier. However, in contrast to this, P002 felt that she was told 'out of the blue' and described the experience: *"We understood that it was there and it was in the family, but we didn't know it was going to affect us as children,"* and then "*They just told me, 'You are a carrier,' and I was shocked. And I asked, 'What does it mean?' And they just said, 'Your children will be affected' and that was it. They didn't say, 'You can speak to this person or that person' or anything, it was just information that was just given to me (crying)."*

The effect of her experience regarding how the information was disclosed to her, and the fact that she did not feel that she could discuss it with anyone or knew who to go to, had a profound effect on P002 and this influenced her disclosure decisions. The finding that experiences of finding out about a condition influenced disclosure decisions was also seen by Forrest *et al.* (2003), who noted that it also influenced individual coping styles.

P002 had informed her children about the condition but did not feel that she could tell them that they could also pass it on: *"I haven't spoken to them because I don't know how. I did tell them that it affects the family but I don't think they know that it could affect them as well."* She also described being scared of informing her children as she was concerned that they would worry about it like she had. She felt she first wanted more information so that she could inform them properly or reassure them. Nondisclosure of information relating to concern over a child's emotional health, the wish to protect relatives from distress and not being well-informed have been described in the literature (Davey, Newson & O'Leary, 2006; Forrest *et al.*, 2003; Gallo *et al.*, 2005; McConkie-Rosell, Heise & Spiridigliozzi, 2009; Metcalfe *et al.*, 2008). Protection of one's child against emotional distress and reluctance to convey bad news was also

expressed by P011 with regards to the possibility that P010's son could be affected as he was being investigated for developmental delay: *"I don't actually want to tell P010 that I see those signs. If it is like that, the doctor must tell her himself."*

The difficulty of informing daughters of their genetic risk of being a carrier, in respect of FXS, was described by McConkie-Rosell, Del Giorno and Heise (2011), who found that the majority of parents did not inform their daughters that they could be carriers, and those that did, struggled to inform them and used less open communication. They suggested that the reason for this may be related to uncertainty of how to describe the possibility of being a carrier, how to inform their daughters, what it would mean for their future and how to answer questions. In the present study, participants' mothers were not interviewed, but the reasons for poor communication cited above may have played a role.

The majority of participants had young children and felt that they were still too young to understand the information regarding inheritance and the implications thereof, which is supported by the literature (Forrest *et al.*, 2003; Gallo *et al.*, 2005). This also ties in with the correct time to tell children about their genetic risk. The majority of the participants stated that disclosure was made when they reached child-bearing age or when they were starting their family. Forrest *et al*. (2003) also found that individuals felt the correct time to inform children was when their first key life decision, that may be affected by the condition, had to be made, such as marriage and having children.

Participants were asked if they had shared information regarding the condition in the family, together with who they had told and what they explained if they had. Only two participants (P006 and P010) said that they hadn't shared information with anyone else. This may be related to the fact that they were the youngest participants in the study, had only recently had their children and were not in a relationship. A summary of who the rest of the participants spoke with is presented in Figure 4.7.

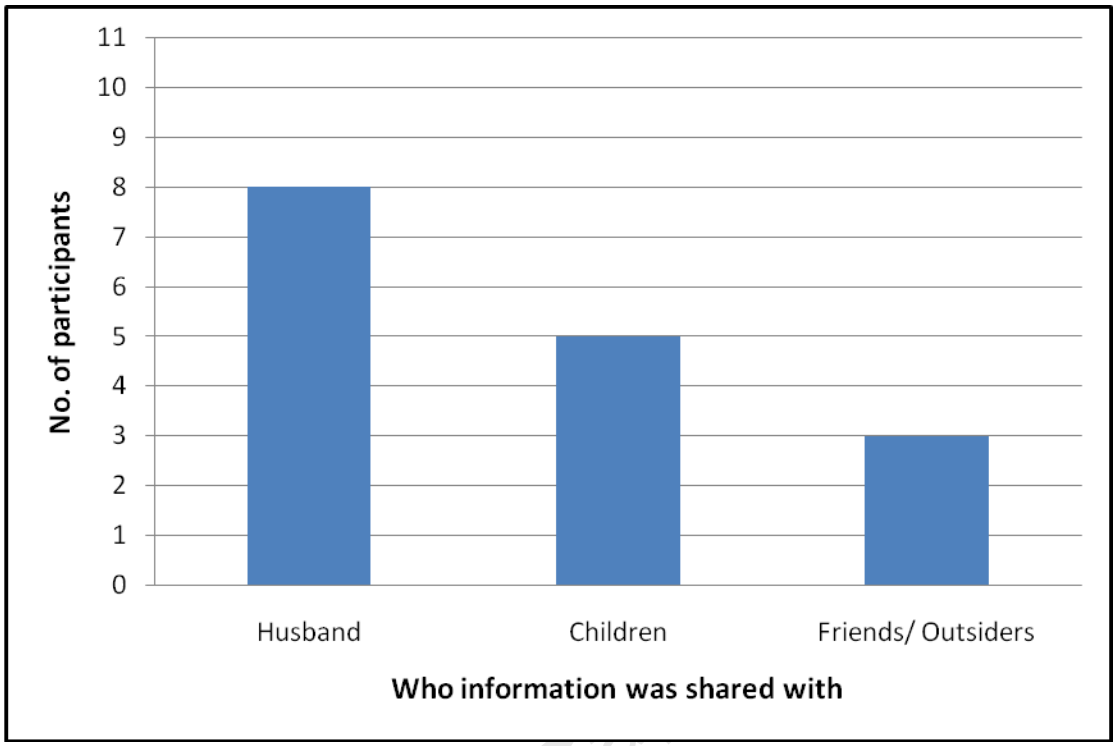

Figure 4.7 Persons with whom participants share information regarding the condition (n=9).

As can be seen in Figure 4.7, the majority of the participants had informed their husband about the condition. However, when asked what information was shared, this was mostly superficial, with the participants indicating that they just informed them about the affected males in the family and did not discuss the genetics of the condition. P009 said: *"I just told him that he is disabled and we didn't talk about it further."* The same applied regarding information provided to children and outsiders. P002 had also not disclosed her risk of having affected children, saying: *"But he doesn't know that it will maybe affect our children or anything, because he thinks it's just in my brothers and sisters, he doesn't know that it can carry on."* When asked if she ever discussed this, she said: *"No, I haven't, because I can't explain it to anybody."*

Only two individuals, P001 and P004, indicated that they had discussed the inheritance of the condition with their spouse, with P001 giving a description of what she had said:

"I would say, it was a sickness that my gran had and all her boys never survived, so it was just carried over to the next generation and my mom and her sisters, they are carriers, and they have got it in their, can I say genes, and that is why they have these retarded boys." She also described what her mother advised her to tell others when she was younger: *"Then my mom said, 'You just tell them that it's something that your granny had, that's passed on to me and your aunts and It's just in the boys and it's a chromosome problem.'"*

4.7.2 Communication about genetic risk and testing in Family X

Participants were asked whether information regarding the genetics of the condition was discussed in the family. Ten of the participants said that it wasn't.

P002: *"We knew it was there, but it was like, nobody had answers. So we never used to talk about it or discuss it with anyone, it was just a thing that we knew about and that's it."*

P005: *"Not when I was involved . . . If I want to know more about the genetics, then I would go to the library and look it up and do my own research and such."*

P007: *"They discuss it very little actually . . . They don't speak about it a lot, we just accept it, we just sit here with our hands folded."*

P008: *"They spoke about it amongst each other."*

P001 was the only participant to indicate that the genetics was discussed and P004 said that it was not discussed but only because *"It's sort of like old news to us now."* However, it is clear from the comments above that the rest of the participants did not feel the same way.

The results were exactly the same with respect to the discussion of carrier testing, with ten participants feeling it wasn't discussed. P001 indicated that it was discussed and

P004 said, "*From speaking to you guys, we know that it is available so we haven't spoken about it."* However, from the findings in Section 4.6, it is apparent that only three individuals really knew that carrier testing was available; these were all sisters of an affected male.

The findings in this study are in contrast to those of Sorenson, Jennings-Grant and Newman (2003), who investigated communication about carrier testing in families affected by Haemophilia A, and found that 60% of the individuals in their sample had discussed carrier testing with family members.

There may be many possible reasons why P001 and P004 had different views to the rest of the participants. They had the highest level of income, a high level of education, the best level of genetic knowledge and they took on the role of facilitators, organising the recruitment of family members into the study. It emerged from the interviews that P001's mother, who had had two affected sons, was very involved in the family and the genetics of the condition (discussed in Section 4.7.3); this may have had an effect on P001's and P004's knowledge of the genetics and testing, as they were very close to each other

P006 indicated that she felt a little resentment that information was not discussed. When asked why she thought her grandmother did not want to talk about the condition in the family and testing she said: *"My mother says that my granny gets heartbroken because she thinks it's her fault or whatever. But if it was me, then yes, I would feel heartbroken, but at least I will think of my children and I will tell them, 'You maybe will get it or maybe you won't get it,' so that they can also know where they stand and how to make plans. Otherwise, if they don't know and they make plans for their life, all of a sudden there will be a setback if they have an affected child."*

The previous comment illustrates that guilt may play a role in preventing communication of genetic information and carrier testing. Although it was not explicitly

said, P002 may also be struggling with guilt feelings that her children may be carriers and this may also be influencing her decision to inform her children. Guilt as a barrier to communication has been described previously (Wilson *et al.*, 2004), and it has been described extensively with regards to X-linked inherited conditions (Anido *et al.*, 2005; James *et al.*, 2006; Kay & Kingston, 2002; Lehmann, Speight & Kerzin-Storrar, 2011).

In respect of the discussion of genetics in the family, five participants (P001, P003, P004, P006 and P010) felt that they could explain the little that they knew about ATR-X syndrome to someone else but ten participants felt that they wanted more information. When asked these questions P011 said: *"No I don't have enough information about this to talk to someone else."* The only participant to indicate that she did not want any more information was P004, who felt she had enough information. She did however say that, if there were new developments, she would want to know.

4.7.3 Responsibility of informing about genetic risk

In order to determine how information was disseminated within Family X, participants were asked whether they thought that there was one individual in the family who took primary responsibility of informing the rest of the family about the condition or the genetics of it. Their responses are shown in Table 4.9.

Table 4.9 Participants' responses to whether a specific individual in Family X takes primary responsibility to inform others in the family about the condition.

P	Who takes primary responsibility to inform the family?
001	Her mother but not anymore. Now herself and P004.
002	Heard it's supposed to be Aunty M† but didn't feel like she would actually give information .
003	"I don't know." Feels that all talk openly and only discuss it when it comes up in conversation.
004	Aunty M, "She is the most learned of all the girls."
005	"You have to go to them and ask them about it, I would have to go to Aunty M."
006	"No, not that I know of, because I know nobody spoke to me about it."
007	"Aunty M, she always do that, she always see that the family comes together."
008	"No one, everyone just talks together."
009	Didn't think anyone really took primary responsibility but felt her sister often asked questions.
010	Aunty M .
011	Aunty M .

†Aunty M is a pseudonym for individual I:1 in nuclear family A (Figure 4.1).

Seven of the participants felt that there was an individual in the family that took the role of 'messenger' (Wilson *et al.*, 2004), namely Aunty M, who would inform the family about the condition and would organise family meetings with the genetic staff. Even though P003 indicated that she did not think there was anyone that took primary responsibility, she mentioned previously that Aunty M had told her that she must inform

her daughter about the possibility of being a carrier. However P002 felt that her aunt did not actually provide her with information, saying: *"I've heard P004 say that my aunt is supposed to be that contact, but she never comes and gives you information, like when there is someone who is coming to draw blood or anything, they don't let you know, and then also (?) will tell you, 'No, it's only for certain members.' Now you would question why? Is there something particular that they looking for, or is there some difference between them and you? So I also feel that, in that way, it's not trustworthy so you don't know if you can go with that, are they going to tell you what's really going on?"*

On the other hand, P001 (daughter of Aunty M), provided insight into how the situation was changing: *"It was first my mother, because she was the main one that would call everybody, but I think my mom's taken a step back now, because both her boys are gone and she thinks the others need to step forward now. She said they need to go forward now, because their boys need the assistance; they need to go and ask or tell their tale. But now, in our generation, it would be me and P004 that arrange, or that would go and tell them, 'You need to go for this and that,' but sometimes you don't get any feedback from them that they actually want to go, or interest."*

This change in the process of the dissemination of information in Family X may be directly contributing towards poor communication in the family and to the feelings described above by P002 above. It seems as though information regarding carrier status and testing was not discussed within nuclear families per se, but rather at family meetings which Aunty M organised with the genetic services; this was, however, not explored in great detail.

The role of only having one 'messenger' may also not have been sustainable in Family X as previous research shows that parents should take the responsibility of informing their children (Forrest *et al.*, 2003; Metcalfe *et al.*, 2008; Wilson *et al.*, 2004). Sorenson, Jennings-Grant and Newman (2003) showed that mothers, in particular, play a pivotal role and act as a source of discussion regarding carrier testing. This implies that the lack

of discussion about the genetics and testing within nuclear families may have been a factor in the participants' lack of knowledge about this and their feelings of not being well-informed.

Family communication about genetics is also dependent on existing norms and patterns that govern family interactions, with existing family conflict or emotional distance acting as barriers to dissemination of information (Davey, Newson & O'Leary, 2006; Forrest *et al.*, 2003; Peterson, 2005; Wilson *et al.*, 2004). It was evident from the interviews that there was definite conflict and tension within Nuclear Family B. P002 clearly withdrew herself from the family and felt resentful towards her brothers and sisters who did not help out more with her affected brother. P004 also implied poor communication with her mother when explaining how upset she was when her mother put her brother in respite care and did not inform her beforehand, saying: *"So I just felt at the time, 'Why didn't my mom talk to us?' Because that would be a last resort."*

P002, P005 and P006 indicated to the researcher that they were happy that they had someone to discuss things with, as this was the first time they were able to talk about it, further emphasising the lack of communication in nuclear family B. P002 tearfully expressed her relief saying*: "You know, I have been worried so much and I'm actually glad that I can speak to someone, so I actually feel better about it now."*

Where communication was more closed, feelings of frustration and distrust were expressed, which is evident in the comment above from P002 where she discussed distrust in the information given by her aunt. This sense of distrust was explicitly stated by P003, *My mother tells us, but then sometimes we don't believe her, sometimes we believe her,"* with reference to her brother's behaviour at home. P006 felt that the family was very guarded regarding the genetics of the condition stating *"They were very secretive; they didn't want to tell people."* A feeling of distrust from the extended family was also implied by P011, who said: *"We are not sure about (*) being affected, so we*

haven't told the other families about it. We will wait until the tests come back. You can't say until you have proof, so we will wait till we have proof and then go to them and maybe they will then give support," implying that, if she did not have proof they may not believe her, and that there is a lack of support generally.

Open communication has been seen to empower families and allow individuals the opportunity to discuss concerns and ask questions, together with providing increased support within families (Metcalfe *et al.*, 2008). This would be beneficial for Family X, with P009 expressing that she wanted more information so she could inform her children: *"If I can get an understanding about what it's about now, and one day they have children and I am still around, then I can tell them about it, where it comes from, what it is, then I can help them again. It's a help for everyone."* With this statement, she was implying that more communication would empower both her and her children. Children from families where there was more open communication were also reported to be more emotionally and psychologically resilient (Metcalfe *et al.*, 2008).

Disclosure of information to more distant relatives may be problematic with information being communicated in a more selective manner and more reports of nondisclosure (Claes *et al.*, 2003; Sorenson, Jennings-Grant & Newman, 2003; Wilson *et al.*, 2004). Claes *et al.* (2003) found that one of the reasons for nondisclosure to distant relatives was that 40% of individuals with a conclusive genetic result assumed that other relatives would pass on the information. Other reasons for nondisclosure can include lack of contact, emotional distance and beliefs that the information wasn't important for certain individuals (Claes *et al.*, 2003; Forrest *et al.*, 2003; Peterson, 2005; Wilson *et al.*, 2004).

This study only investigated the perceptions of four nuclear families within Family X, although there were seven in total. The amount and quality of communication with other nuclear families is unknown and as snowball sampling was used, there is a potential bias that the participants in this study were closer to each other than to the individuals in the other families. It may have also been felt that information regarding ATR-X syndrome

was less important for those nuclear families that did not have an affected relative (families C and D), and information may not have been fully disclosed. However, this view is not necessarily true as nuclear family C would have originally been classified as a family without an affected relative although this is now being reassessed as P010's son may be affected with ATR-X syndrome. The knowledge scores of P007 and P011 support the possibility that distant relatives may have received less information, as they were amongst the lowest scores of the participants, however P010, also a distant relative, had one of the higher scores (Table 4.2). This may be influenced by the process P010 was going through with her son's investigations and the more recent explanations by doctors.

The finding that the majority of the participants in the current study were unaware of the availability of carrier testing , together with similar findings in the literature (Binedell, Soldan & Harper, 1998; Forrest *et al.*, 2003; Varekamp *et al.*, 1990), raise ethical questions surrounding the obligation of genetic services to inform at-risk individuals about testing that may be beneficial to them and their families (Binedell, Soldan & Harper, 1998). In view of this, participants were asked for their opinion regarding who should inform family members, who are unaware of their genetic risk, about this risk and carrier testing. They were asked if the responsibility lies with the family or the doctor. If participants indicated that it was the doctor's responsibility, they were asked if it was appropriate for a doctor to 'cold-call' a family member, without prior contact by a relative, to inform them that they may be at risk. Responses from the participants are presented in Table 4.10.

Table 4.10 Responses regarding responsibility to inform family members at risk.

P	Whose responsibility is it to inform the family about the risk of being a carrier?		
	Family/ Doctor	**Why?**	**If Doctor, would calling to discuss family history with individual who doesn't know be intrusive?**
001	Both	Important to come from both to get the message across. Family can be supportive.	Would not recommend. Face-to-face better
002	Doctor	"You can ask questions and you would be able to understand where it comes from better." "If it's a family member, you don't know whether they understood what was said and if they can give you a true reflection of what is going on."	For own children a joint session will be better as they ". . . know that if I trust the doctor then they can trust whatever information."
003	Both	"If the doctor knows then he has to tell the family and if the family knows, the family must tell."	"For me it will be ok, I don't know about the others."
004	Family	"It's their responsibility. So that they know that they need to ask certain questions when they go to visit the doctor, they need to be aware of the history."	
005	Family	"They are the ones going through the experience of it."	
006	Family	"Because all doctors don't know, like, if my granny goes into hospital they won't immediately know she's a carrier because I mean they won't look for something like that."	
007	Family	"The family knows more about the family, look the doctors know about the condition in the family, but it will maybe better if the family tells because it's not from a stranger, it's from in the family."	
008	Family	"It's the family's responsibility because the doctor has already explained to them so they must distribute it further"	
009	Doctor	"The doctor will explain more to you, what it's about and where it's from, so you will have more understanding that it's possible to be a carrier; but the family will not explain it like that."	"The family can maybe say, but who says that that family member will really take it in."
010	Doctor	"They know more."	"It will be a bit strange. In that situation the family must tell."
011	Doctor	"The doctors can do tests and they can say there's a chance that there could be more in the family."	"The doctors must first do tests before they can say there's a chance in the family."

As can be seen in Table 4.10 above, there were mixed opinions, with five participants indicating it was the family's responsibility to inform individuals, four indicating it was the doctor's responsibility and two indicating that it was a shared responsibility. Of the six participants who were probed further about the doctor contacting an individual directly, half were uncomfortable with this.

There were many reasons given by the participants who indicated that the family should inform individuals, with P005 emphasising that the family knows what it's like and can pass on their knowledge and experiences:

"I think it has to come from the aunties, they must tell the younger generation, they must explain to the younger generation. It's not the responsibility of the doctors because they just did the study of it, but they are the ones going through the experience of it, so they must bring down their experience to the younger generation so they can know what is ahead for them, especially like their emotions, what they think about, what they went through." P007 said that it was better coming from the family than a stranger and said: *"That's why it's better that the family knows more about the disease so that you can explain more to that person, why there will be a chance that her child could be affected."*

Those participants who indicated that the doctor should inform the family mostly gave the reason that the doctor would know more than the family, implying that the doctors are the authority on the matter and thus disempowering themselves. Trust issues relating to communication within the family also seemed to be underlying reasons for P002 and P009.

Although the majority of the participants indicated that the family should take the responsibility for informing relatives of their risk of being a carrier, there were still mixed views. This is in contrast to McConkie-Rosell *et al.* (1997) who showed that all of the individuals in their study felt that an individual should be told about their risk of

being a FXS carrier by a family member first, with further follow-up by a genetic counsellor or doctor. Forrest *et al.* (2003) also showed that the majority of the participants with a family history of Huntington's disease felt that the responsibility to inform relatives lay with the family and not health professionals. However, this was not as clear cut with regards to participants in the above study with a family history of hereditary cancer, which is similar to the findings in the current study.

From the data in Table 4.10, it was clear that some family members felt that joint information giving with a health professional was important and this is supported by the literature (Forrest *et al.*, 2003; Wilson *et al.*, 2004). Support from health professionals in terms of facilitating and assisting with successful communication regarding genetic risk between parents and their child has been recommended (Forrest *et al.*, 2003; Wilson *et al.*, 2004). This may be particularly important for members of extended Family X, where is has been shown that communication regarding genetic risk and testing is poor.

4.8 FAMILY RESPONSE

As a direct result of the research and interviews with participants, several participants showed an interest in having carrier testing. Four individuals made appointments to see the genetic counsellor, one wanted testing, but was waiting to see what her mother's carrier result would be, and three others were awaiting appointments at another tertiary facility due to their place of residence and catchment area for the different tertiary hospitals. P010 was also able to inform the doctors investigating her son for developmental delay about the family history and that testing was available if they felt it was appropriate.

The reason for this sudden interest in testing is not certain. It could be due to increased knowledge about the condition and testing availability (information was provided to participants after their interviews), or the researcher could have served as a reminder for participants. Alternatively, participants may have felt pressured to come for genetic testing as a result of the research.

At the time of writing this dissertation, two participants had received carrier results and two others were unable to make their appointments. They had not yet phoned the genetic services to reschedule. Of the three participants referred to another tertiary facility, one had changed her mind about carrier testing and the other two were still awaiting appointments. As participants had missed appointments and failed to contact the genetic services, there is a concern that the previous lack of uptake of carrier testing may be about to repeat itself.

The main findings in this chapter are presented in Chapter Five.

CHAPTER 5:

CONCLUSIONS

5.1 CONCLUSIONS

The aim of the current study was to investigate the reasons why females in Family X had not presented for carrier testing. In order to achieve this aim, various aspects were assessed, namely investigating the level of genetic knowledge of females who have a relative with ATR-X syndrome, determining the impact of ATR-X syndrome on the family and individuals, investigating current opinions about genetic testing and investigating the communication networks of sharing and transmission of information in Family X

The level of knowledge varied among the participants. None of the participants knew the name of the condition in the family. However, the average level of knowledge, as judged by the responses to the interview schedule utilised in the present study, for the participants was 59% in total. The majority of the participants knew that ATR-X syndrome is inherited or in the family, and they knew that they were at risk of being a carrier. Despite this possibility being known, the fact that no one in the current generation had an affected son may have affected their perception of risk, as many participants spoke about the condition 'skipping a generation'. Higher levels of genetic knowledge seemed to be associated with a higher income level and greater degree of involvement or engagement with the family and genetic services. A good understanding of information is important, as it is required for effective risk communication, dissemination of information and decision making in families.

Certain participants expressed disappointment with the previous genetic research performed, as they had a misperception that they would be informed of their carrier status with that research. This finding highlights the importance of improving informed consent procedures and ensuring that participants have understood the information fully and/or do not have unrealistic expectations. In addition, although results are not

generally delivered through research, if the results of the research are to be disseminated to the family, it should be done in a concrete manner, such as a letter with the outcomes of the research and contact details for further information.

An individual's personal experiences regarding a genetic condition in a family may directly affect their decision to undergo carrier testing. The majority of the participants commented that they had not experienced a negative impact as a result of having male relatives affected with ATR-X syndrome, and that they viewed their affected relatives in a positive light. Themes of normality and acceptance were closely tied to religious convictions and this may tie directly to the participants trying to find meaning in the situation. The participants viewed their relatives' disabilities as personal characteristics rather than abnormalities, which fits with the social model of disability. Negative responses from the community were frequently reported; however, the participants did not feel that this had a negative impact on them. Only one participant indicated that having an affected relative affected her reproductive choices; she reported that she felt too afraid to get married due to her fears that she would have a son with ATR-X syndrome.

More than half of the participants were unaware that carrier testing was available and the majority wanted to know their carrier status. The reasons that participants did not present for testing previously were mostly related to being unaware of the testing, or not knowing who to contact. Other reasons included issues of time, socio-economic reasons, low perception of risk, expectation that the previous research would provide the information and a lack of concern about the condition. The desire for carrier testing was mostly related to wanting to have the knowledge in order to be prepared, or for future generations, rather than for the option of having prenatal testing. In addition, the decision to use prenatal diagnosis was varied amongst participants and was not related to the intention to terminate an affected foetus as all the participants, except one, stated that they definitely would not terminate a pregnancy. This was related to religious convictions.

Many participants described attempting to inform primary health care professionals during pregnancy about their family history; however, most participants were inappropriately reassured or doctors assumed they were referring to other problems. This finding highlights the lack of awareness, and possibly knowledge, of the possible genetic contribution to disease at the primary health care level and has implications, not only for the family concerned, but also for other families with genetic conditions.

There was a lack of dissemination of genetic information within the family. With the exception of two participants, the majority of the participants indicated that ATR-X syndrome was not discussed. Linked to this, the majority also felt that they did not have enough knowledge to explain the condition to others. Other barriers to communication about the condition mentioned were feelings of guilt, lack of contact with more distant relatives and underlying family tensions that dictated communication patterns between certain individuals within the family. The task of disseminating information also seemed to fall on one individual, which is not ideal in a large extended family. In addition, that particular individual no longer wanted to fill that role, which has implications for future generations.

Participants also displayed mixed views regarding who should be responsible for disseminating information in the family, namely the family itself or the doctor. These results indicate that there is a need for genetic counsellors and doctors to help facilitate dissemination within families, especially in the case of research, and to develop tools, such as a summary letter, that may help individuals inform their family of the genetic risks and options available.

Although the small sample size would limit the ability of this research to generalise to other conditions or populations, it does provide valuable insight into issues that are present in families who have an intellectually disabled family member. Communication within families is important, as it can aid in acceptance and coping, decrease anxiety, as

well as inform relatives of the risks related to the inheritance and testing and other options available. Health care professionals should help facilitate the communication process in families.

A genetic counsellor could play an important role in the research process, if and when research results are delivered. They can help participants to understand more about the research implications and options available. Questions could be accurately answered, misunderstandings corrected, and communication within the family facilitated. Genetic counsellors also provide support for individuals and help to discuss the implications of each decision or scenario at different stages. All of these factors mentioned can aid in fully informed decision-making regarding carrier testing.

CHAPTER 6:

RECOMMENDATIONS

6.1 RECOMMENDATIONS

Based on the outcomes of the study, the following recommendations are made:

- When performing research with families, better information should be provided regarding an explanation of the research, the objectives and outcomes. This will ensure informed consent is given and avoid inaccurate or unrealistic expectations of the research. This may include obtaining assent for research with minors (if possible) or re-informing family members of the research when they reach an age where they are able to assent or give consent. A letter informing the family of the purpose of the research, expectations and contact details should be provided to every participant.
- Research outcomes, contact details, and the option of genetic counselling to explain the findings should be provided to every participant, where possible, when the research is complete.
- Researchers should consider involving a genetic counsellor in the research process to ensure that the family members understand more information about the condition in the family and how it may or may not affect them.
- Once the results are delivered, attention should be given to discussing the dissemination of general and risk information to other relatives within a family, together with strategies to improve this.
- A simple fact sheet explaining the condition, its inheritance, the availability of carrier testing and further reproductive options should be given to members of Family X to aid in their understanding This may also help to facilitate dissemination of information to other family members who are unaware of the condition, or who reach child-bearing age. Such a letter could also be used to give to primary care health professionals, and should provide the nearest genetic centres contact details if they require further information.

- If genetic counselling is provided, counsellors should either assist family members in sharing information with estranged relatives to facilitate dissemination of information, or contact the estranged relatives directly themselves, if consent was given by those relatives originally.
- Education of health professionals, especially those at the level of primary care, about genetics may aid in the recognition of inherited or genetic conditions and provide information about the required follow-up. Furthermore, all primary level facilities should be provided with information on the basic referral pathway for genetic services.
- Encouraging individuals to explore carrier testing should not only focus on its application to prenatal testing and TOP, but should encompass a holistic view of the implications for the individual and future generations. It should also be emphasised that genetic counsellors are available to provide support for individuals who may be anxious about their risks and that they are not only concerned with testing.

6.2 FUTURE RESEARCH

It will be of great value to:

- Explore the experiences of obligate carriers within this family and to determine how having affected sons may have had an impact on them.
- Conduct a similar study with individuals who have a family history of a similar condition, such as FXS, due to the overlap of the condition, inheritance, and uptake of carrier testing with the current study, in order to increase the size of the sample.
- Investigate the experiences and attitudes to testing amongst individuals who have any X-linked inherited condition in their family, compared to another mode of

inheritance, to determine issues related specifically to the inheritance pattern, such as guilt due to inheritance through the maternal line.

- Include participants from the entire country, for FXS specifically and X-linked conditions in general, in order to explore the experiences of individuals from other ethnic groups and geographical areas, to aid in generalisability and determine if there are any issues specific to SA.

- In the case of a new diagnosis of FXS, ATR-X syndrome or other X-linked disorders, evaluate the impact of genetic counselling through the use of pre- and post-genetic counselling evaluations.

- Investigate the level of knowledge of genetic related issues amongst non-genetic health care professionals to determine the need for increased education and advocacy.

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APPENDIX I: INTERVIEW SCHEDULE OUTLINE

Participant No:……..…

Recording No:…….

A. SOCIODEMOGRAPHIC INFORMATION

1. Family history

    - Date of birth
    - Marital status (Single/Married/Divorced/Widowed)
    - How many children?
    - Ages of children
    - Any affected children?
    - Do you have brothers and sisters? Are they well? Do they have their own children?

2. What grade did you complete at school?

    - ☐ Grade 12 (matric, std 10)
    - ☐ Grade 11
    - ☐ Grade 10
    - ☐ Grade 9
    - ☐ Grade 8
    - ☐ Grade 7
    - ☐ Other
    - ☐ None

3. Have you started/completed any further courses/training since leaving school?

    - ☐ Yes
    - ☐ No

4. If Yes to question 3, what **and** how many years have you completed?

    - Certificate from college
    - Trade
    - Diploma (beyond Grade 12)
    - Bachelors degree
    - Postgraduate diploma/degree
    - Other

5. Are you currently employed?

    - Yes
        - Permanent (Full-time/part-time)
        - Casual
    - No

6. If Yes to question 5, what kind of work?

7. If No to question 5, reasons for unemployment?

    - Unemployed
    - Housewife
    - Full-time or part-time student
    - Permanently unable to work
    - Retired or pensioner
    - Casual
    - Other

8. How many individuals contribute to the family income?

9. What is the current household income per month?

- ☐ Disability, child support or old age grant
- ☐ Salary income (specify the amount/month)
  - R1-R200
  - R201-R500
  - R501-R1000
  - R1001-R1500
  - R1501-R2500
  - R2501-R3500
  - R3501-R4500
  - R4501-R6000
  - R6001-R8000
  - R8001-R11000
  - R11001-R16000
  - R16000-R30000
  - R30001 or more
  - Unspecified
- ☐ Irregular-casual worker

10. How many people does this income support?

11. Do you have your own form of transport?

- ☐ Yes
- ☐ No

12. If no to question 11, what form of public transport do you use?

- ☐ Lift-club
- ☐ Bus
- ☐ Train

- Minibus Taxi
- Taxi

B. LEVEL OF UNDERSTANDING OF GENETICS

13. What do you understand the cause of ATR-X syndrome to be?

14. How do you get the syndrome?

    - Is it passed on/family disease?
    - Is it something that just happens?

15. How is ATR-X syndrome passed on?

16. Does ATR-X syndrome affect both males and females?

17. What do you understand by the term "carrier"?

    - Are carriers affected of not?

18. What are your chances of being a carrier?

19. What are your chances of having a child with ATR-X syndrome?

20. What are the chances of your unaffected children being carriers?

21. What are the source/sources of your information regarding the inheritance of ATR-X syndrome?

    - Family members
    - Internet
    - Genetic doctors or nurses
    - Other (please specify)

C. IMPACT AND EXPERIENCES OF HAVING FAMILY MEMBERS AFFECTED WITH ATR-X SYNDROME

22. What has been your personal experience with ATR-X syndrome?

    - Living/lived with affected brother
    - Cared for/assisted with caring for a brother/relative
    - Affected relative with whom had contact
    - No contact with affected relative

23. How did/does this affect you (and your family)?

    - Schooling
    - Youth/childhood
    - Lifestyle
    - Early into work market

24. How did/do you feel when in contact with an affected family member?

    - Sad, embarrassed, worried, happy, angry

25. Have your personal experiences with affected family members influenced your reproductive choices?

26. If yes to question 25, how and why?

27. How would you feel about having a child with ATR-X syndrome?

    - Worried, sad, fine, helpless
    - Do you think you'd be able to look after a child with ATR-X syndrome?

28. Do you have support from your family?

    - Who supports you?
    - What do they support with?
    - Psychological support?
    - Amount of contact with family?
        - Frequently
        - Rites of passage

29. What has the community's reaction been to affected family member?

    - Embarrassment, support, judgement,

D. CURRENT OPINIONS REGARDING GENETIC TESTING

30. What is your understanding of the availability of carrier-testing?

31. Would you want to know if you are a carrier? (Reasons for answer)

32. Would you like to undergo carrier testing? (Reasons for answer)

33. Why have you not been for carrier testing yet?

34. Would you consider testing a pregnancy for an affected foetus?

35. If yes to question 34, would you consider terminating an affected foetus? (Reasons for answer)

E. COMMUNICATION WITHIN THE FAMILY

36. How was information regarding your affected relative shared/explained to you?
    - What did they say?

37. Who shared/explained this information with you?

38. Have you shared this information with other immediate or extended family members?

39. If yes to question 38, how did you explain it to them?

40. If no to question 38, why did you not share this information?

41. What do your children understand about the condition?

42. Has the genetics of the condition been discussed in the family?

43. Have you mentioned carrier testing to any immediate or extended family members?

44. If yes to question 42, what did you tell them about it?

45. Is there someone specific in the family who takes primary responsibility for informing other family members about things, specifically regarding ATR-X syndrome in your family?

46. Do you feel confident that you have enough information about the genetic aspect of ATR-X syndrome to explain it to other family members/people?

47. Would you like more information about the genetics of ATR-X syndrome?

48. In your opinion, is it your responsibility or that of the health care professionals to inform your relatives of the potential genetic risk?

    - Family
    - Doctor

49. If answered Doctor in question 48, why do you feel that way?

ONDERHOUD SKEDULE OORSIG: AFRIKAANS VERSION

Deelnemer No:……..…

Rekording No:……..

A. SOSIODEMOGRAFIESE INLIGTING

1. Familie Geskiedenis

    - Geboortedatum
    - Huwelikstatus (getroud?)
    - Hoeveel kinders
    - Ouderdom van kinders
    - Enige kinders wat met ATR-X sindroom geaffekteer is?
    - Het u broers of sisters? Is hulle gesond? Het hulle kinders?

2. Wat was die laaste graad/standerd wat jy op skool voltooi het?

    - Graad 12 (matriek, st10)
    - Graad 11
    - Graad 10
    - Graad 9
    - Graad 8
    - Graad 7
    - Ander
    - Geen

3. Is daar enige ander kursus of opleiding wat jy begin of volooi het nadat jy skool verlaat het?

    - Ja
    - Nee

4. As jy Ja vir vraag 3 beantwoord het, wat het jy gedoen **en** hoeveel jare het jy voltooi?

    - Sertifikaat van Kollege
    - Ambag (Trade)
    - Diploma (na Graad 12)
    - Bacculureurs Graad
    - Nagraadse opleiding of diploma/graad
    - Ander

5. Is u tans in diens? (Werk u op die oomblik?)

    - Ja
        - Permanent (Voltyds/deeltyds)
        - Tydelik
    - Nee

6. As jy Ja vir vraag 5 beantwoord het, watter soort werk doen jy?

7. As jy Nee vir Vraag 5 beantwoord het, wat is die rede vir u werkloosheid?

    - Werkloos
    - Huisvrou
    - Voltydse/deeltydse student
    - Ongeskik vir werk
    - Afgetree of pensioentrekker
    - Tydelik
    - Ander

8. Hoeveel mense dra by tot die familie se inkomste?

9. Wat is die huidige huislike inkomste per maand?

- Disability, child support of old age toelaag (grant)
- Salaris inkomste (per maand)
  - R1-R200
  - R201-R500
  - R501-R1000
  - R1001-R1500
  - R1501-R2500
  - R2501-R3500
  - R3501-R4500
  - R4501-R6000
  - R6001-R8000
  - R8001-R11000
  - R11001-R16000
  - R16000-R30000
  - R30001 of meer
  - ongespesifiseerd
- Onreëlmatige inkomste (tydelike werk)

10. Hoeveel mense word met hierdie inkomste ondersteun?

11. Het jy jou eie vervoer?

- Ja
- Nee

12. As jy Nee beantwoord het vir vraag 11, watter vorm van publieke vervoer gebruik u?

- Ry saam met ander mense
- Bus

- Trein
- Minibus Taxi
- Taxi

B. VLAK VAN BEGRIP VAN GENETIKA

13. Wat verstaan jy is die oorsaak van ATR-X sindroom?

14. Hoe kry ‘n mens die sindroom?

    - Is dit in die familie oordra? Familie siekte?
    - Is dit iets wat net gebeur uit die bloute?

15. Hoe word hierdie sindroom oorgedra in die familie?

16. Affekteer hierdie sindroom beide mans en vrouens?

17. Wat verstaan jy van die begrip “draer”?

    - Is draers affekteer met dit of nie?

18. Wat is jou kanse om ‘n draer te wees?

19. Wat is jou kanse om ‘n kind met ATR-X sindroom te hê?

20. Wat is die kanse dat jou ongeaffekteerde kinders draers is van die sindroom?

21. Watter bronne van inligting gebruik jy met betrekking tot die oorerflikheid van ATR-X sindroom?

    - Familielede
    - Internet
    - Genetiese dokters of verpleegkundiges
    - Ander (Spesifiseer asb)

C. IMPAK EN ERVARINGE VAN FAMILIELEDE WAT GEAFFEKTEER IS MET ATR-X SYNDROME

22. Wat is jou persoonlike ervaring van ATR-X sindroom?

    - Bly/ het gebly met ‘n geaffekteerde broer
    - Sorg/bygestaan met versorging vir ‘n broer/familielid
    - Kontak met ‘n familielid wat geaffekteer is
    - Geen kontak met geaffekteerde familielid

23. Hoe het/nog steeds dit jou (en jou familie) geaffekteer?

    - Skooljare
    - Kinderjare/Jeug
    - Leefwyse
    - Vroeg begin in die werk omgewing

24. Hoe het jy/voel jy wanneer jy in kontak is met ‘n geaffekteerde familielid?

    - Hartseer, skaam, bekommerd, gelukkig, kwaad

25. Het jou persoonlike ervaringe met geaffekteered gesinslede jou keuse oor reproduktiewe besluite beinvloed?

26. As jy Ja geantwoord het vir vraag 25, hoe en hoekom?

27. Hoe sal jy voel om ‘n kind met ATR-X sindroom te hê?

    - Bekommerd, hartseer, geen probleem, hulpeloos
    - Dink jy dat dit sal moointlik wees vir jou om na ‘n kind met ATRX-sindroom te kyk?

28. Kry jy ondersteuning van jou familie?

    - Wie ondersteun jou?
    - Waarmee ondersteun hulle?
    - Sielkundige ondersteuning?
    - Hoeveelheid kontak met familie?
        - Gereeld
        - deurgangsrites

29. Hoe is die reaksie van die gemeenskap teenoor die geaffekteerde familielid?

    - Skaam, ondersteunend, oordeel.

D. HUIDELIKE MENINGS MET BETREKKING TOT GENETIESE TOETSING

30. Wat verstaan jy van die beskikbaarheid van draer toetsing?

31. Sou jy wou weet of jy ‘n draer is van ATR-X sindroom? (Redes vir antwoord)

32. Sou jy bereid wees om getoets te word of jy ‘n draer is? (Redes vir antwoord)

33. Hoekom was jy nie alreeds vir draer toetsing nie?

34. Sou jy dit oorweeg om ‘n swangerskap te laat toets vir ‘n geaffekteerde foetus?

35. As jy Ja geantwoord het vir vraag 34, sou jy dit oorweeg om die swangerskap van ‘n geaffekteerde foetus te beëindig? (Redes vir antwoord)

E. KOMMUNIKASIE BINNE DIE FAMILIE

36. Hoe was inligting met betrekking tot jou geaffekteerde familielid gedeel/verduidelik aan jou?
    - Wat het hulle gesê?

37. Wie het hierdie inligting met jou gedeel/verduidelik?

38. Het jy al hierdie inligting met direkte of uitgebreide familielede gedeel?

39. As jy Ja beantwoord het vir vraag 38, hoe het jy dit aan hulle verduidelik?

40. As jy Nee beantwoord het vir vraag 38, hoekom het jy nie hierdie inligting gedeel nie?

41. Wat verstaan jou kinders van hierdie sindroom?

42. Is die genetika van hierdie sindroom al bespreek met die familie?

43. Het jy al draer toetsing aan enige direkte of uitgebreide familie genoem?

44. As jy Ja beantwoord het vir vraag 42, wat het jy aan hulle gesê?

45. Is daar enige iemand in die gesin wat die verantwoordelikheid geneem het om ander familie lede in te lig oor die sindroom?

46. Voel jy jy het genoeg inligting oor die genetiese aspek van die sindroom om met vertroue dit aan ander gesinslede te kan verduidelik?

47. Sou jy meer inligting oor die genetiese aspek van ATR-X sindroom wou hê?

48. In jou opinie, is dit jou verantwoordelikheid of die van die dokter, om jou familielede in te lig van die potensiale genetiese risikos?
    - Familie
    - Dokter

49. As jy Dokter beantwoord het vir vraag 48, hoekom voel jy so?

APPENDIX II: INFORMED CONSENT AND INFORMATION FORM

MSc in Genetic counselling Research Project

An investigation into the reasons for non-uptake of carrier testing in a family affected by Alpha thalassaemia X-linked mental retardation (ATR-X) syndrome

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

STATEMENT BY PARTICIPANT

I, ……..…, living at (address)

……

confirm that:

1. I have been invited to participate in the above research project which has been initiated through the Division of Human Genetics, University of Cape Town because I have a family history of ATR-X syndrome and I am at risk for being a carrier.

2.1. I understand that the objective of this study is to investigate:

- The level of knowledge of inheritance of ATR-X syndrome in the family;
- The impact of having a family member affected with ATR-X syndrome, and their experiences concerning this;
- How information concerning this condition is shared among the family;

- Socioeconomic reasons that have made it difficult to go for carrier testing; and
- Whether individuals are aware of available carrier testing and their views concerning this.

2.2. I understand that the interview will take place in my home or another venue of my choice and that it may take one or two visits of two hours each.

2.3. I am aware that this is a once-off procedure that will be implemented in 2010 at a time convenient to me and my family.

2.4. I understand that some of the questions may make me angry or sad, but the risks to me from the study are minimal. The researcher will refer me to a genetic counsellor if necessary. She will show me respect, acceptance and empathy during the interview.

3.1. I have been assured that all information will be handled confidentially. Information may be used for a thesis, publications in scientific journals and presentations at professional congresses, but names will not be included.

3.2. I understand that the interview will be tape recorded so that the researcher does not have to write too much during the interview. The tape will be secured in a safe until the research has been written up and will then be destroyed immediately. The data stored on the computer will have a numerical code only and my name does not appear anywhere.

4. I have been assured that the recorded and transcribed information discussed at the meeting will only be made available to the researchers supervisors with my study code number and that they do not know that it refers to my name.

5. I willingly agree to consent in taking part in the study and I have been informed that I may refuse to participate in this project and that I may stop participating at any stage, and that such refusal or stoppage will not in any way negatively affect my future access to medical and genetic services to which I am entitled.

6. ……. has explained the information of the study to me in English/Afrikaans. I am proficient in that language and my questions have been answered satisfactorily.

7. I understand that there will be no medical benefits to me from this study.

8. I have been assured that participation in this project will not lead to additional costs for me or my family and I will not benefit from it financially.

I HEREBY DECLARE THAT I HAVE VOLUNTARILY AGREED TO PARTICIPATE IN THE ABOVE RESEARCH STUDY

Signed at:

(address)…… on……..2010

……. …….……

Participant's signature Witness

I HEREBY DECLARE THAT I AGREE TO HAVE MY INTERVIEW AUDIOTAPE RECORDED

Signed at:

(address)……..…… on……..2010

…… …….……

Participant's signature Witness

IMPORTANT INFORMATION

Dear Participant

Thanks you for your participation in this study. Should you have any questions during the duration of this study regarding:

1. problems as a result of the research, or
2. questions regarding information about the project

Please contact me or Prof. Greenberg at the following telephone number:

Nakita Verkijk: (021) 406-6373
Email: nakita.verkijk@uct.ac.za

Prof Jacquie Greenberg: (021) 406-6299

If you have any questions about your rights as a research participant please contact Dr M Blockman, Chair of the Research Ethics Committee, Faculty of Health Sciences, University of Cape Town Ethics Review Committee on (021) 406-6496.

AFRIKAANS VERSION OF THE INFORMATION AND CONSENT FORM

MSc in Genetiese Berading Navorsingsprojek

‘n Ondersoek na die redes waarom ‘n familie wat geaffekteer is met Alpha thalassaemia X-linked mental retardation (ATR-X) sindroom nie draer toetsing opneem nie.

INLIGTING EN TOESTEMMING VORM

VERKLARING DEUR DEELNEMER

Ek, ……..…, wat woon by (adres)

……

bevestig dat:

1. Ek uitgenooi is om aan die boegenoemde navorsings projek wat deur die Divisie van Mensgenetika, Universiteit van Kaapstad geinisieer is, deel te neem aangesien ek ‘n familie geskiedenis van ATR-X sindroom het en ek ‘n risiko het om ‘n draer to wees.

2.1. Ek verstaan dat die doel van hierdie projek is om die volgende te ondersoek:

- Die vlak van kennis oor die oorerflikheid van ATR-X sindroom in die familie;
- Die impak wat die familie lid met ATR-X sindroom op die familie gehad het en hoe hulle dit ervaar het;
- Hoe die informasie oor hierdie kondisie gedeel en oorgedra word in die familie;
- Sosioekonomiese redes wat dit moeilik maak om vir genetiese draer toetsing te gaan;

- Of individue kennis dra van die beskikbare draer toetse en wat hulle siening hieroor is.

2.2. Ek verstaan dat die onderhoud of by my huis of by ‘n ander plek van my keuse sal plassvind en dat dit een of twee besoeke van twee ure elk behels.

2.3. Ek is bewus dat dit ‘n eenmalige ondersoek is wat in 2010 sal plaasvind op ‘n tyd wat vir my en my gesin gerieflik is.

2.4. Ek verstaan dat van die vra my hartseer of gelukkig mag maak, maar dat die risiko’s van die studie minimal is. Die narvorser sal my na a genetiese raadgewer verwys indien nodig. Sy sal my met respek, aanvaarding en empatie behandle geduurende die onderhoud.

3.1. Ek is verseker dat alle inligting vertroulink behandel sal word. Inligting mag vir ‘n tesis, publikasies in wetenskaplike tydskrifte en aanbiedings by professionele kongresse gebruik word, maar name sal nie ingesluit word nie.

3.2. Ek verstaan dat die onderhoud op band opgeneem sal word sodat die narvorser nie te veel hoef te skryf geduurende die onderhoud nie. Die band sal ‘n kluis gestoor word tot dat die narvorsing opgeskryf is en sal daarna dadelik vernietig word. Die band en die data op die rekenaar sal slegs ‘n numeriese kode op he en my naam sal nie daarop verskyn nie.

4. Ek is verseker dat die inligting wat opgeneem en getranskribeer is slegs aan die narvorser se mentor bekend gemaak sal word, maar dit sal slegs my numeriese studie kode bevat en my naam sal nie daarop verskyn nie.

5. Ek is nie oorreed om aan die projek te neem nie en ek is bewus dat ek mag weier om deel te neem, en ek kan op enige stadium besluit om te onttrek. My ontrekking sal op geen manier my huidige of toekomstige toegang tot die mediese of genetiese dienste, waarop ek geregtig, is beinvloed nie.

6. ……. het die inligting van die projek in Engels/Afrikaans aan my verduidelik. Ek is volt in hierdie taal en my vra is ten volle beantwoord.

7. Ek verstaan dat daar geen mediese voordele vir my sal wees as gevolg van hierdie projek nie.

8. Ek is verseker dal my deelname aan hierdie projek nie tot enige additionele koste vir my familie sal lei nie en dat ek nie finansieel gaan baat daarby nie.

EK VERKLAAR HIERMEE DAT EK VRYWILLIG AAN DIE BOGENOEMDE NARVORSINGS PROJEK DEELNEEM

Geteken te:

(adres)…… op……..2010

…… ……..……

Deelneemer se handtekening Getuie

EK VERKLAAR HIERMEE DAT EK MY ONDERHOUD OP BAND OPGENEEM MAG WORD

Geteken te:

(adres)…… op……..2010

…… ……..……

Deelneemer se handtekening Getuie

BELANGRIKE INLIGTING

Geagte deelnemer,

Baie dankie vir u deelname aan hierdie studie. As U gedurende die verloop van die navorsing enige vra het aangaande:

1. probleme as gevolg van die narvorsing, of
2. vrae aangaande inligting oor die projek

kontak my of Prof. Greenberg gerus op die volgende telefoon nommers:

Nakita Verkijk: (021) 406-6373
Email: nakita.verkijk@uct.ac.za

Prof Jacquie Greenberg: (021) 406-6299

As u enige vrae het in verband met u reg as ‘n deelnemer, kontak Dr M Blockman, die Voorsitter van die Etiese Hersiening Komitee van die Universiteit van Kaapstad by (021) 406-6496.

APPENDIX III: ETHICS APPROVAL DOCUMENTATION

UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6626 • **Facsimile** [021] 406 6411
e-mail: shuretta.thomas@uct.ac.za

22 June 2010

HREC REF: 291/2010

Ms N Verkijk
c/o Dr M Futter
Human Genetics
CLS

Dear Ms Verkijk

PROJECT TITLE: AN INVESTIGATION INTO THE REASONS FOR NON-UPTAKE OF CARRIER TESTING IN A FAMILY AFFECTED BY ALPHA THALASSAEMIA X-LINKED MENTAL RETARDATION (ATR-X) SYNDROME.

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above mentioned study.

Approval is granted for one year till the 30th June 2011.

Please submit an annual progress report if the research continues beyond the expiry date. Please submit a brief summary of findings if you complete the study within the approval period so that we can close our file.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS
Federal Wide Assurance Number: FWA00001637.

S Thomas