AT-RISK INDIVIDUAL'S PERSPECTIVES OF SPINOCEREBELLAR ATAXIA (SCA) PRESYMPTOMATIC TESTING (PT)

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DECLARATION

I, *Deanah Lloyd*, hereby declare that the work on which this dissertation is based' is my own original work (except where acknowledged otherwise) and that neither the complete work nor any part of it has been, currently is, or will be submitted for another degree, at this or any other university.

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ABSTRACT

Since the introduction of presymptomatic testing for Spinocerebellar Ataxia in South Africa, no research has looked at the impact, perceptions or acceptance of such testing within this diverse population. Despite the relatively high frequencies of late onset autosomal dominant conditions in South Africa, the uptake of presymptomatic testing by those at-risk of inheriting these conditions has been lower than that seen internationally. This research project sought to understand these low levels of utilisation, by exploring the perceptions of those at-risk of inheriting Spinocerebellar Ataxia towards presymptomatic testing.

In depth semi-structured interviews were conducted with six individuals at-risk of inheriting Spinocerebellar Ataxia. The interviews were transcribed verbatim and thematically analysed. The four themes that emerged from the data included: 1) Caregiving, 2) Relationships, 3) Being At-Risk and 4) Presymptomatic Testing (PT) Perceptions. These themes explore the significant and long-lasting burdens faced both physically and emotionally by the affected individual as well as their relatives. With no currently available way of preventing or curing the condition, those at-risk described being left with a sense of hopelessness and anxiety about their future. The at-risk individuals' perceptions and fears were often linked to their and their family's experiences of the condition. Additionally, their perceptions of presymptomatic testing, although positive, did not correlate with testing utilisation amongst the participants.

As such, the current underutilisation of presymptomatic testing in South Africa was found to be due to the at-risk individuals' fears of the result and its' perceived consequences, rather than a negative perception of presymptomatic testing. This is significant as it indicates that the current lack of uptake of presymptomatic testing is due to external factors unrelated to the test itself. As such, genetic counsellors should focus their efforts on counselling the individual through their fears as opposed to primarily offering presymptomatic testing. Although these findings contribute to our understanding of this previous understudied population, they cannot be extrapolated to apply to the entire South African at-risk population due to the small sample size of the study. This knowledge however, may assist in improving the presymptomatic testing process by providing greater insight into the population's experiences and perspectives. Thus, it is recommended that future studies explore ways that genetic counselling sessions and the presymptomatic testing process could be altered to incorporate this knowledge.

DEDICATION

To my family,

Those who have supported me along the way

&

those who inspired it but will never get to read it

I hope this makes you proud!

∞

Especially my Parents,

To my mother,

Jackie Lloyd

Who's always been my biggest supporter!

We finally did it!

&

To my late father,

Dean Lloyd

Who always encouraged me to aim for the stars,

I'm sorry you didn't get to see me try

This one's for you!

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List of Terms and Abbreviations

CBD – Cannabidiol

CGPP – Centre for Predictive and Preventive Genetics

ClinG – Clinical Geneticist

DHG - Division of Human Genetics

F/U – Follow up

GC – Genetic Counselling

GCs – Genetic Counsellors

GSH – Groote Schuur Hospital

HCPA – Hospital de Clinicas de Porto Alegre

HD – Huntington Disease

MPTP – Montreal Predictive Testing Program

Neuro – Neurologist

NSGCs - National Society of Genetic Counsellors

PD – Parkinson's disease

Pdoc – Psychiatrist

Physio - Physiotherapist

Psych – Psychologist

PolyQ - Polyglutamine

PT – Presymptomatic testing/ Predictive Testing

SA – South Africa/ Southern Africa/South African

SCA – Spinocerebellar Ataxia

UCT – University of Cape Town

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Chapter 1: Literature Review, Rational, Aims and Objectives

1.1 INTRODUCTION

This chapter describes and critically analyses the available literature relevant to this study, highlighting some limitations and gaps in the current literature. Concluded with the aims, objective and rationale for this study.

A significant gap was identified in the literature with regard to presymptomatic testing (PT) for Spinocerebellar Ataxia (SCA). Where the impact, acceptance and perceptions of PT amongst individuals at-risk for Huntington's Disease (HD) has been widely studied, with less attention being given to the other neurodegenerative conditions such as the SCAs (Rodrigues *et al.*, 2012). As such, relevant research on HD was incorporated due to the similarities between SCA and HD in terms of their aetiology, inheritance and symptoms.

The literature referenced in this study was obtained using several research databases including Google Scholar, Medline, Psychinfo, PubMed, Sabinet African Journals and ScienceDirect. Several variations and permutations of the following phrases were searched: Presymptomatic Testing/Predictive Testing, South Africa, Spinocerebellar Ataxia, Huntington Disease, Genetic Counselling, Perceptions/Perspectives of Presymptomatic testing.

The literature is presented under the following headings:

- Spinocerebellar Ataxia (SCA)
- Being at-risk
- Role of Genetic Counselling (GC)
- Presymptomatic Testing (PT)

1.2 SPINOCERECELLAR ATAXIA (SCA)

The SCAs are a group of more than 40 genetically different ataxia subtypes, characterised by the progressive incoordination of movements caused by the atrophy of the cerebellum (Klockgether, Mariotti and Paulson, 2019; Diallo *et al.*, 2020). These conditions are often split into two subgroups according to their genetic causes, these are non-repeat mutations and repeat expansion SCAs (Afonso-Reis *et al*., 2021). The repeat expansion SCAs are further categorised by those caused by abnormal CAG trinucleotide repeat expansions and those caused by other nucleotide repeats (SCA8, SCA10, SCA31, SCA36 and SCA37) (Afonso-Reis *et al*., 2021). The most common SCAs are caused by an abnormal CAG trinucleotide expansion and are inherited in an autosomal dominant manner (Afonso-Reis *et al*., 2021). These types of SCA often cannot be differentiated based on clinical features or imaging alone, due to the significant overlap of the symptoms and aetiology (Jayadev and Bird, 2013). Despite the significant overlap, the SCAs have been reported to be some of the most genetically and clinically heterogeneous groups of disorders, as illustrated in Table 1.

Table 1: Lists the symptoms that have previously been reported for the polyQ SCAs (Bryer et al., 2003; Schöls et al., 2004; Smith et al., 2012; Jayadev and Bird, 2013 Klockgether, Mariotti and Paulson, 2019; Diallo et al., 2020).

Type of symptom	SCA1	SCA2	SCA3/ Machado-Joseph disease	SCA6	SCA7	SCA17
Coordination & Movement Impairments	○ Gait, stance & limb Ataxia ○ Dysarthria ○ Dysphagia Choreiform movements (Later in illness)	○ Gait & limb Ataxia ○ Dysarthria ○ Titubation/ tremor (Common) ○ Parkinsonism (Rare)	○ Gait & limb Ataxia ○ Dysarthria Restless leg ○ Dystonia ○ Parkinsonism	○ Spastic Gait ○ Episodic Ataxia ○ Dysarthria ○ Dystonia	○ Gait & limb Ataxia ○ Dysarthria	○ Gait & limb Ataxia ○ Dysarthria ○ Akinesia ○ Dystonia ○ Chorea (occasional) ○ Myoclonus ○ Choreiform hyperkinesia
Muscle & Nerve impairments	○ **Pyramidal tract signs** (hyperreflexia & spasticity) ○ Muscle Weakness ○ Later in illness ○ Hyperkinesia - due to inactivity (Nonresponsive to Quinine) ○ Vocal cord paralysis & stridor ○ **Sensory peripheral neuropathy**	○ Hyporeflexia ○ **Sensory peripheral neuropathy**	○ **Pyramidal & extrapyramidal signs** ○ Amyotrophic fasciculation ○ Sensory loss	○ Brisk reflexes ○ Mild peripheral neuropathy ○ Bradykinesia ○ Pyramidal tract signs	○ **Pyramidal tract sign**	○ Hyperreflexia
Cognitive Impairments	○ ↓ saccades ○ Late in the illness ○ Short-term memory impairment ○ Behavioural disorders ○ Severe mood disorders	○ ↓ saccades ○ **Dementia (**Late in illness)	○ ↓ saccade ○ Sleep disturbances due to periodic leg movements ○ Impaired temperature discrimination		○ ↓ Saccades	○ **Dementia** (Early) ○ Paranoid psychosis ○ Mutism ○ ↓ saccades or epilepsy
Visual Impairments	Infrequent ○ ↓ or absent nystagmus (Early sign) ○ Supranuclear	○ Slow ocular saccades with compensatory head movements	○ Nystagmus ○ Pseudo - exophthalmos (bulging eyes) ○ Diplopia	○ Downbeat Nystagmus (Occasional) ○ Fixation suppression of vestibule-	○ **Visual loss due to macular degeneration** ○ Dyschromatoptia or ↓ central	○ Nystagmus

	ophthalmo plegia ○ Staring look ○ ↓ smooth pursuit eye movements	○ Supranuclear ophthalmoplegia	○ Faciolingual myokymia	ocular reflex ○ Diplopia of lateral gaze with inability to maintain fixation (common)	visual acuity (Early sign) ○ Pigmentary retinopathy ○ Optic atrophy ○ Supranuclear ophthalmoplegia ○ Slow saccade movements ○ Ptosis	

Features that have been bolded have been reported as common in that type of SCA.

As evident in Table 1, most of the SCAs are characterised by the progressive incoordination of hand, eye and mouth movements and a wide, unsteady gait leading to disability and premature death (Jayadev and Bird, 2013; Diallo *et al.*, 2018). Apart from these characteristic features some individuals develop cognitive and/or behavioural impairments such as dementia and aggression (Jayadev and Bird, 2013).

The above SCAs and HD are often referred to as the polyglutamine (polyQ) disorders due to their disease-causing mechanisms, a CAG trinucleotide repeat expansion, within the disease-causing gene (Durr, 2010; Watson and Wood, 2012). This results in a corresponding protein with an elongated polyglutamine tract (Jayadev and Bird, 2013).

Generally, the size of the CAG expansion is inversely correlated to the age of onset and severity of the condition (Jayadev and Bird, 2013). As such, the trinucleotide expansion is often categorised as either ‘normal’, ‘intermediate’ or ‘pathogenic’ based on the number of repeats (Jayadev and Bird, 2013). Table 2 summarises the mean age of onset, duration and repeat sizes of the most common polyQ SCAs.

Table 2: Summarises the known aetiology & prognosis of the most common types of SCA (Bryer et al., 2003; Schöls et al., 2004; Smith et al., 2012).

Features	SCA1	SCA2	SCA3	SCA6	SCA7	SCA17
Gene	ATXN1	ATXN2	ATXN3	CACNA1A (Calcium channel)	ATXN7	TBP (Transcriptional factor)
Mean age of onset & range (years)	37 (4 -74)	32 (1 -65)	36 (5 - 70)	52 (30 – 71)	35 (0 -70)	33 (6 – 48)
Average Duration & Range (years)	15 (10 -28)	10 1 -30)	10 (1 - 20)	>25 years (Not life limiting as brainstem function is spared)	20 (1 – 45) Early onset = shorter duration	>8 years
Normal Repeat Lengths (Number of trinucleotide repeats)	6 -38				4 – 19 Most common in SA = 12 (7 -14)	
Intermediate Repeat Lengths (Number of trinucleotide repeats)	None				20 - 35	
Pathogenic Repeat Lengths (Number of trinucleotide repeats)	>39 Most common in SA 47 (Range 42 - 66)				>36 Most common in SA = 56 (39 - 83)	

The polyQ disorders are susceptible to anticipation which is a tendency for the condition to have an earlier onset with an increased severity in the subsequent generations of a family (Jayadev and Bird, 2013). Due to the instability of the expanded trinucleotide repeat during transmission of the gene, leading to further expansion (Jayadev and Bird, 2013). In these disorders anticipation is more common when the expanded allele comes from the paternal side (Jayadev and Bird, 2013). In particular, SCA2 and SCA7 have been shown to be susceptible to extreme anticipation events (Jayadev and Bird, 2013).

1.2.1 PREVALENCE OF SCA

The prevalence of the SCAs internationally is not well known and different literature reports different figures. Some literature reports that approximately three individuals per 100 000 are affected with SCA (Schöls *et al.*, 2004). Reports of the prevalence of inherited ataxias in Africa and SA are scarce, however, available reports estimate a similar annual incidence of polyQ SCAs in SA to that reported internationally, of two per 100 000 (Smith *et al.*, 2012). Furthermore, these numbers are believed to be under-representative due to the financially strained healthcare system that lacks the infrastructure to refer all cases, especially those from low-income and rural areas (Smith *et al.*, 2012; Smith, Greenberg and Bryer, 2016). As such, an accurate prevalence of the condition is unknown.

This is further complicated by the fact that the prevalence of the different types of SCA depends on the population being studied (Schöls *et al.*, 2004). Although SCA3 is reported to be the most prevalent form of SCA globally, it is only seen in isolated cases in SA (Schöls *et al.*, 2004; Smith *et al.*, 2012). With SA's unique population composition, the distribution of SCA in SA has been shown to differ significantly from other countries, with the most prevalent types of SCAs in SA being type 1 and 7, 48.8% and 26.6% of cases, respectively (Bryer *et al.*, 2003; Smith *et al.*, 2012).

1.2.2 TREATMENT OF SCA

Recent gene therapy trials have shown some promise at effectively delaying or stopping polyQ SCA disease progression however until now none of these strategies have reached clinical trials (Afonso-Reis *et al*., 2021). Several gene therapy approaches have been tested in animal models which aimed to either counteract impairments to the autophage pathways, promote neuroprotection, silence CAG-expanded transcripts or correct the pathological mutation(Afonso-Reis *et al.*, 2021). Majority of this research has been for the treatment of SCA3, however it is believed that due to the several shared traits of the polyQ SCAs these approaches should work for all of these conditions. According to Afonso-Reis *et al.,* (2021) the ideal treatment for polyQ SCAs would be gene editing which would allow for the correction of the pathogenic mutation however this therapy still faces numerous challenges such as toxicity and safety risks. For this reason the next best alternative is considered to be the targeting of mutant RNA transcripts with the antisense oligonucleotides and RNA interference-based strategies (Afonso-Reis *et al*., 2021).

Despite the encouraging reports from recent preclinical trials, there is still currently no available cure for the polyQ SCAs (Afonso-Reis *et al*., 2021). Treatment is therefore focused on medications that are known to partially alleviate the manifestation of some symptoms (Abdel-Salam, 2017; Niewiadomska-Cimicka and Trottier, 2019). Accepted treatments include spasmolytic drugs like baclofen and dopaminergic as well as anticholinergic therapies, for any dystonia and benzodiazepines for muscle cramps (Brusse, Maat-kievit and van Swieten, 2007). Despite the availability of these treatments poor efficacy and tolerability has been reported for neuropathic pain in SCA patients, encouraging the search for alternative treatments for many neurologic diseases (Benbadis *et al.*, 2014). More neurological patients than cancer patients were reported to use alternative therapies (Ryan and Johnson, 2002). The reasons for their use included the patients' desires to, feel hopeful, have more control over their medical care and the belief that alternative approaches are non-toxic (Gómez-ruiz *et al.*, 2019).

In particular, Cannabidiol (CBD), derived from the Cannabis plant, has been shown to have neuroprotective properties for HD patients in some preclinical studies, with no psychoactive effects (Benbadis *et al.*, 2014; Abdel-Salam, 2017). Despite the benefits that have been reported, research is conflicting and the international guidelines for the treatment of HD, released by the European Huntington's Disease Network in 2019, does not include this medication (Consroe *et al.*, 1991; Bachoud-Levi *et al.*, 2019). Due to the similarities between endocannabinoid signalling in SCA and HD patients, it is speculated that SCA patients may experience similar benefits with CBD use (Gómez-ruiz *et al.*, 2019). According to a recent review by Gómez-ruiz *et al.*, (2019) research into the therapeutic benefits of cannabinoids for SCA patients is currently under investigation.

Although, research is limited, some clinical trials have supported the safety and efficacy of the use of CBD in the treatment of several symptoms including; spasticity, pain, glaucoma, nausea and vomiting (Benbadis *et al.*, 2014). Additionally, research indicates the usefulness of these medications in treating dystonia, tics, tremors, epilepsy, migraines and weight loss however, these studies need further validation (Benbadis *et al.*, 2014). No direct fatalities (overdoses), have been reported for CBD, this is believed to be due to its lack of effect on the brainstem (Bachoud-Levi *et al.*, 2019; Russell, 2019). The sedative side effects of the substance however, has been reported to have led to indirect endangerment of users (Bachoud-Levi *et al.*, 2019).

1.2.3 BURDEN OF LATE ONSET NEURODEGENERATIVE CONDITIONS

HD has previously been described as the prime example of a family disease, with devastating social and economic burdens for those in the immediate environment (Hayden *et al.*, 1980). The burden of the condition has been attributed to the affected individual's dependence on caregivers and the genetic inheritance of the condition (Aubeeluck and Moskowitz, 2008). It was estimated that for every affected person, the consequences of the disorder are suffered by about ten individuals (Hayden *et al.*, 1980).

Due to the lack of independence of affected individuals, caregiving is both physically and emotionally demanding (Korer and Fitzsimmons, 1987). Many carers have reported feeling as though the 'duty of care' has been placed upon them (Aubeeluck and Moskowitz, 2008). Immediate family members often take on the responsibility of caring for those affected with neurodegenerative conditions, however, in most cases the primary carer is the unaffected spouse (Hayden *et al.*, 1980; Aubeeluck and Moskowitz, 2008). The partners of affected individuals face many challenges including having to care for their partner, the children and the home (Hayden *et al.*, 1980). A particular challenge for unaffected spouses is the responsibility of informing their children of their at-risk status and its meaning (Hayden *et al.*, 1980).

Neurodegenerative conditions, like HD and the SCAs, have been established to impose significant financial burdens on the affected individuals family and community (Hayden *et al.*, 1980). Not only do these conditions lead to a loss of the affected person's ability to earn an income due to an inability to work, but their care generates many expenses (Hayden *et al.*, 1980). In SA, those affected with these conditions receive a monthly grant from the government however, this has been reported to be insufficient (Hayden *et al.*, 1980).

The lack of finances due to the patient and the carer being unable to work also means that families often cannot afford to employ someone to help with the caregiving duties (Aubeeluck and Moskowitz, 2008). Therefore, the responsibility of caring has been reported to have been taken on, at least in part, by children and adolescents as the healthy adults often have to work to support the family (Williams *et al.*, 2007; Williams, Skirton, *et al.*, 2009; Frank and Slatcher, 2009; Kavanaugh, 2014; Kavanaugh, Noh and Studer, 2015).

Additionally, the presence of HD in families has often been reported to result in social isolation (Hayden, MacGregor and Beighton, 1980; Aubeeluck and Moskowitz, 2008; Frank and Slatcher, 2009; Williams, Ayres, *et al.*, 2009). This social isolation has been reported to be the result of repeated social embarrassment and rejection (Hayden *et al.*, 1980; Aubeeluck and Moskowitz, 2008). Whereas, in other research, it has been suggested to be a result of the families' reluctance to disclose the situation to outsiders (Williams *et al.*, 2013; Kavanaugh, 2014), as well as the family structure and the nature of the condition (Frank and Slatcher, 2009).

The strain on family members was found to be further exemplified by the fact that it often repeats itself in successive generations, leading to the unique implications for the family of anticipating the disorder in unaffected family members (Williams *et al.*, 2000). Additionally, the possibility of the disorder being transmitted to successive generations often leads to caregiving extending for decades (Aubeeluck and Moskowitz, 2008).

Research found that the experience of caregiving not only increased the carers' awareness of their genetic risk but also impacted the caregiver's perception of their genetic risk (Dondanville *et al.*, 2018). For some at-risk individuals witnessing the effects of the condition made the risk appear worse (Dondanville *et al.*, 2018). Whereas, for others, caregiving had increased their sense of preparedness and control over the condition making them less afraid of their risks (Dondanville *et al.*, 2018).

1.2.4 FAMILIAL COMMUNICATION

The difficulties experienced by family members of those affected with HD has received little attention in previous research. Thus, it is not surprising that there is even less research available on the effects of SCA on family functioning (Vamos *et al.*, 2007). However, very high rates of family dysfunction were identified in families with HD (Vamos *et al.*, 2007). Family pathologies such as low cohesion and expressiveness as well as high levels of conflict have been reported (Vamos *et al.*, 2007).

The reluctance to inform outsiders is believed to be of specific importance in conditions like HD and SCA, where there is often stigma and secrecy surrounding the condition (Williams *et al.*, 2013; Kavanaugh, 2014). Many studies have reported HD to be a concealed and taboo subject in some families (Quaid *et al.*, 2008; Rawlins, 2010; Wexler, 2010; Keenan *et al.*, 2013) Family trauma was reported as common among HD families and was associated with the amount of communication in the family (Stuttgen *et al.*, 2020). This family trauma included seeing or caring for an affected relative, suicide attempts, death of their relatives, job losses, divorce and abuse (Stuttgen *et al.*, 2020). Deliberate secret keeping within families, has been reported as common in several studies on HD (Cox and McKellin, 1999; Quaid *et al.*, 2008; Forrest *et al.*, 2009; Keenan *et al.*, 2013). Certain situations or events were found to trigger communication of HD risk within families (Stuttgen *et al.*, 2020). These life events included marriages, family planning, symptom onset, receiving PT results or deciding to undergo PT (Stuttgen *et al.*, 2020).

1.3 BEING AT-RISK

Every child of a parent affected with a type of SCA or HD has a 50% chance of developing the condition therefore referred to as being 'at-risk' (Hayden *et al.*, 1980; Taylor, 2005). These individuals live their whole lives with the risk of an inescapable tragic reality therefore, it is understandable that they have described experiencing high levels of anxiety (Hayden *et al.*, 1980). This included fears of physical and mental disability that leads to a loss of their sense of dignity, economic struggles and stigma around the condition (Hayden *et al.*, 1980).

At-risk individuals have been reported to often experience a fear of abandonment, of rejection and of loneliness (Hayden *et al.*, 1980; Dufrasne *et al.*, 2011). These fears were associated with an attitude of extreme dependence and depression (Hayden *et al.*, 1980). At-risk individuals have been reported to experience guilt over imposing their eventual illness on their life partner stating that they would understand if they were to decide to leave the relationship (Dufrasne *et al.*, 2011).

The fear of abandonment and rejection has also been reported to manifest as a reluctance to disclose their genetic status, especially to the individual's partners and children (Hayden *et al.*, 1980; Dufrasne *et al.*, 2011). This reluctance has been speculated to be motivated by shame, fear of ostracism and a tradition of secretive behaviour in families (Dufrasne *et al.*, 2011). Participants expressed guilt of possibly having passed the deleterious gene to their children (Dufrasne *et al.*, 2011). Some individuals were noted to motivate hiding their genetic status in the guise of protecting their children (Dufrasne *et al.*, 2011). Others felt that their children were not emotionally strong enough to receive the information and feared that it would compromise their psychological wellbeing and development (Dufrasne *et al.*, 2011).

Stuttgen *et al.*, (2020) also reported a tendency for individuals at-risk for HD to be very selective about whom they disclose their personal risks too; due to a fear of discrimination or being treated differently. They were reported to tell their close friends and the majority had communicated their HD risk, decisions about PT and the result with their romantic partner, normally while dating and before marriage (Stuttgen *et al.*, 2020).

A recent study reported that for the majority of at-risk individuals, risk communication and/or PT had strengthened the romantic relationships with the significant others, often being the individuals' support partner (Stuttgen *et al.*, 2020). One negative impact of communicating HD risk, that was reported, was that it had put additional strain on the relationship when one of the partners had been unprepared to discuss the risk openly (Stuttgen *et al.*, 2020). The reported positive impact on relationships and the importance of the support provided by significant others led this author to recommend openness between partners (Stuttgen *et al.*, 2020).

Reasons reported by Stuttgen *et al.*, (2020) for why at-risk individuals share their result with their family members included a sense of responsibility, to obtain emotional support, relieve relatives worry (if tested negative) and to prepare relatives for the time of symptom onset. Reasons for not communicating PT results included relatives being in denial and/or a lack of communication about the condition in their family; previous conflict in the family; feeling guilty about having a normal result or the lack of support received from that family member during PT (Stuttgen *et al.*, 2020). Women have also been found to be more willing to share their genetic status with others (Taylor, 2005).

1.3.1 RISK PERCEPTION

The only previous SA study conducted on the attitudes and impact of SCA on unaffected individuals, found that the majority of at-risk individuals had not received GC and were dependent on their relatives for information about the condition (De Villiers, Weskamp and Bryer, 1997). This study found that the majority of at-risk individuals were unaware or denied their risk status (De Villiers, Weskamp and Bryer, 1997). This finding is supported by Futter, Heckmann and Greenberg (2009) who reported that many SA HD family members not only were unaware of their risk and options but also expressed a lack of interest in learning their at-risk status. These individuals were reported to have philosophical beliefs and were very accepting of outcome (Futter, Heckmann and Greenberg, 2009). Other research has reported similar philosophical beliefs in the SA community, suggesting that individuals often adopt fatalistic worldviews (Greenberg *et al.*, 2012). Similarly, instances of denial of the HD risk by some relatives was reported by Stuttgen *et al.*, (2020). This denial was reported to cause tension among relatives and influence family communication patterns (Stuttgen *et al.*, 2020).

In the study by Van der Steenstraten *et al.*, (1994) it was found that those who hadn't gone for PT often reported expecting to be a carrier of the HD gene. In this study, at-risk individuals risk perceptions were shown to be influenced by their age compared to the average age of manifestation of symptoms in their family; as well as the observed behavioural similarities between themselves and the affected parent (Van der Steenstraten *et al.*, 1994).

1.4 ROLE OF GENETIC COUNSELLING (GC)

Establishing and providing genetics services is not a top priority for the SA healthcare system due to the burden associated with the high levels of infectious disease in the country (Greenberg *et al.*, 2012; Sizer *et al.*, 2012; Kromberg, Sizer and Christianson, 2013). Despite this, genetic counselling (GC) is available in a few urban areas of SA, either through tertiary level public hospitals or private practices (Kromberg, Sizer and Christianson, 2013). One such tertiary level hospital is Groote Schuur Hospital (GSH) where a clinic was specially established to treat neurodegenerative conditions in January 1979 (Hayden *et al.*, 1980). Forty years later this clinic is still run once a month at GSH and involves the attendance of all necessary healthcare professionals including a Neuro, Pdoc, ClinG, GCs, Physio and Genetic nurses (See List of Terms and Abbreviations, page 8).

The currently proposed definition for GC by the National Society of Genetic Counsellors (NSGCs) is that it is "the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease." (Resta *et al.*, 2006). Beyond providing information, a main role of GCs is to help explain and facilitate genetic testing and the delivery of results. In SA, genetic testing in the public sector is done in conjunction with the National Health Laboratory Service (NHLS) (Kromberg, Sizer and Christianson, 2013). The testing that is available through the NHLS includes prenatal genetic diagnosis, diagnostic testing, presymptomatic and carrier testing for a variety of different genetic conditions (Kromberg, Sizer and Christianson, 2013).

Several previous research studies have reported on the many cultural and social issues related to genetic services in SA (Kromberg and Jenkins, 1997; Greenberg *et al.*, 2012; Sizer *et al.*, 2012; Kromberg, Sizer and Christianson, 2013). One of the common issues that affects GC in SA is difficulties with language and communication (Kromberg, Sizer and Christianson, 2013). Additionally, the majority of these papers reported on the importance of traditional healers in SA culture, with some suggesting it may lead to the rejection of genetic services (Greenberg *et al.*, 2012; Sizer *et al.*, 2012; Kromberg, Sizer and Christianson, 2013). Furthermore, this research reported the tendency of SAs to think in terms of the collective and to have fatalistic worldviews (Greenberg *et al.*, 2012). An example used in literature is that of ancestor worship, where it is believed that illness is the result of a transgression by the person or their parent (Greenberg *et al.*, 2012). According to Greenberg *et al.,* (2012) these worldviews affect GC as individuals may not take full advantage of the knowledge and choices that are given to them (Greenberg *et al.*, 2012). All of these issues affect how genetic information is delivered and received, therefore, it is essential to have a good understanding of cultural background and how it influences the perception of healthcare services (Greenberg *et al.*, 2012; Rodrigues *et al.*, 2012; Sizer *et al.*, 2012; Kromberg, Sizer and Christianson, 2013). There is still a need for more knowledge surrounding the influence of diverse cultural backgrounds on the acceptance of PT (Rodrigues *et al.*, 2012).

1.5 PRESYMPTOMATIC TESTING (PT)

PT is available to asymptomatic individuals, who are at-risk of having inherited the disease-causing variant from a first degree family member with a neurodegenerative condition (Dufrasne *et al.*, 2011; Rodrigues *et al.*, 2012). This provides at-risk individual the option to reduce their uncertainty about the future by clarifying their status (Dufrasne *et al.*, 2011).

Although widely studied in the case of HD, the various aspects of PT for SCA have received far less attention (Abe and Itoyama, 1997; Goizet, Lesca and Durr, 2002; Rolim *et al.*, 2006; M. Paneque *et al.*, 2007; Rodrigues *et al.*, 2012; Guimarães *et al.*, 2013; Schuler-Faccini *et al.*, 2014; Leite *et al.*, 2017; Paneque *et al.*, 2019; Cahn, Rosen and Wilmot, 2020). The majority of this research has been conducted in Portugal, Brazil and Cuba and has focused assessing the PT protocol and the impact of PT for SCA3 (Abe and Itoyama, 1997; M. Paneque *et al.*, 2007; Guimarães *et al.*, 2013; Schuler-Faccini *et al.*, 2014).

1.5.1 PT PROTOCOL

PT for late onset neurodegenerative conditions is normally performed within the context of a counselling program/protocol (Aktan-collan *et al.*, 2000; Creighton *et al.*, 2003; Dufrasne *et al.*, 2011; Rodrigues *et al.*, 2012; Guimarães *et al.*, 2013; Macleod *et al.*, 2013; Paneque *et al.*, 2019). PT protocols were initially developed for HD, to promote informed decision-making and protect at-risk individuals from potential psychological harm that could be associated with receiving the result (Hawkins, Creighton and Hayden, 2013). Due to early studies that speculated that the PT protocol was essential to reduce risk of catastrophic events in HD patients (Almqvist *et al.*, 1999). The guidelines for PT protocols were revised in 2013 (Macleod *et al.*, 2013).

In Table 3 the current PT protocol used at UCT is compared to other protocols used internationally. Although, there are differences between the different PT protocols, all of the protocols are spread over multiple sessions, involve numerous healthcare professionals and have similar inclusion criteria (Dufrasne *et al.*, 2011; Rodrigues *et al.*, 2012; Hawkins, Creighton and Hayden, 2013; Schuler-Faccini *et al.*, 2014). This is consistent with the latest guidelines for PT (Macleod *et al.*, 2013). Compared to the other testing centres shown in Table 3, UCT has one of the more lengthy PT programs, consisting of four sessions spread over several months. Additionally, compared to the majority of the protocols (except MPTP), the UCT PT protocol has reduced number of follow-up requirements (Dufrasne *et al.*, 2011; Rodrigues *et al.*, 2012; Hawkins, Creighton and Hayden, 2013; Schuler-Faccini *et al.*, 2014). Research has found that the PT process is likely to elicit some anxiety/stress and difficulties adapting for the client and their loved ones regardless of the approach taken by the professionals involved (Dufrasne *et al.*, 2011).

Table 3: Compares the PT protocols reported by several international testing centres.

	UCT, SA (See Appendix A, page 74)	HCPA, Brazil (Rodrigues *et al.*, 2012; Schuler-Faccini *et al.*, 2014)	CGPP, Portugal (Schuler-Faccini *et al.*, 2014)	MPTP, Canada (Dufrasne *et al.*, 2011)	BC, Canada (Hawkins, Creighton and Hayden, 2013)
Team	GCs, Psych, Neuro & GN	ClinG, GCs, Psych, Neuro & Pdoc	ClinG, GCs, Psych, Neuro, Pdoc, SW	ClinG, GCs, Psych & Pdoc	-
Inclusion Criteria	○ 25% & 50% risk ○ ≥ 18 years old ○ Asymptomatic ○ Support Partner	○ 50% risk ○ ≥ 18 years old ○ Asymptomatic ○ Support Partner	○ 50% risk ○ ≥ 18 years old ○ Asymptomatic ○ Support Partner	○ 25% and 50% risk ○ ≥ 18 years old ○ Asymptomatic ○ Support Partner (Not Enforced)	-
1st Visit	GC	GC	○ GC ○ Psych Evaluation	Phone call: Psych (Knowledge & Motives for PT)	○ GC ○ Psych Evaluation
2nd Visit	(4 Weeks Later) Psych Evaluation	(1-2 weeks later) Psych or Pdoc Evaluation	(3 Weeks later) ○ GC ○ SW Evaluation ○ Sign Consent	Psych Evaluation	(Week 3 – 4) ○ Pre –results session
3rd Visit	(4 Weeks Later) Genetic Counselling	(1-2 weeks later) F/U Psych or Pdoc	(3 Weeks later) Results Delivery	(4 weeks later) Confirmation of risk status: ClinG	(Week 4 -5) Results Delivery
4th Visit	(6 weeks later) Results Delivery: GCs & Psych	(1-2 weeks later) F/U GC	-	(4 weeks later) GC	-
5th Visit	-	Result Delivery	-	(4 – 6 weeks later) Results Delivery	-
Neurology Evaluation	Always available on request	Always available on request	Always available on request		Always available on request
Blood Collection	3rd Visit	4th Visit	1st & 2nd Visit	4th Visit	2nd Visit
Result Disclosure	4th Visit	5th Visit	3rd Visit	5th Visit	3rd Visit
Post-test F/U	○ 4 weeks: GCs & GN ○ 8 weeks (Optional): GCs	3 weeks, 6 & 12 months: Psych or Pdoc	○ 3 weeks, 6 & 12 months: Psych or Pdoc ○ 12 months: Neurologist	1 week (Phone Call): Psych	○ 1 or 2 weeks ○ 6 Months
F/U upon request	Psych, Pdoc & GCs	ClinG, GCs, SW & Neuro	ClinG, GCs & SW	Psych & Pdoc	

Abbreviations: UCT, University of Cape Town; HCPA, Hospital de Clínicas de Porto Alegre; CGPP, Centre for Predictive and Preventive Genetics; MPTP, Montreal Predictive Testing Program; ClinG, Clinical Geneticist; GC, Genetic Counselling; GCs, Genetic Counsellors; Psych, Psychologist; Pdoc, Psychiatrist; Neuro, Neurologist; F/U, Follow up.

1.5.2 PT UPTAKE

The uptake and dropout frequencies of SCA PT in SA has not been reported however, the rate of uptake of PT for HD has been reported as approximately 3 individuals per year in SA (Futter, Heckmann and Greenberg, 2009). These levels are much lower than those that have been reported internationally, especially in developed countries (Maat-Kievit *et al.*, 2000; Trembath *et al.*, 2006; Dufrasne *et al.*, 2011; Baig *et al.*, 2016). Futter, Heckmann and Greenberg (2009) speculated that there were several reasons for low uptake of PT in the Western Cape, SA. These reasons included low levels of awareness of the availability of PT amongst HD families, large distances from home coupled with a lack of personal transport and a lack of interest in knowing their risk status (Futter, Heckmann and Greenberg, 2009). They found that living further than 40 km away from the testing centre acted as a barrier to initiating and completing the full PT program as it adds major considerations including travel time and costs, loss of income and accommodation expenses (Futter, Heckmann and Greenberg, 2009). Research has found that greater than 80% of families who have members affected with HD in SA have their own transport and have significant difficulties affording public transport (Futter, Heckmann and Greenberg, 2009). Participants have also been reported to be deferred by the length of the protocol (Dufrasne *et al.*, 2011). Similar findings were reported in an international study on the barriers to HD PT (Hawkins, Creighton and Hayden, 2013). The reported statistics and sociodemographic characteristics of individuals who undergo HD PT are compared between different countries in Table 4.

Table 4: Compares the reported statistics and sociodemographic data of HD PT in different countries around the world

Population	Study Period	Uptake Rate (%)	Dropout Rate (%)	Mean Age at Uptake (Years)	Male: Female Ratio (%)	Reference
Australia, Victoria	1987 - 2004	15.4	14.3	40.4	42.2:57.8	Trembath *et al.*, 2006
Canada	1987 - 2000	18 (12.5 – 20.7)	-	39.3	39.8:60.2	Creighton *et al.*, 2003
Canada, Montreal	1994 – 2008	9.2	22.1	36.4	43:57	Dufrasne *et al.*, 2011
France	1993 – 1999	5	43	34	37:63	Goizet, Lesca and Durr, 2002
Netherlands	1987 – 1997	24	15	35	41:59	Maat-Kievit *et al.*, 2000
Republic of SA	1994-2009	4.5	8.3	35.3		Futter, Heckmann and Greenberg, 2009
United Kingdom	1994 – 2014	17.4	-	37	44.3:54.5	Baig *et al.*, 2016

As can be seen in Table 4 the HD PT dropout rates that have been reported in SA are similar to those reported in Australia, but are lower than those reported internationally (Maat-Kievit *et al.*, 2000; Goizet, Lesca and Durr, 2002; Creighton *et al.*, 2003; Trembath *et al.*, 2006; Dufrasne *et al.*, 2011; Baig *et al.*, 2016). The reasons for withdrawing from the PT protocol that have previously been reported were the participants' fear of not being able to cope with the results or having felt pressured to participate in the first place (Dufrasne *et al.*, 2011).

As is evident in Table 4 above the mean age of HD PT is similar to that seen in Canada, France and the Netherlands (Maat-Kievit *et al.*, 2000; Goizet, Lesca and Durr, 2002; Futter, Heckmann and Greenberg, 2009; Dufrasne *et al.*, 2011). Interestingly, this SA research also identified a difference in the mean age of uptake of PT based on the at-risk individuals experience with the condition (Futter, Heckmann and Greenberg, 2009). Individuals who had no prior experience with the condition were found to present for PT earlier than individuals who had been raised in a family with an affected individual (Futter, Heckmann and Greenberg, 2009). These findings are supported by those reported by (Trembath *et al.*, 2006). Previous research has reported that at-risk individuals often have very variable timelines for when they would undergo PT (Dondanville *et al.*, 2018). In some research the timing of PT was decided based on when the individual was old enough whereas for others the timing was decided based on certain life milestones such as getting into a serious relationship (Dondanville *et al.*, 2018).

Other sociodemographic similarities amongst individuals who undergo PT have also previously been reported. Individuals who have undergone PT have previously been reported to have higher levels of education and earn a higher income than the general population (Bloch *et al.*, 1989; Craufurd *et al.*, 1989; Futter, Heckmann and Greenberg, 2009; Dufrasne *et al.*, 2011). Additionally, as is also evident in Table 4 a trend has been widely established in which the majority of individuals who undergo PT are female (Bloch *et al.*, 1989; Craufurd *et al.*, 1989; Decruyenaere *et al.*, 1995; Almqvist *et al.*, 1999; Maat-Kievit *et al.*, 2000; Goizet, Lesca and Durr, 2002; Creighton *et al.*, 2003; Taylor, 2005; Trembath *et al.*, 2006; Futter, Heckmann and Greenberg, 2009; Dufrasne *et al.*, 2011; Baig *et al.*, 2016). Previous research has suggested explanations for this gender difference including greater involvement of women in family and reproductive decisions as well as having a greater willingness to deal with difficult decisions and consequences (Decruyenaere *et al.*, 1995). Whereas other research has explained this trend by suggesting that women have a higher perception of their own ability to cope with an adverse result (Taylor, 2005).

1.5.3 PT AWARENESS & UNDERSTANDING

Dondanville *et al.*, (2018) reported that the amount of knowledge about PT held by at-risk individuals depended on their age and degree of involvement in support groups as well as conferences. An article by Futter, Heckmann and Greenberg (2009) found that the awareness of PT amongst those at-risk for HD in SA was low. Although individuals at-risk for HD reported several ways in which they had discovered the PT program, the majority of individuals found out through their relatives who had attended the Neurogenetics clinic at GSH. This was deduced to be associated with language barriers caused by resources only being available in English, which was often not the home language of the at-risk individuals. Since this time the resources have been translated into Afrikaans and increased efforts have been employed by GCs to counsel the family members who attend clinics with the affected individuals in order to increase awareness of the PT program (Futter, Heckmann and Greenberg, 2009).

1.5.4 PT PERCEPTIONS & DECISION-MAKING

It has previously been reported that for those at-risk of inheriting a late onset condition the decision whether to undergo PT can be emotionally challenging and complex (Codori, Hanson and Brandt, 1994; Dufrasne *et al.*, 2011). The complexity of the decision has previously been attributed to the perceived equal advantages and disadvantages of PT leading to those at-risk feeling torn between a simultaneous desire to know and not to know their genetic status (Dufrasne *et al.*, 2011).

On the contrary, some at-risk individuals have been reported to perceive going for HD PT as futile due to the lack of treatment or cure and negative perceptions of the public healthcare system in Spain (Rivera-navarro, Cubo and Mariscal, 2015). This is similar to previous findings in SA that many of their family members of individuals with HD have no interest in knowing their at-risk status (Futter, Heckmann and Greenberg, 2009).

Hayden *et al.*, (1980) reported that many at-risk individuals choose to live in denial in order to enjoy their lives and a study by Quaid *et al.,* (2008) found that hope was a crucial factor of living at-risk for HD. They described that some individuals at-risk for HD choose not to go for testing as they wish to sustain the hope that there is a possibility of having a disease-free future (Quaid *et al.,* 2008). These participants sustain hope that they won't get the condition or that at least their risk decreases with age, suggesting that no testing can be a positive step taken to maintain hope through uncertainty, rather than a passive act. This research maintained that linking hope to uncertainty was different from denial. Their justification for this stance is that individuals at-risk often have observed, cared for, been abused by and/or lost many family members to the condition, hence are not in denial about what a life and death with HD looks like. These individuals are afraid of the condition but not in denial about what the future would look like (Quaid *et al.*, 2008). For some individuals at-risk their hope was maintained through the potential for a cure or that their children may be lucky enough not to be affected (Quaid *et al.*, 2008).

Rivera-navarro, Cubo and Mariscal (2015) investigated the factors that influence at-risk individuals' decisions to undergo PT. They found that almost half of their participants thought PT would be beneficial and knowledge about risk status could improve relationships. These individuals felt that the result would provide freedom from uncertainty, if the individual was positive they could adopt coping strategies, whereas if they were negative they could live a life free from concern. However, other participants expressed that going for PT would have a direct negative effect on the individual. These individuals felt that receiving a positive result would provoke constant worry about the onset of the condition and that going for PT would be denying them the opportunity to enjoy life (Rivera-navarro, Cubo and Mariscal, 2015).

Research done on SCA3 found the perceived benefits of PT to be a decrease in uncertainty and the possibility of planning the future (Rolim *et al.*, 2006). Other reasons were informing children of their risk and the possibility of starting medical treatment which is currently unavailable (Rolim *et al.*, 2006). At risk individuals in SA reported concern for their children as a reason for undergoing PT which differs from the self-focused reasons reported internationally (Decruyenaere *et al.*, 2003; Futter, Heckmann and Greenberg, 2009). Most gave several reasons why they went for testing, but their primary purpose involved family planning, informing their children of their status and guilt of passing on the gene (Futter, Heckmann and Greenberg, 2009).

Arguments against PT included anticipated negative consequences of an unfavourable result and the difficulty adapting to the outcome (Rolim *et al.*, 2006). Additionally, some research reported that PT could lead to an absence of hope which has sometimes been fatal which suggests that extra caution needs to be taken when testing for conditions where there is currently no cure (Quaid *et al.*, 2008).

1.6 RATIONALE

Recent research has shown that the cultural, environmental and personal experiences of individuals may influence their perceptions and uptake of PT (Rodrigues *et al.*, 2012; Sizer *et al.*, 2012). Therefore, there is a great need for more knowledge about the acceptance of PT for SCA in diverse societies. The impact, acceptance and perceptions of PT amongst individuals at-risk for HD has been widely studied, but less attention has been given to the other neurodegenerative conditions such as the SCAs (Rodrigues *et al.*, 2012). Some research has been done on SCA in countries in Europe, North and South America but no research has been done on the perceptions of SCA PT in SA (Rodrigues *et al.*, 2012). This is of special significance in the culturally diverse population of SA due to the low levels of uptake of PT that have been noted in comparison to international studies.

1.7 AIM & OBJECTIVES

The aim of this research project was to qualitatively explore the views and perceptions of individuals at-risk of inheriting Spinocerebellar Ataxia (SCA) towards presymptomatic testing (PT), available through UCT, SA.

The objectives of this research study were to explore:

- The participants' experience of being at-risk for SCA
- The participants' perceptions about the SCA PT process
- Factors that may influence the participants' decision whether to undergo PT

Chapter 2: Methodology

2.1 INTRODUCTION

In this chapter, the methodological design of this research study are described. The chapter begins with a brief background of the involvement of the Division of Human Genetics (DHG) with the research population, followed by a description of the study design and population. The data collection and analysis methods are then described in detail. The chapter is concluded by reports on the validity and reliability of the study, as well as the ethical considerations of this study.

2.2 RESEARCH SETTING

The DHG at UCT began investigating the SCAs in the 1970s, after the discovery of a large family with an autosomal dominant ataxia in the Western Cape, SA (Smith, Greenberg and Bryer, 2016). Since the commencement of this research, thousands of individuals from several large families have been diagnosed with different types of SCA (Smith, Greenberg and Bryer, 2016). In SA, to the best of the researchers' knowledge, there is no patient support group for SCA.

Due to the severity of the neurodegenerative conditions (See Section 1.2, page 10), a specialist clinic was established at Groote Schuur Hospital (GSH) in January 1979, to treat these conditions (Hayden *et al.*, 1980). Forty years later, this clinic is still held once a month and involves a multidisciplinary team (See Section 1.4, page 18).

A large part of GC for late onset neurodegenerative conditions involves PT of at-risk relatives (Rodrigues *et al.*, 2012). The DHG at UCT, has offered a PT service since February 1995 (Futter, Heckmann and Greenberg, 2009). Similarly to international PT protocols, PT at UCT consists of multiple spaced out sessions, that allow the at-risk individual time to reflect and make an informed decision about testing (See Section 1.5, page 19 and Appendix A, page 74) (Futter, Heckmann and Greenberg, 2009).

2.3 RESEARCH DESIGN

This study aimed to explore the personal views and perceptions of at-risk individuals towards PT for SCA in SA. Qualitative research was used as it allows for the discovery, description and understanding of social behaviour by exploring individuals' lived experiences (MacFarlane, Veach and LeRoy, 2014). This research strategy therefore required the research participants to draw on their personal experiences and beliefs, resulting in a rich dataset. Additionally, qualitative research has been described as a "natural" design choice for GC research due to the nature of the field and the types of skills possessed by GCs (MacFarlane, Veach and LeRoy, 2014).

As research on this topic is limited in SA (See Chapter 1, page 10), the current study was designed as an in-depth exploration of the views and perceptions of individuals at-risk of SCA towards the PT process. Explorative research examines topics that are not well understood, to develop preliminary ideas and formulate more precise future research questions (Neuman, 2014). This was of particular importance as the population of interest was anticipated to be difficult to access.

2.4 RESEARCH STUDY POPULATION

This research was specifically interested in the views and perceptions of individuals, at-risk of inheriting SCA. For this reason the inclusion criteria of this study stipulated that participants had to be potential carriers of a familial SCA mutation which was defined as being, at either 50% or 25% risk of inheriting the condition. Due to the inheritance pattern of SCA, individuals with a first degree relative with the condition are considered to be at 50% risk (See Section 1.2, page 10). Similarly, an individual is considered to be at 25% risk of inheriting SCA if they have a second degree relative that has been diagnosed with SCA and their at-risk first degree relatives genetic status is unknown. For example, if the participants' at-risk first degree relative has not yet shown symptoms, passed away before displaying symptoms and/or has not undergone genetic testing.

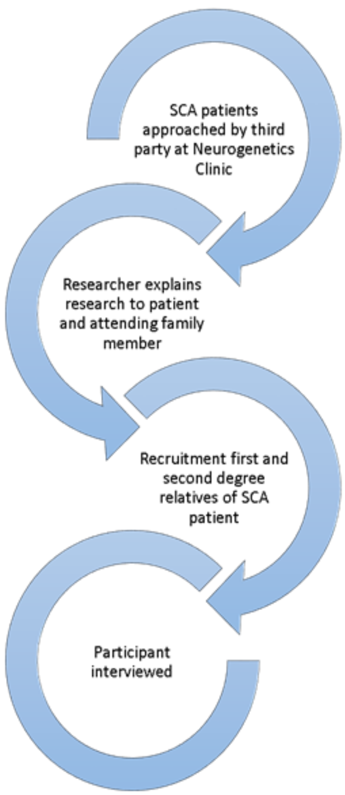
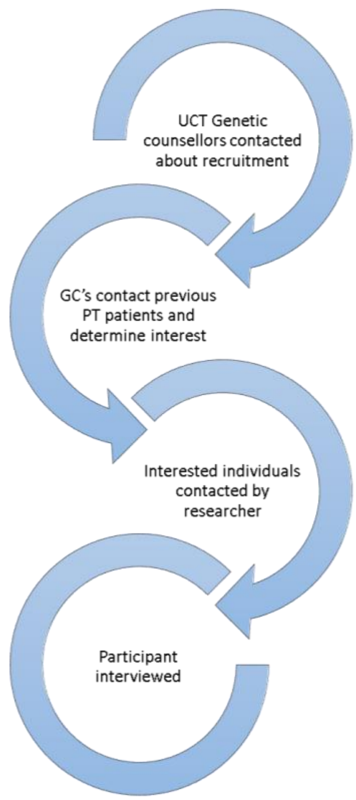
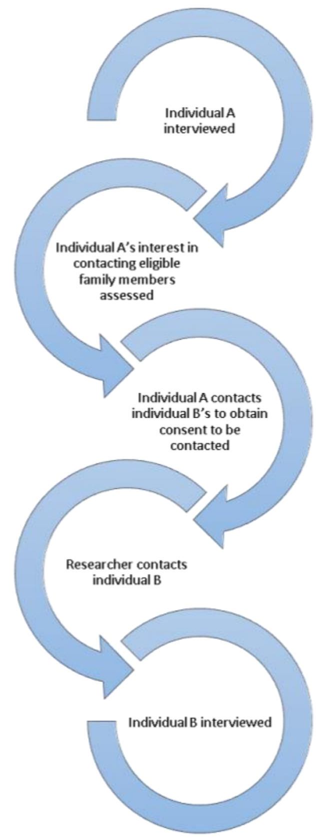
In order to be eligible to participate, individuals had to be 18 years or older and asymptomatic. Asymptomatic was defined as not having been clinically diagnosed with SCA or displaying clinical features, at the time of the interview. These exclusion criteria were incorporated into this study for several reasons. The first reason was to protect these special populations, such as individuals that are vulnerable to coercion or unable to grant voluntary consent to participate in a study (Neuman, 2014). This includes children, incarcerated individuals or individuals who have less than full physical, emotional or mental capabilities (Neuman, 2014). As some types of SCA exhibit symptoms associated with reduced mental capacities this was an exclusion criterion for this study (See Section 1.2, page 10).

Another reason for this exclusion criteria was to decrease heterogeneity in the sample, which would lead to difficulty obtaining prevalent themes from the data (MacFarlane, Veach and LeRoy, 2014). Additionally, this meant that individuals who had completed the PT process and were known to be carrying the SCA mutation were still eligible to participate, as long as they had not yet started exhibiting symptoms of the condition or been clinically diagnosed.

2.5 RESEARCH POPULATION RECRUITMENT

After obtaining ethics approval, recruitment of participants took place over a four-month period in 2019. A multi-pronged approach to recruitment was used, including two methods of purposive sampling and one method of convenience sampling. The recruitment strategies utilised in the current study are illustrated in Table 5.

Table 5: Illustrates the multipronged approach to recruitment utilised in this study

Purposive Sampling		**Convenience Sampling**
Method 1: Neurogenetics Clinic	Method 2: UCT GCs	Method 3: Previous Participants
		

Purposive sampling was proposed as it is known to allow for information-rich cases (MacFarlane, Veach and LeRoy, 2014). This type of sampling is often used in exploratory research, as it allows the researcher to access a very specific or difficult to reach population (Neuman, 2014). The first method of purposive sampling took place at the monthly Neurogenetics clinic run at GSH. The second method of purposive sampling took place through the GCs employed in the DHG, UCT.

The third method of sampling involved participants being recruited by a prior participant, referred to as snowball sampling. Snowball sampling is used when research is interested in a network of people (Neuman, 2014). This type of sampling begins with a few individuals and spreads out based on relationships and links to the initial cases (Neuman, 2014). This sampling method was proposed for this research study due to the difficulties of accessing this at-risk population and to gain access to participants with differing perspectives to those who have attended clinic or gone through the PT process.

The data produced by purposive sampling rarely represents the entire population, but rather finds cases that are especially informative (Neuman, 2014). This is in line with qualitative research as the data yielded is not intended to be generalised to the population (MacFarlane, Veach and LeRoy, 2014).

This study aimed to reach data saturation, which refers to a theoretical point where no new information emerges, and all topics are present in data analysis (MacFarlane, Veach and LeRoy, 2014). The results of the various recruitment methods used are described at the beginning of Chapter 3 (page 37).

2.6 DATA COLLECTION

The qualitative data for this study was collected through several methods, including:

- A Sociodemographic questionnaire (See Appendix B, page 77)
- A Semi-structured interview (See Appendix C, page 78)
- Field notes

Before the commencement of data collection, the interview protocol for this study was piloted. A total of 4 pilot interviews were conducted and the participants' feedback was used to revise the participant questionnaire and interview guide where necessary.

2.6.1 SOCIODEMOGRAPHIC QUESTIONNAIRE

The researcher had no prior knowledge of the participants before their interview. As such, following written consent, participants were asked to fill out a sociodemographic questionnaire (See Appendix B, page 77). The questionnaire reduced the time spent obtaining background information about the participants, so that more in-depth questions could be asked in the interview. The questionnaire consisted of closed ended questions that were utilised in the interview to guide the researcher on how to phrase the questions. For example, the interviews were tailored based on whether the respondent had undergone PT and who in their family was affected. All the sociodemographic information collected in the questionnaires was collected in a table and used to compare and contrast the participants of this study (See Table 8, page 39).

2.6.2 SEMI-STRUCTURED INTERVIEWS

Due to the sensitive nature of the topic under study, individual interviews were the preferred data collection method (MacFarlane, Veach and LeRoy, 2014). The type of interviews conducted in this study were semi-structured in nature. Semi-structured interviews use a set of questions as a guide but includes the use of necessary prompts, pauses and nonverbal communication to encourage elaboration and clarification (MacFarlane, Veach and LeRoy, 2014). Probes are defined as neutral requests or follow-up questions that encourage the participant to clarify ambiguous answers, expand on an incomplete answer or provide relevant responses to the questions (Neuman, 2014). These techniques reduce the likelihood that a participant will misunderstand a question, therefore increasing the reliability of the responses obtained (Neuman, 2014). Importantly, if a participant had questions or conveyed misinformation, they were offered a genetic counselling referral at the end of the interview.

The interviews were conducted in person or telephonically, usually lasting between 40 and 80 minutes. Face-to-face interviews were preferred as it allows for the interpretation of non-verbal cues and allowed the researcher to build a rapport with the participants more easily (MacFarlane, Veach and LeRoy, 2014). However, telephonic interviews were offered to accommodate participants that were unable to do a face-to-face interview due to geographic distance etc.

Due to the researcher's lack of prior knowledge about the participants, each interview was started by taking a family history. This also allow the researcher to build mutual trust with the participant as well as to explore the relationships and feelings surrounding the condition in the family (Weil, 2000).

The open-ended questions in the interview guide (See Appendix C, page 78), were focused on exploring the experience and impact SCA has had on the participants' life and the participants' (as well as their families') perspectives of PT. At the end of each interview, an open question was asked about whether there was anything further the participant wanted to contribute to the study.

In order for the verbal data of the interviews to be analysed, the interviews were voice recorded, and the data was transcribed into a written form (Braun and Clarke, 2006). The interviews were transcribed verbatim; all verbal sounds were thoroughly documented with careful attention placed on punctuation as it can alter the meaning of the data (Braun and Clarke, 2006). The transcripts were checked by the researcher against the original audio recordings to ensure the accuracy of the raw data.

2.6.3 RESEARCHER'S FIELD NOTES

Field notes were taken by the researcher after each interview to note both the physical and verbal behaviours of the participant, as well as features of the setting for data analysis. These included the date, time, setting and any external factors that may have influenced the interview.

2.7 DATA ANALYSIS

The process of data analysis starts when the researcher began to note patterns of meaning and issues of interest in the data (Braun and Clarke, 2006). Data analysis was done in conjunction with data collection so that emerging concepts or questions informed subsequent interviews to improve focus and clarity on specific issues.

This analysis approach was selected as it is useful for researching previously unexplored topics, especially complex phenomena and inner experiences that are difficult to observe (MacFarlane, Veach and LeRoy, 2014). In the current study, a rich thematic description of the entire data set is provided in order to give the reader a sense of the important themes found.

Theme refers to a representation of a patterned response or meaning in relation to the research question that has been identified in the data set (Braun and Clarke, 2006). Although the prevalence of a particular topic was acknowledged and did impact the structure of the themes in this research, the final themes were based on what topics captured something important about the research question.

The data obtained from the semi-structured interviews in this study were analysed by means of thematic analysis, in close discussion with the research supervisor. Thematic analysis is defined by Braun and Clarke (2006) as "a method for identifying, analysing and reporting patterns (Themes) within the data". Thematic analysis offers an accessible and theoretically flexible approach to analysing qualitative data. This method of data analysis was chosen for this research as it has the potential to produce a complex, detailed and rich account of the entire data set (Braun and Clarke, 2006).

The data obtained in this research study was analysed in an inductive manner therefore the themes were extracted from the data without imposing a pre-existing framework (MacFarlane, Veach and LeRoy, 2014). Although, it is important to note that the researcher cannot completely free themselves from the theory however, the analyst tried to limit their engagement with previous literature (Braun and Clarke, 2006).

Themes reported in this study were obtained in a semantic approach. A semantic approach is when themes are identified from the explicit meaning of the data, not beyond the data (Braun and Clarke, 2006). This involves the progression from description of the data (Results) to an interpretation of the data (Discussion). The description of the data involved organising it into patterns based on the content and summarizing these patterns (Braun and Clarke, 2006).

Language allows us to articulate meaning and experiences. For this reason an essentialist/ realist approach was utilised in this study, where language was used to theorise on the motivations, experience and meaning of the data (Braun and Clarke, 2006). This is achieved by assuming a unilateral relationship between meaning, experience and language (Braun and Clarke, 2006).

The thematic analysis was done according to a six phase analysis system published by Braun and Clarke (2006), as illustrated in Figure 1. Although, this analysis system was used, the data analysis often moved back and forth between the different stages. Data analysis is a recursive process involving continuous movement between the raw data, coded data and the analysis that is being produced (Braun and Clarke, 2006).

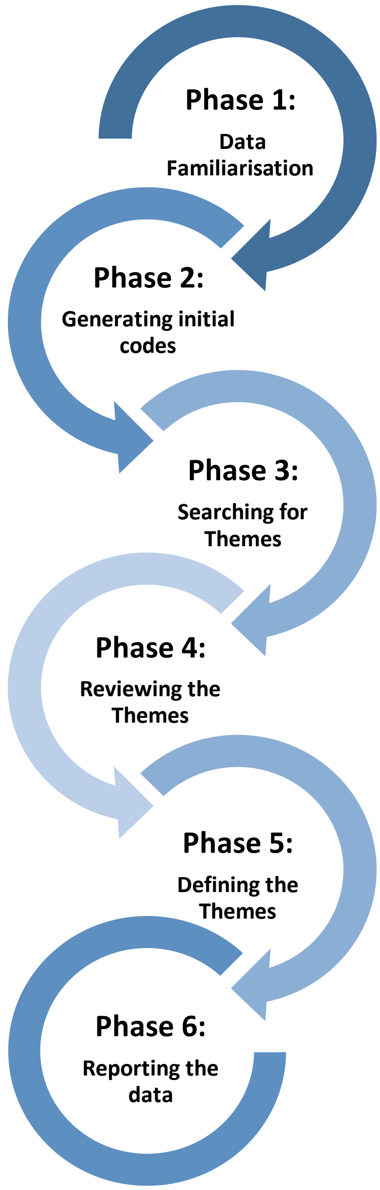


Figure 1: Illustrates the phases of data analysis as proposed by Braun and Clarke, (2006).

Writing was an integral part of analysis and happened throughout the process. In phase one, the researcher jotted down ideas and potential coding schemes and continued to write throughout the coding and analysis process (Braun and Clarke, 2006).

The first phase of data analysis involved familiarisation with the data set. This started during the interviewing process which was an interactive means of obtaining data, the researcher therefore started data analysis with some prior knowledge of and thoughts about the data. This continued during the transcription process. The first interview was transcribed by the researcher, however due to time constraints the remaining transcription was outsourced to an experienced individual. Once complete, all the transcripts were checked for accuracy against the original audio recording by the researcher. During the checking process, all identifying details of the participants were removed from the transcripts, and they were given pseudonyms to protect their anonymity. When necessary, extra details were added in brackets to the data to insure the reader's understanding. For example, jargon used by the participants was followed by the correct English word/s, similarly, context was provided in brackets for vague pronouns. The researcher read the transcripts several times in their entirety to increase familiarity with the data (Braun and Clarke, 2006). Preliminary notes and ideas were documented in the margins of the raw data.

The second phase of the research began by open coding all the transcripts, which involved examining the data and assigning preliminary analytic code to each pertinent statement (Neuman, 2014). A code is defined as a word or phrase that is used to identify a feature of the data that is deemed to be of interest or important (Braun and Clarke, 2006). Coding the data is a method used in thematic analysis to organise the data into meaningful groups. Due to the small sample size in this study, coding was done manually on the printed transcripts, using coloured pens and highlighters to indicate the potential patterns that were identified. A list of the codes used in this research are provided in Appendix D on page 80. An example of how the data was coded is provided in Table 6.

Table 6: Provides an example of how codes were assigned to the raw data

Data Extract	**Assigned Codes**
"Mm… Yes, I don't think I would have been, I might have been in denial for much longer, if it was positive, if I had received it, at the time because I just thought, "it wasn't the time now for me to do all of this" and usually when, when for me, it's like park it, I'll come to it later. I won't deal with it right now. Which is, which is also not fair. I need to deal with things. If it is what it is, then I need to deal with it and move on but I don't think, I didn't think, at the time, that the timing was right, you know? Because I didn't expect her to have such a reaction or uh… a meltdown the way she had, so then I thought "No… let me just deal with her and then see how it is." – Sofia	Reason for delaying testing - Fear of reaction - Not Ready - Support Family Guilt over not Testing Reactions to Testing

The next two phases of the analysis involved identifying the overarching themes and reviewing these themes. This phase was accomplished by writing each code onto sticky notes and creating a thematic map. Braun and Clarke (2006) define a thematic map as "a detailed account of the hierarchical relationship between codes, as well as a description of each". Using this technique allowed the researcher to visualise the data and group similar codes and ideas into a collection of candidate themes and subthemes (Braun and Clarke, 2006). During this phase the transcripts were re-read to determine if the themes were accurate depictions of the data set and to see if any new codes emerged from the data.

Once the preliminary themes were identified, data extracts were collated together within each code to allow for comparison. This was done by copying extracts of the raw data into separate Microsoft Word documents (Themes). Each data extract was added to as many codes as was relevant (See Table 6).

The next phase of data analysis involved identifying the story that each theme told and how it related to the research question (Braun and Clarke, 2006). This phase involved reading the excerpts for each code, comparing the different participants' views, and writing up descriptions of the findings of each section. These descriptions were given to the research supervisor for feedback. Based on the feedback received and re-reading the descriptions of the data, the themes were reviewed and restructured. This involved a process of rereading the raw data and reworking the thematic map. The final thematic map of this study is illustrated in Figure 3 on page 40.

The final phase of the analysis process involved writing up the results in a logical, coherent and non-repetitive manner (Braun and Clarke, 2006). The results of the data analysis are reported in chapter 3 (See page 37) including data extracts as evidence of the prevalence of the theme.

2.8 REFLECTIVE PIECE

From early in my professional career, I levitated towards inherited conditions, particularly the late onset conditions. In reflection, this was most likely fuelled by my own family history of cancer and heart disease, which has resulted in the loss of many of my family members. This motivated my decision to be a genetic counsellor as, I wanted to be able to help these families. My own experiences of loss have improved my ability to empathise with the pain and grief of my patients however, I have to be cautious not to over identify with their struggles. The same was true for the participants in this study, as this could have influenced the direction of the interview and how the data was analysed. To overcome this potential bias the interviews were piloted with colleagues and the data analysis was verified by the research supervisor.

The emotional complexity of the topic was both what inspired, and the most challenging aspect of, this research. The interviews were more emotionally challenging than initially anticipated, with participants describing their experiences of physical and sexual abuse, neglect and abandonment. Having had a privileged and safe life, the frequency and magnitude of trauma that was described was difficult to comprehend. I felt helpless in the confines of my role as the interviewer, as being a training genetic counsellor I felt compelled to step into a supportive and information giving role at several points throughout the interviews. Being aware of my role as a researcher I was very careful to not provide information or support until after the interview was complete, at which point the participants questions were answered, and they were offered a genetic counselling referral.

Due to my genetics background and my tendency to intellectualise, undertaking PT for late onset conditions was something that I could relate to, especially, when the condition was preventable or manageable. However, I had pondered the difficulty of deciding to undergo PT for unpreventable conditions like, HD and found the process of making such a decision curious. Therefore, when the low uptake of PT and lack of information surrounding SCA came to my attention, it brought with it the possibility of investigating a topic that had always fascinated me.

The possibility of investigating the at-risk population of SA's perceptions' of PT was compelling. Due to the cultural diversity of the country, it was anticipated that the perceptions of PT in this population may be unique. It was therefore surprising that majority of the findings of this study were similar to that reported internationally, in HD studies. Additionally, the unique family structures, religions, cultures, socioeconomic statuses and stages of life, of each participant increased the heterogeneity of the dataset, making it challenging to identify the themes. This research did however, identify the unique difficulty of being at-risk for SCA in SA, which has an underfunded healthcare system, limited help services, high levels of violence and extreme differences in socioeconomic statuses.

2.9 VALIDITY AND RELIABILITY

Trustworthiness refers to the believability of the results presented in a study (MacFarlane, Veach and LeRoy, 2014). The trustworthiness of qualitative research can be measured using several criteria. Reliability and validity are ideas used in research to establish the believability, credibility and truthfulness of the findings (Neuman, 2014). These criteria and how they were upheld in this research study are explored in this section.

- Reliability refers to the consistency and dependability of the results (Neuman, 2014).
- Validity refers to the truthfulness of the results i.e. no false or distorted statements, so that the results fit the reality (Neuman, 2014). As measuring validity is challenging in qualitative research, achieving authenticity is said to be more important than finding a single version of the truth (Neuman, 2014).
- Applicability or transferability refers to whether the findings of a study are useful to the profession (MacFarlane, Veach and LeRoy, 2014).

All the resources used for recruitment and data collection were proofed by the studies research supervisor. This ensured that the questions in the sociodemographic questionnaire and interview guide were relevant and comprehensive to achieve the research goal. Subsequently, the resources were piloted with three colleagues and one lay individual to further improve the relevance and flow of the questions as well as to reduce any ambiguity of the questions (See Appendix B, page 77 and Appendix C, page 78).

In qualitative research reliability is difficult to measure, as data collection is an interactive process that is dependent on the setting and a unique mix of measures which cannot be repeated (Neuman, 2014). Additionally, different researchers may analyse the data differently however, these diverse perspectives are seen as beneficial in qualitative research as it helps to identify different aspects of the subject matter (Neuman, 2014). Thus, the research supervisor was involved throughout the data analysis process to ensure accurate interpretation of the data, limit researcher bias and increase the confidence in the results. The validity of the results reported in this research was improved by carefully and objectively analysing the data.

Validity grows as the dense connectivity of the different data sources are recognised by the researcher in detail (Neuman, 2014). To achieve applicability, the researcher set out to clearly describe the sample and the context of the study. Therefore, thick descriptions of the context are provided in the study to make the participants' experiences and perceptions meaningful and transferable.

2.10 ETHICAL CONSIDERATIONS

This section discusses various ethical considerations and how these ethical principles were upheld in the current study, followed by a discussion of the potential benefits and harms for the research participants.

2.10.1 ETHICAL APPROVAL

This study was approved by the Human Research Ethics Committee at the Faculty of Health Sciences of UCT on the 11th of February 2019 (Reference number: HREC REF: 758/2018) (Appendix F, page 84).

2.10.2 CONSENT

Autonomy is the ethical principle that protects individuals from being forced or coerced into participating in a research study. This principle is upheld by ensuring that voluntary consent is obtained from each participant. Informed consent refers to a statement that explains aspects of a study to a participant and asks for their voluntary agreement in participating in a study (Neuman, 2014). In the current study, autonomy was protected through the implementation of several considerations.

To protect the research population from possible coercion, no contact was made with potential participants, by the researcher, until verbal consent was received by a third party. Additionally, contact attempts by the researcher was limited to three per potential participant therefore if the participant was unreachable, avoided making arrangements or declined to participate, contact was ceased. No special benefits were offered for participation in the study, and non-participation had no bearing on the individuals' future medical treatment (Neuman, 2014). Furthermore, no special populations, which may lack the necessary competency to provide informed consent, were recruited for this study (See Section 2.4, page 26).

Following the initial verbal consent, the researcher called each participant to ensure that they were fully informed about the study. When possible a written copy of this information was sent to the participant before the interview, alternatively, a copy was provided following the conclusion of the interview (See Appendix E, page 82). To make sure that the participants' consent was autonomous, the consent form and information sheet was available in English, Afrikaans and Xhosa, as these are the main languages spoken in the Western Cape. Additionally, upon request a translator was available to explain the study and for the interview.

Verbal and written informed consent were obtained from each participant prior to the commencement of the interviews. During the consenting process, the participants were informed, both verbally and in writing, of the following:

- The aims, objectives and process of the study
- Their involvement in the research project was completely voluntary and that they could withdraw from the study at any time as well as refuse to answer any questions during the interview.
- The duration of the interview would be approximately an hour.
- That the interview would be voice-recorded however their involvement would be confidential (See Section 2.10.3 below).

2.10.3 PRIVACY AND CONFIDENTIALITY

Social research often studies sensitive topics and invade the participants' privacy in order to study certain social behaviours therefore special precautions are need to protect the participants' privacy (Neuman, 2014). In order to maintain the ethical principles of privacy and confidentiality several precautions were put in place for the current study.

- Confidentiality refers to the protection of the participant's data from the public so that they cannot be linked to their responses.
- Anonymity refers to protecting the participants' privacy by not disclosing the participants' identities after data collection (Neuman, 2014).

To ensure the previous PT client's confidentiality was protected, the researcher did not access the PT records or contact the clients. Additionally, all of the interviews were conducted in a private setting in the GCs offices at UCT and the participants were aware of the voice recording before the commencement of the interview. Although, a third party was involved in transcribing the interviews, they were given no information, and asked to sign a confidentiality agreement. All potentially revealing paperwork was kept in confidentiality by the researcher, revealing personal details were removed, and the participants were assigned a pseudonym throughout the transcripts and the reporting of the results (See Chapter 3, page 37).

2.10.4 RISKS AND BENEFITS TO PARTICIPANTS

No physical risks to the participants were foreseen for this research study. To prevent any financial burden to the participants for attending the interview, participants who took public transport were compensated for their travel by the researcher.

Due to the sensitive nature of the topic under investigation, some emotional difficulties were possible during the interviews. All participants were informed during the consent process that they did not have to answer any questions they were not comfortable with, and that they could end the interview at any time. The risks were further minimised by the researcher counselling background and skills such as empathy and sensitivity.

Additionally, any participants that needed any further support were referred appropriately. Although the majority of the participants in this study became emotional during their interviews, two participants were flagged as having difficulties coping and were offered a psychology referral. Furthermore, participants' GC related questions were answered after the conclusion of the interview and those who expressed misconceptions or interest in going for PT were offered a GC referral.

Expected benefits to the participants' involvement in this research was twofold. Firstly, the individual interview provided them the opportunity to share their story as well as express their opinions and emotions in a safe place. This may have therapeutic benefits, allowing the participants to make sense of their world. Additionally, this research may consequently improve the genetics services that they receive in the future.

Chapter 3: Results and Discussion

3.1 INTRODUCTION

This research study aimed to explore:

- The participants' experience of being at-risk for SCA
- The participants' perceptions about the SCA PT process
- Factors that may influence the participants' decision whether to undergo PT

In this chapter, the findings of this study are documented and discussed. The chapter begins with a brief summary of the research participants, followed by the results of the thematic data analysis performed. The results are reported and discussed as themes, with verbatim data extracts from the semi-structured interviews. Where more than one participant quoted the same topic, the most significant data extract was provided, based on its content.

3.2 THE PARTICIPANTS

The sample size of this research study was small (6) not reaching the targeted data saturation (See Section 2.5, page 27). The small sample size was attributed to several factors, including a limited time period for recruitment and several challenges with accessing the study population group. One challenge was that the at-risk population are not known to the DHG unless they have attended the Neurogenetics clinic, have come for GC or PT. Additionally, as this is a sensitive population group, where confidentiality is a major concern, therefore, only conservative sampling methods were utilised (See Section 2.5, page 27). The success of each recruitment method utilised in the current study can be seen in Table 7.

Table 7: Summarises the numbers of participants recruited through the various sampling methods utilised in this study (See Chapter 2, page 25)

Recruitment method	Recruitment Period (Months)	Eligible individuals identified (Met Study Criteria)	Individuals who expressed interest in participating	Individuals who presented for interview
1: Clinic	4	0	0	0
2: GCs	4	10	7	5
3: Snowball	4	1	1	1
Total	12	11	8	6

As can be seen in the Table 7, the majority of the participants were recruited using the second purposive sampling method. The first recruitment method was entirely unsuccessful with none of the affected individuals having attended their appointments at the Neurogenetics clinic over this period. The reason for this lack of clinic attendance is unknown. Additionally, the third sampling method only yielded one participant (Noah), as the majority of the participants could not or would not contact their eligible family members about participating in the study. The reasons provided by the participants included; not having any eligible family members i.e. relatives being too young or already symptomatic, knowing that their eligible family members would not be interested in participating (See Section 3.7.3.1, page 64) or not having good relationships with those who were eligible to participate (See Section 3.5, page 46). This outcome is consistent with the findings described in the next sections.

The sampling methods yielded a total of 11 potential participants, over the four-month recruitment period. Of the 11 individuals who gave consent to be contacted by the researcher, eight individuals expressed interest in participating, but only six honoured their appointments. The low yield of recruitment could be attributed to the limited time period of recruitment or indicate that the recruitment strategies used were inadequate. However, considering the previously mentioned low uptake of PT in this population (See Section 1.5.2, page 21) and the findings of the study, this result could indicate the inaccessibility of the at-risk population. Figure 2 illustrates the family history of Sofia and Noah (indicated with arrows) constructed from the information gathered in their respective interviews. The figure shows that the family had eight affected family members **(solid blue symbols)**, resulting in at least 17 at-risk individuals **(indicated with asterisks)**. Of these family members only the affected individuals have been for genetic testing and only Sofia has come forward for PT (but didn't follow through).

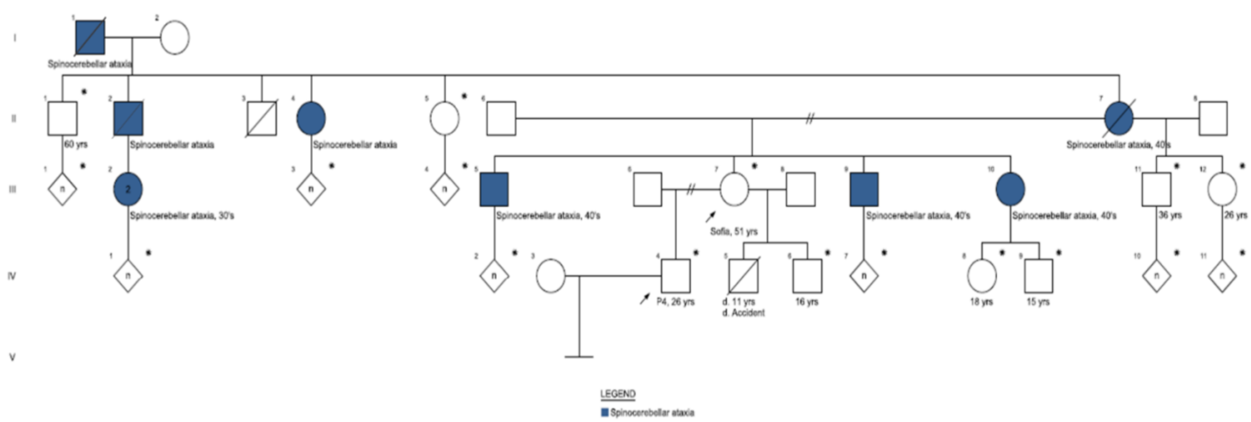


Figure 2: Illustrates the family history of Sofia and Noah (indicated with arrows) constructed from the information gathered during their respective interviews. To protect the anonymity of the participants, some specifics (not essential to this study) have been altered such as genders.

As a result the final number of participants in this study was six at-risk individuals. All but one interview was conducted face-to-face at the UCT medical campus, and the final interview was conducted telephonically. Although only half of the participants indicated English as their home language, all the participants were fluent in English and did not elect to have a translator in the interview. To protect the confidentiality of the participants, pseudonyms are used to illustrate each individual's contribution to this study. The sociodemographic characteristics of the participants are illustrated in Table 8. The table summarises the information that was obtained from the sociodemographic questionnaire filled out before each interview (See Appendix B, page 77).

Table 8: Illustrates the sociodemographic and familial information provided by the six participants in the sociodemographic questionnaire

Participant Code	Gender	Age	Relationship status	No. of Children	First Language	Highest Education level	Type of SCA	Affected Relatives	Risk
Maria	Female	28	Single	1	Xhosa	High School	SCA 7	Mother & Maternal Grandmother	50%
Sofia*	Female	50	Married	2	English	Post Graduate		Mother, Maternal Grandfather, Brothers, Sister & Cousins	50%
Rose	Female	20	Single	1	English	Matric		Mother, Maternal Grandmother, Aunts, Uncles & Cousins	100% (Tested + for familial mutation)
Noah*	Male	26	Married	0	English	Matric		Maternal Grandmother, Maternal Great Grandfather, Aunts, Uncles & Cousins	25%
Juan**	Male	33	Married	1	Afrikaans	Matric	SCA 1	Father, Aunt & Uncle	50%
Ben**	Male	33	Partnership	0	Afrikaans	Post Graduate	SCA 1	Father, Aunt & Uncle	50%

Indication of relationships between participants: *Mother (Sofia) & Son (Noah), **Brothers

As can be seen in Table 8, the age range of the participants was between 20 and 50 years old, with the majority of participants being between 25 - 35 years of age. Additionally, the sample consisted of equal numbers of each gender and the participants had diverse cultural, socioeconomic and educational backgrounds. It is therefore evident that despite the small size, the sample was diverse.

The small sample size is an important limitation of this research project, as it produced variability in the data that led to difficulty interpreting the results. This is especially true considering the diverse ages and cultures as well as socioeconomic and educational backgrounds of the participants. These factors would have impacted the results obtained however due to the small sample size the impact of these factors could not be established. Additionally, the data obtained in the interviews was rich, as the participants provided in-depth descriptions of their experiences. The book on qualitative research by Patton (2015) describes how in depth information obtained from a small number of individuals can be very valuable especially when purposive sampling is used (See Chapter 2, page 25) as stated that:

> *"The validity, meaningfulness and insights generated from qualitative inquiry have more to do with information richness of the cases selected and the observational/analytical capacities of the researcher than the sample size" - (Patton, 2015)*

Based on this concept, despite the limitations of the small sample size the results of this study are still considered valuable, especially considering the limited research that has been done on the perceptions of those at-risk for SCA.

Furthermore, due to the explorative approach used in this study, the findings are not intended to be statistically or conceptually generalisable.

3.3 INTRODUCTION TO THEMES

Through in-depth thematic analysis and careful study of the transcripts, four themes were identified (See Chapter 2, page 25). The themes represent the main patterns and topics that emerged from the interviews. Although the results of this study have been reported as themes, it is important to note that the data was often difficult to disentangle as many of the topics were closely linked. As such, there may be some overlap between the topics discussed in the themes. This is indicated in brackets at the end of a sentence. The themes and sub-themes that emerged in this research are illustrated in Figure 3.

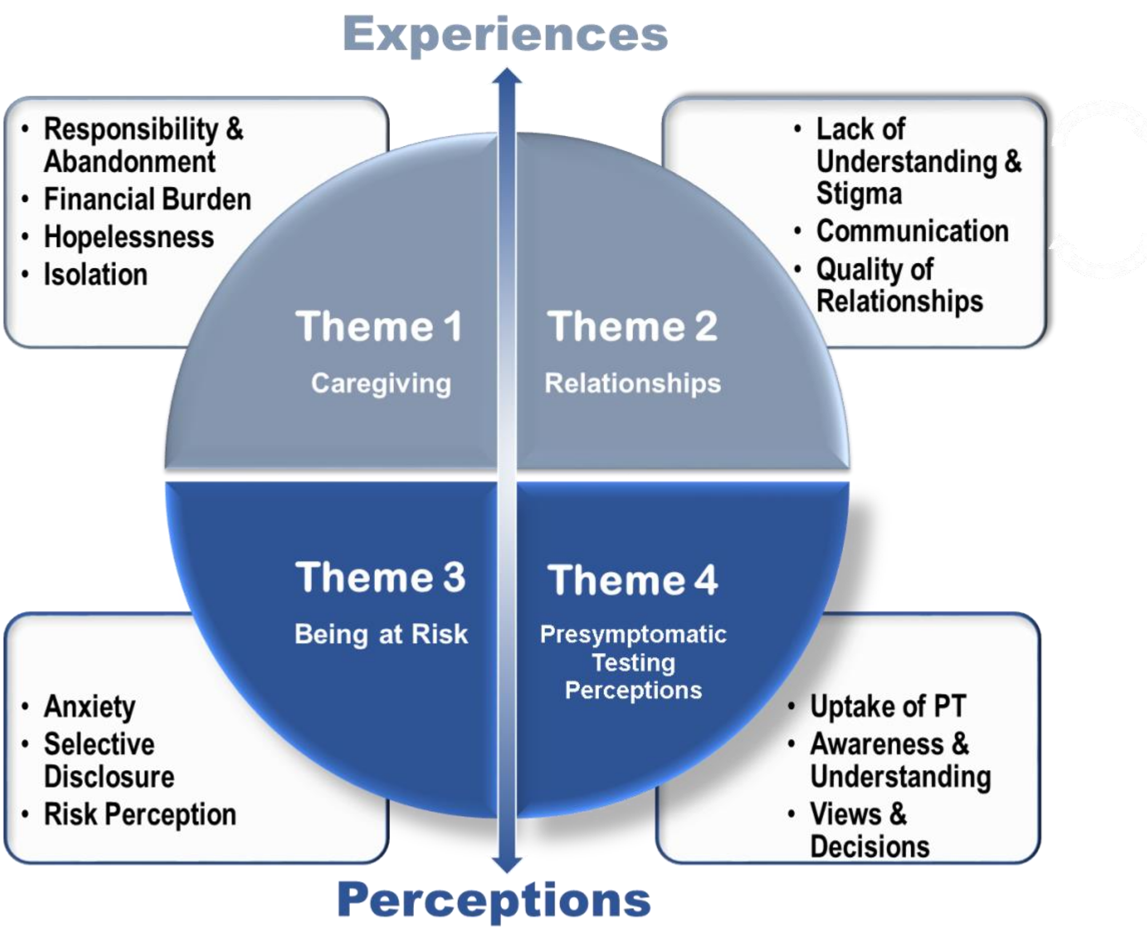


Figure 3: Illustrates the Themes and Subthemes reported in this chapter

As is illustrated in the figure above, the themes are connected, as the participants' experiences of the condition had a major impact on their perceptions of their risk and their decisions. The first two themes cover the main **experiences** of the participants, which emerged from the data. The last two themes cover the participants' **perceptions and decision-making**. Previous research has reported that the cultural, environmental and personal experiences of individuals' influences their perceptions and uptake of PT (Greenberg *et al.*, 2012; Rodrigues *et al.*, 2012; Sizer *et al.*, 2012; Kromberg, Sizer and Christianson, 2013).

3.4 THEME 1: CAREGIVING

> *"…I mean, he, he can't do anything for himself, he, uh… even when he goes to the toilet it's difficult, and the thing is, it's got a huge impact for people around him."- Ben*

Caring for those affected with SCA, places several significant burdens on the individual's family. The debilitating symptoms of SCA result in the affected individual becoming completely dependent on others for their emotional, physical and financial needs (See Section 1.2.3, page 15). Caring has previously been reported to increase the carers' awareness of their risk and impacts their perception of their genetic risk (Dondanville *et al.*, 2018). The experience of caring described in this theme was often linked to the participants' beliefs and fears (See Theme 3, page 51 & Theme 4, page 58).

The participants' experiences of the burden of caregiving are described under the following subthemes:

- Responsibility & Abandonment
- Financial Burden
- Hopelessness
- Isolation

3.4.1 RESPONSIBILITY & ABANDONMENT

> *"She can't even say I am going to take a cup, I want that, so if I am not there, who is going to look around after her?" – Maria*

As discussed in Chapter 1 (See page 10), the progressive loss of independence caused by the symptoms of SCA, results in the need for a full-time caregiver. During the interviews, the role of caregiving was often described as having been taken on by the affected individual's spouse and/or children. This is supported by the findings of previous literature which reported that the spouse was the family member who most often took on the responsibility of caring (Hayden *et al.*, 1980; Aubeeluck and Moskowitz, 2008). However, other research reported that children often take on the role of caring, referring to them as young caregivers (Kavanaugh, 2014).

During the interviews, other relatives were also described to have taken on the responsibility of caring, however, this was often associated with descriptions of abandonment of the affected individual. This was the case with Sofia who, at the time of the interview, was taking care of her affected brother.

> *"No, it is still, like the one brother of mine, the 48-year-old, I had to take him in because his family just abandoned him, didn't wanted to care for him and so I had to take him…" – Sofia*

The experience of affected individuals, being abandoned, emerged frequently in the interviews. These experiences were often associated with the participants' own concerns of abandonment (See Theme 3, page 51).

In the current study, all the female participants had experience with caregiving. These participants often described taking on the role because they felt a sense of responsibility to the affected individual/s. Although these participants acknowledged that it was their decision to take on the role, they also expressed feeling as though they did not have a choice. This feeling of forced sense of responsibility is evident in the extract below and some other quotes of Maria and Sofia in this section.

> *"So, I don't know if, I know it's my choice but sometimes I feel like I don't want to take care of her again, I don't feel like taking care of her [struggling for breath]…[Whispers] and she's my mother!!! Nothing I can do so, if I leave her, then who is going to take care of her as well?" – Maria*

The sense of responsibility that the carer felt was described in one study as a feeling of a 'duty of care' and by another as being "duty-bound' (De Villiers, Weskamp and Bryer, 1997; Aubeeluck and Moskowitz, 2008).

The burden of the role of caregiving was further exemplified for some participants by the nature of the condition, which leads to the repeated need to care in successive generations. For Maria, the responsibility of caring felt never-ending. In her interview she described going from caring for her grandmother to caring for her mother.

> *"…We stay with her (my grandmother) until she passed away in 20…15. 2015 past by and buried her, 2016 my mother started to shake" – Maria*

The strain on family members caused by the tendency of caregiving to extend for decades has been reported in several HD studies (Williams *et al.*, 2000; Aubeeluck and Moskowitz, 2008). This was described as having the unique implication of leading to families anticipating the condition in unaffected family members (Williams *et al.*, 2000). This anticipation of disease onset in unaffected individuals also emerged in this study as "Symptom watching" (See Section 3.6.3.3, page 56).

3.4.2 FINANCIAL BURDEN

"Ya, ya, (Yes, yes,) and I mean it's put a, it's put a lot of like, like, strain on, on everybody and not like emotionally but financially and stuff like that as well. So, um… ya (yes)." – Ben

Throughout the data collection, participants indicated that caring for an individual with SCA, was associated with a number of physical, emotional and financial burdens. Some participants described relying heavily on the monthly disability grant they received from the SA government. The grant was however, also described as not being sufficient to relieve the financial burdens of caring, so many of the caregivers also work to support their relatives. In her interview, Sofia described how she had to put her dream of retiring on hold and adjust her life so that she could care for her brother financially.

> *"I can't, like it's expensive to cart them around, to pay for things, to buy things, to just to see to them in general, when there's no contribution from them. I mean they are on the grant but what is that? Can't really contribute to anything so, I just thought "I can't expect them too." Therefore, I… I'm still working and still gonna (going to) work for the next five years. So, but it's (it is) okay, it now gives me time to make provision for whatever." – Sofia*

Similar findings were reported in a previous SA study on HD where the various financial burdens of caring for an individual with a neurodegenerative condition were described (Hayden *et al.*, 1980). This study is often quoted for its suggestion that for every individual that has HD the consequences are suffered by ten others (Hayden *et al.*, 1980). Of significance is that even though this study was conducted 40 years ago it also reported the disability grant to be insufficient (Hayden *et al.*, 1980).

The participants described the need for continuous healthcare visits as acting as a financial burden, as well as requiring transport to clinics. Previous research done in the Western Cape reported similar difficulties in the HD population in terms of affording public transport and managing the affected individuals' symptoms while travelling (Futter, Heckmann and Greenberg, 2009).

3.4.3 HOPELESSNESS

> *"[Laughs] Ya (Yes), just like you are helpless within it, you don't have enough options." – Sofia*

During the interviews, a sense of hopelessness emerged amongst the participants, both surrounding their own future and that of their relatives. Hopelessness was linked to many of the topics in this study (See Theme 4, page 58). The hopelessness the participants felt, was usually associated with the lack of effective treatments, cures or research available for SCA. Some participants expressed difficulty coming to terms with the lack of available interventions, as is demonstrated in the quote below.

> *"You're still in the hope like 20 years from now, you think to yourself there might be a cure. I mean it's, it's 2020 and we got flying cars and stuff, but I mean, you can't have a cure for this which doesn't make sense." – Ben*

Other participants felt hopelessness as they had no way of easing their relatives' suffering. During the interviews, many participants mentioned how the medication that their relatives were prescribed had been ineffective at relieving their symptoms. In his interview, Juan described feeling hopeless as he could not help relieve his father's suffering.

> *"Ag... ya (yes), everyone is ya (yes), feeling bad, bad for my dad but ya (yes), that's, there's nothing really you can do, otherwise than say, when we go away for weekends, we take him with..." – Juan*

To counteract the hopelessness they felt, some participants described actively searching for hope for their affected relatives such as, taking their relatives to healthcare specialists, searching for clinical trials and/or trying alternative medicines. In particular, the use of alternative medications, such as hemp oil and cannabis pills, emerged frequently in the interviews.

> *"So, they… I mean they are doing well it's just that um… part of this, this disease progression I think it's got to do with um… um… spasms also which is very painful. Which they are battling with because the management that they on currently, is not helping much and there's not much else that they can be given. So, we looking at um… alternatives. What else can we do? What else can we use? So, I'm even looking at hemp oil… for them." – Sofia*

The use of alternative medications to treat the symptoms of various neurological conditions has been reported to be common in previous literature (Ryan and Johnson, 2002; Benbadis *et al.*, 2014). Additionally, the desire to feel hopeful was reported as a reason for alternative medicine use by Ryan and Johnson (2002), however it was not linked to dissatisfaction with the effectiveness of conventional medication as seen in this study. The participants had found alternative medications to be effective at relieving their relative's symptoms.

> *"So, the hemp oil which I've bought for them, um… after two weeks it started having affect and then they had no spasms./…/ Which was wonderful." - Sofia*

These findings cannot be substantiated as there is no available literature on the safety and efficacy of cannabinoid use for SCA patients, however research on the topic is reported to be underway (Gómez-ruiz *et al.*, 2019). Additionally, research suggests that SCA patients may show similar benefits of cannabinoid use that has been reported in HD patients (Gómez-ruiz *et al.*, 2019). Although research into the use of these medications for HD patient has shown some promising results (See Section 1.2.2, page 14), the results are conflicting and the studies limitations require that these findings be validated (Consroe *et al.*, 1991; Abdel-Salam, 2017; Bachoud-Levi *et al.*, 2019; Russell, 2019).

Despite the participants' experiences of the benefits of the use of alternative medicines, they described having experienced some issues with their use. In her interview, Sofia commented on the expense of obtaining the medications for her siblings (See Section 3.4.2, page 42). Whereas, Juan and Ben described the dangers of the use of cannabis pills as it had led to their father falling and breaking his hip.

> *"…like it's the new dagga, dagga medication and, um... ya (yes), that night he said he took one and was fast asleep and he just got up and feel like a new person and he get out of the bed and ya (yes), fall down, broke his hip, had to go for hip surgery and from that time he didn't walk again." – Juan*

A few studies have reported some adverse side effects to CBD use, but these cannot be generalised (Russell, 2019). Some of these findings could however be consistent with the findings of this study, such as the indirect endangerment of users caused by the sedative side effects (Benbadis *et al.*, 2014; Bachoud-Levi *et al.*, 2019; Russell, 2019)

3.4.4 ISOLATION

"I don't socialise that much. /…/ I just stay at home and do nothing. I don't know if I'm used to not going home (out) or anything. I don't have friends, no people, if you tell people this is what is going on and then they will make it a laugh of you. Like, this is what she is going through, this is what is happening in her life, she's I don't know what…"– Maria

The need for constant caring for the affected individual was attributed by some participants to the caregiver experiencing restricted freedom. In her interview, Sofia described being unable to go out as she always had to make arrangements for the care of her brother and how caring for someone with SCA impacted her freedom.

> *"Now it's gone back to having to take care of somebody and you can't move like you want too. You don't have the freedom to go away for weekends and go plan trips overseas so it, it impacts on my life, but I mean he's my brother you know what else can I do? I need to take care of him." – Sofia*

In the interviews, instances of the affected individual refusing to leave their house were described. The participants explained how this had contributed to the caregiver's restricted freedom and isolation because the caregiver felt obligated to stay with the affected individual.

> *"…he's like no, you guys can rather go, I'll look after myself, although he does (knows), he won't be able to look after himself, you understand? Um… and then obviously my mom obviously feeling that she has to stay at home so, ya (yes), there, it's like she's confined to, to a certain area, into town, in the house and stuff like that so." – Ben*

Previous literature has also found a tendency towards social isolation amongst caregivers (Hayden *et al.*, 1980; Aubeeluck and Moskowitz, 2008). Several reasons have been proposed for the caregivers' isolation in previous studies, including the reluctance to tell outsiders about the situation, the structure of the family and the nature of the illness (Frank and Slatcher, 2009). Some of these are discussed in the next theme, such as a lack of familial support, familial conflict and the breakdown of relationships (See Theme 2, page 46). Additionally, as can be seen in the quote from Maria at the top of the section the reluctance to tell outsiders about the condition also came up in the interviews as leading to isolation, this concept is discussed in theme 3 (See Section 3.6.2, page 52). Other previously described factors that did not emerge in association with social isolation in this study included repeated social embarrassment and rejection (Hayden *et al.*, 1980; Aubeeluck and Moskowitz, 2008). Although, these concepts did emerge in different contexts (See Section 3.5.1, page 46).

3.5 THEME 2: RELATIONSHIPS

The presence of SCA, affected all the relationships within and surrounding the participants' families. The severe impact that the presence of HD has on family functioning has been described in previous literature (Vamos *et al.*, 2007). In the present study the participants' experiences of SCA's impact on relationships was highly associated with many of their beliefs and fears (Discussed in Theme 3, page 51 & Theme 4, page 58). Although the impact of the condition on the participants' relationships were unique to their circumstances, some common topics came up in the interviews.

The results are presented under the following subthemes:

- Lack of understanding and Stigma
- Communication
- Quality of Relationships

3.5.1 LACK OF UNDERSTANDING & STIGMA

> *"It's looks I see that's given their way. /…/ Like either it's pity or it's just judgmental." - Noah*

The participants expressed that the broader community had generally been supportive, however some instances of stigma and judgement were described. One of the most common experiences described in the interviews was a lack of understanding of the condition in the community. The participants explained that their relative's movement symptoms had often been misinterpreted, as either old age or the individual being an alcoholic.

> *'Ya, it was, um… like it got, he couldn't walk straight, like a person, like a drunk person." – Juan*

Additionally, all the participants indicated that before they had found out about the diagnosis, they had also misinterpreted the symptoms in their affected relatives and not realised that it was inherited. For most of the participants finding out about the condition had helped them notice the link between their family member's symptoms.

> *"Um… she (Sofia's mother) actually had some symptoms, but we didn't know what it was, at the time and then we could uh… um… sort of go back and think about our grandfather who had same symptoms. At the time we didn't link the two. Then we obviously thought about everything and then when we've known the diagnosis and its symptoms, we knew that, that is how our grandfather was." – Sofia*

For some affected individuals the misinterpretation of their symptoms, had led to the affected individual enduring unpleasant experiences and stigmatisation. For example, some participants mentioned, people staring and making comments when they were in public with their affected loved ones (See Noah quote, top of the section). The stigmatisation experienced by some affected individuals however, had been worse than looks and comments. In his interview, Ben, described how his father had been arrested as he was accused of driving under the influence of alcohol.

> *"He, he, eventually got pulled over by, by ah… police back in the day and they really thought the was drunk and I, it's obviously trying to defend himself and say, guys I haven't been drinking for the last ten years, um… I'm not drinking and stuff, so, this is this condition that I do have, uh… they eventually ended up locking him up for stuff like that, saying that he's under the influence and stuff, and ya (yes), that it, that was another case." – Ben*

One participant described being afraid that people's misinterpretation of her mother's symptoms may put her mother in harm's way.

> *"She is talking to herself and I am scared. She's like going out at 2am talking to herself, shouting. You know in our environment, where we live, if you do those kinds of things people, they will point you like you are a witch, why are you doing this? Why are you doing that?" – Maria*

This lack of understanding and stigmatisation of affected individuals was not, however, limited to the community, also being common within the participants' families. Lack of understanding was described by Juan and Ben in their family, explaining that their mother had thought their father had Motor Neuron Disease (MND)[1]. This familial misconception had led to lasting confusion for some participants about the condition, their risks and PT (See Theme 3, page 51 & Theme 4, page 58).

> *"Uh… my mom all, always thought it was like MND, she told me no it's something similar to MND, what, uh… the, obviously the disease Joost van de Westhuizen[2] had, coz (because) obviously his speech was also affected…" – Ben*

In some of the interviews, the lack of understanding in the participants' family's had led to stigmatisation and abandonment of the affected individuals (See Section 3.4.1, page 41 & Theme 3, page 51). During her interview, Maria described how her stepfather's lack of understanding of the limitations imposed by the condition on her mother, had led to conflict and his eventual abandonment of her mother (See Section 3.4.1, page 41 & Section 3.5.2, next page).

> *"You see now she's (Mother) having this problem and they (Stepfather) say "go away I don't want you anymore because who is going to want you because you can't walk you, who's going to want you because you are not doing this for me anymore." "- Maria*

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[1] Motor Neuron Diseases (MND) are a group of progressive neurodegenerative diseases caused by the degeneration of the motor neurons which lead to the loss of spine and brain function over time.

[2] Famous SA professional rugby union player who was diagnosed with a type of Motor Neuron Disease (MND) called Amyotrophic Lateral Sclerosis (ALS) and passed away from related complications in 2017.

3.5.2 COMMUNICATION

The presence of the condition had affected communication both within families and with the broader community. It is important to note that, similar to previous subthemes, this topic is linked to the experience of caregiving (Theme 1, page 41) and the participants' views and decisions (Theme 3, page 51 & Theme 4, page 58).

The participants' experiences of the effect of SCA on communication, are addressed under the following headings:

- Secrecy
- Conflict & Breakdown

3.5.2.1 SECRECY

"It's somehow become like a taboo subject in our family right now, my mom doesn't speak about it. Not sure why." – Noah

Many forms of secrecy existed in the participants' families. In her interview, Rose recalled how the diagnosis had been hidden by her great-grandmother from the family for years, due to fear of it highlighting her infidelity. This secrecy had led to the affected individuals being stigmatised (See Section 3.5.1, page 46).

> *"Ya (Yes), they just, they thought ya (yes), a lot, my mother says a lot of the people thought the mother was a drunk. And, the uncles were drunks and it wasn't nice growing up like that because someone actually knew in the family what was going on…" – Rose*

Although not a main finding of Keenan *et al.*, (2013) this study reported a similar case where illegitimacy had blocked the transmission of information about HD across several generations.

Familial secrecy was a topic that emerged frequently in Noah's interview, as he described how the condition was a taboo subject in his family, hardly ever being discussed openly (see quote at the top of the section). Furthermore, he described how his family would avoid telling their relatives when they had started to notice symptoms. Additionally, he described how his family had gone to great lengths to keep the condition a secret from him for years. This secretiveness led to Noah feeling anger and resentment towards his family, especially as it could have affected his reproductive choices (See Section 3.7.3, page 61).

> *"(I felt) a bit betrayed. Like, why would you keep something like that from me? Like, that is something that I would have wanted to know. Like, coz (because) like I said I wouldn't want to have kids, if I have it. I wouldn't want to pass that on. Like, what if I was to have kids already. I'm married three years and I had to choose in the beginning of my marriage to have kids and they only told me last year." – Noah*

This participant hypothesised that it made his family feel better not to acknowledge the presence of the condition.

> *"I think that's the reason. Maybe the less they talk about it, the better they will feel about themselves because knowing more scares them, probably." – Noah*

This participant's feelings of betrayal are consistent with the finding by Stuttgen *et al.*, (2020) that not being informed about the risk of HD until adulthood can have a negative impact on the parent-child relationship.

Additionally, as was the case with Sofia decision to tell Noah about his risks, Stuttgen *et al.*, (2020) reported that parents often communicated risk information due to a "triggering event" such as when their child is thinking about getting married or planning children.

3.5.2.2 Conflict & Breakdown

Several aspects of SCA were described to cause conflict and the breakdown of relationships. This is consistent with the findings of previous research involving HD families (Vamos *et al.*, 2007). Like these previous studies the symptoms of SCA were associated with conflict in this study, however, not as common as that reported in HD. This is most likely due to the limited psychological symptoms associated with SCA.

On the contrary to what has been reported in HD literature, the most common cause of conflict described by the participants in this study was the burdens of caregiving (See Theme 1, page 41). The conflict described by the participants surrounding caregiving was often linked to who would take on the role and the quality of care that was being provided. Throughout Maria's interview, she described conflict with and resentment towards her family members, due to their lack of support with the responsibility of caring for her mother and grandmother. As can be seen, this experience affected Maria's current views and decisions about having more children (See Section 3.7.3, page 61).

> *"So I don't want to put my child in the same suffering that I did which is for the past 12 years, past 10 years, past 15 years, it's been so much hard and it seems like in my family I'm the only one that's caring, anyone else, it's (is) not, they don't, they don't even lend a hand" – Maria*

Similarly, Noah described how some of his family members had lost contact after disagreements over how to best care for their affected family member.

> *"He (Grandfather) said that "he could take better care of her (Grandmother)". He didn't… he made it worse./…/ Uh… he…he kept giving her solid food like, chips and things like that, things that hurt her and made her more sick, so… So yeah, he made things, that's why we… we don't speak. That's, that's… the two siblings took grandpa's side." – Noah*

Additionally, the strain on partnerships associated with the condition was mentioned throughout the interviews, often leading to their breakdown (See Section 3.5.2.3, page 50). Maria described how having to care for her mother had left her with no time for her partner and friends, inevitably leading to the loss of those relationships.

> *"Um… We fight and my mother when come back so… but I didn't have time for him so, I was like it's fine let's just continue but you do take care of the baby, that's why I do that's why go to school in silverside. He's paying the fees and all that." – Maria*

3.5.3 QUALITY OF RELATIONSHIPS

The presence of SCA affected the quality of relationships between the affected individual and other family members. This reduction in the quality of relationships was, most often, linked to the symptoms of SCA. For example, Ben described how his parents' relationship had been completely altered by the onset of the condition, where the couple had grown apart emotionally.

> *"It's more like I said, it's more the frustration and everything and I could see that eventually, that, that's playing a major role and that eventually my mom is just obviously trying to, to, to get him in a position or obviously assist him as the best as, as she can but I mean, then eventually you do stuff just because you do it, it's not, there's no, for instance, you just give somebody breakfast in the morning and you just put it there and then you leave, you understand? Eventually that got a whole emotional thing on her and obviously on him. You can't have proper conversations." – Ben*

Additionally, various ways that the condition had affected the participants' parent-child relationships, emerged in the interviews. These experiences seemed to be dependent on the age of the participant, when their parents became symptomatic. In their interviews, Maria and Rose described having similar experiences of growing up with the condition, including physical abuse and the burden of having to care from a young age. These burdens are similar to what has previously been reported among young carers (Forrest Keenan *et al.*, 2007). During their interviews, however, Maria and Rose described having different perceptions of the burden of caring from young, these differences were described in association with the amount of support each had received. This is consistent with the previous findings of a good social support system acting as a protective factor for young carers (Forrest Keenan *et al.*, 2007).

Despite the differences in these participants' experiences, both Maria and Rose expressed feeling that their development had been neglected. Previous research has reported the tendency for the neglect, isolation and invisibility of caregivers, especially young carers whose needs are often overlooked (Frank and Slatcher, 2009).

> *"I wanted to have another baby since I was going to get sick, I wanted to have another child young. I know it sounds stupid but, when I grew up, my mother couldn't teach me anything, not to cook, clean, washing out his school clothes when you come from school, doing, doing all the things that I had to do, my mother never taught me any of that. We had a maid that was at home and she hardly ever took any time to teach me anything. It wasn't her place though." – Rose*

The participants' own parent-child relationships often affected their own reproductive decision-making. As can be seen in Rose's quote above, where she stated that her decision to have her children at a young age was based on the hope - that if she had them young enough - that she could do for her children what her mother could not do for her (teach her), before she became symptomatic. Similarly, the other participants' reproductive and PT decisions were associated with their experiences (See Section 3.7.3, page 61).

Despite being older when their parents had become symptomatic, Sofia, Juan and Ben also described the symptoms of the condition affecting the quality of relationship they could have with the affected parent. For Juan the condition meant that he and his father could not do the activities they used to love doing together. Whereas for Ben it meant he could not have a relationship with his father as he lives far away and his father could no longer talk on the phone.

3.6. THEME 3: BEING AT-RISK

> *"Ya, it is actually quite… overwhelming if you think about all the things, if you sit still and just be in your thoughts, it's quite a lot." – Sofia*

Living with the uncertainty of developing SCA, was often described by the participants as emotionally overwhelming. As mentioned above, the participants' experiences were often associated with their current beliefs and perceptions. The participants' experiences of being at-risk of inheriting SCA and their perception of this risk, are reported under the following subthemes:

- Anxiety
- Selective Disclosure
- Risk Perception

3.6.1 ANXIETY

> *"It's scary. It's scary that… knowing that… that could happen at any time. Conditions could start at any time. Most of the time it starts when I'm much older but the fact that it might happen, it's scary." – Noah*

In the interviews, the participants described experiencing much anxiety surrounding the uncertainty of their risk. The participants' anxiety was often linked to their experiences.

Most of the participants described finding out about SCA in their family as overwhelming and scary. On the contrary, Rose felt relief when learning about the diagnosis, as it explained what she had noticed in her family. She did, however, describe finding out about her personal risk as scary.

> *"It wasn't really a problem because, we were used to it already, she couldn't walk anymore, she was on diapers, we were helping her with feedings and stuff so, we were used to it, so, it wasn't a shock, it was, more of a relief to find out exactly what was going on. After that, we got older and we realized it's genetic. When I read up on it, I was a teenager then, I read up on it then I was like (swore), but genetic means that I can get it, they never said that." – Rose*

Data analysis revealed that most of the anxiety, described by the participants, was linked to their fear of inheriting the condition. The fears associated with getting SCA expressed by the participants, are shown in Table 9.

Table 9: Highlights the common fears described by the participants during the interviews and provides a quote to describe each fear

Fear of Suffering	*"I know that my grandma did not go peacefully. Shoo… she suffered the whole time, until her last. I wouldn't want that happening to me. I'd rather die at a younger age. Quick death. I wouldn't want to suffer like that." –Noah*
Fear of Being a Burden	*"…So I don't want to put my child in the same suffering that I did. Which is for the past 12 years, past 10 years, past 15 years, it's been so much hard." – Maria*
Fear of Abandonment	*"I don't even need a man that, right now, I don't want any dating or anything like that because I am scared that maybe the guy will say, okay, let me marry you, let me do this for you then it ends up the same thing, that, I went through with my mother and my grandmother, so… for me… (Sigh)… I'm good." – Maria*
Fear of Stigmatisation	*"No, I wouldn't want that done to me. /…/ Ya. I don't want them treating me differently. I'd want them to treat me exactly the same way as how they have been treating me before. I don't want anyone's pity." – Noah*

Similar fears and anxiety were reported by Hayden, MacGregor and Beighton (1980) regarding HD. Additionally, they described how those affected with the condition often anticipated abandonment (See Section 3.6.2, below). A study found that the fear of abandonment interplays with the at-risk individuals' fear of being a burden, with these individuals expressing understanding of their relatives' decision to leave (Dufrasne *et al.*, 2011).

Through data analysis, it emerged that the participants' experiences and fears had resulted in behaviours like selective disclosure (discussed in next Subtheme) and self-isolation. Selective disclosure was common amongst all the participants, however, self-isolation was more common amongst the participants who acted as caregivers (See Section 3.4.4, page 45).

3.6.2 SELECTIVE DISCLOSURE

"…I think, the fear of rejection and abandonment is quite huge…" – Sofia

Within the context of this research study, selective disclosure refers to a behaviour where the participants choose to only disclose the presence of SCA in their family to a select few trusted individuals. Previous research has noted this reluctance to inform outsiders of the condition as being of specific importance in disorders like SCA and HD, where secrecy and stigma have often been found to surround the conditions (Williams *et al.*, 2013; Kavanaugh, 2014). In the interviews, the participants described only disclosing the condition to close friends and partners in order to prepare them. One situation that was described to result in disclosure of the condition, was when an individual was going to come into contact with the affected family member, thus would notice the symptoms.

"*Mm… And like my friends, I mean, I've explained it to my friends because they come to my house and when we go out I take him (her Brother) along, so obviously they know something is wrong with him and I had to explain to them what it is and… but they have been very supportive."– Sofia*

Another reason given by the participants, for disclosing the condition, was to prepare their romantic partner for their potential future and to determine whether they would be willing to care for them. Some participants described feeling that they had an ethical obligation to disclose the condition with their partner before marriage.

"She must be prepared, and obviously, I think it will be very selfish if you know you got this disease and at 55, more or less, or at 50 you'll start showing the symptoms. Obviously, stuff will happen, more or less to what happens with my dad and my mom and now she is obviously tied in with you in this and, without her having like, what's the word, without her having like a… she's just there. A choice…" – Ben

Stuttgen *et al.*, (2020) reported that at-risk individuals often communicated their risks with their significant other while dating or before marriage. Whereas other research found that although partners were normally informed about the condition by their partner, this disclosure happened at different times and to different levels of awareness (Keenan *et al.*, 2013). Additionally, this disclosure was found to contribute to the couples coping (Keenan *et al.*, 2013). Partners that had only been told after marriage expressed feelings of anger, bitterness and resentment (Keenan *et al.*, 2013).

The participants described how when they did disclose the condition to their friends and partners, they found it to be very anxiety provoking and scary. The participants' anxiety was most often due to their fear of abandonment.

"Uh… it was scary [Breath Out]. I, I did, I did tell my wife about it before, before getting married. Did explain to her what it could, what could possibly happen and all that. She was still okay with it anyway so, that's why I married her [Laughing] so, I know I have someone to take care of me in my old age when that happens, eventually. So, ya (yes)." – Noah

The majority of participants described how their partners and friends had been very supportive when they had disclosed the condition, offering to come with them for GC and promising to look after them if they became symptomatic in the future. This is consistent with the findings of previous research, which establish that at-risk individuals' romantic partners are often their primary source of support and that risk communication is often beneficial for the relationship (Stuttgen *et al.*, 2020).

"*He was even the one who said, "We must go for", there was genetic counselling here in Groote Schuur, he said "he will go with me if I want too". So, he was very supportive, even now." – Maria*

Despite their partners' reassurances, the participants remained afraid of being abandoned in the future. One participant explained her continued fear, by describing that it's easy to be supportive when the condition is not yet a reality. This participant's fear of abandonment was linked to her decision to delay going for PT (See Theme 4, page 58).

"Ya. So, um, at the time my husband said, I mean he was very supportive, but I was just like wondering, is he really gonna (going to) be accepting of it. It's easy to say now, when there's no result but how will he then respond if it should come, actually when it's a reality and that was a bit overwhelming for me…" – Sofia

As can be seen in the quotes, the fears expressed seemed to be related to the participants' as well as their family's experiences of SCA (See Theme 1, page 41 & Theme 2, page 46). Additionally, it emerged that the anxiety the participants felt about inheriting the condition, was often related to their age and led to behaviours like symptom watching (See Section 3.6.3, below).

The fear of abandonment was reported to manifest as the at-risk individuals' reluctance to disclose their genetic status to their children, not to family outsiders as described in this study (Dufrasne *et al.*, 2011). Interestingly, previous research reported that at-risk individuals often withhold their risk status from their partners and children (Hayden *et al.*, 1980).

3.6.3 RISK PERCEPTION

> *"Oh… heck, I thought I knew but I'm not sure anymore." – Sofia*

All the participants in this study (apart from Noah), had attended at least one GC session (See Table 10, page 58). As such, all the participants should have had their risk of inheriting SCA explained to them. All the participants were aware that they were at-risk of inheriting SCA, however, when asked what their personal risk was, all the participants in this study expressed uncertainty and confusion (See quote above).

This is contradictory to the findings of De Villiers, Weskamp and Bryer, (1997) which reported that the majority of their at-risk participants had not received GC about SCA, were unaware of their risk or were in denial of their risk status. Despite the age of this research, it is considered significant to this discussion as it is the only SA study to date that has explored the awareness and attitudes of those at-risk for SCA. The difference reported here could be attributed to several factors including the age of the study, that the study only recruited at-risk individuals from one family from a rural area, whereas the participants of the current study were mainly recruited by GCs and came from different families from an urban area (See Chapter 2, page 25 & Section 3.2, page 37). However, despite the differences, there were some common findings between the current study and the previous one (See below). The participants' risk perception were often linked to their beliefs and fears.

In this subtheme, the participants' risk perceptions are explored under the following headings:

- Personal Beliefs
- Age Related Concern
- Symptom Watching

3.6.3.1 Personal Beliefs

The participants' risk perception was often based on their personal beliefs of inheritance, rather than the risk given to them by the GCs. This was found in a previous SA study where the at-risk individuals 'perceived' risk did not correlate with their 'assigned' risk (De Villiers, Weskamp and Bryer, 1997). Additionally, at-risk individuals have previously been reported to use a number of 'lay beliefs of inheritance' to determine their risk (Smith *et al.*, 2002)

In this study, some participants' beliefs were based on the inheritance pattern that had been seen in their family. For example, Maria felt that she may get it because she is the firstborn child of her mother.

> *"I… I just saw the pattern. Like, it's a first born on his mother's side and I'm the first born on my mother's side so I said maybe it's going to go with first borns so… I said ah… I need to know." – Maria*

Smith *et al.,* 2002 found a similar perception of risk in their participants based on sequence specific inheritance, but this was based on the concept of if one individual is affected it reduces the risks to other relatives.

Another personal belief that was described to affect the participants' risk perceptions was the perceived similarity between the affected individual and certain family members. Due to his perceived similarity to his affected father, Juan believed he was likely to have inherited the SCA mutation.

> *"Um... ya (yes), I think I will have it one day probably because ya (yes), Uh... me and my dad like, like you say, our genes are the same as well. /…/ But ya (yes) I don't think, I think ya (yes), me and my sister we will probably, probably have it but not my Uh... twin brother./…/ He's more to my mothers' side, the, the genes, the ya (yes), the gene." – Juan*

The resemblance of an individual to an affected relative whether in appearance or temperament being used as a measure of risk has been reported in several studies (Van der Steenstraten *et al.*, 1994; De Villiers, Weskamp and Bryer, 1997)

3.6.3.2 Age Related Concern

The participants' anxiety about and perception of their risk was often influenced by their current age, compared to the average age at which their relatives had started showing symptoms. In her interview, Sofia described that she had found her 40s very stressful as this is when most of her relatives had started showing symptoms.

> *"Yes, it (my 40s) was (were a stressful time for me) because that's when most of my mom and her brothers and sisters started developing symptoms and all my siblings and even my uncle's children, both the boys, they were, they had symptoms in the late 30s. And so, it was a stressful time for me." – Sofia*

Having now surpassed the average age of onset in her family, Sofia, believed that her risk of inheriting the condition should be lowered. She did, however, acknowledge anticipation as a contributing factor which had left her feeling uncertain about her personal risk. The same belief was expressed by a participant who hadn't gone for PT in the Van der Steenstraten *et al.*, (1994) study. Like Sofia this individual had passed the average of onset of the condition in his family therefore expected to have 'escaped' the HD gene.

This age related concern was a common experience amongst the participants. Several of the participants describe not being concerned about their risk when they were young, as they felt they had time. Most of the participants described only starting to worry about their risks and considering PT, when they got close to the average age of onset of the condition seen in previous generations of their family (See Theme 4, page 58).

"I was about 13, but, at that point we never really took note of it coz (because) I thought to myself I was basically still a baby then, I thought to myself, how long am I going to take to get to 30. My mother only got sick at 30, at that point I didn't know that you can actually just get sick at any point in time." – Rose

The tendency of at-risk individuals to use age comparisons in their risk perceptions has been described in several studies in different forms (Van der Steenstraten *et al.*, 1994; Smith *et al.*, 2002). In the current study, this age related concern was suggested by Sofia to be related to young individuals feeling invincible.

"I think they are still a bit too young to grasp the, the intensity of, of the diagnosis like this but uh, but they just aware of it but I don't think they know exactly what it is./…/ As well. Then like, they at the stage when they invincible [chuckles]..." – Sofia

3.6.3.3 SYMPTOM WATCHING

A common topic that emerged during the interviews was symptom watching. In this study, symptom watching refers to the participant's described behaviour of assessing whether they or a relative have started to develop symptoms. Although not reported as 'symptom watching' previous research has described this behaviour in individuals at-risk for HD (Smith *et al.*, 2002). The behaviour was described as an 'over-vigilant symptom search' that allows those at-risk to interpret unusual behaviours as possible precursors of disease onset (Smith *et al.*, 2002).

In the current study, the participants' symptom watching behaviours were often related to their anxiety and fears about developing symptoms. In his interview, Ben described that the behaviour was an involuntary anxiety induced reaction.

"I've been, sometimes I'll just stand like this and suddenly I'll just tilt to the side, and I'm like, why is this happening, is it normal or whatever, so, these, these things are constantly on your mind and you laugh it off and you move on, you understand? So, but, that's exactly how my dad started./…/ It's not like, ya (yes), not looking for it but, in a certain way you feel like, you feel like ya (yes), there are some similarities and uh… ya (yes), which is, which is, like I said which is quite, which is quite scary." – Ben

Symptom watching was often used by the participants to determine their, as well as their families', risk of having SCA. In her interview, Sofia described symptom watching, especially as she got close to the age of onset of the condition in her family (See Section 3.6.3.2, above).

"No, I didn't know at the time, I didn't think about it a lot, in my 30's. And, because there were no symptoms but I thought "Woo… 40's, it might start developing" and every time it's like you looking out for the symptoms, you wanting to put everything down to, could this possibly be a symptom, could this? If you drop something, is this a symptom? You know, like you were just searching and assessing all the time." – Sofia

Similarly, one participant described watching for symptoms in his mother in order to determine his own risk of getting the condition.

> *“I haven’t seen the symptoms in my mom so… so far, I’m hopeful that I might not get it but um… for now, I’m just… I’m watching her.” – Noah*

Other participants also described, watching for symptoms in their relatives, however this behaviour was explained to be due to concern for their relatives. This behaviour of determining the likelihood of getting HD based on the existence of symptoms and signs has been reported in previous literature (Smith *et al.*, 2002).

3.7 THEME 4: PRESYMTOMATIC TESTING (PT) PERCEPTIONS

"Yeah. I would like to know. I'd be scared though, but I would like to know." – Noah

Perception is a difficult concept to define, it has been said to begin with the stimuli we receive from the environment and end with our interpretation of it. The results of this study echo this concept as the participants' beliefs were intertwined with their experiences (Theme 1, page 41 & Theme 2, page 46). Throughout data collection and analysis it was clear that the participants' perceptions of their risk (Theme 3, page 51) and PT were complex topics.

In this theme, the participants' perceptions of PT will be explored under the following headings:

- Uptake of PT
- Awareness & Understanding
- Views & Decisions

3.7.1 UPTAKE OF PT

An understanding of the participants' exposure to GC and the PT process is essential to understanding the results described in this theme. Table 10 provides a summary of the participants' uptake of various stages of the PT process.

Table 10: Summarises the participants' experiences with PT

Participant Name	Attended information session	Initiated PT process	Completed PT process
Maria	Yes	No	-
Sofia	Yes	Yes	No
Rose	Yes	Yes	Yes
Noah	No	-	-
Juan	Yes	No	-
Ben	Yes	No	-

As can be seen in Table 10, only two of the participants in this study had ever undertaken PT and only Rose completed the process, with Sofia dropping out before receiving her results. This low uptake and follow through of the PT process amongst the participants in this study, is consistent with the low levels of uptake described by the GCs at UCT as well as those reported in SA by Futter, Heckmann and Greenberg, (2009). Despite the majority of the participants' lack of uptake of PT, they all expressed an interest in undergoing PT in the future. In the remaining subthemes, the participants' understanding, views and decisions regarding PT are explored.

3.7.2 AWARENESS & UNDERSTANDING

Previous research conducted in the Western Cape found a low level of awareness of PT amongst individuals at-risk for HD (Futter, Heckmann and Greenberg, 2009). In this study this was not the case as the majority of the participants were aware of PT for SCA. The difference in level of awareness reported in these studies, may be due to efforts made to improve awareness in the population following the results of the previous study (Futter, Heckmann and Greenberg, 2009). An alternative explanation, however, is that the purposive sampling methods used in this study yielded participants that had been for GC therefore were aware of the availability (See Table 7 on page 37 , Table 10 on page 58 and Chapter 2, page 25). Interestingly, despite the participants' previous attendance of GC and their awareness of PT, the participants still expressed several misconceptions of the PT process.

The most common topic that emerged with regard to the PT process was its length. Some participants expressed uncertainty about the length of the PT process, with participants showing a tendency to overestimate the number of sessions. One participant described feeling uncertain about the length of the PT process due to limited recollection of what was said in the information session.

> *"Um... it, it sounded like a not a big process but, ya (yes) you have to go a few times, I don't really remember what they said 100% but it, you must go for counselling first, for, I think for ten classes, hour classes and after that you can decide if you want to go for, ya (yes), do the test and give, get the result." – Juan*

For this participant, the perceived length of the PT process acted as a deterrent.

> *"I'll do the test, but ya (yes), don't, mustn't take weeks and months and years." – Juan*

The length of the PT process has been reported in several studies as having acted as a deterrent to PT for some individuals at-risk for HD (Dufrasne *et al.*, 2011; Hawkins, Creighton and Hayden, 2013). On the contrary, another participant expressed appreciation for the amount of support that the PT process provided.

> *"Um… I like the fact that there's support, um… not even only for me but people in general to, to, there is outlets, there is, um… pre-support and then counselling support after which I think is great because, I mean people deal with things differently and the fact there is support for me is great and I think it's good." – Sofia*

Another participant (Ben) did not have a problem with the length of time involved in the PT process, rather the expense that the multiple spread out sessions would incur due to the need to travel. The perceived expense of the numerous sessions seemed to be acting as a barrier for this participant, as he felt it required a lot of preparation.

> *"...And um… and all of those things make sense and I think it's, it's actually set up quite nicely, it is also obviously over a period so um… it is quite an expensive, type of thing that you need to get yourself in the right mind space and stuff like that." – Ben*

The distance required to travel has been reported to constitute a major barrier to the accessibility of PT internationally (Hawkins, Creighton and Hayden, 2013). Additionally, the financial burden and considerations that at-risk individuals who live far from the testing centre face when considering undertaking PT have been reported in a previous SA study (Futter, Heckmann and Greenberg, 2009).

Another aspect of the PT process that emerged in the interviews as a potential barrier to undergoing PT was the need for a suitable support partner. Although the participants can choose anyone to be their support partner during the process, all the participants associated the concept with a romantic partner. Although not a reported finding by Williams *et al.*, (2000) the quotes provided in the results section of this study, indicate a mentality of the spouse being the 'logical choice' for a support partner.

The participants' perceived need for a romantic partner as a support partner acted as a barrier to testing for some participants, as they did not yet have a romantic partner. In his interview, Ben described how he had just gone through a breakup at the time that he had been considering undergoing PT and this had resulted in him delaying testing until he had someone he could share the experience with.

> *"You need to have a person or family member that can assist you while you, while you doing these things, coz (because) I mean, you, you, you wanna (want to) know as a person, you want to know there's somebody that you can, you can, that you can speak to and like I said, fortunately I'm in a position where I do have somebody now, but a year ago, I thought that person I could obviously tell this stuff but that, that, that's not the person I would like to share this with." – Ben*

Whereas for other participants the need for a stable romantic partner had acted as a barrier as her boyfriend had not been perceived as a suitable support partner by the GCs.

> *"No, it's not that. When I started going for testing, the day I was here with (the GCs) them, my, my, they told me I need to get a support for the next time I came, so I'd have to choose either my father, so I said, "Why not his father then. We are having a baby." So, they said "No, it's fine as long as he stays throughout the whole process, especially with boyfriends and stuff you know there's gonna (going to) be a drop out so, they don't really allow it"." – Rose*

The need for a support partner was also reported as a barrier to PT in the Canadian study by Hawkins, Creighton and Hayden (2013). However, the reasons described for why the requirement of a support partner acted as a barrier to PT differed in that their participants did not want to have a support partner through the process (Hawkins, Creighton and Hayden, 2013). Whereas the participants of this study described not having a suitable support partner.

Other less frequent but significant misconceptions emerged in the interviews. The topics included the terminology used, who could be tested and the meaning of the results. These misconceptions may be explained in part, by Ben's description of how emotional he had found the information session.

> *"Ya (Yes), it's something that you obviously need to digest a little and think about it, coz (because) I mean it does affect you, obviously your, your life going forward. Um… and, and the info and stuff that they, that they shared, it's quite an emotional ride as well…" – Ben*

Although the participants expressed some confusion over the PT process, their perceptions of the PT process were generally positive (See Section 3.7.3, below). These findings are supported by some HD studies (Hawkins, Creighton and Hayden, 2013; Stuttgen *et al.*, 2018) which illustrate the need for more flexible and individualised options for PT that take into account an individual's circumstances.

3.7.3 VIEWS & DECISIONS

> *"…the long and the short is that if you have it... um… if you don't have it, great but if you do have it, there is an enormous ripple effect on your life going forward, as well as the people around you…" – Ben*

All the participants in this study, expressed an interest in going for PT in the future. The participants, however, described being conflicted about going for PT because of the potential consequences of testing positive (See quote above). Throughout the interviews, the participants explained both their reasons for wanting to go and not wanting to go for PT, these are shown in Table 11.

Table 11: Highlights the participants perceived incentives and hindrances surrounding undertaking PT

Incentives	**Hindrances**
Relief From Uncertainty *"So I can have peace of mind. Like okay, I will have it one day then I will make peace with that. I don't mind. But, but I just need to know. I don't want to sit and wonder because I've been wondering for so many years but I don't want that anymore. I just said "okay, it's either I do this or I don't. But I do want to know, I will want to know."" –Maria*	Maturity/ Being Ready *"Not, not, I won't say I'm too young but ya (yes), just ya (yes), when you get the result like that and it's positive you must be, ya (yes). Ya (Yes), mentally must be very strong./…/ Ya, ya, (Yes, yes,) I think I'm a bit too young, maybe in two, three, four years' time." – Juan*
Planning the Future *"It's got a huge ripple effect so, if you got a few things in place and you know what's happening or what might happen, you obviously are prepared for the worst for instance."- Ben* - Financial Planning - Family Planning - Goal Planning	Situational Factors *"I decided not to because like I said I was breaking up with that, that girlfriend of mine from three years and stuff and we did live together and everybody had to move out and, like I said, "Ya, it, it wasn't a good time for me and that's the only reason why I decided not to (test)." – Ben* - Significant Life Events - Support Partner - Family Needs
	Survivors Guilt *"Also, the, the survival result… why, why didn't, if it's negative then the guilt why was I negative or why am I negative, you know? /…/ Ya, I will definitely feel um… somewhere, um… I've been spared, why???" – Sofia*
	Hopelessness *"I dono (do not know), I don't wanna (want to) get sick. I don't want to be sick at all. I don't see what kind of a future I have now because I can relate to my brother, what is the point?" – Rose*

Similar incentives for PT have been reported in several international studies on HD (Dufrasne *et al.*, 2011; Dondanville *et al.*, 2018). Interestingly, Dufrasne *et al.*, (2011) reported relief from uncertainty as the most frequent incentive for PT, whereas in the current study the most common reason provided was to plan for the future. As can be seen in Table 11, the participants mentioned a variety of different types of plans that they felt PT would assist them in making. The majority of the plans mentioned, were not for the participants' personal benefit but were centred on preparing the participants' family for the future. These plans were normally associated with explanations of wanting to protect their family from repeating their experiences (See Theme 1, page 41 & Theme 2, page 46). For example, the majority of Sofia reasons for wanting to go for testing were orientated towards her family.

"If I'm also affected then we have to put things in place so that we can all be taken care of." – Sofia

This is contrary to most international research where participants often state personal reasons for going for PT (Decruyenaere *et al.*, 2003). However, the tendency for SA at-risk individuals to give reasons that concern their families more than themselves has been reported before (Futter, Heckmann and Greenberg, 2009). These findings are consistent with Greenberg *et al.*, (2012) finding of how many South Africans think in terms of a collective rather than the individualistic manner of the more Westernised cultures.

Similarly, to Futter, Heckmann and Greenberg (2009), the participants in this study mentioned several plans that motivated them to test, however, the most common was family planning. In the current study, this plan was often associated with the participants' fears of passing the condition on to their children (See Theme 3, page 51). Maria described not wanting to have another child until she knew her mutation status (See Section 3.5.2.2, page 49). Similarly, the participants without children (Noah and Ben) both expressed that testing positive would influence their decision whether to have children.

> *"It has also made me a bit scared to have kids. I wouldn't wanna (want to) pass this on to them and have them deal with it as well. That's why I first wanted to have the test done, to make sure I don't have it. Otherwise, if I do, if I do have it, I don't know what testing they do but if it turns out I do have it, I wouldn't want any kids because I wouldn't want them to have this coz (because) I know it's terrible." – Noah*

As can be seen in the above quote, the participants' reproductive decisions were also associated with their experiences. This differs from the findings of a previous SA study on the perceptions of those at-risk for SCA (De Villiers, Weskamp and Bryer, 1997). This research found that the at-risk individuals' experiences of the condition had little impact on their reproductive choices, with the majority of individuals wanting more children (De Villiers, Weskamp and Bryer, 1997).

Although, the participants expressed interest in going for PT, they also described the reasons why they had not availed themselves of the option of PT (See Table 11, page 61). Similar reasons for delaying going for PT or dropping out of the PT process have been reported in international studies (Dufrasne *et al.*, 2011).

The most significant finding that emerged surrounding the participants' reasons not to go for PT was their struggle to find a good enough reason to test. This was often associated with there being no way of preventing or curing the condition, which made the participants feel that getting a positive result would result in hopelessness (See Section 3.4.3, page 43).

"No, there's nothing more you can do. Ya, (Yes,) there's not options. We don't have a lot of options for this disease so, just deal with the emotions as it happens." – Sofia

One participant described feeling hopeless about his future because there was nothing he could do to prevent the onset of the condition.

"Um… in the week I obviously eat right, and you think to yourself if you, obviously if you live, if you live healthy and stuff it will make a difference but apparently, they say, that doesn't make a difference." – Ben

For the participant who had tested positive the feelings of helplessness had caused a number of psychological consequences, such as depression and lack of ambition.

"Ya, (Yes,) they want me to be accomplished so, I asked him, accomplished to lay in bed?" – Rose

Some participants seemed to relieve the anxiety they felt by maintaining hope. This mentality helped one participant to stop pondering the possibilities and to reach acceptance (See Table 11, page 61).

"I'm more calm about it. If it happens, then it happens, then there's nothing I can (do) about it, so deal with it. /…/ Mm… Ya, (Yes,) mostly about planning but then we can die of something else entirely, any minute of the day so, I thought, "I wouldn't spend too much time on pondering about what ifs." " – Sofia

Previous research studies have reported similar fatalistic mentalities in the SA population (Futter, Heckmann and Greenberg, 2009; Greenberg *et al.*, 2012). However, unlike these previous studies, the fatalistic mentalities of the participants in this study were not associated with negative perceptions of testing but seemed to be an attempt to reduce anxiety or find acceptance in order to cope with their possibly inescapable reality. Other SA research has described individuals using other coping mechanisms like denial to reduce the stress of being at-risk for an incurable condition (Hayden *et al.*, 1980).

An international study found that hope was a crucial part of living with the risk of inheriting HD and suggested that linking hope to uncertainty was different from being in denial (Quaid *et al.*, 2008). They found that some individuals actively choose to not go for testing in order to maintain hope (Quaid *et al.*, 2008).

Despite the participants expressing interest in undergoing PT, all except one of the participants, in the current study, has delayed going for PT to date (See Table 10, page 58). Throughout the interviews, deciding whether to go for PT was described as extremely emotionally overwhelming. Although the participants described several reasons for why they had not gone for PT (See Table 11, page 61), all of their reasons seemed to stem from fear of receiving a positive result and the implications it would have on their life going forward.

"Because I know I'll think about it too much, if I do have it, it will bother me for the rest of my life until it, until I start showing symptoms." – Noah

Dufrasne *et al.*, (2011) described that at-risk individuals are torn between the desire to know and not know their genetic status. The perceived equal advantages and disadvantages of PT for those at-risk was reported to make deciding a stressful experience (Dufrasne *et al.*, 2011). Similar difficulties faced by at-risk individuals when trying to decide about whether to go for PT have been reported in several studies on HD (Codori, Hanson and Brandt, 1994; Dufrasne *et al.*, 2011).

3.7.3.1 Family Perceptions

During the interviews, some participants described their family's perceptions as being more negative than their own. Both Maria and Rose described their siblings not wanting to go for PT.

> *"My brothers did not want to do the testing. I think they both came for the first, [Pause] I think they were here only once with (the GCs) and them, then they decided they didn't want to do it, which I think they should because my brothers look as if they…" – Rose*

This is supported by the findings of previous SA research on HD PT perceptions (Futter, Heckmann and Greenberg, 2009), however, the proposed reasons for lack of uptake differ (See Section 1.5.2, page 21).

The participants stated that very few of their family members had gone for genetic testing or even gone to get diagnosed. In her interview, Rose described how her family often did not go to the hospital to get diagnosed because of the past negative experiences of other family members.

> *"My entire family, and we all know what it is, we've been through generations of it now. I've, since I was born, my mother was sick, my uncle was sick, one of my mother's cousins was sick, she never came to a hospital. She's never been here. They don't have on record, she, coz (because) when my grandmother came I think, or my uncle, they were of no help to him, like he explained so my cousin just decided no, my mother's cousin. She passed away and then my mother got sick and my mother's brother was sick and now, my mother's brother, all three of their kids have it." – Rose*

This negative perception of the public healthcare system emerged in association with other topics in the data. In his interview Ben described not wanting to attend a public hospital due to a negative perception of the service.

> *"…If you didn't have money then, eventually, he, he should have probably ended, ended up in like, a state hospital and then you obviously know what the story is over there, anything can happen over there, you understand." - Ben*

Previous research has reported similar perceptions of the futility of PT for HD due to the lack of available cure or treatment and a negative perception of the public healthcare system in Spain (Rivera-navarro, Cubo and Mariscal, 2015).

Chapter 4: Conclusion

4.1 INTRODUCTION

In the following chapter the findings, strengths and limitations of the current study are described. The implications of this research for GC practice as well as recommendations for future research are explored.

4.2 CONCLUSION

Compared to HD, international research on the experiences and perceptions of those at-risk for SCA is scarce (Abe and Itoyama, 1997; Lima *et al.*, 2001; Goizet, Lesca and Durr, 2002; Gonzalez *et al.*, 2004; Rolim *et al.*, 2006; H. M. Paneque *et al.*, 2007; M. Paneque *et al.*, 2007; Paneque *et al.*, 2009, 2019; Leite *et al.*, 2017; Cahn, Rosen and Wilmot, 2020). Similarly, in SA only one study has explored the perceptions of those at-risk for SCA, however, this research was conducted before the availability of direct mutation testing (De Villiers, Weskamp and Bryer, 1997). This gap in the literature is of significance, as a deeper understanding of how at-risk individuals cope with the knowledge of their risk and make decisions regarding PT is essential in providing appropriate genetic services and support to this population. This is especially important with regard to the PT service offered at UCT, as, despite the relatively high frequencies of SCA in SA, the uptake of PT has been lower than that seen internationally (Harper, Lim and Craufurd, 2000; Evers-kiebooms *et al.*, 2002; Creighton *et al.*, 2003; Trembath *et al.*, 2006; Futter, Heckmann and Greenberg, 2009; Dufrasne *et al.*, 2011; Smith *et al.*, 2012; Smith, Greenberg and Bryer, 2016). The current research project sought to understand these low levels of uptake and fill in the gaps in the literature, by exploring the perceptions of those at-risk of inheriting SCA towards PT in SA.

The demands SCA placed on the participants' families were identified as significant. The physical, emotional, social and economic burdens of the condition were described by all participants regardless of their role in the family. Although, the caregivers bear the majority of the burden of the condition. The social and emotional burdens of the condition were further highlighted by the consequences on the family structure and communication difficulties. A high level of family dysfunction was evident in the data including conflict, secrecy, abuse, neglect and abandonment. Abandonment was a particularly common experience, where relatives of the affected individual felt they couldn't or wouldn't take on the burden of caring.

Throughout the topics explored in this research, the association between the participants' experiences and their perceptions was evident. Their experiences influenced their perceptions of the condition as well as that of their risks, fears and decisions. An example evident throughout Chapter 3 (page 37), is how the experience of stigma, abandonment and burden of caring were often linked to the participants own fears of abandonment- which influenced their behaviours such as selective disclosure and delaying uptake of PT.

The non-engagement of the SCA at-risk population was further indicated by the difficulties experienced in recruiting participants for this study. Not only were low levels of Neurogenetics clinic attendance identified, but the participant's lack of willingness to recruit relatives, suggested negative perceptions of the PT and/or the healthcare services within this population. The data further indicated negative perceptions of PT and the healthcare system amongst the participants' relatives. The participants' explanations for these perceptions included a sense of hopelessness and previous negative experiences with the healthcare system. This is similar to the reduced tendency to undergo PT that was found to be linked to a negative perception of the public healthcare system in Spain, which has a similar uptake rate as SA (Futter, Heckmann and Greenberg, 2009; Rivera-navarro, Cubo and Mariscal, 2015).

Unlike their relatives, the participants in this study generally expressed positive perceptions of the PT process. This result could be a result of an ascertainment bias (See Section 4.4, page 67). Despite their positive perceptions, the inflexibility of the PT protocol had acted as a deterrent for some, particularly the perceived length, expense and need for a support partner. This is consistent with previous research done in HD which found the inflexibility of the PT program to act as a barrier to uptake (Futter, Heckmann and Greenberg, 2009; Hawkins, Creighton and Hayden, 2013).

Despite the participants' positive perceptions and expressed interest in PT, all but one had delayed going for PT to date. The decision to undergo PT was described as complex and emotional, with the participants expressing the simultaneous want to and not want to go for PT. The decision to delay testing was due to a fear of the consequences of the result. These findings are similar to those of previous research in HD, which highlighted the need for GCs to be aware of the complexity of the decision and understand that for some at-risk individuals choosing not to undergo PT can be a healthy coping strategy (Quaid *et al.*, 2008).

In the light of these findings, it is recommended that future research investigates the negative experiences and perceptions of SCA PT in more detail, as well as more creative and adaptable solutions to personalising the PT protocol. Previous suggestions have included utilising telemedicine and supporting other healthcare providers (such as general practitioners) in the provision of PT. However, these options need to be further evaluated to determine their safety, in order to prevent adverse events (Almqvist *et al.*, 2003; Hawkins, Creighton and Hayden, 2013). This issue is pertinent not only to this area of genetic services but to uphold the ethical principle of Justice in ensuring that all services are available to everyone who needs them (McCarthy Veach, LeRoy and Bartels, 2003).

4.3 STRENGTHS OF THE STUDY

This research study is the first in depth exploration of the perceptions of those at-risk for SCA towards PT to be undertaken in SA therefore fills a significant void in the literature, providing much needed insight into this extremely diverse at-risk population group. As such, it highlighted several important issues that need to be addressed in the provision of genetic services for these patients as well as issues that need further investigation.

The research sample was balanced with respect to gender and included at-risk individuals from diverse cultural and ethnic backgrounds. Furthermore, the fact that most of the participants had been for GC ensured that they had enough knowledge to provide meaningful feedback on the topic. These characteristics of the research sample produced a rich data set.

4.4 LIMITATIONS OF THE STUDY

The difficulties faced with recruitment resulted in data saturation not being reached. Additionally, the recruitment was inherently biased towards at-risk individuals who self-selected to discuss these issues, and it was difficult to access individuals who had not been for GC or PT as they were not known to the DHG. As such, the majority of the participants were at-risk individuals who had previously been for GC, therefore didn't provide alternative and possibly more negative perceptions of the PT process and personal risk. Furthermore, all the participants interviewed lived in urban areas, therefore the perceptions of PT highlighted in this study are more representative of urban dwelling individuals. This constraint may also indicate the difficulty in accessing such individuals for clinical care. These ascertainment biases may therefore be responsible for the positive perceptions of GC, healthcare and PT that were expressed by the research sample. For these reasons the results of the study cannot be extrapolated to apply to the entire at-risk population. This research can however function as a starting point for future research on the topic.

4.5 IMPLICATIONS FOR GENETIC COUNSELLING (GC) PRACTICE

The present study highlighted many practical implications for the GC of at-risk individuals. The misconceptions of the condition, their risks and the PT process demonstrates the need for alteration to the current GC information session. As explored in theme 4, the participants of this study found the information session to be very emotionally overwhelming, which led to lack of recall. This is an important finding for the field of GC as the main goal is to provide the client with information so that they can make an informed decision (Resta *et al.*, 2006). Possible changes that could be incorporated is providing clients with additional resources such as videos or altering the session itself, this could be done by taking breaks or having multiple sessions.

The results of this study illustrate the lack of support available to those at-risk for SCA, both from their family and the community. Unlike HD, there is no support group for SCA. The establishment of a support group would address some of the support issues that this population currently faces, as well as increase awareness of the condition and decrease the current misconceptions held by the population. Furthermore, the family dysfunction identified in this study indicates the need for GCs to explore family issues and identify individuals who are in need of more support. Future research could focus on the need for a support group for this population group and how this could be achieved.

Based on the results from the present study, the following points are suggested to be addressed during GC in order to improve the client's understanding and need for support:

- The clients' experiences of SCA in their family and the past trauma associated with this experience.
- The clients' fears surrounding being at-risk as well as the implications of the result.
- The clients' feelings of hopelessness about the future.
- Family functioning and support.
- Increased empathy and awareness of the difficulty of deciding to undergo PT.
- Increased understanding of the decision about PT.

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Appendices

APPENDIX A: UCT PRESYMPTOMATIC TESTING (PT) PROTOCOL

UNIVERSITY OF CAPE TOWN

DIVISION OF HUMAN GENETICS

Level 4, Falmouth Building, Faculty of Health Sciences, Observatory 7925, Cape Town, South Africa **Fax: 021-406-6826, Telephone: 021-406-6297**

UNIVERSITY OF CAPE TOWN PREDICTIVE TESTING PROTOCOL FOR LATE-ONSET NEURODEGENERATIVE DISEASES

The predictive test for late-onset neurodegenerative disease is a process which allows an individual at-risk for having inherited the gene for a late-onset neurodegenerative disease a chance of knowing whether he or she has the affected gene, before showing signs of the disease.

To take the test is a very serious decision as the knowledge of your test result will remain with you for life. Therefore, it is important that you are well informed and understand the programme and procedures you will have to go through before being given your result. A programme or protocol has been recommended by international genetic counselling teams based on their experiences in dealing with individuals and families at-risk for the disease. The protocol outlined below is a guideline of the minimum required sessions. Additional sessions or a neurologist or psychiatrist referral may be arranged at the discretion of those involved in the process.

Predictive testing is not generally available to

- individuals under 18 years of age;
- pregnant couples; or
- Individuals who have only recently become aware of a late-onset neurodegenerative disease being in their family as it is advisable to wait for a year before undergoing the predictive testing programme.

If, after careful consideration, you decide to undergo the test, you will be requested to come to the Groote Schuur Hospital Neurogenetic Clinic or the Division of Human Genetics on at least five occasions to see the different members of the genetic counselling team.

FIRST MEETING (GENETIC COUNSELLOR)

The genetic counsellor will ask you for your family history and explain the protocol. He/she will ask you for your reason for requesting a predictive test and will explain the inheritance pattern of the disease and the methods and limitations of the predictive test.

1. As you know, the affected gene for the late-onset neurodegenerative disease in your family has been found and we are now able to offer a blood test that will predict whether you will get the disease.
   IMPORTANT: *It is very important at the beginning that you understand that there is approximately 1% possibility that the test may not show a clear result with absolute certainty. If this occurs in your case, then unfortunately your risk of*

carrying the gene remains the same as before you entered the programme (i.e. 50%). When the result is given, it could be one of three:

* *Positive* - you have the affected gene and will develop the symptoms at some stage in the future. We have no way of knowing when and how it will present.

* *Negative* - based on our current knowledge of this gene, you will not develop the late-onset neurodegenerative disease.

* *Uninterpretable* - no result. You are still at-risk and have a 50% chance of carrying the affected gene.

2. We strongly recommend that you inform your family doctor of your decision to undertake the test. If you do not have a family doctor, we recommend you find one. As part of the policy of this programme, we believe that the on-going medical care and support your doctor can give you is very important to you and your family. A letter will be sent to your doctor to inform him/her about the programme after the third visit.
3. The decision whether to undertake testing can be stressful and waiting for the result can be stressful. The results, even "good news" can take time for adjustment. Having support is essential and we therefore strongly advise that you choose a family member or a trusted friend to accompany you to all the meetings as they will also be able to provide support after the test result is given to you.
4. The result will be given to you approximately six weeks after your blood samples have been taken and will be strictly confidential. No result will be given to you by telephone. Written confirmation of your result will be sent to the genetic centre that referred you. With your permission, your family doctor will be contacted and given the result.
5. If at any stage in the programme you decide you do not wish to continue, the decision is entirely yours. Your decision will in no way prejudice our relationship with you or your family. We will be happy to continue to offer you all the support and help you need.
6. To ensure confidentiality, family members who request testing together will attend individual counselling sessions with the genetic team members.
7. Because the process of being tested for late-onset neurodegenerative disease and dealing with the results will be stressful and is often disruptive to a person's life it is best to choose a time to be tested when complicating factors from the outside are at a minimum.
    - For example, while in the middle of a divorce or break-up of a relationship, or at a stressful time at university or college or work is not a good time to be tested.
    - Testing at a time of celebration may not be optimal, for example right before or after marriage, or during important holidays.
    - Likewise, soon after the birth or death of a family member testing should be delayed.
    - Predictive testing results may impact on health and life insurance, it is important to consider these implications before embarking on the testing protocol.
    - It is useful to make a decision about whether or not to be tested even if the decision is not a yes or no answer. For example, deciding not to be tested for a certain period of time (next year, or after I turn 30), can help you put this aspect of late-onset neurodegenerative disease aside for a period of time until you are ready to readdress testing issues in future.
8. It is important that, before undertaking the predictive test, you plan about who you will tell about your decision and when. It is also important to plan about who you will tell your result and when. Will you tell them on the same day that you are given your result? Exactly how and when do you plan to tell them? Will you tell them by phone or letter or at a family get together? What if you change your mind and do not want them to know at the moment or at all? Do you plan to tell the people at work about your decision to be tested or your test result?
9. If you have attended the support service of a therapist, psychologist, religious professional or psychiatrist during a difficult time in the past, it may be useful to discuss your decision about testing with this person. This is particularly important if you have had prior problems with depression, anxiety or stress.

DISCRETIONARY MEETING (NEUROLOGIST AND ANOTHER MEMBER OF THE GENETIC TEAM) (APPROXIMATELY FOUR WEEKS AFTER FIRST MEETING)

The neurologist will perform a neurological examination to exclude early symptoms.

SECOND MEETING (PSYCHOLOGIST) (APPROXIMATELY FOUR WEEKS AFTER PREVIOUS MEETING)

1. You must be accompanied by your support partner to this meeting.
2. A psychologist will assess your past and current levels of psychological functioning.
3. During this meeting the psychologist will discuss your reasons for requesting predictive testing as well as the possible effects that a positive or negative result may have on you, your partner and your family. Counselling may vary widely. For example, people who have the gene may suffer a sense of shock and grief however well they may have been prepared beforehand. People whose risk is negative may feel relief but at the same time suffer guilt and anxiety. For those with no result their feelings could be anger and frustration.
4. You will be asked to make an appointment to see the genetic counsellor approximately one month after this meeting.
5. It may be necessary to include another interview in the pre-test period if either you or we may need further information or discussion.

THIRD MEETING (GENETIC COUNSELLOR AND GENETIC NURSE IN ATTENDANCE) (APPROXIMATELY FOUR WEEKS AFTER PREVIOUS MEETING)

1. You must be accompanied by your support partner.
2. At this meeting the genetic team will need your written consent to take blood samples from you. Again there will be careful explanation of the test and the manner in which the final result will be given: about six weeks after the blood sample has been taken you will be contacted to make an appointment to see the genetic counsellor and psychologist when you will be given the final result.
3. Your GP will be contacted once your blood has been taken and a letter will be sent to him/her about the test. No result will be given to you over the telephone, whatever the result may be.
4. Due to the complexity of the test it may take longer than six weeks

FOURTH MEETING (PSYCHOLOGIST, GENETIC COUNSELLOR AND/OR GENETIC NURSE IN ATTENDANCE) (APPROXIMATELY SIX WEEKS AFTER PREVIOUS MEETING)

IMPORTANT: It is important that you plan what you will do after you have received your result at this session. Will you go directly home and who will be there? Will you take some time off work or from family responsibilities?

1. You will be contacted and an appointment made to finally receive your result. No result will be given over the telephone, whatever it might be. Please note that the genetic nurse does not know the result when she calls you.
2. The genetic team in attendance, and again only with your consent, will give you the result. You must be accompanied by your support partner at this meeting. You will be given a short recess alone with your partner after the test result has been given and this will be followed by a discussion to answer any questions you may have.
3. Once the result has been discussed with you and again, with your consent, your GP will be informed telephonically.
4. The genetic nurse will make an appointment for one month later for a follow-up visit.

FIFTH MEETING (GENETIC COUNSELLOR AND GENETIC NURSE IN ATTENDANCE) (APPROXIMATELY FOUR WEEKS AFTER PREVIOUS MEETING)

1. You may bring your support partner to this session if you wish but may also attend on your own if you would prefer to do so.
2. During this visit the genetic counsellor will revise your test result with you and the effects this has had on you, your partner and your family. Counselling may vary widely but will generally focus on how you are coping with this knowledge and to who you have disclosed your test result and their reactions to this information.
3. The genetic counsellor will make a further follow-up visit for one month later if you would like it.

Contact person: Sister Nicci Adams
Tel: (021) 404 6235 or 406 6304
E-mail: nicci.adams@uct.ac.za

APPENDIX B: SOCIODEMOGRAPHIC QUESTIONAIRE

Participant Questionaire

For Researcher's Purposes

Participant No. ____________ Recording No. ____________

Date of Interview: ____________

Type of Interview:

Face-to-Face	Telephonic

Venue: ____________

Participant to fill out

Full Name: ____________ Surname: ____________

Current Age: ____________

Gender:

Female
Male

Relationship status:

Single
Married
Divorced
Widowed
Other

First Language:

English
Afrikaans
Xhosa
Other

If other Please specify: ____________ If other please specify: ____________

Highest Education:

Primary School
High school
Undergraduate
Postgraduate

Current Employment:

Full Time
Part Time
Unemployed

If employed, what do you do? ____________

Which area do you live in? ____________

Who is or was affected with SCA in the family?

Father	Mother	Aunt	Uncle	Cousin
Father's Mother	Mother's Mother	Brother	Sister	
Father's Father	Mother's Father	Son	Daughter	

If other please specify: ____________

Have you ever attended Neurogenetics Clinic at Groote Schuur?	Yes	No	Maybe
Have you ever gone for Genetic Counselling?	Yes	No	Maybe
Do you know about Presymptomatic testing for SCA?	Yes	No	Maybe
Have you ever undergone Presymptomatic testing for SCA?	Yes	No	Maybe
If No, have you ever considered going for presymptomatic testing?	Yes	No	Maybe
If Yes, did you follow through with the testing?	Yes	No	Maybe

APPENDIX C: SEMI-STRUCTURED INTERVIEW GUIDE

Open-ended interview Guide

Participant no. _______________ Recording no._______________

Date: _______________ Venue: _______________

Family History

- Parents/ Children/ Siblings
- Affected individuals
    - Diagnosis age?
        - How did it affect them/ the family?
    - How old were you?
        - Did you live with them?
        - How did the diagnosis affect you?
    - Who takes care of them?
        - How is it looking after/living with them
    - What were their symptoms?

Experience of SCA

- Who cares for them?
- Did you ever live with the affected person?
- What were their symptoms?
    - What do you know about the condition? Where did you get this information?
- What is it like looking after/living with them?
- What has been the hardest part of this for you?

Experience affected you/the family?

- Lifestyle
  - Work choices
  - Finances
  - Hospital visits
  - Education
- Reproductive choices
- Relationships
  - Work
  - Family
    - Does your family talk about it?
  - Friends
  - Community engagement
    - Who knows about the condition
    - How do they react?
    - Do you talk about it?
    - How do people treat the affected person?

Personal risks

- What do you believe is your risk?
  - Why is this your risk?
- How do you feel about this risk?
- How does it feel to live with this risk?

Presymptomatic testing knowledge

- What do you know?
  - How do you feel about the process?
- I see you.....
  - Have been for testing?
  - Haven't been for testing?
  - Plan to go for testing?
- What influenced your decision?
  - Travel/Transport
  - Time
- How does your family feel about the process?
  - Is your family supportive of your decision?
  - Who supports you
  - Has anyone else gone for testing?
  - Do you think anyone else in your family would be prepared to talk to me?
- Is there anything else you want to tell me?

APPENDIX D: LIST OF CODES

Abandonment of affected

Acceptance

Adjustment

Affected persons perspective

Age

Age related concerns

Alternative Medicines

Anticipation

Balance

Behavioural problems

Beliefs about risks

Big implications

Community

Community Understanding

Conflict

Consequences of PT

Current treatment ineffective

Dementia

Depression

Difficult decision

Difficult to handle

Distancing from affected

Emotional rollercoaster

Emotionally Overwhelmed

Exhausting

Experience of being at-risk

Experience of Healthcare

Experience of PT

Factsheet

Isolation

Knowledge of PT

Lack of Support/ Unappreciated

Letting them down

Limited Movement

Loss of eyesight

Loss of Independence

Loss of Speech

Meaning of Results

Misinterpretation of cause

Misunderstanding of Terminology

No Clinical trials

Not pleasant to witness

Noticeable & Progressive

Pain/ Spasms

Parent-child Relationships

Prognosis

PT length

Reasons against PT

Reasons for PT

Regret

Relief from Hopelessness

Relived Experience

Reminder of Risks

Reproductive choices

Risk Awareness

Risk disclosure & Understanding

Risk Perception

Search for hope

Familial Perceptives on PT

Familial Understanding

Fear

Financial burden

Finding out about risk

Freedom Restricted

Genetic Counselling Experience

Guilt

Have to do everything for affected

Hopelessness

Information Session

Selective Disclosure

Sense of Responsibility/ Forced Responsibility

Sibling relationships

Similarities between affected family members

Stigma

Stolen Dreams

Support

Support Partner

Sympathy

Symptom watching

Symptom watching in relatives

APPENDIX E: PARTICIPANTS INFORMATION SHEET & CONSENT FORM

UNIVERSITY OF CAPE TOWN

GROOTE SCHUUR HOSPITAL

DIVISION OF HUMAN GENETICS
Faculty of Health Sciences
University of Cape Town
Observatory, 7925
South Africa

Dear Participant,

Thank you for being willing to participate in my masters research project which is titled "At risk individual's perspectives of Spinocerebellar Ataxia (SCA) presymptomatic testing".

SCA is a condition that runs in families and leads to progressive problems with coordination of movement and speech. Although there are at least 31 different forms of SCA, the most common types in South Africa are type 1, 2 and 7. Although there is currently no known cure for these conditions, it is possible to determine who will get the condition, using a genetic test that has been available through UCT, since 1994. This genetic testing is referred to as presymptomatic or predictive testing.

This research project aims to explore the views and perceptions, of individuals with a family history of SCA, towards the presymptomatic/predictive testing process for SCA.

This study has been initiated through the Division of Human Genetics at the University of Cape Town and is for a minor dissertation for the completion of a master's degree in Genetic Counselling.
You have been invited for involvement in this research because:

- You have a first or second degree relative that has been diagnosed with a type of SCA
- You are eligible to undergo the presymptomatic/predictive testing process through UCT

Should you wish to participate, I would like to talk to you about your perception and views of the presymptomatic/predictive testing process available through UCT and what factors contributed to your decision whether to undergo this testing process. The interview will take place at the Genetic Counselling offices at the University of Cape Town, Division of Human Genetics, 4th Floor Falmouth Building or over the telephone. If you need assistance with transport costs to UCT to take part in this interview, you will be compensated. The interview should take about an hour and will be voice recorded. Some parts of the interview may be used in the reporting of this study however, all identifying information, such as your name, will be kept confidential and only be known by the researcher. No personal information will be shared with anyone. At your request, a translator will be present during the interview if you are uncomfortable speaking in English. If a translator is required, the interview may take about two hours.

Your participation is entirely voluntary, meaning that you can withdraw from the study at any point, with no consequences to you or your family. Any health care that you are receiving from our clinics or anywhere else will not be affected by your decision whether to take part in this study. This being a research study, there will be no medical benefits to you. Some of the questions that will be asked may be of a sensitive manner. If you feel that you do not want to answer a question, you can tell the interviewer that you want to skip the question, no explanation required. If you feel that you need further assistance or explanation, a referral to the appropriate health care professionals will be arranged by the interviewer. Contact details are given below for the University of Cape Town, Division of Human Genetics.

Yours sincerely,

Signature Removed

Deanah Lloyd
MSc (Med) Genetic Counselling Student

STATEMENT BY PARTICIPANT

I, ____ confirm that:

1. I understand that the objective of the study is to understand how individuals at risk for Spinocerebellar Ataxia (SCA), in the Western Cape Province of South Africa, perceive the presymptomatic testing process for SCA.
2. I understand that I voluntarily choose to participate in this study and if I choose to no longer continue that my decision will not in any way affect the health care services I currently receive at GSH.
3. I understand that a genetic counselling session can be arranged if I would like to obtain more information or discuss anything further.
4. I understand that all information collected will remain confidential and will be used for research purposes only.
5. I understand that the interview will be recorded for research purposes. All voice recordings will be safely stored away in locked cupboards and information stored on a password-protected computer. I understand that only the researcher, her supervisors and examiners will have access to the data. All recordings will be destroyed upon completion and publication of this study and all identities will remain anonymous.
6. I understand that the interview will take place in English and that the researcher will be administering the interviews herself. I understand that if I do not feel comfortable communicating in English and require a translator, a suitably trained individual will be used to translate the interview and supplementary documentation.
7. I understand that this study has been approved by the registered Human Research Ethics Committee at the Faculty of Health Sciences at the University of Cape Town. I have been given contact details should I wish to contact the committee about how I was treated as a research participant.
8. I have the researchers contact details if I would like to contact her regarding further questions about this study.
9. ____________________________ has explained the information of this study in English or in ____________________________ through the use of a lay translator and I understand this information.

PARTICIPANT CONSENT FORM

I,____(Full Name and Surname) hereby declare that I have voluntarily agreed to participate in the above-mentioned research study and that the interview can be voice-recorded.

Signed at: _________________________ (Address of venue) on______________________ (Date).

____________________________	_________________________
Participant Name	Witness Name
____________________________	_________________________
Participant Signature	Witness Signature

If you have any questions regarding your rights as a research participant, please contact the Human Research Ethics Committee at the Faculty of Health Sciences of the University of Cape Town.

Professor Marc Blockman (Chairperson of the Human Research Ethics Committee): Tel: (021) 406 6496

If you have any questions regarding the research or the research procedure, please contact the researcher or her supervisor:

Ms. Deanah Lloyd (Researcher): Tel: 072 336 7390 | Email: llydea001@myuct.ac.za
Dr Tina-Marié Wessels (Supervisor): Tel: (021) 406 6373 | Email: tina.wessels@uct.ac.za

APPENDIX F: HREC APPROVAL LETTER

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

11 February 2019

HREC REF: 758/2018

Dr T Wessels
Division of Human Genetics
FHS

Dear Dr Wessels

PROJECT TITLE: AT RISK INDIVIDUAL'S PERSPECTIVES OF SPINOCEREBELLAR ATAXIA (SCA) PRESYMPTOMATIC TESTING (PT) (MSc Candidate - Ms D Lloyd)

Thank you for your response letter dated 29 January 2019, addressing the issues raised by the Human Research Ethics Committee (HREC).

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

Approval is granted for one year until the 28 February 2020.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: Miss Deanah Lloyd will also be involved in this study.

Please quote the HREC REF in all your correspondence.

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

We acknowledge that the student: Miss Deanah Lloyd will also be involved in this study.

Please quote the HREC REF in all your correspondence.

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

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

Signature Removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical

Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.