

Ashkenazi Jewish Genetic Testing:

Utilisation of Services, Genetic Knowledge and Perceptions of Stigma

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Candidate's Declaration

I, Kara Stoler, declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Science in Medicine in Genetic Counselling at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

Kara Stoler

August 2013

Dedication

For My Family:

My husband Darren- your support and encouragement has truly given me the motivation to get me through the past two years. Thank you for your constant love, kindness and affection.

My mother, Reneé and my parents in-law, Annette and Roy- thank you for all the support and love over the past few years. I am truly grateful for your never-ending faith in me.

My brother, Michael- you have always been my biggest supporter and I am so proud of what we have accomplished together and apart.

Abstract

Genetic carrier testing programmes originated in different ethnic groups to establish whether an individual or his/her partner carries an inherited recessive genetic mutation that could cause a serious genetic condition in a couple's offspring if both are carriers.

Molecular genetic analysis has shown that despite migration and physical separation, Jewish individuals have retained their religious, social and genetic identity over many years through a common religion, dialect, customs and marriage within the community. Therefore, a number of conditions have a higher incidence in the Jewish population due to the founder effect. There are a number of serious life-threatening conditions prevalent in the Ashkenazi Jewish population that display an autosomal recessive inheritance pattern. These conditions are deemed worthy of genetic carrier testing to identify couples who are at risk and assist them in making appropriate reproductive choices.

This research study focused on the Ashkenazi Jewish genetic testing programmes available to the Jewish community in Johannesburg, South Africa (SA) and it explored the uptake of genetic carrier testing. It also aimed to assess genetic knowledge related to carrier risks and the autosomal recessive inheritance pattern, and to evaluate the personal or social perception of stigma associated with being a carrier of an Ashkenazi Jewish condition.

The study sample included Ashkenazi Jewish men and women in Johannesburg, SA between the ages of 18 and 40 years. The study was advertised through several Jewish community resources. Data was collected through an online structured questionnaire over a one month period. All information was cleaned and coded in an Excel spreadsheet and then analysed.

There were 298 individuals who participated in this study with 32.6% (97/298) male and 67.4% (201/298) female. From the total number of participants in the study, 44% (130/298) had genetic carrier testing. The participants who had testing chose to be tested when they were either single, dating or engaged. The timing would therefore have

implications for participants as individuals would be aware of different reproductive options available at different stages. This study found that knowledge with regard to understanding genetics of the autosomal recessive pattern of inheritance for the common Ashkenazi Jewish genetic conditions was poor. Participants did not fully understand the implications of being a carrier of a genetic condition and underestimated the frequency of the genetic condition. Finally, no stigma for being a carrier of a genetic condition was found in the sample overall or when assessed for personal or social stigma. This finding indicated that there may be less stigma in the community in Johannesburg, South Africa.

This study highlights the need for genetic services to be promoted further in the Ashkenazi Jewish community through educational programmes so that individuals are encouraged by their community and health care professionals to test for the 9 common Ashkenazi Jewish conditions. An increase in genetic carrier testing would allow more individuals to make informed reproductive decisions.

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Abbreviations

AJ	Ashkenazi Jewish
AJs	Ashkenazi Jews
BLM	Bloom syndrome
CD	Canavan disease
CF	Cystic fibrosis
CVS	Chorionic villus sampling
FANC C	Fanconi Anemia, Group C
FD	Familial dysautonomia
GP	General practitioner
GSD	Glycogen storage disease, Type 1A
HEX A	Hexosaminidase A
IVF	In vitro fertilisation
JJCF	Johannesburg Jewish Community Forum
MLIV	Mucopolysaccharidosis IV
n	Sample Size
NHLS	National Health Laboratory Service
NPD-A	Niemann-pick disease, Type A
PGD	Preimplantation genetic diagnosis
SA	South Africa
SABJE	South African Board of Jewish Education
SCD	Sickle cell disease
TSD	Tay-Sachs disease
Wits	University of the Witwatersrand

Definitions

These definitions were included as they are referred to throughout the research report:

Modern-orthodox Jewry Jews who attempt to synthesise Jewish values and the observance of Jewish law within the secular world.

Non-observant Jewry Jews who identify themselves as Jewish but do not follow any customs or laws.

Traditional Jewry Jews who observe some of the Jewish customs and high holidays.

Ultra-orthodox Jewry Jews who attempt to live a life separated from the secular world as they strictly follow Jewish law and customs.

1 INTRODUCTION AND LITERATURE REVIEW

Certain genetic conditions occur more frequently in specific population groups than in the general population. One of the reasons for this is a phenomenon known as the “founder effect,” whereby individuals in a specific population group originate from a small gene pool and therefore share similar genetic information (Klugman & Gross, 2010). Increased genetic knowledge and technology have improved the identification of common pathogenic mutations in various populations such as the Ashkenazi Jews (AJs), French Canadian, Afrikaner, Greek and African American communities (Angastiniotis & Hadjiminias, 1981; Davignon & Roy, 1993; Grover, Shahidi, Fisher et al., 1983; Loubser, Edge, & Fieggen, 2008; Ostrer, 2001). Genetic carrier testing programmes were initiated to test asymptomatic individuals who were at a high risk of carrying a genetic mutation for a particular genetic condition. Genetic carrier testing for autosomal recessive conditions has precipitated an increase in the prevention of disease and promotion of informed reproductive decision making amongst populations at a higher risk for specific genetic conditions (Markel, 1992).

Genetic carrier testing programmes in high-risk populations, such as the AJs, are available worldwide. Alongside the Tay-Sachs disease (TSD) testing programme that began in the 1970’s, developments in molecular genetics led to the development of genetic carrier testing for other genetic conditions in the AJ population (Kaback, Lim-Steele, Dabholkar et al., 1993).

Of the approximately 13 million Jewish individuals worldwide, more than 90% are categorised as Ashkenazi Jewish with a minority being Sephardic Jews (Ostrer, 2001). Ashkenazi Jews originate from Eastern European countries such as Germany, Poland, Russia, Lithuania and Austria while Sephardic Jews are from Spain, Portugal, North Africa and the Middle East. While these two groups do share many religious and traditional practices, they also differ in many cultural aspects. They also differ somewhat with respect to genetic conditions as a different panel of conditions has been found to be

more prevalent in Sephardic Jews such as β -thalassemia, G6PD deficiency and Glycogen Storage Disease Type III. In South Africa (SA), there are approximately 70 000-75 000 Jewish individuals, with 50 000 residing in Johannesburg (personal communication, South African Board of Jewish Education [SABJE] 2012). The majority of South African Jewry are Ashkenazi, while only a small proportion of about 1000 individuals are of Sephardic origin (personal communication, David Saks, SABJE 2012).

Currently, in Johannesburg, genetic carrier testing programmes offer testing for 9 common AJ autosomal recessive genetic conditions, which is in line with many international centres. The genetic conditions tested for in Johannesburg, South Africa include Tay-Sachs disease (TSD), cystic fibrosis (CF), familial dysautonomia (FD), Canavan disease (CD), Fanconi anaemia (FANC C), glycogen storage disease type 1a (GSD), Niemann-Pick Disease type A (NPD-A), Bloom syndrome (BLM) and mucopolidosis type IV (MLIV). Details of the individual diseases are provided in Appendix A. Other centres in the world, such as the Victor Centers for Jewish Genetic Diseases in Philadelphia, Boston and Miami in the United States of America, include testing for up to 19 AJ conditions (Victor Centers for Jewish Genetic Diseases, 2012).

This study focused on the Ashkenazi Jewish genetic carrier testing programmes for the 9 common AJ genetic conditions available in Johannesburg, SA. The history of genetic carrier testing programmes will be discussed with reference to the AJ community both internationally and in Johannesburg. Participants testing choices were reviewed and their knowledge with regard to AJ autosomal recessive genetic conditions evaluated. The psychosocial implications of carrier genetic testing were also considered. As very few studies worldwide have addressed the personal and social stigma associated with testing positive as a carrier, this study focused on these particular aspects.

1.1 Principles of Genetic Carrier Testing Programmes

Genetic carrier testing, also referred to as carrier screening, may be offered to the general population, or as targeted screening programmes for high risk populations, or for specific

at-risk individuals such as siblings. The aim of genetic carrier testing is to identify individuals and couples who are carriers of a genetic mutation, potentially putting them at risk of having offspring with a serious autosomal recessive genetic condition. For a condition to manifest, two genetic mutations are required. The identification of two genetic mutations in an affected individual means that both genes are not functional and therefore the production of a specific protein is disrupted. This includes different mutations in the same gene, also known as compound heterozygosity. When two carriers of mutations for the same recessive condition have children, there is a 25% risk with each pregnancy of having an affected child, a 50% chance of having a child who is a carrier and a 25% chance of having a child who is neither affected nor a carrier. The purpose of genetic carrier testing is to allow couples to be informed about their reproduction options, which in turn may decrease the occurrence of serious genetic conditions.

Several factors as outlined in Table 1.1, are considered integral to the success of a population based carrier testing programme; characteristics of the disease itself, characteristics of the screening and diagnostic tests and characteristics of the targeted population group (Laberge, Watts, Porter et al., 2010; Vallance & Ford, 2003). Ashkenazi genetic testing is a modification of this as it does not screen the whole population in a systematic way. Rather, individual members of the population can opt to pursue AJ genetic carrier testing.

Table 1.1: Factors required for population based genetic carrier testing programmes

A. Disease Characteristics	1. Well defined population at risk
	2. Prevalent and severe disease
	3. Limited phenotypic variability (predictability of disease severity)
	4. Lack of effective treatment
B. Characteristics of Testing	1. Straightforward interpretation of the test results
	2. High test sensitivity for carrier detection
	3. Cost effectiveness
C. Attitude of the Community	1. Involvement of the community
	2. Support of families and advocacy groups
	3. Consensus in favour of avoiding affected births

1.1.1 Overview of Genetic Carrier Testing Programmes

Targeted genetic carrier testing programmes in high risk population groups began in the 1970's with TSD in the AJ population, sickle cell disease (SCD) in the African American population and β -thalassemia in the Greek and Mediterranean communities (Cao, Rosatelli, & Galanello, 1996; Grover et al., 1983; Kaback, Zeiger, Reynolds et al., 1974). The genetic carrier testing programmes for TSD, and β -thalassemia remain successful models for the prevention of severe autosomal recessive genetic conditions (Angastiniotis & Hadjiminias, 1981; Kaback, 2001). Both of these programmes have achieved significant reductions in disease incidence (Laberge et al., 2010). Other programmes, such as the SCD programme in the United States of America have been less successful, owing to poor community involvement.

Tay-Sachs disease is a fatal condition that affects the nervous system, resulting in death between 2 to 5 years of age (Kaback & Desnick, 2001). The TSD programme has achieved a 90% decrease in the incidence of this condition among the AJ population in the United States of America (Kaback, 2001).

Thalassaemia is an inherited blood disorder where the body produces insufficient haemoglobin, the protein in red blood cells that carries oxygen. Beta thalassaemia occurs when there is a defect in the beta globin protein production. Survival rates for individuals with β -thalassemia have increased over the years because of improved treatments and they currently live for approximately 30 years (Cousens, Gaff, Metcalfe et al., 2010). In Cyprus, β -thalassaemia was considered a serious health concern with an incidence of 1/150 births and placed a large burden on the annual health budget (Angastiniotis & Hadjiminias, 1981; Cao et al., 1996). The incidence of the condition has substantially decreased due to genetic carrier testing in the Mediterranean, specifically in Cyprus, Sardinia and Italy (Laberge et al., 2010).

Although some screening programmes, like TSD and β -thalassaemia, have been very successful, SCD screening, initiated in the late 1970's in New York City, failed (Markel, 1992). The failure of the SCD programme resulted not only in stigmatisation of African Americans, but also in the misunderstanding of the differences between being an asymptomatic carrier and being affected with the condition (Markel, 1992).

The highest prevalence worldwide of SCD has been recognised in sub-Saharan Africa where millions of healthy individuals are sickle cell carriers (Diallo & Tchernia, 2002; Tshilolo, Kafando, Sawadogo et al., 2008). Many individuals die in early childhood from SCD. It is encouraged to have testing before marriage or prenatally in these areas. There is no current information that could reveal whether or not implementation of population screening is enforced in these African countries (e.g. Democratic Republic of Congo). Anecdotally, it has been noted in genetic counselling clinics in Johannesburg that this might not indeed be the case for some families. A number of immigrants from African countries north of the South African border have affected children and report not having

been tested before marriage or prenatally.

In a number of countries, such as Saudi Arabia in the Middle East, laws are in place that make premarital testing compulsory for SCD and thalassaemia before a marriage is approved in high risk populations (Alswaidi, Memish, O'Brien et al., 2012). However, studies have shown little success in decreasing high-risk marriages (Alhamdan, Almazrou, Alswaidi et al., 2007; Alswaidi et al., 2012). Therefore, the literature highlights the necessity for the implementation of educational programmes and increased availability of genetic counselling for high risk population groups (Alhamdan et al., 2007).

1.2 The History of Genetic Carrier Testing Programmes in the Ashkenazi Jewish Population

As previously mentioned, the history of Jewish genetic testing began with genetic carrier testing for TSD in the 1970's with the New York Jewry in the United States of America (Kaback et al., 1974). Physicians in several Jewish neighbourhoods worked together to educate Jewish women about TSD and their genetic risks, and offered them testing (Kaback et al., 1993). The initial stigma associated with testing was reduced by educating individuals, which resulted in a decrease in the number of children being born with TSD (Klugman & Gross, 2010).

In the early 1980's, The Committee for Prevention of Genetic Diseases, also known as Dor Yeshorim, began a genetic carrier testing programme for TSD for the ultra-orthodox community in New York, United States of America (Ekstein & Katzenstein, 2001). This programme promoted anonymous testing in young adults in an effort not only to prevent disease, but also to avoid the perceived stigma, which was proposed to be an outcome of knowing one's carrier status. The Dor Yeshorim testing programme meets the needs of the ultra-orthodox Jewish community, and has become a successful model of "genetic compatibility" testing for matchmaking purposes (Ekstein & Katzenstein, 2001). Matchmaking, also known as shidduchim, is a practice in the ultra-orthodox community whereby a couple is set up for the purpose of marriage by a professional matchmaker

based on their religious beliefs, values and personality attributes.

By 2001, through the Dor Yeshorim programme, more than 120 000 individuals had been tested with 118 689 tested specifically for TSD, more than 60 000 compatibility assessments performed, and 295 potential marital matches deemed inadvisable (Ekstein & Katzenstein, 2001). In later years, the genetic testing programme expanded to modern orthodox communities in the United States of America and major cities in Europe, while still maintaining its strict guidelines of testing premarital young adults anonymously (Ekstein & Katzenstein, 2001; Frumkin, Raz, Plesser-Duvdevani et al., 2011). Currently, the programme is available in the United States of America, Canada, Europe, Israel and Australia (Broide, Zeigler, Eckstein et al., 1993; Burnett, Proos, Chesher et al., 1995; Frumkin & Zlotogora, 2008). To date Dor Yeshorim still only offers genetic carrier testing for the 9 common AJ genetic conditions as opposed to the expanded panel offered in some international centers, which will be discussed in the following section.

1.2.1 Expansion in Genetic Carrier Testing Programmes

Many Ashkenazi carrier testing programmes now exist and include testing for nine or more common autosomal recessive conditions (Gross, Pletcher & Monaghan, 2008). This is evident in Israel and the United States of America, where genetic carrier testing panels for common AJ conditions are increasing to accommodate the needs and trends observed in these large communities. Scott, Edelman, Liu et al., (2010) recounted their successful experience with increasing the AJ testing panel to 16 conditions in the New York metropolitan area from 1996-2009, for which the AJ community was very supportive. With this expanded testing panel, they reported that 1 in 3 AJ individuals might be a carrier of at least one of the conditions and 1 in 24 of two conditions. The study also recommended testing both partners in conjunction with genetic counselling (Scott et al., 2010).

Testing centers in the United States of America, particularly in New York, Chicago, Philadelphia (Albert Einstein Medical Center), Boston (Tufts Medical Center and Floating

Hospital for Children) and Florida (University of Miami Miller School of Medicine) have expanded their testing panel to include 19 conditions commonly found in the AJ population (The Chicago Center for Jewish Genetic Disorders, 2008; Victor Centers for Jewish Genetic Diseases, 2012). The 19 conditions include the 9 common AJ conditions discussed previously and Dihydrolipoamide Dehydrogenase Deficiency, Familial Hyperinsulinism, Gaucher's disease, Joubert Syndrome, Maple Syrup Urine disease, Nemaline Myopathy, Spinal Muscular Atrophy, Usher syndrome Type 1F, Usher syndrome Type III, Walker-Warburg (The Chicago Center for Jewish Genetics pamphlet, 2012). While the current testing panel includes the 9 common autosomal recessive AJ genetic conditions with a typically severe prognosis, the additional conditions presented above do not all have the same debilitating or fatal outcome.

1.3 Common Ashkenazi Jewish Genetic Conditions

The AJ conditions range in frequency and birth rate in the community worldwide due to different community sizes. The overall rate for a Jewish individual to carry one of the 9 common autosomal recessive Ashkenazi Jewish conditions is approximately 1 in 5 (Fares, Badarneh, Abosaleh et al., 2008; Gross et al., 2008). Individuals may carry more than one autosomal recessive Ashkenazi genetic condition (Fares et al., 2008).

While genetic carrier testing panels have expanded in some centres, in Johannesburg, testing for the 9 common autosomal recessive genetic conditions are offered to individuals of AJ descent. A full description of these conditions can be found in Appendix A (ACOG Committee on Genetics, 2009; Charrow, 2004; Ekstein, Rubin, Anderson et al., 2004; Jenkins, Lane, & Kromberg, 1977; Storm, Crossley, Redman et al., 2004).

There are a number of other genetic conditions in the AJ community, which also occur at an increased frequency. However they are not included in the current AJ genetic carrier testing panel for a number of reasons including: the complexity of testing, penetrance (proportion of individuals with the mutation who exhibit clinical symptoms), inheritance patterns, treatment options, adult onset of symptoms, genetic testing costs and the

implications for other family members (Klugman & Gross, 2010). These conditions include Gaucher's disease, hereditary breast and ovarian cancer syndrome and torsion dystonia. Testing for these conditions is generally recognised as being advantageous in appropriate circumstances as it gives individuals the opportunity to make life-style changes, allows them to participate in early surveillance, and prophylactic surgery or other treatment that can reduce the likelihood of progression or even prevent the development of these conditions (Charrow, 2004).

1.4 Ashkenazi Jewish Carrier Testing Programmes available in Johannesburg, South Africa

Two independent AJ carrier testing programmes are available in Johannesburg, SA as discussed in section 1.2 and 1.4.1. The first carrier testing programme, Dor Yeshorim, although based in New York and in Israel, holds an annual blood collection day in Johannesburg. The other carrier testing programme is available at all times through the Division of Human Genetics, National Health Laboratory Service (NHLS) and the University of the Witwatersrand (Wits). Both programmes have distinct characteristics and requirements, but ultimately offer the same testing panel for the 9 common autosomal recessive Ashkenazi genetic conditions (Appendix A). Genetic testing is available locally for some other conditions in the context of carrier, predictive, symptomatic and/or prenatal testing. For example, genetic testing for Gaucher's disease and hereditary breast and ovarian cancer syndrome is offered at the Division of Human Genetics, NHLS and Wits in the context of a suggestive family history for the reasons discussed in 1.3. The two programmes will be discussed in more detail in sections 1.4.1 and 1.4.2.

1.4.1 Dor Yeshorim

Dor Yeshorim was established in New York in 1983 by Rabbi J. Ekstein, an ultra-orthodox Jew, to address the concerns of genetic carrier testing in this group of Ashkenazi Jews (Ostrer, 2001; Raz, 2009). As discussed in section 1.2, the programme is commonly used for matchmaking purposes in a community where arranged marriages are the norm, and the termination of a pregnancy is in general prohibited by Jewish Law (Zlotogora, 2009).

The programme has been encouraged by leading rabbis and has thus become a pre-requisite in ultra-orthodox matchmaking (Raz, 2009). The programme tests for the same 9 common AJ genetic conditions available locally (Appendix A) and has been shown to be successful globally in the ultra-orthodox Jewish community with a high acceptability of more than 95% (Raz, 2009). As Frumkin et al., (2011 p 4) state, “the programme has received both praise for its high uptake and success in reducing the number of births of affected children, as well as criticism for compromising personal autonomy and perpetuating the stigmatisation of presumed carriers.”

Dor Yeshorim carrier testing began in 2008 in Johannesburg, and takes place annually on a specified date at a Jewish community centre or when required for matchmaking/dating purposes.

Testing opportunities are advertised through religious Jewish schools, Jewish community newspapers and synagogue newsletters. Once individuals have had their blood taken, the samples are transported by a local Dor Yeshorim representative to New York (United States of America) to be analysed at several quality-controlled laboratories. Samples from across the world are coded with numbers and the results are stored on the Dor Yeshorim database for future matchmaking purposes (Ekstein & Katzenstein, 2001). No names are recorded on the blood sample, as results are not given to individuals. Individuals have the opportunity to contact Dor Yeshorim telephonically and give their personal code with a potential partner’s code to determine if they are genetically compatible before dating and/or a marriage is arranged. Matches are either described as “advisable” or “inadvisable.” Matches that are considered inadvisable are discussed with a Dor Yeshorim representative, and a genetic counselling referral is offered to a couple since they have both been identified as carriers for the same genetic condition and are at risk of having affected offspring (Ekstein & Katzenstein, 2001).

1.4.2 Division of Human Genetics, National Health Laboratory Service, University of the Witwatersrand and Lancet Laboratories

The Division of Human Genetics, National Health Laboratory Service (NHLS) and the University of the Witwatersrand (Wits) began testing for Tay-Sachs carrier status by enzyme analysis in the 1970's (Jenkins et al., 1977). In 2004, genetic carrier testing by DNA testing was offered for four autosomal recessive genetic conditions (TSD, FANC C, CF and CD), which, by 2008, had expanded to include the 9 common AJ genetic conditions (Appendix A). At present, TSD enzyme and molecular testing are done concurrently. The detection of one pathogenic mutation typically identifies the individual as a carrier, however only the most commonly known mutations are tested for and rare mutations may be missed. Appendix A lists the detection rates for the 9 common AJ genetic conditions.

Testing may be arranged by an individual's general practitioner, gynaecologist or another medical professional through Lancet Laboratories, which collects, bills and sends the samples for genetic analysis to the Division of Human Genetics, NHLS and Wits. Alternatively, blood can also be taken at the Division of Human Genetics, NHLS and Wits. Individuals interested in being tested may contact the Division of Human Genetics, NHLS already to book a genetic consultation to discuss their risks and testing options. The turn-around time for genetic testing is dependent on the tests requested, such as carrier or prenatal testing. Considering the urgent nature of prenatal testing, every effort is made to ensure the promptness of these results. Results are either sent to the referring medical professional or discussed with the patient directly at a follow-up appointment or telephonically by a genetic counsellor or geneticist.

Initially, carrier testing for TSD was based on the measurement of hexosaminidase A (Hex A) enzyme levels with an approximately 97% detection rate (Monaghan, Feldman, Palomaki et al., 2008). Enzyme activity is decreased in carriers with TSD but enzyme testing was found to overestimate the number of carriers. In Johannesburg, enzyme analysis is done on all individuals requesting TSD testing, as it is a cheaper option to begin with when doing TSD testing. If the enzyme activity is abnormal and an individual is

found to be a borderline carrier, a DNA test may clarify an individual's carrier risk. Full DNA testing is used to detect three common Hex A mutations commonly found in the AJ population (Yoo, Astrin, & Desnick, 1993). Full DNA testing generally detects 98% of AJ carriers for TSD since 2% of carriers in laboratory testing produce a false negative result (Monaghan et al., 2008).

The full testing panel of the 9 common AJ genetic conditions was previously performed using the Elucigene Ashplex 1 and 2 kit, which have recently been discontinued, and a CF kit that is still available. However, the NHLS has established an in house assay, which detects the same mutations in their laboratory for the AJ community in Johannesburg, SA. Ashplex 1 detected eight mutations in four of the most common diseases: TSD, FD, CD and FANC C. Ashplex 2 detected seven mutations in four different conditions, namely MLIV, GSD, NPD-A and BLM. Cystic fibrosis is tested separately using the Elucigene CF30 kit (introduced in July 2006), which uses allele specific amplification technology that identifies point mutations or small deletions in 30 CF gene mutations. There are 5 specific CF mutations that account for 97% of the CF alleles in the AJ population and are included in the CF30 kit (Abeliovich, Lavon, Lerer et al., 1992).

Between November 2001 and January 2007, a retrospective audit was performed at the NHLS, which examined the uptake of genetic carrier testing performed within the AJ population (Robinson, Essop, Mitchell et al., 2007). During that time period, 488 samples were received for testing for either the TSD enzyme only, or for the 9 common AJ genetic conditions including TSD. A number of samples (11) were rejected for different reasons. The majority of individuals (349 samples) had only TSD enzyme testing done. The results identified 28 carriers, 9 borderline carriers and 312 non-carriers. One hundred and twenty eight individuals underwent full Ashkenazi testing for the 9 common conditions, which identified 10 TSD carriers, 5 CF carriers, 2 NPD-A carriers, 1 FD carrier, 1 CD carrier, 1 BLM carrier, 2 MLIV carriers, 3 FANC C carriers and 103 non-carriers of any of the 9 conditions. The overall frequency of carriers detected for the 9 common AJ conditions at the NHLS was reportedly 1 in 8 (Robinson et al, 2007). Tay-Sachs disease enzyme testing was the more frequently requested genetic carrier testing method due to its known status in

the AJ community and among health care professionals and possibly due to the cheaper cost of this test (Robinson et al, 2007).

An updated audit at the NHLS was recently performed by the researcher to examine the number of individuals who had AJ genetic testing at the NHLS between 2007-2012. Over the five years, 876 samples were received for testing the common AJ genetic conditions, with 10 samples being rejected for various reasons. Tay-Sachs disease was still the most common AJ test performed with 669 enzyme tests carried out. Of those tested for TSD using enzyme analysis, 51 carriers and 25 borderline carriers were identified. One hundred and ninety-seven (197) individuals had the full AJ genetic testing performed (9 common AJ diseases and TSD enzyme). Of these, 12 were carriers for TSD, 9 borderline carriers for TSD, 7 FD, 4 CD, 5 FANC C, 3 MLIV, 2 GSD, 3 NPD-A, 4 BLM and 8 for CF. Seven individuals were found to be carriers for more than one disease mutation. Twenty-two individuals requested testing for a specific condition. Eight Ashplex 1 kits only were run, 7 Ashplex 2 kits only and 7 CF 30 kits. Of these, 2 were carriers for TSD, 1 CD, 1 BLM, 3 GSD and 2 CF. These tests may have been done to establish if an individual was a carrier for a specific condition if his/her partner was already found to be a carrier of the condition or if there was a family history of a condition.

The similarities and differences between the two genetic carrier testing programmes are summarised in Table 1.2.

Table 1.2: A comparison of the genetic carrier testing programmes: Dor Yeshorim and Division of Human Genetics, NHLS, Wits

Dor Yeshorim	Division of Human Genetics, NHLS, Wits
Tested when single for matchmaking purposes. Testing of married or engaged couples is not permitted.	Tested at any life stage: single, dating, engaged, married, pregnant couple
Both potential partners need to have had the test and receive a code to be checked by a matchmaker for compatibility	Individual testing- if one individual is found to be a carrier of a particular condition, the partner will choose to be tested for that condition only
Carrier status is never disclosed- testing is anonymous. Participants receive a unique identifying code but no result	Carrier status is disclosed with a medical laboratory report
If a match is deemed inadvisable, the matchmaker will not introduce the couple or at a later stage of dating, the Dor Yeshorim representative will speak to the couple who may be referred to genetic counsellors for further information	Genetic counselling is offered for reproductive risks and informed decision making
Every individual in a family needs to be tested: no cascade screening. Many individuals are tested and the results of family members are unknown.	Cascade screening for family members who may be at risk (process of systematic family tracing). Need to test fewer individuals
Programme costs are highly subsidized and thus testing is cheaper for the individual.	High programme cost for individuals, as done as a commercial test. Cascade testing can decrease cost in couples and families
Testing happens annually at communal locations in Johannesburg, or by special arrangement. Samples sent to New York, United States of America for analysis and personal codes are stored there.	Tested at Division of Human Genetics, NHLS and/or Lancet Laboratories at anytime

The benefits and challenges that exist in each of the testing options have yet to be explored in formalised research. It is important not only to determine why individuals choose to have testing or not, but also as to why one programme is chosen over another, as well as to ascertain whether individuals have an accurate understanding of their genetic risks and the implications thereof, and whether they are able to make informed choices. It is important

to explore genetic knowledge of carrier testing to understand perceptions in the Jewish community better.

1.5 Psychosocial Aspects of Genetic Carrier Testing

The literature has shown that the number of genetic conditions tested for in the AJ community internationally is increasing (Scott et al, 2010). Considering that an increased number of individuals with genetic conditions could be reached in this way, it is possible that the number of individuals seeking genetic carrier testing may also rise. It is therefore imperative to review the psychological and social aspects that arise through genetic carrier testing, to improve health communication, genetic counselling services and interventions for individuals and families (Cameron & Muller, 2009).

1.5.1 Understanding Genetic Risks and Genetic Knowledge

Education is a fundamental part of any genetic carrier testing programme. Genetic carrier testing programmes have been successful, but it is important to question whether individuals truly have an accurate understanding of the genetics and their risks. Research has shown that a poor understanding and/or misconceptions about genetic testing concepts and the meaning of the consequences for an individual and his/her family do exist (Lanie, Jayaratne, Sheldon et al., 2004). Several studies have shown that long-term retention of the meaning of test results is reduced, while others found higher levels of understanding when individuals had continuous access to information (Axworthy, Marteau, Brock, et al., 1996; Hegwer, Fairley, Charrow et al., 2006). The benefits of genetic awareness were demonstrated in a group of ultra-orthodox individuals who had higher genetic knowledge scores compared to less observant individuals. These individuals had been exposed to Dor Yeshorim, lived in a “Jewish centered” environment and had attended Jewish day school (Hegwer et al., 2006).

An individual’s understanding of his/her genetic risk is a debated subject in the field of genetics. Most genetic assessments offer individuals information about the likelihood of the development of a particular condition (Cameron & Muller, 2009). Risk communication

and understanding in a genetic counselling context involve patients feelings, beliefs and reactions to the overall concept of risk (LeRoy, Veach & Bartels, 2011). The manner in which individuals respond, cognitively comprehend and emotionally perceive a genetic risk is distinctive (Cameron & Muller, 2009). Research has shown that individuals have limited perception of risk information, and so they often extract the “gist” of the probability and then categorise their own risk as either low, moderate or high (Reyna, 2008). Genetic counsellors attempt to ensure that patients truly comprehend the meaning of their risk in order to make informed decisions.

1.5.2 Decision Making with regard to Genetic Carrier Testing

The motivation for genetic carrier testing has been described as an individual’s desire to increase his/her certainty of disease risk (Esplen, Madlensky, Aronson et al., 2007). Yet, some individuals still remain concerned about the psychological consequences of testing, while others are concerned about how it will relate to health insurance coverage (Godard, Pratte, Dumont et al., 2007). Few studies have addressed decision making with regard to AJ genetic carrier testing worldwide.

An individual’s needs dictate which genetic testing programme (Section 1.4.1 and 1.4.2) is used. This is demonstrated in an Israeli qualitative study amongst modern-orthodox Jews about their preferences for testing, either by an anonymous confidential programme (Dor Yeshorim) or an open testing programme (Frumkin et al., 2011). Diverse opinions were evident when participants explained their choices for testing with the different programmes. Some individuals reported social pressure from their community to use Dor Yeshorim testing. These individuals were critical of the programme as it dictated whom they could marry, whilst hiding information about their carrier status. Others felt that this programme offered them the cheapest and quickest way of testing (Frumkin et al., 2011). Overall, participants agreed that Dor Yeshorim is relevant for arranged marriages but not for “love marriages” where a couple’s commitment may already be made (Frumkin et al., 2011). In Frumkin et al’s study (2011), individuals whose matches were deemed inadvisable, still chose to get married but sought additional information about their situation from genetic counsellors. Some couples may seek genetic counselling after an

inadvisable match while others often do not pursue a potential spouse because of their carrier status (Ekstein & Katzenstein, 2001). These findings are relevant to the current study as an individual's preference to have genetic carrier testing may be informed by similar reasoning to that described above. Based on this, it is recommended that individuals needs and choices should be considered in the context of genetic counselling, especially with regard to genetic testing preferences.

1.5.3 Personal and Social Perceptions of Stigma of Genetic Carrier Testing

Research suggests that there may be psychosocial implications to knowing one's carrier status (Lewis, Skirton, & Jones, 2011; Moffett & Ross, 2011). This knowledge may be separated into aspects that question an individual's processing of the information, how it may be incorporated into their own self-image, what his/her emotional response will be to learning his/her carrier status and how genetic carrier testing programmes could lead to possible stigmatisation and discrimination. Lewis et al., (2011) reviewed several studies that assessed the psychological and social effects of knowing one's carrier status for a range of conditions. Emotional factors that were recognised were feelings of stigmatisation, anxiety and guilt (Lewis et al., 2011). One study found that individuals at risk for hereditary breast cancer have been shown to feel stigmatised as they consider themselves as feeling isolated, different or labeled. As a result, women with a low self-esteem were found to feel in general more vulnerable and distressed (Den Heijer, Seynaeve, Vanheusden et al., 2011).

Stigma can be defined as “an outcome that occurs when the negative social meanings attached to the discrediting attribute become linked to the individual” (Berger, Ferrans & Lashley, 2001). Stigma may be separated into five categories: the experience of actual discrimination towards a carrier, attitudes towards an affected individual, perceived or felt stigma, self directed stigma and discriminatory and stigmatising practices in health, services, legislation, media and educational materials (Van Brakel, 2006). Research has shown that an individual's health may be negatively influenced by knowing his/her carrier status for genetic conditions (Kenen & Schmidt, 1978; Van Brakel, 2006). An individual may have pejorative feelings towards him/herself, as well as being concerned for his/her

public persona (Kenen & Schmidt, 1978; Van Brakel, 2006). As shown with sickle cell disease in the 1970's and cystic fibrosis in the 1990's, affected individuals have been stigmatised and discriminated against through job opportunities or insurance coverage as a result of their carrier status (Kronn, Jansen & Ostrer, 1998; Markel, 1992; Wilfond & Fost, 1990). Revised research in this area is minimal but the principles addressed above still remain in the field of genetics.

For the purpose of this study, it is important to mention the goals of the Dor Yeshorim carrier testing programme. This particular programme's primary goal is to prevent a child being born with a genetic condition. Secondly, the programme aims to ensure that no social stigmatisation or discrimination takes place by the community, insurance carriers or employers (Ekstein & Katzenstein, 2001; Kronn et al., 1998). The Dor Yeshorim pamphlet states that their "programme was established to provide protection from predominantly Jewish genetic diseases, while safeguarding individuals from the psychological stigma of carrier status knowledge" (Dor Yeshorim Pamphlet, 2011). The rationale behind the programme is that not knowing one's carrier status reduces stigmatisation as carriers are never identified and cannot be labeled as "defective" (Raz, 2009). This is central in observant communities where couples are matched based on their similar backgrounds. The health of each partner and their future offspring is of great concern and young men and women are encouraged to marry at an early age with the purpose being to create a large healthy family (Ekstein & Katzenstein, 2001). Dor Yeshorim is effective in observant communities in that if a family is known to have a child who is a carrier; there is a fear that the marriageability of their other children and relatives could be threatened (Raz & Vizner, 2008).

Some studies have indicated that the anonymity provided by the Dor Yeshorim programme reinforces the power and burden of stigma as a result of non-disclosure (Raz & Vizner, 2008). The perception that being a carrier of a genetic condition is "bad" (Raz & Vizner, 2008), is echoed by one participant's opinion towards Dor Yeshorim, "Everyone wants to know what they got. This makes Dor Yeshorim anachronistic...it's better to know for yourself and to tell your partner. To confront it" (Frumkin et al., 2011).

1.5.4 Anxiety related to Genetic Carrier Testing

There are many components to consider when taking anxiety and its effect on genetic testing into account. Previously, anxiety was considered a motivating factor for individuals to be tested (Goodman & Goodman, 1982). However, this led to individuals using fear as a motivational force to make emotional choices rather than informed decisions (Goodman & Goodman, 1982). Lewis et al., (2011) showed that anxiety increased when individuals considered genetic carrier testing for a number of reasons that include: a fear of being a carrier of a genetic condition, what it would mean for their health and how it would affect their future offspring. Individuals felt that their status as carriers would affect their future social and reproductive behaviour (Levin, 1999). Other studies illustrated an increase in anxiety after individuals learnt more about the conditions and the carrier rate (Hegwer et al., 2006; Henneman, Bramsen, Van der Ploeg et al., 2001; Sher, Romano-Zelekha, Green et al., 2003). Anxiety related to genetic carrier testing has been shown to dissipate, subsequent to genetic counselling and written educational information (Bekker, Denniss, Modell et al., 1994; Watson, Marchant, Bush et al., 1992). Other individuals who were not pregnant yet and so had time to consider their reproductive options, were shown to display low levels of anxiety (Lewis et al., 2011) This supports the idea that screening for carrier status at an earlier stage of life is preferable as the benefits appear to outweigh the disadvantages.

1.6 Genetic Counselling and Reproductive Testing Options

The National Society of Genetic Counsellors (NSGC) defined genetic counselling as,

“the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease. This process integrates the following: Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence. Education about inheritance, testing, management, prevention, resources and research. Counselling to promote informed choices and adaptation to the risk or condition” (Resta, Biesecker, Bennett et al, 2006).

Genetic counsellors are health care professionals who assess the risk of genetic or inherited conditions in individuals, couples, their offspring, as well as of other family members. Genetic counsellors gather appropriate information, present the available options and facilitate informed decisions with their patients. It is common for genetic counsellors to address the fear and discomfort associated with the process of genetic testing in order to uncover which choice carries the least amount of ambivalence for the patient. Due to the sensitive nature of genetic tests, communication, support and non-directiveness is essential in genetic counselling (Turnpenny & Ellard, 2008).

Individuals or couples seeking genetic carrier testing for genetic conditions in general should ideally receive genetic counselling prior to testing. This is not always the case, as some individuals or couples are encouraged to have testing done by their general practitioner or gynaecologist, who request testing and communicate the results to their patient directly foregoing the necessity of genetic counselling. When a genetic counsellor consults with an individual or a couple, reproductive and genetic testing options are discussed so that informed choices can be made, especially in cases where two carriers of the same condition are identified. The consultation is important as a complete family pedigree is necessary for any other concerns to be addressed. Decisions around prenatal testing may not be straightforward and options for termination become complicated, particularly when religious parameters are involved as will be discussed further on.

1.6.1 Genetic Counselling in Johannesburg, South Africa

In Johannesburg, SA, genetic counselling is offered at the Division of Human Genetics, NHLS and Wits via clinics held at Donald Gordon Medical Centre, and several state tertiary hospitals. There are also genetic counsellors available for counselling who are in private practice. The departmental audits discussed in section 1.4.2 shows that TSD is still the condition for which genetic carrier testing is performed most often. Genetic counselling could therefore improve individuals and health care professionals knowledge about what genetic carrier testing is available. Genetic counsellors are trained professionals who are considered well educated regarding genetic conditions. At times, other medical professionals may counsel patients about their genetic risks, which may be

problematic since genetic conditions are complex and accurate and up-to-date information is necessary for a patient to make an informed choice.

1.6.2 Prenatal Testing and Reproductive Genetics

Prenatal genetic testing provides information about genetic conditions in an unborn fetus and is available locally in most private antenatal care settings, and in some state tertiary hospitals. It allows couples to make informed decisions regarding reproductive options and termination should a genetic condition be identified in a fetus. When both members of a couple are identified as being carriers of a genetic condition, a number of reproductive options are available. When pregnant, these include prenatal diagnosis by invasive techniques, such as chorionic villus sampling (CVS), amniocentesis, cordocentesis. Prior to a pregnancy, options include pre-implantation genetic diagnosis (PGD), artificial insemination by a donor, egg donation and/or adoption. The more invasive procedures provide definitive diagnoses but carry higher risks to the mother and/or the fetus such as early induction of labour and early miscarriage. It is an essential responsibility of the genetic counsellor to discuss options with a couple so they can be informed of all potential risks and outcomes.

1.6.2.1 Pre-implantation Genetic Diagnosis

Generally, an individual's desire to have healthy offspring is a fundamental parental instinct. With advancing technology in genetics, individuals are now able to pursue certain health and wellness advantages prior to a pregnancy. For example, PGD gives a carrier couple the opportunity to screen the DNA of embryos fertilised *in vitro* (IVF) and have only the unaffected embryos implanted (Handyside, Kontogianni, Hardy et al., 1990). However, PGD is only available to couples in whom the genetic mutations are known.

Pre-implantation genetic diagnosis takes place in combination with IVF and is therefore subject to similar pregnancy success rates. About 30% of IVF cycles lead to a successful pregnancy and 83% of those pregnancies result in a live birth (Popovsky, 2007).

1.6.3 Health and Medical Concerns in the Ashkenazi Jewish Population

Ultra-orthodox individuals usually seek medical help within their community and thereafter ask for rabbinic guidance about other resources. These individuals are often sceptical about seeking help outside of their community and so certain medical practices are not utilised (Ekstein & Katzenstein, 2001).

Procreation is a fundamental expression of Jewish life and Jews are encouraged to have children, fulfilling the Torah commandment in Genesis 1:28. “to be fruitful and multiply.” The issue of ending a pregnancy is a difficult one, as opinions vary over when life begins. Some interpret the Jewish Law (*halachah*) as saying that a fetus is “mere water until the 40th day after conception,” which is equivalent to approximately 6-7 weeks gestation (Mittman, Bowie, & Maman, 2007). Within Jewish law, termination of a pregnancy is only permitted under two circumstances; if a mother’s life is in danger, a termination may be carried out as her life is given the highest priority, or if the mother’s mental health is threatened, a termination may be performed (Brown, 1990).

A study undertaken in Israel showed that religious beliefs influenced the acceptance of invasive prenatal testing in Jewish women over 35 years of age when offered an amniocentesis. Ultra-orthodox women chose no testing, while 36% of the orthodox, 62% of the modern/traditional and 94% of the non-observant/secular women chose invasive testing (Sher et al., 2003). This research suggests that groups with different levels of Jewish observance regard reproductive issues differently.

1.6.3.1 Understanding Jewish Beliefs and Values

An individual’s religion, value system and principles influence decision making processes (Anderson, 1999). While some individuals follow religious rules strictly, others may follow a more traditional path or none at all. Judaism is not homogeneous; there are many subgroups, such as ultra-orthodox/haredi, hasidim, modern orthodox/traditional, reform, conservative and non-observant/secular (Fine, 1995; Kaback, 2001). Each group is defined by their own traditions, belief systems and practices. Such differences are evident when

assessing for example, ultra-orthodox versus Modern/Traditional Jewry (Berkowitz, 2008; Ekstein & Katzenstein, 2001). According to Mittman et al., (2007 p 231), “Orthodox Jews legitimize their normative behaviour almost exclusively through rabbinical precedence and Jewish law and tend to have limited contact with the secular world.” Traditional/Modern Jews, “tend to be more lenient in their religious practices, although less so than non-orthodox Jews, and are less concerned with asking a rabbi about what Judaism demands of them, but rather define it for themselves” (Fine, 1995 p 156). These differences in levels of religious observance may determine which medical practice each subgroup follows, and consequently, how these subgroups regard genetic carrier testing. The subgroups are not distinct and difficult to define.

1.7 MOTIVATION FOR RESEARCH

There is no published information about genetic carrier testing in the South African Jewish population. This is the first study which examines the genetic carrier testing programmes in the AJ population in Johannesburg, with a particular focus on AJs at different self-reported religious levels. More information regarding the utilisation by different subgroups will assist genetic professionals in determining which individuals use the service and when and why they request genetic testing to be done. This information will also illustrate whether certain aspects of the genetic service could be improved, as well as provide insights into genetic counselling for AJ autosomal recessive conditions in Johannesburg, SA.

Evaluation of participants’ knowledge with regard to genetic risks will guide genetic services to address any particular gaps identified from this study. The information gained from this study could also allow insight into the perception of stigma from a personal and social level. This study could contribute important information to the study of genetic conditions in the Ashkenazi Jewish community of SA, which may add value to genetic services for this population.

1.7.1 Aims

The first aim of the study was to investigate factors contributing to the utilisation of AJ genetic carrier testing services. The study also aimed to assess genetic knowledge related to carrier risks and to the autosomal recessive inheritance pattern. It also aimed to evaluate whether there were personal or social perceptions of stigma associated with being a carrier of an AJ condition.

1.7.2 Objectives

- a. To assess factors that influence the utilisation of the two Ashkenazi genetic testing programmes available in Johannesburg, SA (Division of Human Genetics, NHLS/Wits and Dor Yeshorim).
- b. To examine participants' genetic knowledge with regard to genetic risks and carrier status for the 9 genetic conditions tested in the AJ population.
- c. To establish if there are any psychosocial issues (e.g. stigmatisation) amongst those who have used Ashkenazi testing programmes available in Johannesburg, SA.
- d. To compare individuals who have undergone AJ genetic carrier testing and those who have not been tested.

2 SUBJECTS AND METHODS

This chapter describes the participants who took part in the study and the methods used to conduct the research. It includes a description of how the study was designed and implemented as well as the characteristics of the participants. The chapter concludes with a description of the manner in which the data were collected and analysed, as well as important ethical considerations.

2.1 Research Design and Procedure

The study used an online structured questionnaire to collect data. Descriptive statistics were used to analyse the data. The study began by gathering information through a literature review about the Jewish community and AJ genetic carrier testing, both locally and internationally.

A preliminary questionnaire was created and piloted to volunteers, which helped to refine the questions and clarify any ambiguity. Once changes were made, the study was advertised in several areas in an attempt to attract volunteers within the Ashkenazi Jewish community. All online questionnaires were collected and the data were analysed. Results were generated (Chapter 3) and conclusions (Chapter 4) were drawn from these results and discussed in conjunction with other research literature.

2.2 Setup and Scope

The study took place in Johannesburg, SA and targeted both male and female AJs between the ages of 18-40. As discussed previously (Section 1), the Jewish community in SA is predominantly AJ and so the study focused on this population. The study initially hoped to achieve a sample size of 150 participants but over the one-month of advertising it, a total number of 298 responses were collected and then analysed.

2.3 Participants

Participants included in this study were AJ individuals living in Johannesburg, SA who had or had not undergone AJ genetic carrier testing. Ashkenazi men and women aged 18 to 40 years were invited to participate. Subjects had to complete the online questionnaire between the 2nd May and the 1st June 2012. Sephardic Jews were excluded, as they are a minority group in Johannesburg and their genetic profile is different. Individuals not currently living in Johannesburg were discouraged from participating in the study by stating the Johannesburg-centric aim of the study in the information sheet (Appendix C) and also by advertising in Johannesburg based media only (discussed in the following section).

2.3.1 Participant Recruitment

A written advertisement to participate in the study was inserted in numerous Jewish community media. These included: weekly synagogue newsletters, the Jewish Report newspaper and an Internet community forum. Staff at all advertising facilities were contacted telephonically or by email and informed of the study. The reason to advertise the study on different sites was to recruit a wide sample of Jews with different levels of Jewish observance who accessed community information from different sources. The wording of the advertisement may be found in Appendix B.

Advertising took place over a one month period from the 2nd of May to 1st June 2012. The advertisement was placed three times on an Internet community forum, known as Johannesburg Jewish Community Forum (JJCF), which is an online newsletter in which individuals advertise for personal or professional reasons. Individuals who sign up to this forum receive daily emails with 25 advertisements, which are sent out to approximately 5 500 Jewish individuals. The advert was placed once in the Jewish Report, a weekly newspaper. Unfortunately, the advertisement only appeared in the final week of data collection due to their space constraints. It was also published in several synagogue newsletters over the advertising period, including the Chabads' of Strathavon, Norwood, Sandton, Savoy and Waverley and Ohr Somayach Glenhazel, Sunny Road Shul Glenhazel

and Ohr Somayach Sandton. Most synagogues have weekly newsletters that are distributed to congregants by email, on notice boards and/or in pamphlets. The advert was also placed in King David Jewish Day School newsletters.

2.3.2 Sampling Strategy

The sampling strategy selected for this study was purposive (Jupp, 2006), using only volunteer Ashkenazi Jews in Johannesburg, SA (Appendix C). An element of snowball sampling was identified in this study as participants recruited other individuals to participate. From the large amount of responses in a short time, it was apparent that there was a good response to the study. Individuals described hearing about the study via email and social networks on the Internet as seen through the online questionnaire whereby participants chose “other” in section 1 question 8 and qualified it with an answer.

2.4 Research Tool

The research tool was a structured questionnaire. Section 4 was modified from a previous study which assessed HIV and stigma (Berger et al., 2001). Their stigma scale was freely accessible on the Internet. The full questionnaire was designed by the researcher in discussion with the supervisors to answer questions about aspects of genetic carrier testing in the local AJ population (Appendix C). The questionnaire was adapted for online data collection by a website developer. The website domain, www.jewishgenetics.co.za was registered in March 2012, and participants were invited to complete the questionnaire online.

2.4.1 Information sheet, informed consent and completion of the online questionnaire

Participants were prompted and guided to continue with the questionnaire from the information sheet and consent form. Once data collection was complete on the 1st June 2012, the website was no longer available. A notification was created on the website that thanked potential participants for their interest in participating in the study and notified

them that the study was complete (Appendix D).

2.4.2 The online questionnaire

The web based online questionnaire was completed anonymously and took approximately 20 minutes to complete. Once a participant had read the information page and consented to continue by ticking a consent box, the questionnaire followed. Participants could not advance until all questions were completed and only then could they submit the questionnaire.

The online questionnaire consisted of 72 questions, which were divided into five sections: 1) Demographics, 2) Utilisation of testing services, 3) Knowledge, 4) Social Perception Stigma Scale (Berger et al., 2001), and 5) General questions. The questionnaire comprised the following details:

Section 1: Demographics (9 Questions)

- The demographic items included age, gender and relationship status (Questions 1 to 3). The purpose of these questions was to determine what life stage an individual was currently at, for example, single, engaged or married. The purpose of knowing this information was to understand at which stage in life individuals would want testing and whether it was influenced by their relationship status.
- Questions 4 and 5 established how many children a participant had and if they were planning on having more children.
- Question 6 and 7 asked participants the level of their Jewish observance. It was difficult to determine a participant's level of Jewish observance and so a Likert scale (Likert, 1932) was included in which an individual could rate themselves from 0 to 10 and then give a reason for this choice. Zero was characterised as non-observant and 10 as ultra-orthodox.
- Question 8 was aimed at assessing how individuals heard about the study. This question determined how the study was accessed.

- Question 9 asked whether the participants knew anyone with a genetic condition. This was to assess whether a participant's experience and/or knowledge of a condition influenced practice and risk perception.

Section 2: Utilisation of testing services (15 Questions)

The questions in this section were designed to focus specifically on uptake of AJ genetic carrier testing. Question 1 established whether an individual had had an AJ genetic test. The questions that followed changed depending on their first answer. If the answer to question 1 was positive, the following points were addressed (questions 2 to 8):

- The testing programme used
- The life stage at which an individual was tested
- Who recommended the testing
- How results were communicated
- Whether an individual was found to be a carrier or if the result was unknown.

If the response to question 1 was negative, the questions following this response were (questions 9 to 11):

- Whether an individual planned to be tested in the future,
- At what life stage would he/she pursue said testing
- Through which genetic carrier testing programme would he/she be tested

Questions 12 to 15 were used to explore the individual levels of anxiety caused by genetic carrier testing and about being a carrier. These questions explored whether or not an individual worried about being a carrier for a genetic condition and if they felt it would affect their future. The questions also attempted to elicit whether or not the participants felt AJ genetic testing was important for the community.

Section 3: Knowledge (7 Questions)

The questions in this section were used to evaluate the participants' knowledge of genetic

risks, including carrier risks based on the AJ carrier rate, autosomal recessive inheritance pattern and the presence of symptoms in carriers. A variety of scenarios were presented that included being a carrier or being affected with an AJ genetic condition as a result of an individual's parents' carrier status. Questions were asked in a multiple-choice format so that individuals could choose the answer they believed was correct. These questions were chosen to determine this groups overall knowledge and level of understanding of genetics. The questions were deemed important to assess knowledge relating to understanding the risks in autosomal recessive inheritance. This knowledge would be important for individuals to understand their test results.

Section 4: Perception of stigma (39 Questions)

As no validated scales for measuring stigma in genetic carrier conditions exist, the questions in this section were modified from a validated HIV stigma scale (Berger et al., 2001). The adapted HIV stigma scale was previously used successfully in other studies, involving genetic conditions (Moffett & Ross, 2011). Questions were adapted by changing terminology to fit the genetic context. Two statements from the HIV stigma scale were excluded from this study as the statements were considered inappropriate in this context. These two statements were: “people with HIV lose their jobs when their employers find out” and “most people believe that a person who has HIV is dirty.”

This section assessed participants' perceptions of stigma by asking them to respond as to how they would feel if they were a carrier of an autosomal recessive AJ genetic condition. This part of the questionnaire was done using a Likert scale. A neutral option was also added to this section of the questionnaire to determine if individuals were impartial to stigma. The inclusion of a neutral option and the adaptation of questions for genetic carrier testing may have altered the true validity of the original scale. A statistician was consulted and did not feel the validity would be impacted.

Section 5: General (2 Questions)

The last two questions of the questionnaire were created to assist in future genetic counselling education programmes and awareness campaigns. Participants were asked whether they would find verbal information about Ashkenazi Jewish genetic conditions valuable and what other methods of communicating information they would find useful.

2.4.3 Pilot Study

A pilot study was carried out using 6 participants who volunteered. They were Jewish work colleagues. These questionnaires were not included in the final cohort. Their responses to the questionnaire helped to assess internal consistency of the questions and to clarify any confusion or ambiguity. Small changes were made to clarify questions, by changing a few words. No additional modifications were made to the questionnaire.

2.5 Data Collection

Data was collected through an online questionnaire. Once a participant submitted the completed questionnaire, the researcher received the results via email in an Excel spreadsheet. The website designer coded the responses to format continuously in Excel. The Excel spreadsheet contained all the responses and was updated with each submission. The collected data was cleaned by coding certain answers and correcting spelling mistakes before data analysis began.

2.6 Data Analysis

This was a descriptive study and most of the data generated were calculated as frequencies and percentages. Variables were coded and the data in the Excel spreadsheet were analysed using an Excel Statistical Analysis application. Both univariate and multivariate tests were used to identify the similarities and differences in the utilisation of genetic testing programmes between the participants' understanding of genetics and their perceptions of stigma, measured by the modified HIV Stigma Scale (Berger et al., 2001).

Responses were calculated and are presented graphically in tables and figures as percentages (Chapter 3). Percentages were rounded off to the nearest whole number. A statistician was consulted to verify the data analysis.

2.6.1 Carrier stigma: Independent sample t-test

In section 4 of the questionnaire, participants were asked to consider, hypothetically, how being a carrier of an AJ genetic condition would affect them personally and socially, with particular emphasis on the perception of stigma. An independent sample t-test was performed to assess the significance of stigma. The independent-sample t-test evaluates the difference between two independent or unrelated groups (Kirkwood & Sterne, 2003). A modified model of scoring as that in Berger's HIV stigma Scale was used and recorded as follows: strongly disagree= 1; disagree= 2; neutral= 2.5; agree= 3; strongly agree= 4 (Berger et al., 2001). Neutral was added to the scale so that participants who did not have a strong opinion either way could be considered. A score of less than 2.5 would indicate little or no stigma and a score of greater than 2.5 would indicate stigma. Two items were reverse scored: questions 5 and 14. Items that are reverse scored invert the numerical value when the data are scored. This is done in order to ensure internal consistency. After reversing the scores on these two questions for analysis, scores were added up per individual to give a cumulative score. The range of possible scores was determined by the number of items on the scale (39), and the number of responses available (1-4). For this study the range was 39-156 (1x39 items to 4x39 items). Given that every individual answered 39 questions on stigma, the lowest score one could get was 39, indicating no stigma and the highest score was 156, indicating the highest possible stigma. For calculation purposes, each individual's total score was divided by 39 to get his/her average total stigma score. A new adjusted stigma score was executed by subtracting 2.5 from all the scores so that the scores ranged from -1.5 to 1.5 rather than from 1 to 4. This centered the range of score on zero. Therefore, if participants had a score of zero, they were neutral. If their average score was below zero, there was no stigma and if their score was above zero, there was stigma.

2.6.1.1 Personal and Social Stigma

The personal meaning associated with being a carrier of a genetic condition defined personal stigma (questions 2-5, 8, 12, 14-17, 20, 24, 25, 28, 29, 34, 35-36). Social stigma related to an individual's social relationships and identity with reference to being a carrier of an AJ genetic condition (questions 1, 6, 7, 9-11, 13, 18, 19, 21-23, 26, 27, 30, 31, 32, 33, 37-39) (Appendix C, Section 4).

The same approach as above (Section 2.6.1) was applied when the significance of personal and social stigma was assessed. There were 18 and 21 questions on personal stigma and social stigma, respectively. The lowest score one could obtain for personal stigma was 18 and the highest was 90. For social stigma, the lowest score was 21 and the highest 105. Scores were then divided by 18 or 21 to create an average score. A new adjusted stigma score was formulated by subtracting 2.5 from all the scores so that the scores ranged from -1.5 to 1.5. This centered the range of score on zero. An individual who scored above zero was one who felt stigma personally or socially and an individual who scored below zero was one without personal or social stigma.

2.6.2 Correlation analysis

Correlations are utilised to investigate the relationship between two quantitative, continuous variables. Pearson's correlation coefficient (r) is a measure of the strength of the association between two variables (Kirkwood & Sterne, 2003). In order to conclude the significance of comparing two variables, an r value of 0.5 or higher would need to be found.

Correlation analysis was undertaken by examining the whole sample on Excel 2011 using a Pearson's correlation coefficient to assess relationships between the following variables:

- Level of observance and genetic knowledge
- Level of observance and those tested/not tested
- Genetic knowledge and stigma

- Genetic knowledge and those tested/not tested
- Genetic knowledge and age
- Age and stigma
- Age and those tested/not tested
- Gender and stigma

Variables were calculated as follows:

- Knowledge: 7 questions were asked in section 3 of the questionnaire. Participants' answers were added together and they were given a score out of 7. This created a composite knowledge score.
- Level of observance: participants were asked to self-rate their level of Jewish observance on a scale of 0 to 10.
- Age: ages were grouped into four categories (18-25, 26-30, 31-35, 36-40). The ages in each category were then averaged to achieve a single number to use in calculations as this removed working with a range. The midpoint of each category was used.
- Gender: men were assigned a 0 score and women a 1.
- In section 2 of the questionnaire, participants began by answering whether or not they had had genetic carrier testing. Participants either gave a "yes" or "no" answer. For statistical purposes, those who responded "yes" were coded as 1 and those who responded "no" were coded with a 0. Correlational analysis was carried out with the two variables.
- Stigma: in section 4 of the questionnaire, 39 questions to determine the overall stigma associated with potentially being a carrier of an AJ genetic condition were asked. Participants' scores were calculated as described in Section 3.5.

2.7 Ethical Considerations

Anonymity and confidentiality of all participants who volunteered for the study was maintained as no identifying information was accessed through the online questionnaire.

Participants were made aware that they could withdraw from the survey at any time online. Informed consent was assumed by the participants' online acceptance to continue from the information sheet to the questionnaire and when they submitted their questionnaire. Participants could not withdraw once they had submitted the questionnaire. The participants were invited to contact the Division of Human Genetics, National Health Laboratory Service (NHLS) if they required any further information or had any questions and appropriate contact details were provided.

The research protocol was submitted in February 2012 and ethics approval was granted by the Human Research Ethics Committee (Medical), Faculty of Health Sciences, the University of the Witwatersrand, reference number M120284 on the 24th of February 2012 (Appendix E).

3 RESULTS

In this chapter, the results generated from all participants' completed online questionnaires are presented. The data were analysed using descriptive statistics and are presented graphically in tables and figures. The chapter begins with an outline of the participants' demographics. Following this, the data regarding utilisation of AJ genetic testing is presented, including both individuals who had genetic carrier testing and those who did not. Lastly, the two main findings with respect to participants' knowledge and perception of stigma are calculated and displayed.

3.1 Demographics of Participants

Two hundred and ninety-eight individuals completed the online structured questionnaire over a one month period from 2nd May to 1st June 2012. There were 1 215 total views on the website, www.jewishgenetics.co.za, over that time period, with 34 additional questionnaires started but not completed. Due to the anonymity of the website design, it is not possible to determine the number of times an individual accessed the website. The total number of views may not be reflective of the number of individuals who accessed the website since some individuals may have viewed it more than once from a single IP address.

3.1.1 Age and Gender

The individuals who participated in the study included 33% male (97/298) and 67% (201/298) female participants. Participants were categorised into four age groups ranging from 18 to 40 years. Figure 3.1 illustrates the distribution of these age categories. Most of the participants, 42% (126/298) were in the 26 to 30 year age group.

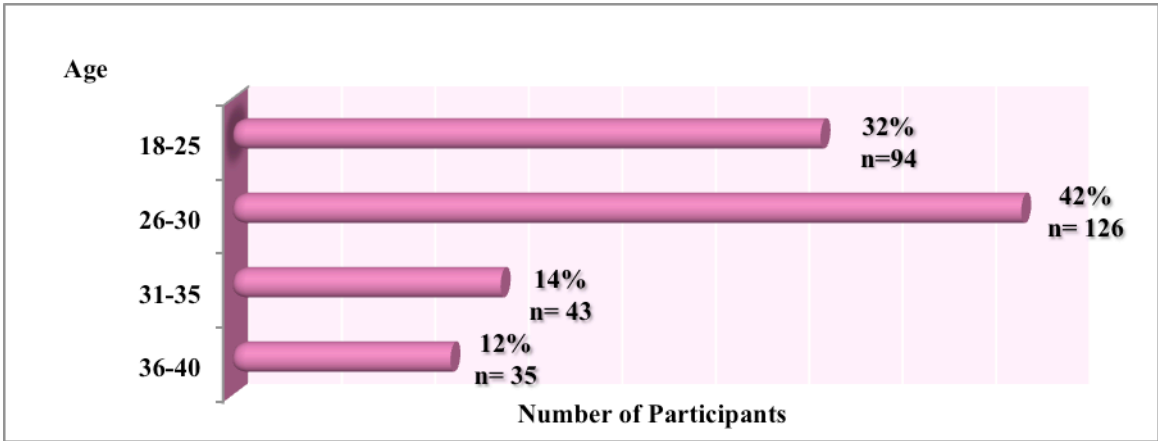


Figure 3.1: Distribution of the age categories of participants (n=298)

3.1.2 Relationship Status

Participants were further assessed by their relationship status at the time of participating in the study (Figure 3.2). Most of the participants, 48% (142/298) were married for the first time and 42% (126/298) were single and had never married.

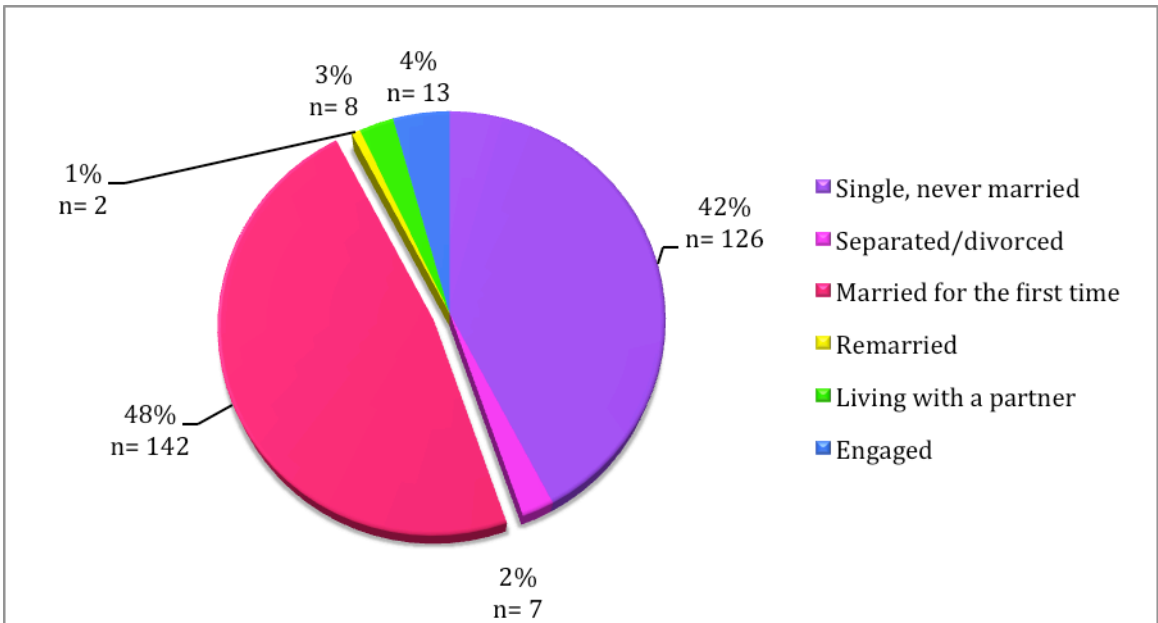


Figure 3.2: Participant's relationship status (n=298)

3.1.3 Number of Children

Participants were asked how many children they currently had and if they were planning

more children in the future. Figure 3.3 shows the number of children ranging from 0 to more than 6. None of the participants had 5 children. From the total sample, 68% (203/298) had no children and 32% (95/298) had children. Of those with children, most participants had 1 (14%, 41/298) or 2 children (13%, 38/298). Of those with children, most participants had 1 (14%, 41/298) or 2 children (13%, 38/298).

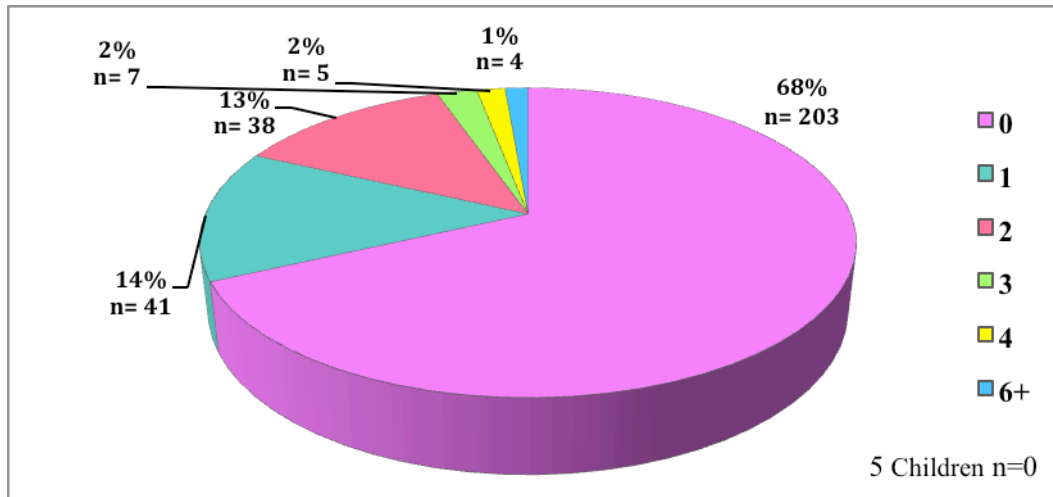


Figure 3.3: Number of children per participant (n=298)

A large proportion, 88% (263/298) of individuals reported that they planned to have more children in the future while 12% (35/298) of individuals did not plan on having more children.

3.1.4 Self-rated Level of Jewish Observance

Participants were asked to rate their level of Jewish observance subjectively, ranging from 0 to 10, with 0 being described as non-observant and 10 being ultra-orthodox. As seen in Figure 3.4, a large proportion of participants, 58% (171/298) rated their level of Jewish observance at 7 or above. The highest level of Jewish observance (10) was self-rated by 5% (16/298) of the participants.

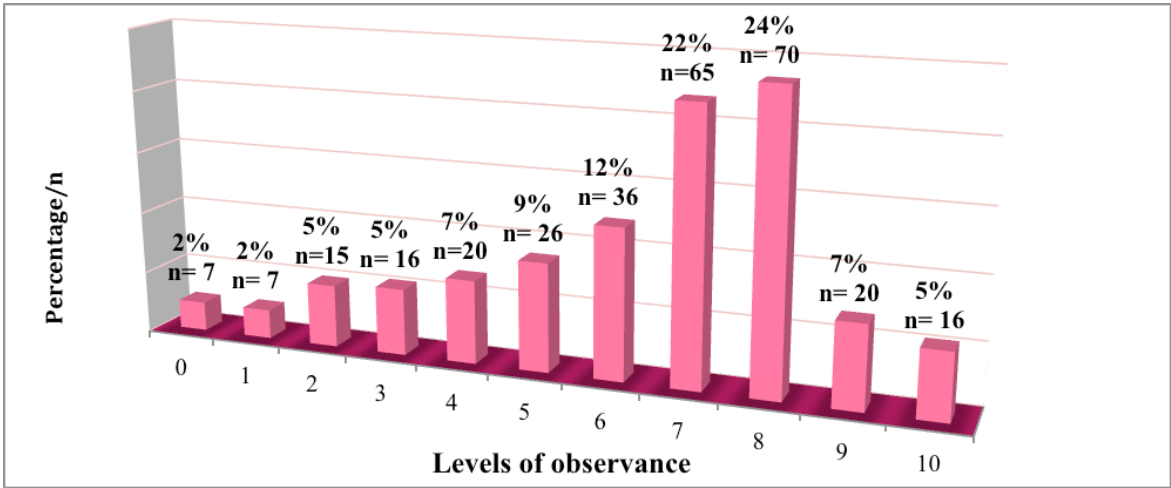


Figure 3.4: Self-rated levels of Jewish observance among participants (n=298)

3.1.5 Publication and Advertising of the Study

The study was advertised at several sites, including synagogues, Jewish day schools, one Jewish newspaper and one Jewish community Internet forum (JJCF). Thirty seven percent (109/298) of the participants became aware of the study through the Internet forum, followed by 31% (93/298) who heard about the study through a friend (Figure 3.5).

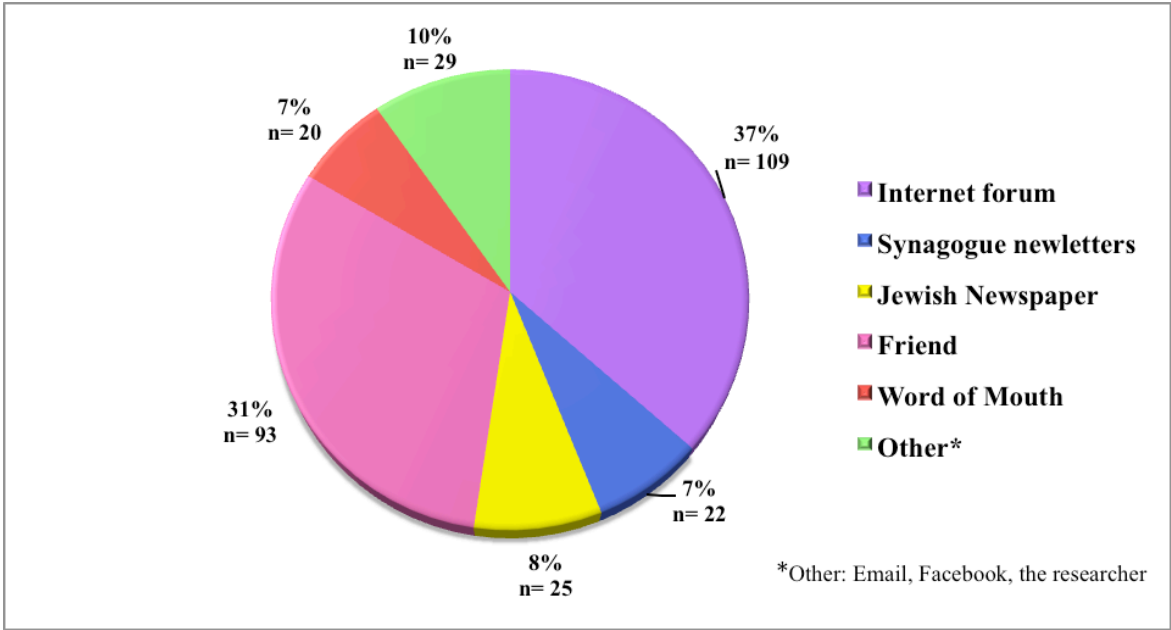


Figure 3.5: Participants access to the study (n=298)

3.1.6 Personal Experience with a Genetic Condition

The final question in the demographic section enquired as to whether individuals knew someone with a genetic condition. Most participants, 55% (165/298) did not know anyone with a genetic condition, while 45% (133/298) knew someone who had a genetic condition. The most commonly reported genetic conditions are illustrated in Figure 3.6. These responses account for 57% (76/133) of participants who answered “yes” to the above question. Other conditions were reported at a lower frequency.

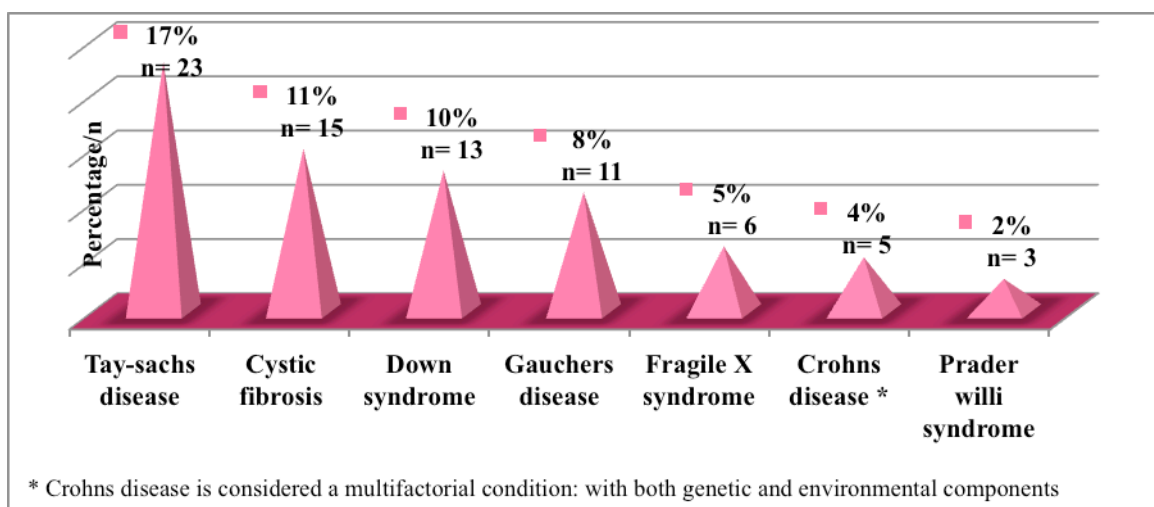


Figure 3.6: Genetic conditions commonly reported by participants who had personal experience of conditions (n= 76)

3.2 Utilisation of Ashkenazi Jewish Genetic Testing Programmes by Participants

This section was divided into two parts depending on the participants’ response to the first question, which enquired as to whether or not an individual had had Ashkenazi genetic testing. Those individuals who responded yes completed a different set of questions to those individuals who reported that they had not been tested.

Forty four percent (130/298) of the participants reported having had Ashkenazi genetic testing, while 56% (168/298) had not been tested.

3.2.1 Participants who had previously had Genetic Carrier Testing

Participants who had previously been tested were asked to complete questions 2-8 of the online questionnaire in section 2.

3.2.1.1 Genetic Carrier Testing Location

Of those who had been tested, the testing locations differed and are presented in Table 3.1.

Table 3.1: Genetic carrier testing location (n= 130)

Location	n	Percentage
Lancet Laboratories	83	64%
Division of Human Genetics, NHLS and Wits	16	12%
Dor Yeshorim	23	18%
Other*	8	6%

*In Israel or through a school programme.

3.2.1.2 Life-stage at which Genetic Carrier Testing was Performed on Participants

Of the 44% (130/298) of participants who were tested, the life-stage at which they chose to be tested differed (Figure 3.7). Many of the participants chose to be tested either when they were single (23%, 30/130), dating (24%, 31/130) or engaged (28%, 37/130).

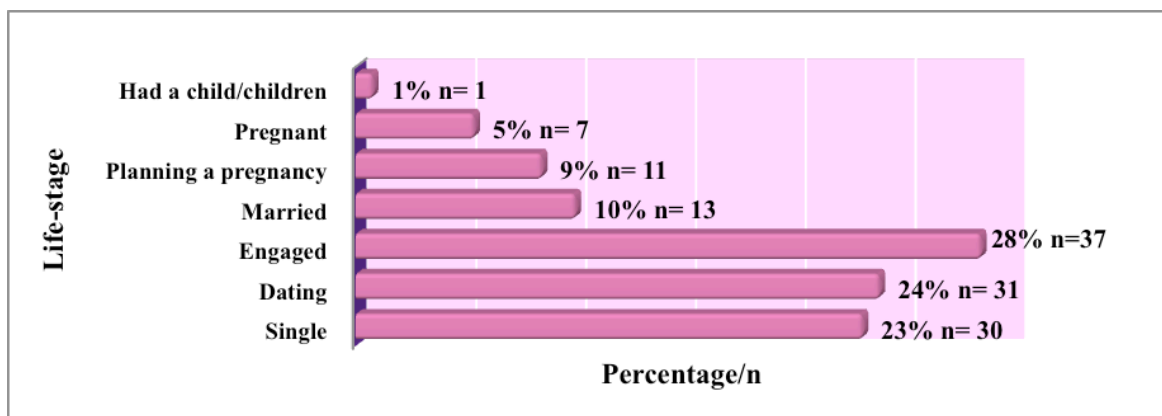


Figure 3.7: Life-stage at which genetic carrier testing was done (n= 130)

3.2.1.3 Type of Genetic Carrier Testing Performed on Participants

Of the 130 participants who had genetic carrier testing, the choice of which genetic carrier testing panel was requested varied (Table 3.2). Almost half of the participants (48%, 62/130) tested for the full Ashkenazi genetic carrier testing panel of 9 conditions.

Table 3.2: Genetic carrier testing panels performed on participants (n=130)

Question: Which genetic test did you have?	n	Percentage
Full Ashkenazi genetic testing panel (9 condition)	62	48%
Tay-Sachs disease only	55	42%
Gauchers disease only	2	2%
Smaller panel (Ashplex 1 or 2)	4	3%
Did not know	7	5%

Of the participants who were tested, a large proportion, 70% (91/130) reported not being a carrier of an AJ genetic condition, while 16% (21/130) of participants were reportedly carriers, and 14% (18/130) did not know their carrier status.

3.2.1.4 Testing Motivator and Communication of the Genetic Carrier Testing Results

This study assessed the participants' reasons to be tested and further examined how their

carrier results were communicated to them (Table 3.3). There was not one particular motivator for genetic carrier testing as results were divided among family, parents, education/school, gynaecologist and general physicians.

Table 3.3: Genetic carrier testing motivator (n=130)

Question: Who prompted you to be tested?	n	%
1. Family	13	10%
2. Parents	15	12%
3. Partner	7	5%
4. Future Partner	8	6%
5. Friends	7	5%
6. Rabbi	3	2%
7. Information pamphlet	5	4%
8. Education/school	22	17%
9. Other*	50	39%

* Other: (Broad category- responses coded and the most commonly reported are included) 18% (9/50) referred themselves to be tested, 26% (13/50) were prompted by their gynaecologist, 36% (18/50) by their general physician and 2% (1/50) by a matchmaker .

Significantly, the most commonly reported means of communication of the results was feedback from participants’ doctors (39%, 51/130), while the least reported communication was from a genetic counsellor (7%, 9/130). (Table 3.4).

Table 3.4: Communication of genetic carrier testing results to participants (n=130)

Question: How did you receive your results?	n	%
1. Doctor	51	39%
2. Dor Yeshorim representative*	19	15%
3. Genetic counsellor	9	7%
4. Gynaecologist	19	15%
5. General Practitioner	14	10%
6. Other**	18	14%

* Dor Yeshorim representatives do not give individuals their actual result. Couples are told that the match is either advisable or not.

** Other: (Broad category-responses coded and the most commonly reported included) Mail: 22% (4/18), Laboratory: 17% (3/18), Never given results: 28% (5/18), Never checked results: 6% (1/18) and Nurse: 17% (3/18).

3.2.2 Participants who did not previously have Genetic Carrier Testing

Of the 56% (168/298) of participants who did not have genetic carrier testing, most of the participants, 79% (134/168), reported that they would be tested in the future, while 21% (35/168) reported that they would not be tested.

3.2.2.1 Life-stage at which Genetic Carrier Testing would be Performed

Figure 3.8 illustrates at which life-stage the 79% (134/168) of participants planned to undergo Ashkenazi genetic testing. The life stage chosen most frequently by participants' was when they begin dating (30%, 40/168), followed by when planning a pregnancy (27%, 36/168). Interestingly, no participants reported that they would undergo genetic carrier testing when they were either pregnant or engaged.

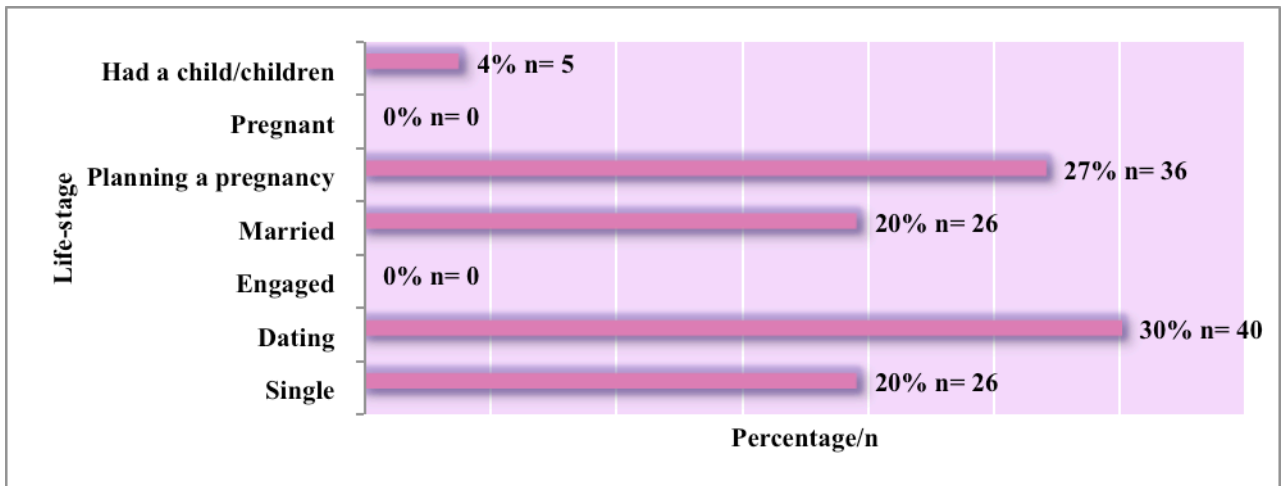


Figure 3.8: Life-stage at which participants planned to have genetic carrier testing (n= 133)

3.3 Attitudes of Participants towards Genetic Carrier Testing

When asked the question: “do you feel that individuals should have Ashkenazi screening tests?”, most of the participants, 47% (139/298), responded “strongly agree” or “agree” 37% (110/298), with only 14% (43/298) responding “neutral” and 2% (6/298) who did not agree.

When participants were asked, “do you feel it is important to know one’s carrier status for a genetic condition?”, 51% (152/298) strongly agreed and 39% (117/298) agreed, while only 6% (19/298) responded as being “neutral” and 3% (10/298) reported that they disagreed or strongly disagreed.

3.3.1 Anxiety of Genetic Carrier Testing

In order to assess anxiety, participants were asked whether or not they were worried about being a carrier of a genetic condition. The results showed that 30% (89/298) of the participants were indifferent, while 40% (130/298) were not worried and 30% (88/298) were worried.

When asked the question: “do you believe being a carrier of a genetic condition will affect your future?” 66% (198/298) felt that being a carrier of a genetic condition would affect one’s future, while 21% (63/298) were impartial and 12% (37/298) did not agree.

3.4 Understanding of Genetic Carrier Risks by Study Participants

Genetic and carrier risks were evaluated with seven multiple choice questions (Appendix C), which determined the participants’ understanding and knowledge of the inheritance pattern of AJ autosomal recessive genetic conditions, their knowledge of carrier risks, the risk of having affected offspring and their understanding of the implications of being a carrier of an AJ genetic condition. The responses to knowledge-based questions were arranged into three categories; “correct”, “incorrect” and “did not know”. The results are shown in Table 3.5 and Table 3.6.

Table 3.5: Questions of genetic carrier risks to assess participants knowledge (n= 298)

Question	Answer	Correct Answer		Incorrect Answer		Do not know	
		n	%	n	%	n	%
1 What is an individual's overall chance of being a carrier for at least ONE of the common AJ conditions?	1/5	38	13%	111	37%	149	50%
2 What is an individual's chance of <i>being a carrier</i> for a genetic condition if ONE of his/her parents is a carrier of a condition?	50%	105	35%	106	35%	87	30%
3 What is an individual's chance of <i>having a genetic condition</i> if ONE of his/her parents is a carrier of a condition?	< 1%	70	23%	145	49%	83	28%
4 What is an individual's chance of <i>being a carrier</i> of a genetic condition if BOTH his/her parents are carriers of a condition?	66%	18	6%	201	67%	79	27%
5 What is an individual's chance of <i>having a genetic condition</i> if BOTH his/her parents are carriers of a condition?	25%	67	23%	149	49%	82	28%
6 What is an individual's chance of <i>having a genetic condition</i> if BOTH his/her parents are carriers but of two different conditions?	< 1%	67	23%	106	35%	125	42%

A composite knowledge score was formulated to determine participants' overall score out of 7 questions. The results showed that no participants achieved a full score of 7. The majority of participants got 0 or 1 question correct, 26% (78/298) and 30% (89/298) respectively. Sixteen percent (48/298) of the participants got 2 correct, 10% (29/298) got 3

correct, 9% (28/298) got 4 correct, 7% (21/298) got 5 correct and 2% (5/298) got 6 correct. The mean score on knowledge was 1.7 with a standard deviation of 1.6, thus suggesting a poor knowledge of genetic concepts required to make informed choices about testing.

Table 3.6: Symptoms associated with being a carrier of a genetic condition (n= 298)

Question: If an individual is a carrier of a genetic condition, what symptoms will be noticeable?			
Answer	n	%	
No symptoms	155	52%	
Very few symptoms	17	6%	
Many symptoms	3	1%	
Only symptoms characteristic of that specific condition	42	14%	
Do not know	81	27%	

Participants were also asked about the type of symptoms a carrier of a genetic condition might be expected to have (Table 3.6 describes the responses). The results show that only 52% (155/298) of respondents chose the correct answer of no symptoms and 21% (62/298) had incorrect responses. Of those who chose the incorrect answer, 14% (42/298) said that an individual would have symptoms that are characteristic of that specific condition, while 6% (17/298) reported very few symptoms and 1% (3/298) chose many symptoms. An additional 27% (81/298) did not know the answer to the question.

3.5 Carrier Stigma

Scores were assigned, calculated and adjusted as discussed in section 2.6.1, and an independent sample t-test was performed to assess the significance of stigma (using a significance level of $\alpha=0.05$). The sample mean was -0.53, the standard deviation was 0.46 and the median was -0.46. The resultant t-statistic for this test was -22.6 with $p=1.0$. The null hypothesis was not rejected confirming that individuals were neutral and did not perceive stigma. Figure 3.9 reflects that the vast majority, 91% (269/298), of participants had a negative score which meant that they did not feel stigmatised by being a carrier.

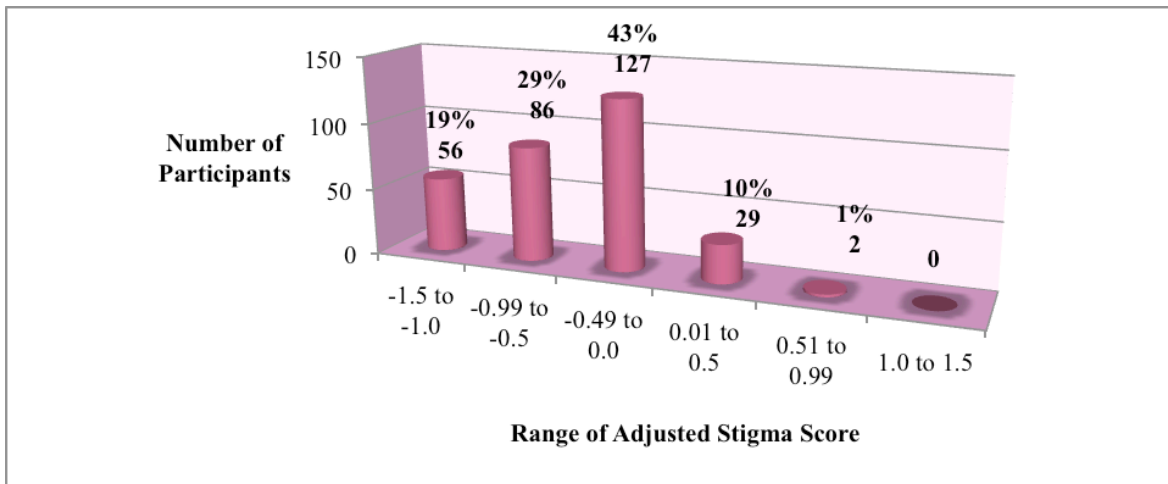


Figure 3.9: Range of adjusted stigma scores for carrier stigma (n= 298)

3.5.1 Personal and Social Stigma

Stigma was further divided into personal and social stigma, with participants being asked 18 and 21 questions respectively (section 2.5.1.1).

An independent sample t-test was performed with a null hypothesis that individuals are neutral with no personal stigma, while the alternative hypothesis was that individuals feel personal stigma with regard to carrier status. The sample mean was -0.42, the standard deviation was 0.49 and the median was -0.36. The resultant t-value for this test was -14.99, which corresponded to a p-value of 1.0. Therefore, the null hypothesis was not rejected, meaning there was no stigma personally attached to being a carrier of an autosomal recessive genetic condition.

Another independent sample t-test was performed with the null hypothesis that individuals are neutral with no social stigma, and the alternative hypothesis that individuals stigmatise others socially. The sample mean was -0.63, the median was -0.57 and the standard deviation 0.47. The resultant t-statistic for this test was -23.44, which corresponded to a p-value of 1.0. Again, the null hypothesis was not rejected, meaning that no social stigma was found to be associated with being a carrier of an autosomal recessive genetic condition.

3.6 Correlational Analysis

Correlations were performed using the variables described in 2.5.2 to determine whether or not a relationship existed between any two variables compared. Table 3.7 shows that all the correlation coefficients calculated were below 0.5, therefore no significance was found between any of the variables. The researcher chose not to use personal and social stigma as separate variables in this particular analysis since no stigma was identified in either groups with previous calculations.

Table 3.7: Correlational Analysis

Variable 1	Variable 2	Pearson Coefficient (r)
Knowledge	Level of observance	0.12
Knowledge	Stigma	-0.21
Knowledge	Individuals tested/not tested	0.16
Knowledge	Age	-0.09
Level of observance	Individuals tested/not tested	0.30
Age	Stigma	-0.07
Age	Individuals tested/not tested	0.11
Gender	Stigma	0.14

4 DISCUSSION

This study gives an overview of a sample of the individuals who identify themselves as Ashkenazi Jewish living in Johannesburg, SA. The results have indicated whether or not, and by whom AJ genetic carrier testing programmes are utilised. The study further assessed individuals' attitudes towards genetic carrier testing, their knowledge of carrier risks and the autosomal recessive inheritance pattern of genetic conditions. The results concluded with an examination of the psychosocial factors associated with genetic carrier testing, namely anxiety and carrier stigma. Stigma was also explored further with reference to personal and social influences.

This chapter will discuss any relevant aspects of these results, including the importance of future research and the potential applicability of the results within the practice of genetic counselling for Ashkenazi Jews who come for genetic carrier testing.

4.1 Demographics of the Participants

Ashkenazi Jewish men and women were the population of interest in this study. One of the main focuses of the study was whether or not AJ genetic carrier testing was being utilised in this particular population. The following interesting findings in the demographic sections were: age and gender of the participants, marital status and number of children and self-rated level of Jewish observance.

4.1.1 Age and Gender of the Participants

The highest response rate to the questionnaire was seen in the 26 to 30 year age group, followed by the 18 to 25 year age group. These results may indicate easier access and familiarity with the Internet in younger participants. Studies have shown that while Internet usage is growing exponentially, the percentage of adults who use the Internet is highest between individuals who are 18 to 29 (Zickuhr & Madden, 2012). Underwood,

Kim & Matier (2000) found that lack of access to, and familiarity with the Internet may undermine the participation of underrepresented minorities in Internet surveys. This may be a factor that clarifies the lower response rate in individuals over the age of 30 in this study (26%). Another factor could be that the study was less relevant to those who had had their children and were not planning on expanding their families further.

Most of the participants in this study were female 67%. This result is different to other studies that found that more men respond to surveys than women, particularly with respect to Internet-based questionnaires (Bech & Kristensen, 2009; Sax, Gilmartin, & Bryant, 2003). For example, Sax et al., (2003) showed that men were more inclined to respond to Internet surveys while women preferred paper surveys. It is difficult to determine why this study found that more females responded. One may postulate that the places the study was advertised could have played a role in this outcome or perhaps the topic of the study was more relevant to females than males.

4.1.2 Marital Status and Number of Children

The majority of participants reported that they were either married for the first time or single/never married. It was interesting to find that even though there was a large number of married participants, 68% of the sample reported having no children. This may be due to a bias of those who responded to the survey as it may have been more relevant to those planning a family. As seen in this study, 42% of the participants were between 26 to 30 years of age and so this finding may be attributed to the trend of having children at a later age (Cooke, Mills, & Lavender, 2012).

The study found that those participants who had children reported having typically 1 or 2 children. Only a small minority of participants had more than 3 children. Research in the United States of America has shown that ultra-orthodox individuals have a much higher rate of fertility (Wertheimer, 2005). The average fertility rate for Jewish women has been shown to range between 1.86- 2.65, while more tradition Jews generally have 3.3 children and ultra-orthodox between 6.6-7.9 children in a family (Sperling, 2010; Wertheimer,

2005). Similar fertility rates are evident in Israel where the average fertility rates for religious women is ~7.5 births per woman while the fertility rate of ~2.8 children per woman is observed in the general Israeli population (Landau, 2003; Remennick, 2006).

While it is not possible to directly compare these findings to the current cohort, it is noteworthy that the majority of participants (58%) self-rated their level of Jewish observance as ultra-orthodox and so one might have expected an increased number of children. Further research is needed to determine what factors play a role in the apparently more conservative family sizes of AJs in Johannesburg.

4.1.3 Self-rated Level of Jewish Observance

Participants rated their level of Jewish observance and were additionally asked to explain why they rated themselves as they did. These qualitative responses were interesting to examine, but were difficult to include in the study as the responses were subjective and could not be coded into similar groupings. There was also the concern from the researcher of a personal bias. When the researcher attempted to examine the self-rated scale by participants, it was found that many individuals chose a different number but characterised their religious observance with similar open-ended responses. For example, one participant chose 6 and one chose 8 but they both considered themselves to observe the same Jewish customs. Since the Jewish community in SA, especially in Johannesburg, is religiously diverse, quantifying participants levels of religious observance would have been challenging to perform objectively.

This question overall was difficult to characterise and the researcher proposed that those individuals who rated themselves as a 0 or 1, are more likely to be non-observant or secular and a 7 or above is more likely to be religiously observant. This study found that most individuals, 58%, classified themselves as religiously observant (Figure 3.4). The results may also be biased, as perhaps individuals who responded are more involved in the community based on their participation through the Jewish media advertising methods.

There were fewer responses in the lowest and highest levels of Jewish observance (Figure 3.4, page 38). A possible reason for this may be explained by the recruitment methods chosen for this study. When the study was designed, there was concern that individuals in the above two groups may be overlooked because of issues such as access to the Internet, interaction and participation in the Jewish community, lack of participation in Jewish media (Internet community forum and Jewish Newspaper) and/or not associating themselves with a Jewish identity. Both groups may therefore not be represented adequately for an even distribution of levels of observance to be considered. The researcher feels that it may be useful to use different recruitment methods in a follow-up study to determine if similar findings would have occurred had a larger participant sample been used and shown to be more evenly distributed. For example, recruitment could be carried out through personal interviews with those who identify themselves as ultra-orthodox with no access to the Internet. Individuals who appear to be less involved would be harder to identify, but using social media such as twitter and facebook, may be a more accessible channel to them.

4.1.4 Publication and Advertising of the Study

Participants were recruited by publishing the study in several Jewish community resources (section 2.1.1) in an attempt to draw individuals from different backgrounds (from non-observant or secular to ultra-orthodox). These places were purposefully chosen to reach different groups of Jewry with varying levels of Jewish observance. Most participants responded through the Internet community forum, JJCF, which has an estimated 5 500 users of which the majority may be more religious.

Many individuals viewed the website (perhaps on more than one occasion), with 298 completed questionnaires submitted and 35 discarded. The number of incomplete questionnaires may be due to the length of the questionnaire or a lack of interest. It is not possible to determine how many times an individual looked at the website or if individuals who initially did not complete the questionnaire, completed it at a later stage and were included in the study. Lower response rates were seen from the Jewish newspaper and synagogue newsletters, which could be due to timing. Individuals may have encountered

the printed advertisements on a Saturday, which is a Jewish day of rest (Jewish Shabbat), and so an inability to access the study online immediately might have resulted in a non response.

Many participants had heard about the study through friends or by word of mouth, indicating that the community is eager to participate in research and future research is possible in this population. Research has shown that Jews are enthusiastic to participate in research since the outcomes have implications for their own health (Rothenberg & Rutkin, 1998). Overall, the study illustrates that successful recruitment via the methods chosen in this study is possible as a larger sample size than initially calculated was easily obtained. Had the study been advertised for a longer period of time or more broadly, the sample size may have increased and been more representative of the community. However, this was not possible due to time constraints and the researcher achieved almost double the sample size as originally proposed.

4.1.5 Personal Experience with a Genetic Condition

Clinical geneticists and genetic counsellors understand the implications of genetic conditions and the risk to individuals and their families. Genetic counselling involves facilitating adaptation to a genetic risk or condition (Biesecker & Erby, 2008). The study found that 55% of the participants had no personal experience of an individual who has a genetic condition and so their knowledge about genetics may be poor. Forty five percent of the participants had interacted with someone who has a genetic condition. The most commonly reported known genetic condition was TSD, which was expected, as it is the most universally known AJ genetic condition (Section 3.1.6). Following this was CF, which is another well-known AJ genetic condition. The study did not explore the interaction or relationship participants reported in more depth so it is difficult to establish if this would have affected their decision-making abilities with regard to genetic carrier testing.

As the conditions are still relatively rare, it is possible that participants did not distinguish

between carriers and affected individuals. Gaucher's disease was known by 8% (11/298) of the participants. As previously discussed, Gaucher's disease, is an autosomal recessive genetic condition prominent in the AJ population but is not included in the full AJ genetic testing panel as it has a late onset and treatment is available. Other conditions that occur at similar frequencies in most populations include Down syndrome, Fragile X syndrome, Prader Willi syndrome and Crohn's disease. Most responses to this question were correctly recognised as genetic conditions so this question reflected a good understanding of what constitutes a genetic condition. The conditions reported are seen not only in the AJ population, but also in the general population. Educational programmes and genetic counselling can improve individuals' knowledge and understanding of genetic conditions overall and not just their risks.

4.2 Utilisation of Ashkenazi Jewish Genetic Carrier Testing Programmes by Study Participants

In this section, the use of AJ genetic carrier testing programmes was evaluated. Participants were asked whether or not they had had AJ genetic carrier testing and depending on their response, were guided to different questions on the online questionnaire. Section 4.2.5 deals specifically with recommendations from other studies that may be important to incorporate into current genetic counselling practices.

4.2.1 Participants who had previously had Genetic Carrier Testing

Of the 44% who had AJ genetic carrier testing. Lancet Laboratories send their samples to the Division of Human Genetics, NHLS Laboratory to have the testing performed. Most of the participants were tested through Lancet Laboratories or the Division of Human Genetics, NHLS and Wits. Results show that they tested the majority, 76%, of the participants. A minority was tested through the Dor Yeshorim programme (18%). The availability of Dor Yeshorim is limited as genetic carrier testing is generally undertaken once a year only at a local community center. Therefore it was expected that higher test numbers would be tested through Lancet Laboratories and the Division of Human Genetics, NHLS and Wits, as genetic carrier testing is available all the time, and both

laboratories are generally accessible across Gauteng and have been in place for many years.

While the Dor Yeshorim programme was established to meet the needs of the ultra-orthodox community, it was interesting to find that although a large proportion of the sample classified themselves as more religiously observant, the number of those tested through Dor Yeshorim was low. The Dor Yeshorim programme tests individuals only when they are single and will not test individuals who are engaged or married. This therefore affects the number of individuals who are tested through the Dor Yeshorim programme in Johannesburg. There may also be a bias in the sample, as individuals who classify themselves as ultra-orthodox, may not respond to such a study due to their religious practice of not using the Internet. Some individuals belong to very religiously observant communities and may refrain from the use of Internet in general but only use it for work purposes. This issue is echoed by the Dor Yeshorim programme as although it is an international programme, there is no website available to access information. Other factors impacting the participation in this study may have included time constraints, a lack of awareness of this study due to the publicising methods and/or a lack of interest in taking part in this study. Another factor may be that Dor Yeshorim was less accessible to many of the participants who responded from the 26 to 30 age group, as Dor Yeshorim began testing in Johannesburg only 5 years ago and so they would not have had the opportunity to be tested through their programme.

4.2.1.1 Life-stage at which Genetic Carrier Testing was Performed

Of concern was the finding that many of the participants chose to be tested when they were either engaged or dating. This has implications for their future since doing genetic carrier testing when they are already in a committed relationship is not ideal due to the stress a result may put on a couple. However, reproductive options such as PGD are available but couples may not know about them. Research has shown that genetic carrier testing done in high school and/or when an individual is unmarried may be preferable because reproductive options can be addressed earlier if an individual is identified as a carrier (Barlow-Stewart, Burnett, Proos et al., 2003; Mitchell, Capua, Clow et al., 1996).

Only 23% of the participants were single when they had genetic testing. There are certain benefits of being tested when single, including choosing a different partner and being aware of reproductive options available such as PGD should their future partner also be identified as a carrier of the same condition. It is possible that individuals do not get tested when they are single as they do not understand their genetic risks, feel it is not relevant or do not know about the genetic tests available, and therefore are never tested or neglect being tested until a time that they feel is suitable. Having genetic carrier testing later when a couple is already pregnant or not having it at all, may have consequences like an affected child being born because a couple was unaware of their genetic risks. This is plausible since it was noted that many participants test only when encouraged by their general practitioner or gynaecologist. This relates to the important responsibility of health care professionals to increase awareness and advocate for earlier testing. The community also needs to be involved in spreading an awareness about genetic carrier testing and the need for individuals to participate in testing.

4.2.2 Type of Genetic Carrier Testing on Performed

Of the 130 participants who had been tested, 48% tested for the 9 common autosomal recessive AJ genetic conditions. Four participants were tested for a smaller panel of conditions, which may have been because their partner completed the full AJ genetic testing panel and was found to be a carrier of a specific condition. So the partner was tested only for that specific condition. Alternatively testing was done before the full panel was in place in 2008. A further 42% of the participants had been tested for TSD only, performed by assessing an individual's enzyme activity. Tay-Sachs disease is the most well known AJ genetic condition with the highest carrier rate and is therefore a commonly chosen test. It appears that a large number of individuals are only offered testing for TSD and may be unaware of the other conditions common in the AJ community. As previously shown in the Division of Human Genetics NHLS audit in section 1.4.2, most individuals are still only having testing for TSD. The discrepancies between these two sets of results are concerning as which result is more reflective of current practice is not currently distinguishable. This supports the great need for genetic education and awareness to be

increased not only amongst health care professionals but also AJ community leaders and members.

Testing for Gaucher's disease is offered when there is a clear family history of the condition or when an individual has symptoms of the condition. In this study, only two individuals reported being tested for Gaucher's disease. At present testing for Gaucher's disease is not incorporated into the 9 common AJ genetic carrier testing panel due to the cost of the test. The condition's prognosis is comparatively less severe than the neurodegenerative and fatal conditions of the 9 common AJ genetic carrier testing panel. There is treatment available for Gaucher's disease and some affected individuals live without any clinical manifestations.

In future, the AJ genetic carrier testing panel in Johannesburg, SA, may increase to include additional conditions seen at a higher frequency in the AJ population as offered in the United States of America by some private laboratories (Scott et al., 2010). Scott et al., (2010) have expanded their panel to include 16 AJ genetic conditions in New York, United States of America (Section 1.2). This panel has gained acceptance in the Jewish community and such a programme would likely be accepted in the local AJ community too. These conditions (Section 1.2.1) may be important to consider for the expansion of the current 9 AJ genetic carrier testing panel. However, increased awareness through education about genetic carrier testing and the services currently available should be implemented first before the testing panel is increased. It is also important to mention that the implementation of such a panel would necessitate more patients requiring genetic counselling. This is a concern currently as there are significant staff shortages (i.e laboratory and genetic counselling staff) in the Division due to budget restraints and a lack of resources including personnel.

4.2.2.1 Participants' Carrier Status

The carrier rate for an AJ genetic condition worldwide is 1 in 5 (Fares et al., 2008; Gross et al., 2008). A carrier rate refers to the number of individuals in a population who have

inherited a single copy of a specific recessive gene mutation. Seventy percent of the participants in this study who had testing, were reportedly found not to carry a common AJ autosomal recessive condition, and 16% were found to be carriers which is in line with the expected carrier rate. This may not be a true reflection of the accurate carrier rate as the participants may have had different tests performed. Those who did not know their carrier status, (14%) were identified as having been tested through the Dor Yeshorim programme so their results were not disclosed to them.

Research into the psychological impact of population based carrier testing for CF over a 3 year follow-up, showed that some individuals may not be able to recall their carrier status after time has passed (Axworthy et al., 1996). The study showed that in the long-term, retention of the meaning of test results is poor. This was reflected in individuals who were tested for CF in London, United Kingdom, of whom 20% of the carriers and 50% of the non-carriers could not recall their carrier status three years after receiving their results (Axworthy et al., 1996). This is a concerning factor and further highlights the question as to when is the most appropriate time for individuals to be tested. The researcher therefore infers that it is important to improve the performance of test-related counselling before and follow-up programmes after to ensure the main objectives are met such as providing information on carrier status and informed reproductive decisions. Counselling before genetic carrier testing would ensure that an individual would understand his/her carrier risks based on a specific pattern of inheritance and that he/she would better understand the conditions. Follow-up sessions should include results giving in a sensitive manner and discussion about reproductive options should a positive result be confirmed.

4.2.2.2 Testing Motivator and Communication of the Genetic Carrier Testing Results

Participants were asked who prompted them to be tested and the resultant findings have several implications; it was expected that general physicians (GP) and gynaecologists would have encouraged AJ genetic carrier testing. However, from the options participants chose in the questionnaire (section 2; question 5), it was apparent that health care professionals still prefer to test for TSD over the full AJ genetic testing panel. This is of concern since the carrier status of many individuals may be missed, which will have

consequences for the individual, their family and their offspring. It is therefore imperative that health care professionals are continuously educated with regard to genetic carrier testing opportunities so that the correct information is given to patients. Subsequently, individuals and couples could make informed decisions, particularly for reproductive purposes.

Since most of the individuals described themselves as more religiously observant, it is surprising to find that rabbinic referrals in this study account for only 2%. Steiner-Grossman & David (1993) established that rabbis are often in a position to discuss AJ genetic testing with religious couples, but that they may neglect to do so in detail due to their own lack of knowledge and preparedness. Along with many Jews, rabbinic leaders may misjudge the carrier rate of AJ genetic conditions. Since only a small number of babies are born every year with a genetic condition, misperceptions are created that consider genetic conditions as rare. Many conditions are rare individually but common collectively in high-risk population groups.

This study further found that there is a low rate of information being conveyed through information pamphlets and schools (Section 3.2.1.4). Research studies have reiterated the need for an increase in education and awareness to ensure that more individuals are aware of the availability of AJ genetic testing programmes (Acharya, Lang & Ross, 2009). This holds true for the local population too, who would benefit from an increase in their knowledge and awareness about genetic carrier testing for AJ conditions. However, this is hard to achieve at present due to not only the high costs of marketing such awareness but also the limited members of staff available. Perhaps the creation of a website with a specific focus on Ashkenazi Jewish genetic testing would be feasible. This would allow a large number of individuals to be educated about their risks and their reproductive options. The need for genetic counselling following a positive result should be strongly emphasised.

The results of this study show it is important to consider the manner in which results are communicated. It has been shown that an individual's doctor or gynaecologist usually relays carrier results. The least frequent manner in which results are communicated is

through a genetic counsellor. This finding may illustrate that fewer individuals seek genetic counselling, which may show a lack of knowledge about the genetic counselling service and a need to promote the service to the AJ community. Sixty four percent of the cohort were tested through Lancet Laboratories, where genetic counselling is not offered routinely. Results may be fed back to patients through the health care professional who requested the test.

One needs to consider whether or not the recipients understand the implications of the results and if not, seek clarification from an informed source. At the Division of Human Genetics, NHLS, results are only made available once a genetic counsellor has discussed the testing implications with the patient. In this study two individuals who were reportedly tested in the United States of America, received their results through the mail. This goes against the policy of the Division of Human Genetics, NHLS and Wits. Research has shown that individuals misinterpret genetic concepts (Lanie et al., 2004) and this current study confirms this, evident from the participants' lower comprehension of genetics.

4.2.3 Participants who had previously not had Genetic Carrier Testing

Of the 56% (168/298) participants who had not had AJ genetic carrier testing, most described a desire to be tested in the future. This finding was encouraging as it may confirm that participants are aware that genetic carrier testing is available or perhaps that it would be important for them to have genetic carrier testing. Some participants reported that they would not choose to be tested as they already have children. This could indicate that either their family is complete or that they have a misconception that if they already have healthy children, future children are not at-risk. Others were not interested in genetic carrier testing, 21%, as their partner had already been tested and was found not to be a carrier of an AJ genetic condition. This is appropriate as two carriers would need to be identified for offspring to be at risk. If an individual's partner had been found to be a carrier of an autosomal recessive AJ genetic condition, the other partner should be offered testing for that particular condition and thereby know the risks for future offspring to be affected.

4.2.3.1 Life-stage at which Genetic Carrier Testing would be Performed

Many participants specified that they would prefer to participate in AJ genetic carrier testing when they were either dating or planning a pregnancy, while fewer participants felt that they would be tested when they are single or married. This is a noteworthy finding since most AJ genetic testing programmes promote testing ideally in early adulthood, and particularly when an individual is single as previously mentioned in Section 4.2.1.1. It has also been shown that anxiety is increased for genetic carrier testing when a couple is contemplating a pregnancy or are already pregnant (Ormond, Iris, Banuvar et al., 2007). Genetic services need ideally to address this issue so that individuals can be informed of their genetic carrier risks prior to being involved in a relationship or pregnancy. It is also important to mention that the timing of testing will affect and potentially limit the testing options available. For example, the turn around time for results may take between 6-8 weeks so couples planning a pregnancy would need to be aware of that time frame. Other couples who are already pregnant would need to discuss prenatal options for testing and what a positive test result would mean for the pregnancy if both parents are found to be carriers. In general, different genetic carrier testing options would apply to each situation, which supports the need for genetic counselling at the appropriate time.

4.2.4 Factors in implementing Genetic Carrier Testing

This study shows that there are many different factors involved in the utilisation of genetic carrier testing and so presented below are some suggestions from other studies to improve uptake of services.

The original AJ population genetic carrier testing programme was initiated in Montreal in 1972. Senior students were educated in high school, offered genetic carrier testing for TSD and then offered genetic counselling when their results were given to them (Beck, Blaichman, Scriver et al., 1974). The programme was evaluated 20 years later and it was found that the average uptake of voluntary testing in the high school based programme was 67% (Mitchell et al., 1996). As a result of the genetic carrier testing programme in high schools, the incidence of TSD in Quebec decreased by 95% (Mitchell et al., 1996).

In 1981, Austein, Seashore & Mick assessed the feasibility of screening single Jewry for TSD using a sample of college students at Yale University in the United States of America. The study established that 32% favoured testing in high school, 21.3% in college, 33.7% before marriage, and 8.4% before a pregnancy. Most students wanted to know their carrier status while single or before marriage. The study also revealed that mate selection would not be affected by an individual's carrier status (Austein et al., 1981). The study supported genetic testing at an earlier life stage, specifically on college campuses as this site was shown to improve efficiency of delivery. Genetic carrier testing has been offered to high school students over the years as it is viewed as a critical time for education and making informed decisions. School-based programmes have proven to be successful in some countries like Australia and Canada, but the involvement and the support of the community is essential for its success (Barlow-Stewart et al., 2003; Mitchell et al., 1996). An individual's parents would need to consent to a high school programme if individuals were under 18 years of age.

As seen with the success of the Dor Yeshorim programme in the ultra-orthodox community, the support and encouragement of the community and rabbinic leaders has been tantamount to its growth worldwide. This is currently an issue in the local community as the need for awareness and education about genetic carrier testing needs to be promoted and established in the community.

Whether or not mandating genetic carrier testing for AJ genetic conditions would be beneficial for reproductive purposes, is a question that needs to be explored further. As seen in Section 1.1.1, the mandate to test high-risk population groups has not been shown to decrease high-risk marriages in some cases. As far as this study is concerned, there is a need for evaluation and reflection about the best time and at what life-stage individuals should be tested. Perhaps more research is necessary for appropriate genetic services to be implemented and developed further in the AJ community in South Africa and worldwide.

This study shows that most respondents who had not been tested, would be receptive to having AJ genetic carrier testing in the future. For those 21% (35/168), who stated that they would not be interested in testing, the main reasons were that their spouse had been tested and was found to be negative and/or they had already had their children. Both of these responses are understandable since the risk of a genetic condition would have decreased. Others stated that their spouse had converted to Judaism so there was a smaller chance of him/her being a carrier of an AJ genetic condition, as he/she would be part of a different population group and less likely to carry the same genetic condition. Ashkenazi Jews have been somewhat successful in retaining their genetic profile over many years, but this does not mean that other population groups are exempt from the same conditions. So it would still be important to test a spouse for the more common conditions such as CF and TSD. Lastly, other participants responded that they were not interested in being tested at all. One cannot determine if this is attributable to a genuine lack of interest or if their awareness of genetic conditions is poor. Other individuals said they did not know about testing and if they did they may be inclined to have genetic testing. Educational programmes about genetic risks are provided in the AJ community in Johannesburg, but their frequency of these needs to be increased. For example, programmes are incorporated into some Jewish day schools, Rabbinic Associations and Jewish media such as pamphlets and community forums. Education about genetic risks and AJ conditions is critical to establish health interventions that are encouraged by community leaders and health care professionals.

4.2.5 The Future Implications of Genetic Carrier Testing

Section 4.2 has shown that most individuals are generally only tested for TSD, while the 9 common AJ conditions are often not tested for by medical professionals. As discussed in section 4.2.2, testing practices locally are problematic based on this finding. Once issues around acceptance of the current programme and improved community engagement have been dealt with, it will be possible to introduce additional improvements to the existing programme. For example, the issue of expansion could be dealt with and implemented. The first concern is how can the local panel of 9 AJ conditions be expanded if the uptake is already low. Secondly, pan ethnic testing needs to be considered as a result of

intermarriage within the AJ community and other religious groups. This refers to groups that are independently distinguishable but are then encompassed into one group of people. Other conditions may start to factor in when genetic carrier testing is offered since the founder effect for AJs may be less common in the future and other conditions may become more prevalent (Klugman & Gross, 2010).

To address these two concerns, initially additional research would need to be done not only to determine the acceptance of an expanded programme but also to implement an educational programme within the AJ community. Educational programmes should focus on medical professionals as this would increase referrals for genetic carrier testing. Ideally, genetic carrier testing should be carried out in consultation with trained genetic counsellors who can address patient concerns. This can only be achieved if the AJ community and medical professionals obtain a more thorough genetic education that includes discussion of their risks and what genetic carrier testing is available.

4.3 Attitudes towards Genetic Carrier Testing

Motivations and attitudes towards genetic carrier testing is very individualised. Some individuals demonstrate a desire to know their risk for a genetic condition which prompts them to be tested (Esplen et al., 2007). The majority of individuals supported having AJ genetic testing. Additionally, 90% of participants showed that they valued knowing their carrier status. Jallinoja, Hakonen, Aro et al., (1998) found that most individuals approve of genetic testing in general, but have some ambivalence towards certain aspects of the testing such as the concern of genetic discrimination, the potential increase in termination of pregnancies, anxiety in decision making situations and ignorance about genetics. They indicated that the most acceptable purpose for genetic testing was the “right to know about one’s genes so that one can influence one’s own health and life” (Jallinoja et al., 1998). Although this study highlighted no opposing attitude towards genetic carrier testing, other research has shown that some individuals do not value genetic carrier testing and future research in this area may be beneficial.

4.3.1 Anxiety regarding Genetic Carrier Testing

Anxiety with regard to genetic carrier testing was explored using two questions in this study that displayed interesting results. Participants were first asked if they worried often about being a carrier of a genetic condition, and most responded that they were not concerned. Participants were then asked if they believed that being a carrier of a genetic condition would affect an individual's future. Over 66% of those individuals responded that being a carrier of a genetic condition would affect an individual's future. This study did not ask participants in what way it would affect their future but an assessment of this would be beneficial. Anxiety has been shown to be elevated in carriers as those individuals feel that their carrier status "would affect their future social and reproductive behaviour" (Levin, 1999). This is a conceivable reason as to why so many participants felt that being a carrier of a genetic condition would affect their future. This has been echoed in a study by Lewis et al., (2011) who demonstrated that carriers of a genetic condition like CF have intensified anxiety when considering what their carrier status will mean for them and their future offspring.

Anxiety related to genetic carrier testing has been found to dissipate with time, subsequent to genetic counselling and written educational information (Bekker et al., 1994; Watson et al., 1992). Ormond et al., (2007) ascertained that balancing the information given to an individual or couple could control anxiety. Information needs to be considered not only on a case by case basis but also how much detail or brevity is necessary (Ormond et al., 2007). This reaffirms the importance of genetic counselling ideally prior to, but also after genetic carrier testing to address individuals' different needs, coping mechanisms and emotional reactions.

The research literature has also proposed that in general, religious and spiritual beliefs influence risk perception and decisions about undergoing genetic carrier testing (White, 2009). Although this notion was not explored in this study, some religious individuals whose spiritual values are important may find genetic carrier testing in opposition to their moral beliefs. Interestingly, religious and spiritual values have been shown to assist individuals in coping with their genetic risks (White, 2009). Both issues need to be

acknowledged in a genetic counselling setting and perhaps a limited religious assessment should be done to determine any conflicts with genetic carrier testing.

In general, anxiety is influenced by a number of factors which all play a role in an individual's decision to undergo genetic carrier testing. From this study, one cannot determine if anxiety was influenced by an individual's genetic misconceptions, religious beliefs and coping strategy. Individuals who took part in the study who had genetic testing may also have shown less anxiety as they may have not been found to be a carrier or their results were relayed a while ago and the concern has dissipated. Although anxiety was found to be prevalent amongst the participants, a lack of stigma was also identified. Unfortunately this could not be explored further in the context of this study as more qualitative responses would have been needed to address this.

4.4 Understanding of Genetic Carrier Risks by Study Participants

As discussed in Section 1, the AJ population is associated with a predisposition to specific autosomal recessive conditions because of the founder effect (Klugman & Gross, 2010). Due to the increased frequency of these conditions in the AJ population, there should be an awareness aimed at establishing an individual's understanding of implicit genetic risks, including the inheritance pattern and reproductive risks associated with a particular condition. Such an awareness should be provided by the community leaders, medical professionals, genetic counselling department through pamphlets and information evenings.

This study utilised seven multiple-choice questions to assess the participants' understanding of the genetics and carrier risks for AJ genetic conditions. As previously mentioned, the questions in this section were designed to examine core autosomal recessive concepts. Questions were used to gain an understanding of what individuals from the study population understood. From the seven questions asked, not one participant got all the answers correct. As shown in section 3.4 the majority of participants got 0 or 1 question correct and so a poor level of understanding was evident. The study showed that participants underestimated the carrier rate of 1 in 5 since only 13% (38/298) chose the

correct answer while 50% (149/298) did not know the correct answer. This underestimation of the carrier rate may be due to a lack of knowledge of the genetic risks for AJ genetic conditions or the misconception that genetic conditions may be viewed as rare. Many individuals may not have genetic carrier testing in their lifetime or get tested later in life, as they may be unaware of the genetic carrier testing opportunities available or feel it unnecessary, as it does not affect them. These perceptions may have serious reproductive consequences such as having an affected child. Many participants displayed a low level of understanding, which could influence an individual's uptake of genetic carrier testing as individuals may not understand the implications. Furthermore, a poor level of understanding carrier risks may relate to less stigma and anxiety.

Participants were asked to determine their knowledge of being a carrier for an AJ genetic condition and of being affected with an AJ genetic condition. It is clear from the results many could not distinguish between the two. So, besides a poor understanding of the inheritance pattern for an autosomal recessive genetic condition, some participants had no familiarity with genetic concepts as indicated by the number of "do not know" responses. Similar studies confirm that there is significant misunderstanding about the inheritance pattern, health and reproductive implications of genetic conditions (Acharya et al., 2009; Lanie et al., 2004). Incorrect information is passed down in families due to their own lack of accurate understanding (Acharya et al., 2009). Misconceptions are also noted in the literature which underpin the stereotype (prevalent amongst ultra-orthodox AJs) that being a carrier is always bad so one should not know their carrier status (Raz & Vizner, 2008). This misconception was not seen in this study as minimal stigma was identified. It is therefore essential that information be given in an understandable and clear manner so that no misconceptions arise. Morren, Rijken, Baanders et al., (2007) found that the most preferred source for genetic information was the general practitioner, followed by information sheets and the medical specialist. This emphasises the need to develop alternative educational modalities that promote genetic literacy (Acharya et al., 2009). As previously mentioned, educational programmes in Jewish schools or at rabbinic conferences, are available in the AJ community in Johannesburg but their success needs to be evaluated further so that improvements may be made where necessary.

In the questionnaire, section 3 question 7, participants were asked about the symptoms that a carrier of an autosomal recessive AJ genetic condition might have. The responses further highlighted the limited understanding of autosomal recessive genetic conditions (Table 3.6, page 44). Whilst carriers of certain genetic conditions may display milder symptoms of that condition, carriers of the common AJ genetic conditions will not have any symptoms. Although 52% of the participants chose the correct answer of no symptoms, 21% had incorrect responses. From those incorrect responses, 6% chose the option “very few symptoms,” which was designed to be a vague category but also meant to test their understanding of genetics. This finding indicated the inadequate understanding of what it means to be a carrier for an AJ autosomal recessive genetic condition. It is possible that this lack of understanding might contribute to the respondents’ view that being a carrier would affect their future (Section 4.3.1.1). The question may have also been poorly phrased and participants may have misunderstood the purpose of the question.

Overall, the findings reveal that awareness in the AJ cohort in Johannesburg is inadequate. Due to this inadequacy, the uptake of genetic carrier testing in the AJ community may be poorer since the purpose of genetic carrier testing may not be well understood. As mentioned previously in section 1.1, genetic carrier testing is in place in many high-risk population groups to prevent the frequency of autosomal recessive genetic conditions. The number of individuals who utilise genetic carrier testing and the low level of understanding of genetic risks supports the finding of decreased awareness.

It is important to mention that an equivalently low level of understanding has been found in other research. Raz and Vizner (2008) conducted a small study in the ultra-orthodox community in Israel and found that misunderstandings were common regarding the genetic basis of carrier matchmaking. Participants were very concerned about the debilitating effect their carrier status or a genetic condition would have on their children’s matchmaking opportunities (Raz & Vizner, 2008).

Morren et al., (2007) examined the relationship between genetic knowledge and genetic testing when making informed decisions. The study noted that higher levels of genetic knowledge are associated with a more favourable attitude towards genetic testing. This is a critical consideration in order to improve the awareness and services of genetics, especially for the common AJ genetic conditions.

4.5 Carrier Stigma: Personal and Social

Negative connotations are generally found when labels or undesirable names are placed on individuals or groups. Research shows that individuals are ambivalent to disclose their carrier status out of a fear that they may be shunned or ostracised by misinformed or uninformed individuals (Rosner, 1998). This may present a cognitive barrier to genetic carrier testing, as individuals fear the psychological burden of being identified as a carrier of a genetic condition. The Dor Yeshorim programme claims to reduce such a supposed burden through their programme but has in fact been described elsewhere as retaining and reinforcing stigmatisation of carriers (Raz & Vizner, 2008).

Numerous research studies emphasise the stigma or psychological distress attached to being a carrier for a genetic condition such as CF and Duchenne muscular dystrophy (Lewis et al., 2011; Moffett & Ross, 2011). Studies show that an individual may experience personal stigma by knowing his/her carrier status that in turn may negatively affect his/her health. This individual may internalise a derogatory attitude towards him/herself, as well as being concerned for his/her social interactions (Frumkin et al., 2011; Kenen & Schmidt, 1978; Van Brakel, 2006). As previously mentioned, some individuals at risk for hereditary breast cancer perceive themselves as being stigmatised and this affects their self-esteem. This perception of stigma also strongly correlated with increased levels of breast cancer specific distress (Den Heijer et al., 2011). Although stigma is important to examine with regard to other genetic conditions, individuals who are found to have a genetic predisposition to cancer are at a greater risk of manifesting the condition as it is autosomal dominant (50%) while the AJ conditions are autosomal recessive (25%).

For the purpose of this study, stigma was divided into three parts: overall stigma, social, and personal stigma. Studies have found that some individuals felt stigmatised based on their carrier status while others reported no stigma. Hegwer et al., (2006) described high school students who were told of their carrier status for TSD did not report feeling stigmatised. While, Lewis et al., (2011) reviewed a number of articles that reported feelings of stigmatisation, anxiety and guilt are evoked when knowing one's carrier status. A similar conclusion was found Gordon, Walpole, Zubrick et al., (2003) who recognised that carriers of CF felt less positive and angry about their positive test result. Social stigma was also found to be attached to carrying a gene mutation. This study found that neither personal nor social stigma appears to be associated with being a carrier for an autosomal recessive AJ genetic condition in the community of Johannesburg as little or no stigma was identified in this cohort. It is difficult to determine why no stigma was found in this study but it should be investigated further using a qualitative approach as it is different to other studies. Perhaps this is an important issue to consider in countries where stigma is evident, but this may not be the case in the AJ community in Johannesburg, SA. Reasons for the identification of stigma in other studies could be based on an increased knowledge and awareness in that community or discriminatory laws in certain places. Reproductive options such as PGD are also recently available and these may reduce the concerns around carrier status. Once again, additional research is necessary to tease out these issues more completely.

While the Dor Yeshorim programme claims to protect individuals from discrimination and stigma, some feel that the programme perpetuates the stigma of being a carrier of a genetic condition due to nondisclosure (Raz, 2009). As discussed above, little or no stigma was found in this cohort. This finding has many implications such as an inadequate level of knowledge and awareness about AJ genetic conditions and carrier testing. It also showed that participants were eager to learn their carrier status and since little or no stigma was found, perhaps the rationale for the Dor Yeshorim programme is not applicable in the Johannesburg AJ community. This requires additional research specifically with regard to the utilisation of the Dor Yeshorim programme.

Dor Yeshorim has been cited as an example of a carrier matching programme that has adapted to a specific religious groups needs (Frumkin et al., 2011). However, the programmes expansion into other Jewish groups has been questioned due to its rationale and strict guidelines (Frumkin et al., 2011). The Jewish population in Israel presents a framework for distinguishing between the different subgroups since 8% of the Jewish population is ultra-orthodox and 10% are traditional (Landau, 2003). Frumkin et al., (2011) assessed individuals attitudes towards genetic carrier testing in traditional Jews in Israel and found that stigma was reduced with personal knowledge and autonomy connected with testing in an open setting in which results are provided to patients. The study asserted that the programme would not find the same success that has been seen in the ultra-orthodox community if implemented in more traditional Jewish groups. The sample in this study was not evenly distributed so it is difficult to assess testing trends in reference to levels of observance.

4.6 This Study's Implications for Genetic Carrier Testing and Counselling

With advances in molecular technology, the possibility of having a child affected with an AJ genetic condition is lower if a couple follows the appropriate genetic carrier testing process. According to Collins, Halliday, Kahler et al., (2001), the main reason why people do not present for genetic counselling, or more importantly genetic carrier testing, is because they are not aware of its existence. This leaves couples with greater anxiety if something serious is discovered in their baby during a pregnancy or after birth, as they had no prior knowledge of potential genetic conditions.

Research in the Jewish community, especially regarding genetics, has been more focused on the ultra-orthodox community. Historically, Jewish individuals have been interested and willing to participate in genetic research, which has been seen over the years since the inception of the TSD enzymatic screening program in the 1970s (Monaghan et al., 2008). In an ultra-orthodox setting, rabbis often play a key role in a couple's prenatal decisions and counselling for genetic issues is part of the rabbi's role (Steiner-Grossman & David,

1993). In some ultra-orthodox Jewish communities, it is apparent that medical personnel are trusted less because they seemingly show less sensitivity towards specific Jewish issues (Mittman et al., 2007). As a result, fewer referrals are made and rabbis are forced to deal with genetic issues. Many rabbis have reported feeling poorly prepared to provide counselling on genetic issues and have expressed a need for additional training (Steiner-Grossman & David, 1993). It is imperative that genetic counsellors be aware of Jewish values and that they display sensitivity and understanding to associated cultural issues.

Research has shown that there may be a need for genetic counsellors and medical personnel to interact with rabbinic leaders, especially in ultra-orthodox communities in order to prepare them for discussing genetic issues (Steiner-Grossman & David, 1993). Through such interactions genetic counsellors and medical personnel may learn important beliefs and values upheld in Judaism that will enable them to understand patient needs better. It is important for health care professionals, especially genetic counsellors, to be perceptive to the attitudes and feelings of their patients in order to facilitate an acceptable solution for any contradictory feelings regarding genetic testing (Jallinoja et al., 1998).

This study has identified that there is minimal social or personal stigma present in the Johannesburg AJ community, therefore a genetic carrier testing programme like Dor Yeshorim may be premised on unfounded fear and anxiety in some communities. Rather, there is a need for individuals to access resources, which would better inform them of their carrier risks and testing opportunities. Following this, genetic counselling services would be appropriate if a positive result is confirmed or if an individual needs clarification. The Dor Yeshorim programme may characterise some matches as incompatible but couples now have reproductive options when both are identified as carriers for the same genetic condition. Healthy offspring may be achieved through PGD. This reproductive technology permits couples to screen the DNA of embryos fertilised *in vitro* and to implant those that match the parents' desired genetic profile (Handyside et al., 1990; Popovsky, 2007). With increasing education and awareness of genetic carrier risks, more individuals may choose genetic carrier testing as there are suitable reproductive options if both members of a couple are identified as being carriers.

In general, this study had some important findings that have great implications for the current genetic services available at the Division of Human Genetics, NHLS and Wits. As previously mentioned, the AJ community in Johannesburg is diverse and the needs of all levels of observance need to be considered further. Recruitment for genetic carrier testing of these different groups needs to reach all AJ Jewry, especially for those unaffiliated with their community or Judaism in general. At present, the publicity of genetic carrier testing takes place in some Jewish Day Schools, at rabbinic associations and in some community synagogues. There are also AJ pamphlets available through the Division of Human Genetics, NHLS and Wits. This study assists in evaluating the present publicity and awareness in the AJ community in Johannesburg.

4.7 Summary of Findings

This study aimed to determine the utilisation of genetic carrier testing for AJ living in Johannesburg, and to ascertain participants' genetic knowledge. It also aimed to assess the amount of personal or social stigma that is associated with genetic carrier testing. Based on the results of the study, the described objectives were met, and the overall aim achieved. In summary the following points were identified:

- One of the objectives of this study was to assess factors that influenced the utilisation of one Ashkenazi genetic testing programmes over the other available in Johannesburg, SA (Division of Human Genetics, NHLS/Wits and Dor Yeshorim). This objective was not achievable as the majority of participants had testing through Lancet Laboratories and the Division of Human Genetics, NHLS and Wits (76%), while only 18% had testing through the Dor Yeshorim programme.
- There was a relatively even distribution of individuals who had AJ genetic testing and those who had not. Importantly, the life-stage at which testing was performed showed that most individuals get tested when engaged or dating, and that fewer were tested when single. As previously discussed, testing at an earlier stage in life gives individual's wider reproductive options. Encouragingly, participants who had not been tested previously, conveyed a wish for genetic carrier testing in the future. Those individuals had a preference to be tested when they were dating or planning

a pregnancy. A couple would ideally need to be tested prior to a baby's conception as more reproductive options would be available.

- Knowledge amongst participants, with regard to understanding autosomal recessive pattern of inheritance for the common AJ genetic conditions, was poor. Therefore participants did not fully understand the implications of being a carrier of a genetic condition and underestimated the occurrence of the genetic conditions. It is difficult to assess from this study what impact inadequate knowledge has on testing decisions.
- There was minimal stigma reported in the sample, even when it was assessed in two separate components: personal and social stigma. This finding implies that the AJ community in Johannesburg, SA may not be as affected by stigma as some countries in the world, like Israel and United States of America, who also have AJ genetic carrier testing programmes. This may also be due to an ascertainment bias.
- A low level of anxiety for being a carrier of a genetic condition was found in this study. However, participants did feel that being a carrier of a genetic condition would affect their future. The manner in which participants felt it may affect their future was not explored except with regard to stigma, which was shown not to be of concern for these individuals.
- No correlations were found between individuals who had undergone genetic carrier testing and those that had not been tested with regard to the following categories: age, gender, level of observance and stigma.

4.8 Limitations of this Study

- Due to the anonymity of the online questionnaire, follow-up for elaboration on answers or for further questioning could not be carried out.
- In retrospect, the study did not include some questions, which may have been useful, including questions about the 9 common AJ conditions, reproductive choices such as termination of an affected pregnancy and the availability of PGD. This limited the scope of the research.
- Most participants reported hearing about the online questionnaire through the Internet. This finding illustrates that there is a high response rate through social

networks and Internet forums, a consideration for future research. This recruiting method may have excluded individuals who do not access the Internet except for work purposes.

- Participants were recruited in an opportunistic manner and although the sample size was larger than expected (n= 298), a large proportion of ultra-orthodox Jews and non-observant Jews may have been missed due to the sites where the study was publicised. Ultra-orthodox Jews may have not known about the study due to limited Internet access. Individuals who responded to the questionnaire may have been more involved in the Jewish community and so the study may have missed individuals who do not have a strong Jewish identity. Participants may have also been more knowledgeable and therefore had better testing.
- The study only focused on the AJ community in Johannesburg so other places in South Africa were excluded. Other places may also not have the same exposure to resources due to smaller community numbers.
- Finally, the stigma scale was modified from a scale that was validated for an infectious disease (HIV), and the focus of our study was a genetic condition. Unfortunately there are no standardised scales that examine stigma related to a genetic carrier status. Therefore, study data may not be a true reflection of the degree of stigma as not all questions may have been truly relevant. The section was also asked in a theoretical manner as participants were not known carriers with experience.

4.9 Recommendations

Based on the findings of this study the following recommendations can be suggested:

- From the number of individuals who had and did not have AJ genetic testing, it seems evident that there is a need for community outreach/educational programmes to be expanded not only to attract young adults to be tested voluntarily, but also to educate other members of the community of the genetic carrier testing available, the optimal time to test, the carrier risks and reproductive options for themselves and family members.
- General practitioners, gynaecologists and other health care professionals should be

offering testing to all young adults during routine clinical encounters.

- Individuals should be encouraged to participate in the full AJ genetic testing programme rather than TSD only. Education programmes are necessary for health care professionals to be informed about current genetic carrier testing opportunities.
- There should be an increase in referrals and information from rabbinic and Jewish community leaders. This may occur if there is an improvement in communication between such individuals and health care workers, especially genetic counsellors. Marriage programmes are in place by the Jewish community and perhaps education and referrals may be increased through these programmes.
- It is advisable that genetic carrier testing be done late in high school or university, so young adults can have some time to make informed decisions before marriage as this gives them a wider range of reproductive options.
- Other educational opportunities should be provided through mass media, lectures presented to the general public, training of health professionals, as well as posters and pamphlets in medical rooms with large Jewish clientele.
- With regard to the genetic counselling service offered, improvements and community awareness needs to take place. Education about genetic carrier risks for AJ genetic conditions and reproductive options should be encouraged amongst rabbinic leaders, medical doctors and at Jewish schools.
- To gain improved insights into the underpinnings of this anxiety, additional research involving one-on-one interactions with genetic counsellors and participants perhaps of a qualitative nature, would prove beneficial.
- Ultimately, it is recommended that targeted genetic carrier testing should be offered to all AJ in Johannesburg and the rest of SA, as they are a high risk population group for specific genetic conditions in an acceptable way. Involvement from the community is essential for an increase in awareness and knowledge to take place.
- The same is true for the expansion of genetic carrier testing in other high-risk populations such as the Afrikaner, Indian and Black populations. It would also be critical for these communities to support a programme for testing common genetic conditions.

5 FUTURE RESEARCH

As our understanding and awareness of genetics with regard to AJ genetic conditions increases, so too may the number of individuals presenting for targeted genetic carrier testing from high risk population groups. With the number of genetic conditions increasing continuously, additional genetic counselling services and testing will be needed to benefit individuals living in Johannesburg and the rest of South Africa.

The success of such programmes is multifactorial; firstly, the programme needs to address certain characteristics of the genetic conditions, including whether the condition is well defined in a population, whether it is a prevalent and severe disease, if the disease is predictable, and does it have effective treatment. Secondly, the characteristics of the genetic testing need to be addressed with regard to high test sensitivity and ease of interpretation of the results. Finally, and most importantly, is the attitude of the community: whether they are involved, supported by families and advocacy groups, and whether there is a consensus to avoid affected births.

Along the same lines, research examining individuals attitudes towards genetic carrier testing could be explored in the context of anonymous testing versus open testing programmes. Psychological and social attitudes such as anxiety could also influence whether individuals seek genetic carrier testing. A future study could offer genetic counselling to assess knowledge and risk perceptions prior to, and/or after, genetic carrier testing for an AJ genetic condition. It would also be interesting to have a control group who would not receive genetic counselling, which would help determine a basic level of knowledge and risk perception before interventions.

The researcher proposes that further research is necessary in the AJ communities of Johannesburg and the rest of SA to determine the strengths and weaknesses of the current genetic carrier testing programmes available. As previously discussed, some testing programmes internationally have expanded their testing panel to include up to 19 AJ genetic conditions, so the feasibility of implementing that in the local community would

need to be assessed. This study may be built upon in future research, and perhaps include some qualitative elements to truly understand testing motivations and concerns.

Finally, research is also needed to assess the impact of intermarriage within the AJ community and other religious groups to establish if pan ethnic testing may be required in the future. This would potentially alter the way genetic carrier testing is done as the founder effect may be less relevant. Other genetic conditions may need to be included in a pan ethnic testing that would allow for a larger number of conditions to be tested. This is important to consider for the growth of genetic services in South Africa.

6 CONCLUSION

For genetic carrier testing to have the greatest impact in the AJ community, it is necessary to consider initial strategies for gaining access to the maximum number of individuals within the target population that is realistically achievable. Genetic counselling is important in the context of educating individuals or at-risk couples about their genetic risks. Their role post-testing is of supreme importance to provide support for those who test positive. It seems that many health care professionals, as well as the AJ community, are not aware of the value of such a service. Therefore this study demonstrated that the Division of Human Genetics, NHLS and Wits has a responsibility not only to promote the genetic counselling services available but also to educate health care professionals, AJ community leaders and community members about the genetic carrier testing options and counselling services available. More awareness and referrals amongst health care professionals and rabbinic leaders in this community will result in greater testing opportunities, and allow individuals to make informed choices regarding their reproductive options. For example, information evenings, educational seminars and a dedicated website for increasing awareness may be beneficial. Such programmes should also be accessible in other parts of South Africa where there are smaller number of Jews living.

This study also found that there has been an increase in genetic carrier testing for the common 9 AJ genetic conditions, but it seems as if TSD only is still encouraged at a significant rate. The education of health care professionals in Johannesburg and the rest of SA, especially general practitioners and gynaecologists, needs to be a focus so that they are aware of the 9 AJ genetic conditions. The hope of this is that health care professionals will refer patients for the full AJ testing panel and not just for TSD. This needs to be considered before the panel is expanded since other medical centres in the world, such as in New York, have already increased their testing panel to 16 or more AJ genetic conditions, and these have been supported by their respective Jewish communities.

This study may be used as a useful model to understand genetic testing programmes in

other communities at high risk for specific genetic conditions. It has also highlighted the need for broader educational services to be implemented in high risk populations such as a website and/or engagement with a community to increase awareness about genetic carrier testing.

Thus, genetic carrier testing is recommended for the Johannesburg community when testing in the AJ population. Unfortunately the practicality of such a set up is difficult as currently the Division of Human Genetics, NHLS and Wits have a very small number of genetic counsellors, who would not be able to accommodate a large number of testing and genetic counselling cases. This staff shortage is sadly not being addressed at a national level and so the future of genetics in SA is unclear. Through this study, it is clear that instilling a more active concern within the AJ community and medical professions in Johannesburg is essential so that there will be an increased awareness around understanding genetic conditions and the genetic carrier testing programmes available.

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David Saks (Associate Director of Beyachad).

8 Appendices

Appendix A: The 9 common Ashkenazi Jewish Genetic Conditions in the Genetic Testing Panel

1. Tay-Sachs disease (TSD)

- Description: Neurodegenerative condition. Presents in the first year of life. Deficiency in the β -hexosaminidase A (Hex A), which causes a build up of a cell membrane glycolipid, Gm2 ganglioside, within the lysosome, which ultimately results in cell loss especially in the CNS.
- Mean survival-5 years
- Genetic mutations tested: 1278insTATC, IVS12+1G>C
- Detection rate: approximately 98%
- Incidence and carrier rate worldwide-1:3000 and 1 in 30 respectively
- Carrier rate in South Africa-1 in 20

2. Cystic fibrosis (CF)

- Description: Chronic debilitating condition of thickened mucous secretions affecting multi-organ systems, especially the lungs, gastrointestinal tract, sweat glands and the male reproductive tract. Cystic fibrosis is caused by mutations in the *CFTR* gene on chromosome 7, which regulates chloride channels.
- Mean survival-35 years
- Genetic mutations tested: W1282X, Δ F508, N1303K, G542X, 3849+10kbC>T, 1717-1G>A (AJ mutations only)
- Detection rate: Approximately 94%
- Incidence and carrier rate worldwide-1: 2500-3000 and 1 in 29 respectively

3. Canavan disease (CD)

- Description: Progressive neurodegenerative leukodystrophy. Deficiency of aspartoacylase that leads to accumulation of *N*-acetylaspartic acid in the brain and urine.
- Mean survival-early childhood
- Genetic mutations tested: 845A>C, 693C>A

- Detection rate: approximately 97% to 98%
- Incidence and carrier rate worldwide-1:6 400 and 1 in 38 respectively

4. Familial dystautonomia (FD)

- Description: Sensorimotor neuropathy that leads to inadequate development of the sensory and autonomic systems, which results in significant gastrointestinal reflux, lung disease, decreased pain and temperature perception, absence of tears and blood pressure abnormalities. Caused by a reduction in non-myelinated neuronal and myelinated axons.
- Mean survival-20 years
- Genetic mutation tested: R696P, 2507+6T>C
- Detection rate: approximately >99%
- Incidence and carrier rate worldwide-1:3700 and 1 in 30 respectively

5. Fanconi Anemia Type C (FANC C)

- Description: Progressive bone failure, congenital abnormalities (absent thumbs, radial hypoplasia, cardiac, renal, gastrointestinal and neurologic abnormalities) and a predisposition to malignancy. Occurs as a result of chromosome breakage and an increased sensitivity to DNA cross-linking agents
- Mean survival- childhood/adolescence
- Genetic mutation tested: IVS4+4A>T
- Detection rate: approximately 99%
- Incidence and carrier rate worldwide-1:32 000 and 1 in 89 respectively

6. Niemann- Pick Type A (NPD-A)

- Description: Progressive neurodegenerative condition. Due to a deficiency of the sphingomyelinase enzyme, resulting in accumulation in the lysosome
- Mean survival- early childhood \pm 9 years old
- Genetic mutations tested: R496L, fsP330delC, L302P
- Detection rate: approximately 97%
- Incidence and carrier rate worldwide-1:32 000 and 1 in 70 respectively

7. Bloom Syndrome (BLM)

- Description: Short stature, sun- sensitive skin lesions, increased risk of cancer and other health problems. Results from chromosomal instability due to deficiency of the *BLM* gene.
- Mean survival-late 20's
- Genetic mutation tested: 2281del16/ins7
- Detection rate: approximately >99%
- Incidence and carrier rate worldwide-1:40 000 and 1 in 110 respectively

8. Mucopolipidosis IV (MLIV)

- Description: Lysosomal storage condition that is characterised by growth delays, severe intellectual disabilities and ophthalmological anomalies. Abnormal membrane endocytosis that leads to accumulation of lipids and mucopolysaccharides in the lysosome.
- Mean survival- adulthood
- Genetic mutations tested: 511-6944del, 5534A>G
- Detection rate: approximately 95%
- Incidence and carrier rate worldwide-1:62 500 and 1 in 127 respectively

9. Glycogen storage disease 1a (GSD)

- Description: Accumulation of glycogen and fat in the liver and kidneys. Due to a deficiency of the enzyme D-glucose-6-phosphatase (G6Pase).
- Mean survival- childhood
- Genetic mutation tested: R83C
- Detection rate: approximately 95%
- Incidence and carrier rate worldwide-1:20 000 and 1 in 74 respectively

Appendix B: The Study's Advertisement

Advertisements were worded as follows: "Ashkenazi Genetic Testing: Novel research is being conducted by a Jewish MSc Masters student, through the Division of Human Genetics, National Health Laboratory Service (NHLS) and the University of the Witwatersrand to assess individuals attitudes and utilisation of Ashkenazi testing programmes available locally. If you are between 18-40 and have/have not undergone genetic testing, we kindly ask you to take part in our research ANONYMOUSLY at

www.jewishgenetics.co.za. Your participation will assist us in refining the programme for the South African Jewish community”

Appendix C: Information Sheet, Consent Form and Structured Questionnaire

- **Information Sheet**

Ashkenazi Jewish Genetic Testing: Utilisation of Testing Services, Genetic Knowledge and Perceptions of Stigma

Investigator: Kara Stoler, MSc (Med) Genetic Counselling Student

Good day, my name is Kara Stoler and I am currently completing my Masters degree in Genetic Counselling at the University of the Witwatersrand (Wits) in the Division of Human Genetics.

My research focuses on studying Ashkenazi Jews who utilised Ashkenazi genetic testing and those who have not had any testing. In this study I would like to evaluate the testing programs available in Johannesburg, the use of the programs, participants knowledge of genetics and if there are psychological and social implications of being tested. The study has been established to understand the Jewish community's needs, beliefs and understanding with regard to genetics. This area has received little attention until now so this study has great benefits for future services.

I would like to invite you to take part in this research study by completing an online anonymous questionnaire consisting of a number of different questions related to you and your experiences of genetic testing services. It should take no longer than 20 minutes. The questionnaire includes questions regarding your demographic information (e.g. where you live, relationship status, etc.), your experiences with Ashkenazi genetic testing, what you know about genetics and your perceptions of the testing.

Your participation in this study is completely voluntary. No personal information will be asked of you, so your involvement will be completely anonymous. The researcher will not be able to identify any participants. You also have the right to withdraw from the study at any time without any consequences for you or the researcher by not completing the online questionnaire.

Please **DO NOT** use outside sources to answer questions. Please be honest in your answers. All questions must be answered before final submission.

If you have any questions about your participation or would like more information about

being tested, please do not hesitate to contact the Division of Human Genetics, National Health Laboratory Service and Wits at 011 489 9223.

On behalf of the research team, and myself we appreciate your participation and look forward to implementing the study's findings in the future.

Thanks you for participating in the study.

Ms. Kara Stoler – B.A Honours Psychology and Visual Arts, MSc (Med) Genetic Counselling student

Prof. Amanda Krause – MBBCh (Wits), PhD, Associate Professor and Head of Clinical Section,

NHLS and Wits

Ms. Chantel van Wyk – MSc (Med) Genetic Counselling, Associate Lecturer and Genetic Counsellor, NHLS and Wits

- **Informed Consent**

I hereby consent to taking part in this research study by Kara Stoler on the utilisation of Ashkenazi genetic testing services, genetic knowledge and implications of potential stigma amongst Ashkenazi Jews in JHB, SA.

I understand that:

- No identifying information will be asked: participation is voluntary.
- I may withdraw from the study at any time by not completing the online questionnaire.
- Direct quotes from the online questionnaire may be used in the research report.
- There are no direct risks or benefits involved in my participation.

Please tick the box if you accept the above terms and would like to continue to the questionnaire.

Date _____

- **Structured Questionnaire**

Please do not use outside sources to answer the questions!

All the questions below focus on the recessive Ashkenazi genetic conditions in the Ashkenazi screen and the testing that is available for each of them. Please keep this in mind when answering each question.

Section 1: Questions about Demographics

1. Age

- 18-25
- 26-30
- 31-35
- 36-40

2. Gender

- Male Female

3. Relationship status

- Single, never married Married Engaged
- Separated/divorced Remarried
- Widowed Living with a partner

4. Children

- 0
- 1
- 2
- 3
- 4
- 5
- 6 or more

5. Do you plan to have any/more children in the future

No

Yes

6. How would you rate your level of Jewish observance?

(0 being non-observant and 10 being ultra-orthodox observant)

Non-observant	0	1	2	3	4	5	6	7	8	9	10	Ultra-orthodox observant

7. Explain why you rated yourself as you did in Question 6

8. How did you hear about this study?

Newspaper/ Newsletter

Synagogue

Friend

Word of mouth

Internet forum

Other (please specify) _____

9. Do you know anyone with a genetic condition?

No

Yes

• **If yes** what is your relationship to that individual

• **If yes,** what is the name of the condition affecting that individual

Section 2: Questions regarding utilisation of Ashkenazi testing programs

1. Have you had any Ashkenazi genetic testing?
 - No
 - Yes
 - (if yes please answer questions 2-8 and move onto question 12)
 - (if no please skip to question 9-11)
 - * Will be directed online to right questions

2. Which program were you tested through?
 - Division of Human Genetics, NHLS, Wits
 - Lancet Laboratories
 - Dor Yeshorim
 - Other (please specify) _____

3. Briefly discuss your reason for choosing to be tested through that program

4. At what stage of your life did you undergo Ashkenazi genetic testing? Were you...
 - Single
 - Dating
 - Engaged
 - Married
 - Planning a pregnancy
 - Pregnant
 - Had a child/children

5. Which genetic test did you have?
 - Full Ashkenazi genetic testing (9 conditions)
 - Tay Sachs disease
 - Gauchers disease
 - Other (please specify) _____
 - Do not know

6. Who/or what prompted you to be tested for an Ashkenazi genetic condition?

- Family
- Parents
- Partner
- Future partner
- Friends
- Rabbi
- Information pamphlet
- Education/ school
- Other (please specify) _____

7. How did you receive your results?

- Doctor
- Dor Yeshorim representative
- Genetic Counsellor
- Gynaecologist
- General Practitioner
- Other (please specify) _____

8. Were you shown to be a carrier of an Ashkenazi genetic condition?

- No
- Yes
- Do not know

**** If you answered *No* to Question 1, Section 2, please continue:**

9. Would you be interested in carrier screening testing for Ashkenazi genetic conditions in the future?

- No
- Yes

- **If No-** please briefly discuss why not

- **If Yes**, at what stage of your life would you choose to be tested

- Single
- Dating
- Married
- Planning a pregnancy
- Pregnant
- Had a child/children

10. Are you aware of testing programs available?

- No
- Yes

11. Which testing institute would you choose in the future?

- Division of Human Genetics, NHLS, Wits
- Lancet Laboratories
- Dor Yeshorim
- Other (please specify) _____

- **Why?**

Please select your response to Questions 12-15

		Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
12	In General, do you feel that individuals should have Ashkenazi genetic screening tests?	SD	D	N	A	SA
13	Do you feel it is important to know one's carrier status for a genetic condition?	SD	D	N	A	SA
14	Is the possibility of being a carrier for a genetic condition something you often worry about?	SD	D	N	A	SA
15	Do you believe being a carrier of a genetic condition will affect an individual's future?	SD	D	N	A	SA

Section 3: Questions regarding knowledge about risks

1. What is an individual's **overall** chance of being a carrier for at least **ONE** of the common Ashkenazi Jewish conditions?
 - 1 in 5
 - 1 in 20
 - 1 in 50
 - 1 in 100
 - Do not know

2. What is an individual's chance of **being a carrier** for a genetic condition if **ONE of his/her parents is a carrier** of a condition?
- Less than 1%
 - 25%
 - 50%
 - 66%
 - 75%
 - 100%
 - Do not know
3. What is an individual's chance of **having a genetic condition** if ONE of his/her parents is a carrier of a condition?
- Less than 1%
 - 25%
 - 50%
 - 66%
 - 75%
 - 100%
 - Do not know
4. What is an individual's chance of **being a carrier** of a genetic condition if **BOTH his/her parents are carriers** of a condition?
- Less than 1%
 - 25%
 - 50%
 - 66%
 - 75%
 - 100%
 - Do not know

5. What is an individual's chance of having a genetic condition if BOTH his/her parents are carriers of a condition?
- Less than 1%
 - 25%
 - 50%
 - 66%
 - 75%
 - 100%
 - Do not know
6. What is an individual's chance of having a genetic condition if BOTH his/her parents are carriers but of two different conditions?
- Less than 1%
 - 25%
 - 50%
 - 66%
 - 75%
 - 100%
 - Do not know
7. If an individual is a carrier of a genetic condition, what symptoms will be noticeable
- No symptoms
 - Very few symptoms
 - Many symptoms
 - Only symptoms characteristic of that specific condition
 - Do not know

Section 4: Questions with regard to Social Perceptions: Stigma

This study is looking at perceptions of stigma associated with being a carrier of an Ashkenazi Jewish genetic condition. This set of questions asks about feelings and experiences individuals might have if he/she were a carrier of an Ashkenazi Jewish genetic condition.

This may not be true for you but we ask that you answer by imagining yourself as if you were/are a carrier of an Ashkenazi Jewish genetic condition.

Please note: This section may seem repetitive at times but has been designed like this to ensure its validity

		Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
1	In many areas of my life no one should know that I am a carrier of an Ashkenazi Jewish genetic condition	SD	D	N	A	SA
2	I would feel guilty if I am a carrier of an Ashkenazi Jewish genetic condition	SD	D	N	A	SA
3	Telling someone that I am a carrier of an Ashkenazi Jewish genetic condition would be risky	SD	D	N	A	SA
4	I would work hard to keep my carrier status a secret	SD	D	N	A	SA
5	I would never feel ashamed of being a carrier	SD	D	N	A	SA

6	People who are carriers are treated as outcasts	SD	D	N	A	SA
7	It would be easier to avoid relationships than worry about telling someone that I am a carrier	SD	D	N	A	SA
8	Being a carrier would make me feel “tainted”	SD	D	N	A	SA
9	If I learnt I was a carrier I would feel isolated socially	SD	D	N	A	SA
10	Most people think that a person who is a carrier is imperfect	SD	D	N	A	SA
11	Most people who are carriers are rejected when a partner finds out	SD	D	N	A	SA
12	I would be very careful who I tell that I am a carrier	SD	D	N	A	SA
13	If I learnt I was a carrier, I would worry that people will discriminate against me	SD	D	N	A	SA
14	I would never feel the need to hide the fact that I am a carrier	SD	D	N	A	SA
15	I would worry that a partner may judge me when they learn that I am a carrier	SD	D	N	A	SA
16	Being a carrier may be hard for me	SD	D	N	A	SA
17	I would be hurt by someone learning that I am a carrier	SD	D	N	A	SA
18	I would worry that people who know I am a carrier will tell others	SD	D	N	A	SA
19	Some people would act like it is my fault that I	SD	D	N	A	SA

	am a carrier					
20	I would lose relationships by telling people I am a carrier	SD	D	N	A	SA
21	People's attitudes about carriers would make me feel worse about myself	SD	D	N	A	SA
22	People who are carriers would lose their jobs when their employers find out	SD	D	N	A	SA
23	Most people believe that a person who is a carrier is tainted	SD	D	N	A	SA
24	I would feel I am not as good a person as others because I am a carrier	SD	D	N	A	SA
25	Being a carrier would make me feel that I'm a bad person	SD	D	N	A	SA
26	Some people who would know I am a carrier may grow more distant	SD	D	N	A	SA
27	Most people are uncomfortable around a carrier	SD	D	N	A	SA
28	I would regret telling some people that I am a carrier	SD	D	N	A	SA
29	As a rule, telling others that I am a carrier would be a mistake	SD	D	N	A	SA
30	Some people would avoid me once they know I am a carrier	SD	D	N	A	SA
31	People I care about would stop calling after learning I am a carrier	SD	D	N	A	SA
32	Some people close to me would be afraid others will reject them if it becomes known I am a	SD	D	N	A	SA

	carrier					
33	People would physically back away from me when they learn I am a carrier	SD	D	N	A	SA
34	I would stop socialising with some people because of their reactions to me being a carrier	SD	D	N	A	SA
35	I would lose friends by telling them I am a carrier	SD	D	N	A	SA
36	I would tell people close to me to keep the fact that I am a carrier a secret	SD	D	N	A	SA
37	People who know I am a carrier would ignore my good points	SD	D	N	A	SA
38	People would seem afraid of me once they learn I am a carrier	SD	D	N	A	SA
39	When people learn you are a carrier they would look for flaws in your character	SD	D	N	A	SA

Section 5: General Questions

1. Would you find information evenings beneficial in understanding Ashkenazi Jewish genetic conditions and risks?

Yes

No

2. Please indicate other methods in which you feel information could be provided

(May choose more than one)

Website

Pamphlets

Educational seminars

Newspapers/Magazines

Other _____

Appendix D: Notification that the Study was Complete on the Website

Thank you for your interest in participating in the study titled:

Ashkenazi Jewish Genetic Testing:
Utilisation of Services, Genetic Knowledge and Perceptions of Stigma

The study has reached our required sample numbers.

If you require any information on Ashkenazi Jewish testing or wish to contact our department for genetic counselling services,
Please kindly contact the National Health Laboratory Service

011 489 9223/4

Results of the study will be posted by December 2012

Thank you

Kara Stoler
MSc (Med) Genetic Counselling Student

Appendix E: Ethics Clearance Certificate



UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Ms Kara Stoler

CLEARANCE CERTIFICATE

M120284

PROJECT

Ashkenazi Jewish Genetic Testing: Utilization of Services, Genetic Knowledge and Perceptions of Stigma

INVESTIGATORS

Ms Kara Stoler.

DEPARTMENT

School of Pathology/Div. Human Genetics

DATE CONSIDERED

24/02/2012

DECISION OF THE COMMITTEE*

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE

CHAIRPERSON.....

Handwritten signature of Professor PE Cleaton-Jones.

(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Prof Amanda Krause

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.

I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...