A retrospective review of the prenatal genetic counseling services in state healthcare hospitals of Johannesburg, South Africa

Asante Tshwane

Student number: 2305138

Supervisor: Mrs Elzette Gilfillan

Co – supervisor: Mr Barry Shingwenyana

A research report (in the format of a "submissible" paper) submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Science in Medicine (Genetic Counselling) by Research and Coursework

Johannesburg, 2025

NATIONAL HEALTH LABORATORY SERVICE
School of Pathology, University of the Witwatersrand
DIVISION OF HUMAN GENETICS
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Hospital Street, Johannesburg, 2001 | PO Box 1038, Johannesburg, 2000
[T] +27 11 489 9223 | [M] +27 78 080 8841 | [F] +27 11 489 9226 | [E] human genetics@nhls.ac.za

22 January 2025

Re: Research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, by Ms Asante Tshwane in partial fulfilment of the requirements for the degree Master of Science in Medicine (Genetic Counselling)

Dear examiner,

Thank you for agreeing to examine the research report submitted by Ms Asante Tshwane (2305138) entitled "A retrospective review of the prenatal genetic counselling services in state healthcare hospitals of Johannesburg, South Africa". This research report is being submitted by the candidate in the format of a "submissible" paper. This report contributes 30% towards the final mark of the MSc (Med) Genetic Counselling degree for which the candidate is enrolled.

The candidate and her supervisors have chosen to submit the paper to the Journal of Genetic Counseling. This is an international peer-reviewed journal published by Wiley. The submissible paper attached is therefore written in concordance with author guidelines of the stipulated journal. These guidelines have been attached for your reference in the appendices section of this document. The only deviation from these guidelines is that the manuscript has been presented as one complete document (including tables and figures) for ease of marking, rather than being submitted separately.

The research protocol has also been attached as an appendix for the purpose of providing an extended literature review and further context to the study. The protocol has already been assessed and approved by the Faculty of Health Sciences Post-Graduate Assessors Committee and is therefore not for examination.

Please refer to the Table of Contents for a complete list of the contents provided in this research report.

Yours sincerely,

Asante Tshwane (Candidate)

Elzette Gilfillan (Supervisor)

Barry Shingwenyana (Co-supervisor)

Declaration

I, Asante Tshwane, declare that this research report (in the format of a "submissible paper"), is my own, unaided work. It is being submitted for the degree of Master of Science in Medicine (Genetic Counselling) at the University of Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other university.

_____

Asante Tshwane

Student number: 2305138

20 June 2025

Contribution of the candidate to this paper:

Declaration: Student's contribution to article and agreement of co-authors

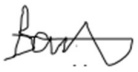
I, Asante Tshwane, student number 2305138, declare that this Research Report, entitled "A retrospective review of the prenatal genetic counseling services in state healthcare hospitals of Johannesburg, South Africa" is my own work and that I contributed significantly towards research findings presented in the paper intended for publication below.

Signature of student:  Date: 20 June 2025

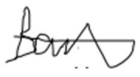
Name of Supervisor 1: Mrs Elzette Gilfillan

Signature of Supervisor 1:  Date: 20 June 2025

Name of Supervisor 2: Mr Barry Shingwenyana

Signature of Supervisor 2:  Date: 20 June 2025

Agreement of Co-Authors: By signing this declaration, the co-authors listed below agree to the use of the article by the student as part of her Research Report.

	Name	Signature	Date
Author 1	Asante Tshwane		20/06/2025
Author 2	Elzette Gilfillan		20/06/2025
Author 3	Barry Shingwenyana		20/06/25

Abstract

Congenital disorders (CDs) contribute significantly to the global burden of disease, particularly in low and middle-income countries. In South Africa, CDs are the fourth leading cause of early neonatal death. While CDs with genetic origins cannot be prevented, earlier identification through prenatal screening and diagnosis offers an effective means of intervention and care. Genetic counseling is vital in prenatal care, assisting in patient education and information giving regarding screening and diagnostic outcomes, prognosis, and options going forward. However, there is still limited data detailing these services in the South African context. This study aimed to evaluate the prenatal genetic services provided by genetic counsellors at several state hospitals in Johannesburg over a two-and-a-half-year period. A total of 525 files belonging to patients who were referred for prenatal genetic counseling from July 2019 to December 2021 were reviewed. The mean age (standard deviation) was 35 ± 8 years and 59.2% (311/525) of the cohort was of advanced maternal age (AMA). The Black population group accounted for 89.7% of the patients seen, of which the most spoken home languages were isiZulu, Sepedi, and Sesotho. The primary reasons for referral were AMA and abnormal ultrasound findings. The uptake of prenatal invasive testing was 39.8% (141/354) and patients were more likely to undergo testing when referred for ultrasound findings ($p < 0.001$). Several reasons were reported for declining testing, with the majority (41.1%; 74/180) indicating concerns about the risk of miscarriage. Twenty-seven confirmed genetic diagnoses were made via genetic testing, namely 26 cases of chromosomal aneuploidy and one single gene condition. Lastly, patients were more likely to terminate a pregnancy with a confirmed genetic diagnosis ($p < 0.001$). These findings provide an overview of the prenatal genetic counseling services in these settings and offers insights into the decision-making patterns of patients in the Johannesburg state healthcare landscape.

Acknowledgements

I would like to express my gratitude to my supervisors, Mrs Elzette Gilfillan and Mr Barry Shingwenyana for their time, effort, and guidance throughout the completion of this study and this report.

I would like to thank my classmates for the coffee runs and shared experiences. The journey would not have been the same without your continuous support. It was truly a collaborative effort.

Thank you to my family and friends for being the best support system. I would like to express my most heartfelt gratitude towards my mom and my sister for their unwavering support. Their sacrifices have provided many opportunities for me. I am truly appreciative. Thank you to my grandmother for always believing in me and covering me in prayer.

My deepest thanks goes to God. Tsotlhe di diragetse ka thato le tumelo ya Modimo le badimo. Ke lebogile go menagane.

Table of contents

List of tables

List of figures

List of abbreviations

AMA	Advanced maternal age
CD	Congenital disorder
CHBAH	Chris Hani Baragwanath Academic Hospital
CMA	Chromosomal micro-array analysis
CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
CNS	Central nervous system
COVID-19	Coronavirus disease 2019
CVS	Chorionic villus sampling
FA	Fetal anomaly
FISH	Fluorescent in situ hybridisation
FM	Fetal medicine
HCP	Healthcare practitioner
NHLS	National Health Laboratory Service
NIPT	Non-invasive prenatal testing
NSGC	National Society of Genetic Counsellors
NT	Nuchal translucency
QF-PCR	Quantitative fluorescent polymerase chain reaction
REDCap	Research Electronic Data Capture
RMMCH	Rahima Moosa Mother and Child Hospital
SD	Standard deviation
TOP	Termination of pregnancy
mTOP	Medical termination of pregnancy

Research report in the format of a "submissible" paper

To be submitted to the Journal of Genetic Counseling

A retrospective review of the prenatal genetic counseling services in state healthcare hospitals of Johannesburg, South Africa

Asante Tshwane[1] | Barry Shingwenyana [1]| Elzette Gilfillan [1]

[1] Division of Human Genetics, National Health Laboratory Service and School of Pathology, Faculty of Health Sciences, the University of the Witwatersrand, Johannesburg, South Africa

Short running title: A retrospective review of prenatal genetic counseling in Johannesburg state hospitals

Corresponding author: Asante Tshwane

Email address: asantetshwane@gmail.com / 2305138@students.wits.ac.za

147 De Korte Street, Braamfontein, Johannesburg, 2001

Conflict of interest statement

A Tshwane, E Gilfillan, and Barry Shingwenyana have no conflicts of interest to declare.

Ethics statement

Ethical clearance was obtained from the Human Research Ethics Committee (Medical) at the University of the Witwatersrand (WITS) (Ethics clearance certificate: M240612). For confidentiality purposes, the data was anonymised. The data was stored on a secure password protected computer. Furthermore, access to the identifying information was only granted to the researcher and the supervisors.

Animal studies: The authors did not conduct any animal studies.

Data availability statement

The study data is available upon request.

Abstract for journal submission

Congenital disorders (CDs) contribute significantly to the global burden of disease, particularly in low and middle-income countries. In South Africa, CDs are the fourth leading cause of early neonatal death. While CDs with genetic origins cannot be prevented, earlier identification through prenatal screening and diagnosis offers an effective means of intervention and care. Genetic counseling is vital in prenatal care, assisting in patient education and information giving regarding screening and diagnostic outcomes, prognosis, and options going forward. However, there is still limited data detailing these services in the South African context. This study aimed to evaluate the prenatal genetic services provided by genetic counsellors at several state hospitals in Johannesburg over a two-and-a-half-year period. A total of 525 files belonging to patients who were referred for prenatal genetic counseling from July 2019 to December 2021 were reviewed. The mean age (standard deviation) was 35 ± 8 years and 59.2% (311/525) of the cohort was of advanced maternal age (AMA). The Black population group accounted for 89.7% of the patients seen, of which the most spoken home languages were isiZulu, Sepedi, and Sesotho. The primary reasons for referral were AMA and abnormal ultrasound findings. The uptake of prenatal invasive testing was 39.8% (141/354) and patients were more likely to undergo testing when referred for ultrasound findings ($p < 0.001$). Several reasons were reported for declining testing, with the majority (41.1%; 74/180) indicating concerns about the risk of miscarriage. Twenty-seven confirmed genetic diagnoses were made via genetic testing, namely 26 cases of chromosomal aneuploidy and one single gene condition. Lastly, patients were more likely to terminate a pregnancy with a confirmed genetic diagnosis ($p < 0.001$). These findings provide an overview of the prenatal genetic counseling services in these settings and offers insights into the decision-making patterns of patients in the Johannesburg state healthcare landscape.

What is known about this topic?

In the context of prenatal care, genetic counseling is an important tool for providing psychological support and advisory services regarding appropriate testing and management options. Despite its recognised importance, limited data exists on this service in the South African context, particularly in Johannesburg.

This paper adds to the topic: As the first audit of these services in the Division of Human Genetics, this study provides insights into the decision-making patterns of patients in the Johannesburg state healthcare sector and also serves as a starting point for future departmental research into this service.

Keywords: Prenatal, Genetic counseling, Johannesburg, South Africa

1. Introduction

1.1 Congenital disorders

Congenital disorders (CD), or birth defects, are structural or functional abnormalities that develop between conception and birth (WHO, 2023). CDs may be detected prenatally, at birth, or later in life. The known causes of CDs fall mainly into three categories, namely genetic (15%), environmental (7% -10%), and multifactorial (20% - 25%) (EUROCAT, 2004). However, a large proportion of CDs cannot be attributed to a specific cause. In South Africa, CDs are the fourth most common contributor to early neonatal death (Rhoda et al. 2018). Yet, the extent to which these cases can be linked to a specific aetiology remains unclear due to the paucity of research in this area. Reportedly, 70% - 85% of CDs can potentially be prevented or mitigated by appropriate care (Czeizel, 2005; Christianson et al. 2006). While CDs caused by genetic factors cannot be prevented, earlier identification efforts have been an effective medium of intervention and care. This is largely attributed to improvements in prenatal screening and prenatal diagnosis for high-risk pregnancies, emphasising the value of prenatal investigations (Christianson et al. 2006).

1.2 Indications of a high-risk pregnancy

A pregnancy is classified as high-risk when the mother, the unborn child, or both are at an elevated risk of adverse outcomes, before or after birth. Common referral criteria for prenatal genetic counseling include advanced maternal age (AMA), defined as pregnant women aged 35 years and older; consanguinity; soft markers and fetal abnormalities detected on ultrasound; known or suspected family history of genetic conditions; history of pregnancies with genetic or structural abnormalities; parents with a chromosomal rearrangement; recurrent miscarriages; and exposure to teratogens during pregnancy (Aalfs et al. 2004). AMA is associated with an increased risk of fetal aneuploidy, whereby there is an abnormal number of chromosomes within a human body cell. Notably, the most common aneuploidies are Trisomy 13,18, and 21 (Lampret et al. 2008). Trisomy 13 and 18 are linked to an elevated risk of mortality shortly after birth, with most cases resulting in intrauterine death and only 5% - 10% surviving beyond the first year (Kroes et al. 2014). In contrast, children with Trisomy 21, also known as Down Syndrome, have a better prognosis and higher life expectancy (Driscoll and Ross, 2009).

1.3 Prenatal screening

Prenatal screening aims to identify high-risk pregnancies and is available to pregnant women of all ages. This is done in combination with fetal ultrasounds, obstetric examination, and family history taking (Nicolaides et al. 2011). Fetal ultrasounds are a routine part of prenatal care, conducted throughout a pregnancy. Two important ultrasounds are conducted during the first two trimesters of pregnancy. First trimester ultrasounds assess the fetal growth, presence of the nasal bone, risk of pre-exlampsia, and the size of the nuchal translucency (NT). This includes a nuchal translucency (NT) scan, conducted between

11 to 14 weeks of gestation, which assesses the amount of fluid in the fetal nuchal fold. An NT thicker than 3mm may be associated with an increased risk of a variety of cardiac, skeletal, and genetic abnormalities such as Trisomy 21 (Kroes et al. 2014; Zhang et al. 2019). The fetal anomaly (FA) scan is a second trimester screening option performed between 18 to 24 weeks. This ultrasound screens for major structural abnormalities as well as soft markers. Ultrasonographic soft markers are minor, observable findings known to be predictive of aneuploidies. Commonly detected soft markers are hypoplasia of the nasal bone, choroid plexus cysts, short long bones, echogenic intracardiac foci, and echogenic bowel (Smith-Bindman et al. 2001; Papp et al. 2008). Further investigations such as prenatal diagnostic testing are necessary when screening outcomes indicate an increased likelihood of a fetus affected with an underlying aneuploidy or other genetic abnormalities.

1.4 Prenatal diagnosis

Three invasive prenatal diagnostic procedures are available to perform further investigations such as genetic testing. These are performed under continuous ultrasonographic guidance and sterile conditions. Chorionic villus sampling (CVS) is performed as early as 11 to 14 weeks of gestation. Amniocentesis and cordocentesis are performed in the second trimester, with amniocentesis typically conducted between 16 to 22 weeks and cordocentesis after 18 weeks gestation and onwards. These procedures carry risks for miscarriage, which are largely dependent on the operator's skill and experience. Experienced operators performing amniocentesis and CVS demonstrate a fetal loss rate of a 0.17 % - 0.52% (Bakker et al. 2016), while cordocentesis is associated with a 1.3% risk. Minor complications include vaginal bleeding, cramping, and amniotic fluid leakage (Driscoll and Ross, 2009; Wilson et al. 2015). Based on screening outcomes, diagnostic samples undergo cytogenetic analysis such as karyotyping, fluorescent in situ hybridisation (FISH), quantitative fluorescent polymerase chain reaction (QF-PCR), chromosomal microarray analysis (CMA), as well as single gene testing to confirm or exclude the presence of genetic abnormalities.

1.5 Prenatal genetic counseling: considerations in the South African context

According to the National Society of Genetic Counselors (NSGC), genetic counseling entails helping individuals to comprehend and adjust to the medical, psychological, and familial implications of genetic factors that contribute to disease (Resta et al. 2006). The 4th edition of Guidelines for Maternity Care, published in 2015 by the South African National Department of Health, proposed the implementation of prenatal genetic counseling services as a key feature of state hospitals. Notably, South African healthcare comprises both private and state sectors, with 80% of the population relying on state services and 20% on private care (Cottino et al. 2022). State hospitals typically employ an income-based classification system to cover medical expenses.

In 2013, Kromberg et al. reported that only 10% of the national genetic disease burden was addressed, with most services solely available at tertiary hospitals in four of the nine provinces in the country. In

addition, they also reported on the sparse number of registered genetic counselors. Thus, genetic services in the country are generally limited. Currently, the South African state healthcare system does not offer CMA routinely in the prenatal setting. At the National Health Laboratory Service (NHLS) Johannesburg, one of the state diagnostic pathology services, QF-PCR has been available since 2001 for aneuploidy detection in both pre- and postnatal cases. While there is a reduced and unbalanced utilisation of this test in the country, QF-PCR has proven to be useful given the lack of resources due to the aforementioned reasons (Cottino et al. 2022).

1.5.1 Decision making in pregnancy

In the prenatal setting, genetic counseling is a source of psychosocial support and guidance on appropriate testing and management choices, making it a vital aspect of prenatal care (Malope et al. 2023). The South African Choice on Termination of Pregnancy Act of 1996 imposes strict guidelines on termination of pregnancy (TOP) at different gestational ages. Following a prenatal diagnosis of a CD, parents have options regarding the management of pregnancy and can decide to either continue with pregnancy or undergo TOP. Although TOP has been legalised in South Africa, it continues to be marked by considerable stigma. Often, the right of choice is negatively impacted by the fear of being shunned by the community (Harries et al. 2007). Moreover, prospective parents are tasked with making decisions that correlate with their moral, ethical, and religious beliefs (Scott et al. 2013). Psychological and financial strains exist in the decision to continue with a pregnancy wherein a CD is diagnosed (Mazibuko et al. 2022). These encompass emotions of guilt and disappointment, as well as the burden of addressing the expenses of life-long medical interventions. Thus, the decision to terminate a pregnancy is complex and there are many factors that contribute to the choices that are made. Given the diversity in South Africa, there may be unique considerations in the provision of genetic counseling services in this context. This highlights the necessity of research that provides insights into the services in these settings as well as the decision-making processes of patients.

Therefore, this study aimed to evaluate the prenatal genetic services provided by genetic counselors at several state tertiary hospitals in Johannesburg over a two-and-a-half-year period. This was achieved by:

i. Describing the demographics of prenatal cases seen for genetic counseling in the Johannesburg state healthcare system from July 2019 to December 2021;
ii. Determining the main reasons for referral for genetic counseling;
iii. Assessing the common soft markers and abnormalities detected on ultrasounds scans during the first and second trimesters;
iv. Analysing the uptake of invasive testing, types of genetic testing performed on diagnostic prenatal samples, as well as their outcomes;

v. Assessing the main contributing factors towards decision-making around uptake of invasive testing and pregnancy outcomes.

2. Methods

2.1. Participant characteristics

This study was a retrospective file review, involving an audit of prenatal clinic records of women who were seen by a genetic counselor from the Division of Human Genetics, at NHLS/WITS. These prenatal genetic counseling services were offered at fetal medicine clinics at NHLS/WITS affiliated state hospitals, specifically Chris Hani Baragwanath Academic Hospital (CHBAH), Rahima Moosa Mother and Child Hospital (RMMCH), and Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

2.2. Data collection

The initial period for data collection was July 2019 to July 2024. This was not achieved due to inconsistencies in certain data fields from patient files and subsequent time constraints. Therefore, this study comprised 525 files recorded over a two-and-a-half-year period from July 2019 to December 2021. These files were retrieved through the Division of Human Genetics Research Electronic Data Capture (REDCap) (Harris et al. 2009). The Division of Human Genetics REDCap was implemented in July of 2018. During the first year of implementation, some patient information continued to be documented on physical hospital files, and the process of transferring data from these files into REDCap was underway. Moreover, the database at the time had fewer data fields compared to the current version. Therefore, to ensure more comprehensive data collection, this retrospective study focused on reviewing prenatal genetic counseling files from July 2019. Notably, the study period coincides with the COVID-19 pandemic. This resulted in a national lockdown, halting health care services such as genetic counselling. Thus, data may not be truly representative of the normal delivery and utilisation of these services.

Specific database fields were used to perform an exhaustive search, generating a report of all the records on REDCap. This report was imported onto Microsoft excel. Each clinic record was reviewed for patient demographics (maternal age, ethnicity, and home language) and pregnancy information (reason for referral, ultrasound screening findings, uptake of invasive testing, genetic diagnosis, and decision regarding pregnancy).

2.3. Data analysis

The study comprised of continuous and categorical data. R software was used to perform the analysis, and the data was summarised with descriptive statistics. Continuous data was tested for normality using the Shapiro-Wilk test. Normally distributed data was reported as mean and standard deviation with a 95% confidence interval. Continuous data not meeting normality was represented by median and interquartile range values. Categorical data was described with percentages. Chi-square tests were

performed to test for significant differences in the distribution of two or more categorical variables. Fisher's Exact tests were used to evaluate relationships due to the small expected count sizes in the data. Monte Carlo simulations were also added to assess variables with large contingency table sizes. Statistical significance was set according to a p-value of < 0.05.

3. Results

3.1. Participant characteristics

A total of 525 files belonging to women who were referred for prenatal genetic counseling from July 2019 to December 2021 were included in this retrospective review. The demographic characteristics of these patients are summarised in Table 1 below. The majority of patients were seen at CMJAH. The maternal age ranged from 16 to 46 years with a mean age of 35 years (SD =8). Ninety percent of the patients seen belonged to the Black population group. Majority of these individuals were isiZulu speaking, followed by Sepedi and Sesotho (see supplementary Table 1).

Table 1: Sociodemographic characteristics of the study cohort (N=525)

Variable	Overall N = 525; n (%)	CHBAH N = 51 (9.7%)	CMJAH N = 308 (58.7%)	RMMCH N = 166 (31.6%)
Number of patients seen (year)				
2019	101 (19.2%)	3 (5.9%)	58 (18.8%)	40 (24.1%)
2020	234 (44.6%)	8 (15.7%)	197 (64.0%)	29 (17.5%)
2021	190 (36.2%)	40 (78.4%)	53 (17.2%)	97 (58.4%)
Maternal age – Mean (SD)	35 (8)	36 (7)	32 (8)	33 (7)
Maternal age classification[2]				
AMA (≥ 35 years)	311 (59.2%)	21 (41.2%)	214 (69.4%)	76 (45.7%)
Non-AMA (< 35 years	213 (40.6%)	30 (58.8%)	93 (30.2%)	90 (54.2%)
Population group				
Black	471 (89.7%)	50 (98.0%)	281 (91.2%)	140 (84.4%)
Mixed Ancestry	19 (3.6%)	1 (2.0%)	10 (3.2%)	8 (4.8%)
White	16 (3.1%)	0 (0.0%)	7 (2.3%)	9 (5.4%)
Indian	11 (2.1%)	0 (0.0%)	8 (2.6%)	3 (1.8%)
Asian	1 (0.2%)	0 (0.0%)	0 (0.0%)	1 (0.6%)
Non-South African[1]	7 (1.3%)	0 (0.0%)	2 (0.7%)	5 (3.0%)

[1]Foreign patients are selected as other and their country of origin is specified; [2] Values may not add up to 100% as a documented date of birth and classification of maternal age was missing in one file.

3.2. Reason for referral for genetic counseling

There were 595 documented referral reasons for the patients seen by the genetic counselors. More than one reason for referral was recorded for 70 patients. These were categorised into 11 groups, as seen in Table 2. Overall, the major referral groups were AMA, abnormal findings on ultrasound, poor obstetric history, previous child with a genetic condition or CD, and suspected or confirmed genetic diagnosis.

Under ultrasound findings, 110 patients were referred for soft markers and 99 patients were referred for structural abnormalities detected on ultrasound. There was a significant difference in the reasons for referring patients for prenatal genetic counseling across the various hospitals ($p = 1 \times 10^{-5}$). At CMJAH, patients were more likely to be referred for AMA, whereas patients at CHBAH and RMMCH were more likely to be referred for abnormal findings on ultrasound.

Table 2: Comparison of the reason for referral at each tertiary hospital

Variable	Overall N = 595[1]	CHBAH N = 54[1]	CMJAH N = 347[1]	RMMCH N = 195[1]	P-value [2]
Reason for referral					1×10^{-5}
AMA	225 (38.0%)	13(24.0%)	172 (50.0%)	40 (21.0%)	
Family history [3]	9 (1.5%)	3 (6.0 %)	4 (1.2%)	2 (1.0%)	
Findings on ultrasound	209 (35.0%)	16(30.0%)	85 (25.0%)	108 (55.0%)	
Grief counseling	4 (0.7%)	1 (1.9%)	3 (0.9%)	0 (0.0%)	
Consanguinity	2 (0.3%)	0 (0.0%)	1 (0.3%)	1 (0.5%)	
Other prenatal screening outcomes	5 (0.8%)	0 (0.0%)	2 (0.6%)	3 (1.5%)	
Patient with/suspected genetic condition	14 (2.4%)	5 (9.3%)	7 (2.0%)	2 (1.0%)	
Poor obstetric history	52 (8.7%)	3 (5.6%)	35 (10.0%)	14 (7.2%)	
Previous child with a genetic condition or CD	36 (6.1%)	6 (11.0%)	19 (5.0%)	12 (6.2%)	
Routine NT scan	3 (0.5%)	3 (5.6%)	0 (0.0%)	0 (0.0%)	
Suspected or confirmed genetic diagnosis	36 (6.1%)	4 (7.4%)	19 (5.5%)	13 (6.7%)	

[1]n (%) ;[2] Fisher's Exact test with Monte Carlo simulations; [3] Family history of a known or suspected genetic condition

3.3. Common soft markers and abnormalities detected on ultrasound

As illustrated in Figure 1 below, a total of 209 individual soft markers were detected via ultrasonography during the first and second trimesters of pregnancy in 159 patients. These markers included intracardiac echogenic foci, increased NT or nuchal fold, absent or hypoplastic nasal bone, short long bones, and other less frequently observed soft markers. Among 159 patients who presented with soft markers, 44.0% (70/159) were of AMA and 55.3% (88/159) were not of AMA. Notably, these values do not add up to 100% due to an undocumented date of birth in one of the patient files. Isolated soft markers were observed for 117/159 patients, whereas 42/159 patients had two or more co-occurring soft markers. Lastly, 54/525 patients presented with soft markers in combination with structural abnormalities.

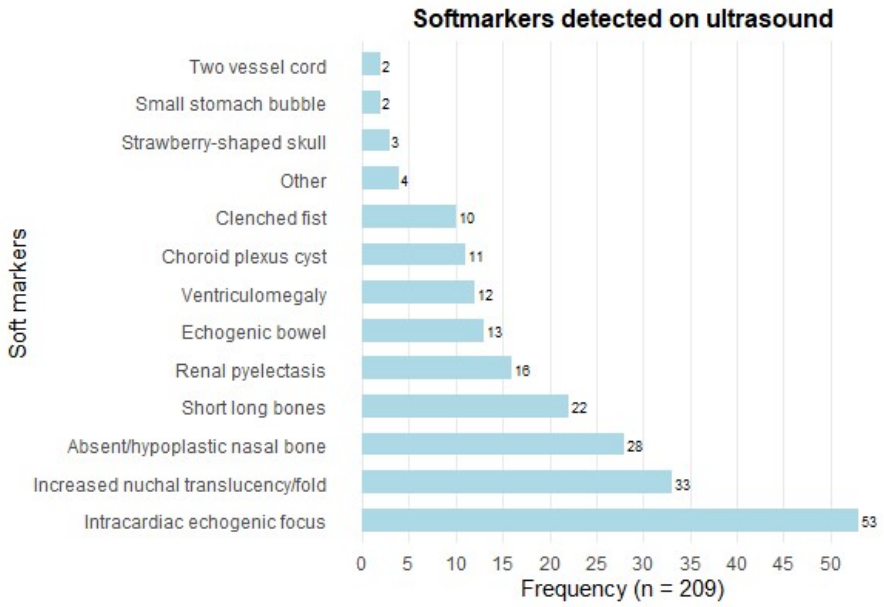


Figure 1: A graph illustrating the commonly detected ultrasonographic soft markers in the study cohort.

One hundred and nine patients (N = 109) presented with structural abnormalities on ultrasound. Among these patients, 284 individual structural abnormalities were detected (Figure 2). The majority of these abnormalities occurred in the musculoskeletal system (27.5%; 78/284), followed by the central nervous system (CNS) (25.4%; 72/284), cardiovascular system (14.8%; 42/284), and the gastrointestinal tract (12.0%; 34/284). Patients of AMA and those not of AMA accounted for 42.2% (46/109) and 57.8% (63/109) of these cases, respectively.

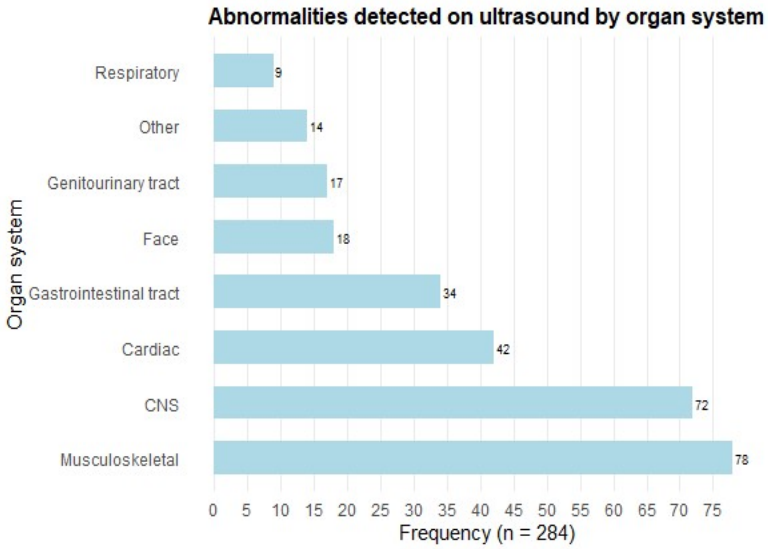


Figure 2: A graph illustrating the abnormalities detected on ultrasound in the study cohort.

3.4. Factors affecting decision-making regarding invasive testing and testing outcomes

Prenatal invasive testing was offered to 67.4% (354/525) of the patient cohort. Decision regarding invasive testing was grouped according to three outcomes: accepted, awaiting decision, and declined. Awaiting decision refers to patients who did not make a decision at the time of the consultation. As seen in Table 3, the uptake of invasive testing was 39.8% (141/354), with 50.8% (180/354) of patients declining and 9.3% (33/354) being unable to reach a decision.

There was a significant difference in the decision to pursue testing between women of AMA and those who were not of AMA ($p = 0.003$); women of AMA were more likely to decline testing or struggle to reach a decision during the consultation. Notably, a higher proportion of patients who were offered testing were of AMA (243/354). A significant difference was observed in the distribution of referral reasons and decision-making ($p < 0.001$), where patients were more likely to undergo testing when referred for findings on ultrasound (supplementary Table 4). However, further analysis revealed no significant difference in decision-making regarding testing between patients who only presented with soft markers and those who only presented with structural abnormalities ($p = 0.3$); both groups were equally likely to pursue invasive testing. No association was found between the choice to pursue testing and the specific type of soft marker ($p = 0.8$), or the specific type of structural abnormality ($p = 0.5$) detected via ultrasonography (see supplementary Tables 2 and 3).

Table 3: Comparison of the decision regarding invasive testing by maternal age classification and abnormal findings on ultrasound

Variable	Overall N = 354[1]	Accepted N = 141[1]	Awaiting decision N = 33[1]	Declined N = 180[1]	p-value[2]
Maternal age classification					0.003
AMA	243 (68.6%)	82 (58.2%)	24 (72.7%)	136 (75.6%)	
Non-AMA	111 (31.4%)	59 (41.8%)	9 (27.3%)	43 (23.9%)	
Ultrasound findings					0.3
Soft markers only	88 (24.9%)	43 (30.4%)	15 (45.5%)	30 (16.7%)	
Abnormalities only	22 (6.2%)	15 (10.6%)	3 (9.1%)	4 (2.2%)	

[1]n (%); [2]Pearson's Chi-squared test

3.4.1. Reason for declining invasive testing

Overall, 180 of the 354 patients who were offered testing, declined. There were 157 documented reasons speaking to the rationale behind this decision. Reasons relating to the same or similar themes were quantitatively analysed and grouped together. Most patients declined testing due to the perception of risk to pregnancy, followed by the decision not to terminate an affected pregnancy, preferring to wait

for a FA scan, religious beliefs, and wishing to decide with their partner. In total, 41.1% (74/180) of patients declined testing due to the fear of miscarriage risks, which was grouped under perception of risk to pregnancy. Other reasons under this category included low-risk perception, referring to a low perceived age-related risk, as well as the fear of preterm labour risks (see supplementary table 5).

Table 4: A summary of the reasons for declining invasive testing

Variable	**Overall** N = 180; n (%)
Reason for declining testing	
Would TOP regardless of testing outcomes	1 (0.6%)
Not reported	23 (12.8%)
Pregnancy risk perception	81 (45.0%)
Religious beliefs	9 (5.0%)
Waiting for a FA scan	25 (13.8%)
Wished to discuss with partner	9 (5.0%)
Would not terminate an affected pregnancy	32 (17.8%)

3.5. Invasive testing and outcomes

Prenatal genetic testing was organized according to the invasive procedure performed, and a summary is provided in Table 5. A total of 119 genetic tests were requested and performed on amniotic samples (112/119; 94%); CVS samples (5/119; 4.2%); and umbilical cord blood samples (2/119; 1.7%). In terms of genetic testing, QF-PCR aneuploidy testing was the most requested, followed by karyotype, and single gene testing. Of the 119 pregnancies that were tested, 27/119 (22.7%) were confirmed to be affected with a genetic condition and one fetus (1/119; 0.01%) was confirmed to be a carrier of Spinal Muscular Atrophy (SMA). The specific types of chromosomal aneuploidies are documented in supplementary Table 6.

Table 5: A summary of the genetic tests performed and the outcomes

Variable	Overall N = 119 (100%)	Karyotype N = 19 (16.0%)	QF-PCR N = 98 (82.4%)	Single gene N = 2 (1.7%)
Test result				
Chromosomal aneuploidy	26 (21.8%)	5 (26.3%)	21 (21.4%)	0 (0.0%)
Single gene condition	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (100%)
No genetic abnormality detected	71 (59.6%)	9 (47.3%)	62 (63.2%)	0 (0.0%)
No result available [1]	20 (16.8%)	5 (26.3%)	15 (15.3%)	0 (0.0%)

[1] Patient consented to testing during the consultation, but no genetic test results were available for the study

3.6. Decision-making around pregnancy

A total of 305 of 354 patients who were offered testing continued with their pregnancy, while 48 of these 354 patients underwent a termination of pregnancy. No association was observed between maternal age and the decision to continue or terminate a pregnancy ($p = 0.1$); both groups were equally likely to continue with the pregnancy. However, the diagnostic outcome via genetic testing had a significant impact on the decision-making process ($p < 0.001$). Patients were more likely to terminate a pregnancy with a confirmed genetic diagnosis. See supplementary Table 6 for genetic diagnoses made.

Table 6: Comparative analysis between Maternal age classification and Pregnancy diagnostic outcome on the decision to terminate or continue with a pregnancy

Variable	Continued with pregnancy N = 306 (86.4%)	Termination of pregnancy N = 48 (13.6%)	p-value [1]
Maternal age classification			0.1
AMA	175 (57.2%)	21 (43.7%)	
Non-AMA	130 (42.5%)	27 (56.3%)	
Pregnancy diagnostic outcome			<0.001
Confirmed genetic diagnosis	7 (2.3%)	12 (25.0%)	
No genetic abnormality	73 (23.9%)	3 (6.3%)	
No result available	9 (2.9%)	4 (8.3%)	

[1]Fisher's Exact test with Monte Carlo simulation

4. Discussion

4.1. Prenatal genetic services - referrals

The demographic composition of the patient cohort is representative of the population distribution in the city of Johannesburg, where the Black population group accounts for 80% of the residents (Cooperative Governance and Traditional Affairs, 2020). The majority of the patients in the study were isiZulu speaking, followed by Sepedi and Sesotho, which also mirrors the predominant Black population group in the region. Regarding maternal age, more than half of the patients were of AMA which can be explained by the provision of services in the state sector. In the South African state healthcare system, local clinics identify women who are at a higher risk of adverse pregnancy outcomes and refer them to fetal medicine units based in tertiary hospitals. There, the women gain access to prenatal services such as specialized fetal ultrasonography, genetic counseling, and invasive procedures to perform genetic testing (Wessels & Koole, 2018). Due to financial constraints and limited resources, prenatal testing for chromosomal abnormalities is offered on the basis of maternal age, along with other screening criteria which constitute a high-risk pregnancy (Bhorat et al. 2018).

This study also observed that genetic counselors were more likely to see patients for specific referrals depending on the tertiary hospital attended. Out of the three hospitals, only CMJAH was found to have AMA as the most common referral indicator. In contrast, the remaining two hospitals were more likely to refer patients for soft markers and structural abnormalities detected via ultrasonography. This observation could be attributed to the referral pathways from both the primary hospitals in the surrounding areas and the healthcare practitioners (HCPs) at the tertiary hospitals, as well as the criteria implemented to determine the necessity of genetics referrals. Therefore, these referral pathways could benefit from the implementation of standardized guidelines to ensure more consistent delivery of services across the different hospitals. This can be achieved through collaboration with pertinent HCPs and the establishment of mutually-agreed upon referral criteria between the referring hospitals and the genetic counseling team.

4.2. Contributing factors towards the uptake of invasive testing

4.2.1. Patient perceptions and personal beliefs

Fifty percent of patients who were offered testing declined this option. Most patients cited the fear of a procedure-related pregnancy loss as the major motivating factor behind this decision. Notably, two patients miscarried subsequent to an invasive procedure, one of which had a negative QF-PCR result. Other motivating factors included the unwillingness to terminate an affected pregnancy, waiting for additional assessments, partner support, as well as religious beliefs. These findings are contrary to Du Toit et al. (2021) who conducted a review on the factors influencing the uptake of prenatal genetic screening and invasive testing among pregnant women of AMA (>37 years) at Tygerberg Hospital. The authors reported unwillingness to terminate an affected pregnancy as the primary reason for declining

an invasive procedure. This may be explained by differences in communication of procedure-related pregnancy loss risks and balancing this with the age-related risks of a genetic condition. The 1:200 risk of miscarriage, as communicated in our consultations, may be generally perceived as minimal. However, it is possible that any level of risk could have been considered unacceptable by the patients in our study. Du Toit et al. (2021) also revealed that decision-making was not influenced by the presence of a partner during the consultation. In contrast, nearly 10% of individuals in our patient cohort wished to commit to a decision with their partner.

4.2.2. *Maternal age*

Overall, 39.8% (141/354) of patients in our cohort accepted testing. Of the 243 patients who were of AMA and were offered testing, 82 accepted, resulting in a 33.7% uptake in this group. Notably, 30.5% (25/82) of these patients did not present with abnormal ultrasound findings nor have a second indication for testing. This rate is higher than the 17.8% uptake reported by Du Toit et al. (2021) amongst women older than 37 years of age at Tygerberg Hospital. However, it is similar to findings by Urban et al. (2011) who conducted a retrospective analysis of patient records at Groote Schuur Hospital in Cape Town. The authors revealed poor attendance for AMA counseling services and of those receiving counseling, approximately 31% opted for amniocentesis. This value differed from the increased acceptance of amniocentesis for referrals based on abnormalities detected on ultrasound, which prompted them to conclude that maternal age, as a screening criterion, performed poorly in comparison to other indicators.

Further analysis between the reasons for referral and the choice to pursue testing, in the current study, revealed an association between these variables. Notably, patients referred for abnormal ultrasound findings showed a higher uptake of invasive testing compared to the AMA group. The association between AMA and the increased risk of chromosomal aneuploidies has long been documented and communicated to patients (Lampret et al. 2008). The South African Health policy also maintains that all women who are of AMA should have access to amniocentesis. Yet, research continues to show a reduced uptake of this service (Urban et al. 2011). Further exploration to elucidate the contributing factors towards this phenomenon could be beneficial for this prenatal genetic counseling landscape. A potential approach would be to conduct interviews with women of AMA who have underwent genetic counseling, to investigate whether they perceived the consultations as beneficial. Interviews could further capture how counseling influenced their understanding and decision making, and note the aspects considered to be most or least effective.

4.2.3. Abnormal findings via ultrasonography

Based on the types of soft markers and abnormalities seen, it may be inferred that a significant proportion of patients attended prenatal genetic counseling before 22 weeks gestation. Commonly detected soft markers in this patient cohort are consistent with other literature (Smith-Bindman et al.

2001; Papp et al. 2008). There were more patients who solely presented with soft markers in comparison to patients who solely presented with abnormalities. This is expected since soft markers are often transient and can be found in pregnancies that are not affected by a genetic condition; whereas structural abnormalities tend to be more definitive (Kroes et al. 2014; Zhang et al. 2019). Following this reasoning, it may be hypothesised that patients would be more likely to test for abnormalities. However, statistical analysis revealed that the choice to pursue testing was not significantly influenced by the type of abnormal ultrasound finding, soft marker or abnormality. Additionally, no associations were found between the specific type of soft marker or the specific type of abnormality and the decision to undergo testing.

4.3. Cytogenetic testing outcomes

Prenatally, QF-PCR aneuploidy testing accounted for 82.4% (98/119) of the tests requested, while 16.0% (19/119) were karyotypes. This discrepancy is expected because the NHLS Johannesburg employs this test as a first line approach for aneuploidy detection. Notably, QF-PCR is less time consuming and has a greater economic value than traditional karyotyping. This is beneficial given both the limited resources and financial constraints present in this setting (Cottino et al. 2022). Of these QF-PCR tests, 21.4% (21/98) were positive and 63.2% (62/98) were negative. Positive QF-PCR results also accounted for 80.8% (21/26) of the total chromosomal aneuploidies identified. In total, diagnostic testing identified 13 cases of Trisomy 21, 7 cases of Trisomy 18, two cases of Trisomy 13, one case of mosaic Trisomy 16 as well as one case of mosaic Trisomy 17. Turner Syndrome and Triple X syndrome were the only two sex chromosomal aneuploidies observed. These results encompass all testing indications.

The majority of the aforementioned trisomies were consistent with the soft markers and abnormalities that were seen on ultrasound. However, 13 out of 19 pregnancies tested for structural abnormalities on ultrasound had a negative QF-PCR test result. Internationally, CMA is the first line prenatal diagnostic test for abnormalities detected on ultrasound, unless the abnormalities are convincingly in keeping with aneuploidy. This is an additional newer technology that is seemingly more favourable than karyotyping, based on its ability to uncover Copy Number Variations (CNVs) in DNA (Zhang et al. 2019). As previously mentioned, this test is currently not available in the state prenatal setting. The question remains whether further testing, in the form of CMA, should be offered in cases where reasonable suspicion of a chromosomal abnormality persists, despite a negative QF-PCR test result. This is an important consideration for genetic counsellors who would have to gauge patient willingness for more testing.

Notably, results for 16.8% (20/119) of the tests requested were unavailable despite these patients consenting to testing. It is possible that patients later chose to forgo testing and to not attend their

booking. However, test results may have also been reported under an incorrect name or hospital number due to spelling inconsistences and human error.

4.4. Pregnancy management

While no statistical significance was established between maternal age classification and the decision to continue or terminate a pregnancy, a higher proportion of patients belonging to the non-AMA classification group underwent the procedure. Previous findings have proposed that young South African women may be more likely to opt for TOP (Ndwambi & Govender, 2015). Perceived readiness for parenthood, financial status, relationship problems, and the need to complete their schooling were found to be the motivating factors behind this decision.

In South Africa, there are no conditions for a medical TOP (mTOP) in the first 12 weeks of the pregnancy case. During 13 to 20 weeks of gestation, mTOP is dependent on the following: (i) the medical practitioner is of the opinion that continuing the pregnancy would present risks of injury to the woman's physical or mental health; (ii) a considerable risk of gross mental or physical malformation to the fetus; (iii) the pregnancy resulted from rape or incest; and (v) continuation would affect the woman's social or economic circumstances. Following the 20th week of gestation, mTOP is permitted based on endangerment to the mother as well as the risk of injury and severe abnormalities to the fetus. At this stage, two medical practitioners must agree upon offering a mTOP (CTOP Act, 1996).

Patients were more likely to terminate a pregnancy affected by a genetic condition. Though not substantial, a higher proportion of women in this group were of AMA. TOP was carried out for seven cases of Trisomy 21, four cases of Trisomy 18, one case of Trisomy 13, as well as the mosaic Trisomy 16. The motivating factors behind terminating an affected pregnancy were not explored in this study. However, previous research provides insights into plausible reasons for this decision regarding pregnancy. Firstly, there are psychological and financial strains in the decision to continue with a pregnancy where a CD was diagnosed. Mothers of children with CDs report experiences of emotional pain, guilt, denial, and disbelief. Moreover, depending on the severity of the CD, children may require life-long interventions. This means that some mothers must pause their educational endeavours in order to care for their children (Mazibuko et al. 2022). There is also an economical burden related to frequent medical visits and loss of work opportunities (Dambi et al. 2015). Altogether, these factors highlight the complexities in the decision to terminate.

4.5. Study limitations

This study aimed to review patient files from July 2019 to July 2024. Data collection was constrained due to inconsistencies in the presence of certain data fields at particular time points, which extended the collection process as certain information was not uniformly recorded in the same place. This also impacted comprehensive capture of gestation at consultation as well gestational age at ultrasound. Physical FM ticksheets used during the pandemic required downloading. Consequently, patient data

was manually entered onto the excel spreadsheet. Due to the impact of the pandemic on the delivery of genetic services, test results required manually searching on the national database. This study is being submitted as part of the research component of the MSc (Med) Genetic Counselling degree, which is a one- year programme. Therefore, due to time constraints, only files from July 2019 to December 2021 were analysed. However, the remaining files will be analysed prior to submission to the selected journal as data collection is planned to continue.

5. Conclusion

This study provides an overview of the prenatal genetic counseling services and testing practices in our setting, highlighting potential drawbacks and areas for improvement. Abnormal ultrasound findings were stronger indicators for invasive testing than AMA, reflecting how patients understood and responded to their perceived risk. Qualitative research, in the form of interviews, could uncover the informational and emotional needs of patients in such cases. The fear of procedure-related pregnancy loss was the main deterrent for invasive testing in this cohort. The utilization of QF-PCR as a first-line testing approach is effective in detecting common aneuploidies. However, the feasibility of offering further testing should be evaluated in cases where there remains suspicion of a chromosomal abnormality despite a negative QF-PCR result. Inconsistent referral patterns indicate a need for more standardized practices as well as improved collaboration with other HCPs to ensure equitable service delivery. These findings provide a foundation for guideline development, future research and promotes a contextual and patient-centered approach to prenatal genetic counseling practices.

Author contributions

E Gilfillan and B Shingwenyana designed this study and supervised the research. A Tshwane, E Gilfillan, and B Shingwenyana were involved in the retrieval and interpretation of the data. Data analysis was performed by A Tshwane. A Tshwane drafted this manuscript. This was then reviewed by E Gilfillan and B Shingwenyana. All authors provided final approval prior to submission. A certificate of ethical clearance is provided in Appendix B.

Acknowledgements

A Tshwane, E Gilfillan, and B Shingwenyana would like to acknowledge the genetic counsellors who conducted the consultations as well as Dr Clarence Yah who provided assistance with statistics queries.

References

1. Aalfs, C., Mollema, E., Oort, F., De Haes, J., Leschot, N., & Smets, E. (2004). Genetic counseling for familial conditions during pregnancy: An analysis of patient characteristics. *Clinical Genetics*, *66*(2), 112–121. https://doi.org/10.1111/j.0009-9163.2004.00279.x
2. Bakker, M., Birnie, E., Robles de Medina, P., Sollie, K. M., Pajkrt, E., & Bilardo, C. M. (2017). Total pregnancy loss after chorionic villus sampling and amniocentesis: a cohort study. *Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology*, *49*(5), 599–606. https://doi.org/10.1002/uog.15986
3. Bhorat, D. I., Chauke, D. L., Coetzee, E., Geerts, L., Lombaard, H., Nicolaou, E., Pistorius, D. L., & Soma-Pillay, P. (2018). *Challenges and Controversies in Prenatal Genetic Screening in the South African Context*.
4. Choice on Termination of Pregnancy Act of 1996 (1996). https://www.gov.za/documents/choice-termination-pregnancypact
5. Christianson A, Howson CP, Modell B. (2006) *March of Dimes: Global Report on Birth Defects, the Hidden Toll of Dying and Disabled Children*.
6. Cooperative Governance and Traditional Affairs. (2020). *Profile: City of Johannesburg metro.*
7. Cottino, L., Sahibdeen, V., Mudau, M., Lekgate, N., & Krause, A. (2022). QF-PCR: A valuable first-line prenatal and postnatal test for common aneuploidies in South Africa. *Journal of Community Genetics*, *13*(3), 355–363. https://doi.org/10.1007/s12687-022-00587-y
8. Czeizel, A. E. (2005). Birth Defects Are Preventable. *International Journal of Medical Sciences*, 91–92. https://doi.org/10.7150/ijms.2.91
9. Dambi, J. M., Jelsma, J., & Mlambo, T. (2015). Caring for a child with Cerebral Palsy: The experience of Zimbabwean mothers. *African Journal of Disability*, *4*(1). https://doi.org/10.4102/ajod.v4i1.168
10. Driscoll, D. A., & Gross, S. (2009). Prenatal Screening for Aneuploidy. *New England Journal of Medicine*, *360*(24), 2556–2562. https://doi.org/10.1056/NEJMcp0900134
11. Du Toit, N. (2021). Uptake rate of prenatal genetic screening and invasive testing in pregnant women over the age of 37 in Tygerberg Hospital and factors influencing this [Master of medicine dissertation, Stellenbosch University]. Stellenbosch University Research Repository. http://hdl.handle.net/10019.1/1239030

12. EUROCAT, W. (2004). A review of environmental risk factors for congenital anomalies. *EUROCAT, European surveillance of congenital anomalies: Newtownabbey, University of Ulster, Northern Ireland*.
13. Goel, N., Morris, J. K., Tucker, D., de Walle, H. E. K., Bakker, M. K., Kancherla, V., Marengo, L., Canfield, M. A., Kallen, K., Lelong, N., Camelo, J. L., Stallings, E. B., Jones, A. M., Nance, A., Huynh, M. P., Martínez-Fernández, M. L., Sipek, A., Pierini, A., Nembhard, W. N., Goetz, D., … Morgan, M. (2019). Trisomy 13 and 18-Prevalence and mortality-A multi-registry population based analysis. *American journal of medical genetics. Part A*, *179*(12), 2382–2392. https://doi.org/10.1002/ajmg.a.61365
14. Harries, J., Orner, P., Gabriel, M., & Mitchell, E. (2007). Delays in seeking an abortion until the second trimester: A qualitative study in South Africa. *Reproductive Health*, *4*(1), 7. https://doi.org/10.1186/1742-4755-4-7
15. Harris, P. A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., & Conde, J. G. (2009). Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of biomedical informatics*, *42*(2), 377–381. https://doi.org/10.1016/j.jbi.2008.08.010
16. Kroes, I., Janssens, S., & Defoort, P. (2014). Ultrasound features in trisomy 13 (Patau syndrome) and trisomy 18 (Edwards syndrome) in a consecutive series of 47 cases. *Facts, views & vision in ObGyn*, *6*(4), 245–249.
17. Kromberg, J. G. R., Sizer, E. B., & Christianson, A. L. (2013). Genetic services and testing in South Africa. *Journal of Community Genetics*, *4*(3), 413–423. https://doi.org/10.1007/s12687-012-0101-5
18. Lampret, Julie, Lane, Tony, & Christianson, Arnold. (2008). QF-PCR for prenatal diagnosis of common aneuploides in women of advanced maternal age. *SAMJ: South African Medical Journal*, *98*(2),68-69. http://www.scielo.org.za/scielo.php?script=sci_arttext&pid=S0256-95742008000200004&lng=en&tlng=en.
19. Lildballe, D. L., Vogel, I., Petersen, O. B., & Vestergaard, E. M. (2014). Diagnostic performance of quantitative fluorescence PCR analysis in high-risk pregnancies after combined first-trimester screening. *PubMed*, *61*(11), A4964–A4964
20. Malope, M. F., Stewart, C., Fieggen, K. J., & Wessels, T.-M. (2023). The decision-making process of pregnant individuals offered termination of pregnancy for serious congenital abnormalities. *Patient Education and Counseling*, *112*, 107745. https://doi.org/10.1016/j.pec.2023.107745
21. Mazibuko, T. B., Ramukumba, T., & Ngwenya, N. (2022). The lived experiences of mothers who have children with congenital abnormalities in the Gert Sibande district. *Curationis*, *45*(1). https://doi.org/10.4102/curationis.v45i1.2250

22. Merkatz, I. R., Nitowsky, H. M., Macri, J. N., & Johnson, W. E. (1984). An association between low maternal serum alpha-fetoprotein and fetal chromosomal abnormalities. *American journal of obstetrics and gynecology*, *148*(7), 886–894. https://doi.org/10.1016/0002-9378(84)90530-1
23. Ndwambi, A., & Govender, I. (2015). Characteristics of women requesting legal termination of pregnancy in a district hospital in Hammanskraal, South Africa. *Southern African Journal of Infectious Diseases*, *30*(4), 22-26.
24. Nicolaides, K. H. (2011). Screening for fetal aneuploidies at 11 to 13 weeks. *Prenatal Diagnosis*, *31*(1), 7–15. https://doi.org/10.1002/pd.2637
25. Practice Bulletin No. 162: Prenatal Diagnostic Testing for Genetic Disorders. (2016). *Obstetrics and gynecology*, *127*(5), e108–e122. https://doi.org/10.1097/AOG.0000000000001405
26. Papp, C., Szigeti, Z., Tóth-Pál, E., Hajdú, J., Joó, J. G., & Papp, Z. (2008). Ultrasonographic Findings of Fetal Aneuploidies in the Second Trimester – Our Experiences. *Fetal Diagnosis and Therapy*, *23*(2), 105–113. https://doi.org/10.1159/000111588
27. Resta, R., Biesecker, B. B., Bennett, R. L., Blum, S., Estabrooks Hahn, S., Strecker, M. N., & Williams, J. L. (2006). A New Definition of Genetic Counseling: National Society of Genetic Counselors' Task Force Report. *Journal of Genetic Counseling*, *15*(2), 77–83. https://doi.org/10.1007/s10897-005-9014-3
28. Rhoda, N., Velaphi, S., Gebhardt, G., Kauchali, S., & Barron, P. (2018). Reducing neonatal deaths in South Africa: Progress and challenges. *South African Medical Journal, 108*(3a), s9-s16. doi:10.7196/SAMJ.2017.v108i3b.12804
29. Scott, C. J., Futter, M., & Wonkam, A. (2013). Prenatal diagnosis and termination of pregnancy: Perspectives of South African parents of children with Down syndrome. *Journal of Community Genetics*, *4*(1), 87–97. https://doi.org/10.1007/s12687-012-0122-0
30. Smith-Bindman, R., Hosmer, W., Feldstein, V. A., Deeks, J. J., & Goldberg, J. D. (2001). Second-trimester ultrasound to detect fetuses with Down syndrome: a meta-analysis. *JAMA*, *285*(8), 1044–1055. https://doi.org/10.1001/jama.285.8.1044
31. Todd, C., Haw, T., Kromberg, J., & Christianson, A. (2010). Genetic Counseling for Fetal Abnormalities in a South African Community. *Journal of Genetic Counseling*, *19*(3), 247–254. https://doi.org/10.1007/s10897-010-9278-0
32. Urban, M. F., Stewart, C., Ruppelt, T., & Geerts, L. (2011). Effectiveness of prenatal screening for Down syndrome on the basis of maternal age in Cape Town. *South African Medical Journal*, *101*(1), 45. https://doi.org/10.7196/SAMJ.4188
33. Watcham, S. J., Schön, S., & Christianson, A. L. (2007). Neglect in the care of pregnant South African women of advanced maternal age. *South African medical journal* ,*97*(11), 1064-1069

34. Wessels, T. M., & Koole, T. (2019). “There is a chance for me”–Risk communication in advanced maternal age genetic counseling sessions in South Africa. *European journal of medical genetics*, *62*(5), 390-396. https://doi.org/10.1016/j.ejmg.2018.12.014
35. Wilson, R. D., Gagnon, A., Audibert, F., Campagnolo, C., Carroll, J., Wilson, R. D., Audibert, F., Brock, J.-A., Campagnolo, C., Carroll, J., Chong, K., Gagnon, A., Johnson, J.-A., MacDonald, W., Okun, N., Pastuck, M., & Vallee-Pouliot, K. (2015). Prenatal Diagnosis Procedures and Techniques to Obtain a Diagnostic Fetal Specimen or Tissue: Maternal and Fetal Risks and Benefits. *Journal of Obstetrics and Gynaecology Canada*, *37*(7), 656–668. https://doi.org/10.1016/S1701-2163(15)30205-X
36. World Health Organisation (WHO). (2023). Congenital Disorders. https://www.who.int/news-room/fact-sheets/detail/birth-defects
37. Zhang, Z., Hu, T., Wang, J., Li, Q., Wang, H., & Liu, S. (2019). Prenatal Diagnostic Value of Chromosomal Microarray in Fetuses with Nuchal Translucency Greater than 2.5 mm. *BioMed Research International*, *2019*, 1–9. https://doi.org/10.1155/2019/6504159

Appendices

Appendix A: Supplementary tables and figures

Supplementary Table 1. Comprehensive sociodemographic characteristics of the study cohort (N=525).

Supplementary Table 2. Comparison of the common ultrasonographic markers and decision regarding invasive testing

Supplementary Table 3. Comparison of the abnormalities on ultrasound and decision regarding invasive testing

Supplementary Table 4. Comparison of reason for referral by decision regarding invasive testing

Supplementary Table 5. A comprehensive summary of the reasons for declining testing

Supplementary Table 6. A summary of the pgenetic tests and outcomes, stratified by the type of invasive procedure (pre-natally)

Appendix B: Ethics Clearance certificate

Appendix C: Approved research protocol

Appendix D: Turnitin Report and Plagiarism declaration

Appendix E: Author guidelines for Journal of Genetic Counseling

Appendix A: Supplementary tables and figures

Supplementary Table 1. Comprehensive sociodemographic characteristics of the study cohort (N=525).

Variable	Overall N = 525 [1]; n (%)	CHBAH-FM N = 51[1](9.7%)	CMJAH-FM N = 308 [1](58.7%)	RMMCH-FM N = 166 [1](31.6%)
Total number of patients seen (year)				
2019	101 (19.2%)	3 (5.9%)	58 (18.8%)	40(24.1%)
2020	234 (44.6%)	8 (15.7%)	197 (64.0%)	29(17.5%)
2021	190 (36.2%)	40 (78.4%)	53 (17.2%)	97(58.4%)
Maternal age – Mean (SD)	35 (8)	32 (8)	36 (7)	33 (7)
Unknown	1	0	1	0
Maternal age classification				
AMA (≥ 35 years)	311 (59.2%)	21 (41.2%)	214 (69.4%)	76 (45.7%)
Non-AMA (< 35 years	213 (40.6%)	30 (58.8%)	93 (30.2%)	90 (54.2%)
Unknown	1	0	1	0
Population group				
Black	470 (89.7%)	50 (98.0%)	280 (91.2%)	140 (84.4%)
Mixed Ancestry	19 (3.6%)	1 (2.0%)	10 (3.2%)	8 (4.8%)
White	16 (3.1%)	0 (0.0%)	7 (2.3%)	9 (5.4%)
Indian	11 (2.1%)	0 (0.0%)	8 (2.6%)	3 (1.8%)
Asian	1 (0.2%)	0 (0.0%)	0 (0.0%)	1 (0.6%)
Unknown	1	0	1	0

Other	7 (1.3%)	0 (0.0%)	2 (0.7%)	5 (3.0%)
Ethnolinguistic group				
Afrikaner	12 (2.4%)	0 (0%)	6 (2.0%)	6 (3.7%)
English-speaking	4 (0.8%)	0 (0%)	2 (0.7%)	2 (1.2%)
European	7 (1.4%)	0 (0%)	4 (1.4%)	3 (1.9%)
Hindi	2 (0.4%)	0 (0%)	0 (0%)	2 (1.2%)
Muslim	6 (1.2%)	0 (0%)	2 (0.7%)	4 (2.5%)
Ndebele	26 (5.1%)	1 (2.0%)	19 (6.4%)	6 (3.7%)
Sepedi	56 (10.6%)	0 (0%)	42 (13.6%)	14 (8.6%)
Sotho	55 (10.4%)	13 (25.5%)	23 (7.8%)	19 (11.4%)
Swazi	4 (0.8%)	0 (0%)	2 (0.7%)	2 (1.2%)
Tsonga	21 (4.1%)	3 (5.9%)	12 (4.1%)	6 (3.7%)
Tswana	36 (7.1%)	3 (5.9%)	13 (4.4%)	20 (12.0%)
Venda	19 (3.7%)	2 (3.9%)	10 (3.4%)	7 (4.3%)
Xhosa	39 (7.7%)	6 (11.8%)	23 (7.8%)	10 (6.2%)
Zulu	136 (25.9%)	20 (39.2%)	89 (28.9%)	27 (16.3%)
Unknown	17	0	13	4
Other	67 (12.8%)	3 (5.9%)	33 (10.7%)	31 (18.7%)

Supplementary Table 2. Comparison of the common ultrasonographic markers and decision regarding invasive testing

Variable	Accepted N = 95[1]	Awaiting decision about testing N = 20[1]	Declined N = 45[1]	p-value[2]
Soft markers on ultrasound				0.8
Absent/hypoplastic nasal bone	15 (15.8%)	1 (5.0%)	5 (11.1%)	
Choroid plexus cyst	8 (8.4%)	0 (0.0%)	2 (4.4%)	
Clenched fist	3 (3.2%)	1 (5.0%)	2 (4.4%)	
Echogenic bowel	6 (6.3%)	1 (5.0%)	2 (4.4%)	
Increased nuchal translucency/fold	14 (14.7%)	5 (25.0%)	7 (15.6%)	
Intracardiac echogenic focus	22 (23.2%)	8 (40.0%)	18 (40.0%)	
Other	0 (0.0%)	1 (5.0%)	2 (4.4%)	
Renal pyelectasis	8 (8.4%)	2 (10%)	3 (6.7%)	
Short long bones	8 (8.4%)	1 (5.0%)	2 (4.4%)	
Small stomach bubble	2 (2.1%)	0 (0.0%)	0 (0.0%)	
Strawberry-shaped skull	2 (2.1%)	0 (0.0%)	0 (0.0%)	
Two vessel cord	1 (1.1%)	0 (0.0%)	0 (0.0%)	
Ventriculomegaly	6 (6.3%)	0 (0.0%)	2 (4.4%)	

[1]n (%); [2] Fisher's Exact test with Monte Carlo simulation

Supplementary Table 3. Comparison of the abnormalities on ultrasound and decision regarding invasive testing

Variable	Accepted N = 73[1]	Awaiting decision about testing N = 17[1]	Declined N = 24[1]	p-value[2]
Abnormalities on ultrasound				0.5
Cardiac	14 (19.1%)	2 (11.8%)	4 (16.7%)	
CNS	13 (17.8%)	3 (17.6%)	8 (33.3%)	
Face	4 (5.5%)	4 (23.5%)	0 (0.0%)	
Gastrointestinal tract	12 (16.4%)	2 (11.8%)	3 (12.5%)	
Genitourinary tract	4 (5.5%)	0 (0.0%)	1 (4.2%)	
Musculoskeletal	21 (28.8%)	5 (29.4%)	6 (25.0%)	
Other	3 (4.1%)	1 (5.9%)	0 (0.0%)	
Respiratory	2 (2.7%)	0 (0.0%)	2 (8.3%)	

[1]n (%);[2] Fisher's Exact test with Monte Carlo simulation

Supplementary Table 4. Comparison of reason for referral by decision regarding invasive testing

Characteristic	Accepted N = 162[1]	Awaiting decision about testing N = 39[1]	Declined N = 202[1]	p-value[2]
Reason for referral				<0.001
AMA	44 (27.2%)	16 (41.0%)	123 (60.9%)	
Family history of/suspected genetic condition	0 (0.0%)	0 (0.0%)	2 (1.0%)	
Other screening outcomes	2 (1.2%)	0 (0.0%)	2 (1.0%)	
Patient with/suspected genetic condition	1 (0.6%)	0 (0.0%)	3 (1.5%)	
Poor obstetric history	7 (4.3%)	2 (5.1%)	13 (6.4%)	
Previous child	6 (3.7%)	2 (5.1%)	6 (3.0%)	
Routine NT scan	0 (0.0%)	0 (0.0%)	3 (1.5%)	
Suspected or confirmed genetic diagnosis	22 (13.6%)	0 (0.0%)	5 (2.5%)	
Ultrasound findings	80 (49.4%)	19 (48.7%)	45 (22.2%)	

[1]n (%); [2] Fisher's Exact test with Monte Carlo simulation

Supplementary Table 5. A comprehensive summary of the reasons for declining testing

Variable	Overall N = 180; n (%)
Reason for declining testing	
Accepted TOP	1 (0.6%)
Not reported	23 (12.8%)
Pregnancy risk perception	81 (45.0%)
Miscarriage risk	64
Miscarriage risk and would not terminate	10
Low-risk perception	5
Pre-term labour risk	1
Prefers to pursue testing after delivery	1
Religious beliefs	9 (5.0%)
Waiting for a FA scan	25 (13.8%)
Wished to discuss with partner	9 (5.0%)
Would not terminate an affected pregnancy	32 (17.8%)

Supplementary Table 6. A summary of the genetic tests and outcomes, stratified by the type of invasive procedure (pre-natally)

	Amniocentesis			Chorionic Villus sampling		Cordocentesis
Characteristic	**Karyotype** N = 17[1]	**QF-PCR** N = 93[1]	**Single gene** N = 2[1]	**Karyotype** N = 2[1]	**QF-PCR** N = 3[1]	**QF-PCR** N = 2[1]
Test result						
Mosaic Trisomy 17	1 (6.3%)	0 (0.0%)	0 (0.0%)			
Beta-thalassaemia	0 (0.0%)	0 (0.0%)	1 (50.0%)			
Confirmed carrier of SMA	0 (0.0%)	0 (0.0%)	1(50.0%)			
Mosaic Trisomy 16	1 (6.3%)	0 (0.0%)	0 (0.0%)			
Normal	9 (52.9%)	59 (63.4%)	0 (0.0%)		3 (100%)	
Normal	9 (52.9%)	0 (0.0%)	0 (0.0%)			
Triple X syndrome	0 (0.0%)	1 (1.1%)	0 (0.0%)			
Trisomy 13	1 (6.3%)	1 (1.1%)	0 (0.0%)			
Trisomy 18	0 (0.0%)	6 (6.6%)	0 (0.0%)			1 (50.0%)
Trisomy 21	1 (6.3%)	11 (11.8%)	0 (0.0%)	1 (50.0%)		
Turner Syndrome	0 (0.0%)	1 (1.1%)	0 (0.0%)			
Not confirmed or excluded	4 (23.5%)	14 (15.1%)	0 (0.0%)	1 (50.0%)		1 (50.0%)

[1]n (%)

Appendix B: Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Ms Asante Tshwane M240612 MED24-04-578

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M240612 MED24-04-578

NAME: (Principal Investigator)	Ms Asante Tshwane
STUDENT/STAFF NO:	2305138
DEGREE:	MSc Genetic Counselling
DEPARTMENT:	School of Pathology Human Genetics NHLS
PROJECT TITLE:	An overview of prenatal genetic counselling services in state healthcare hospitals of Johannesburg, South Africa
DATE CONSIDERED:	21/06/2024
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Mrs Elzette Gilfillan and Mr Barry Shingwenyana
APPROVED BY:	Paul Ruff Paul Ruff (Aug 5, 2024 15:18 GMT+2) Prof P Ruff, Chair, HREC (Medical)
DATE OF APPROVAL:	29/07/2024 **EXPIRY DATE:** 29/07/2029

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to Committee. **I agree to submit a yearly progress report** in July each year until study is closed. Failure to submit annual report will result in ethics clearance certificate suspension. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in June and will therefore be due in the month of June each year. Unreported changes to the application invalidate the clearance given by the HREC (Medical). Email signed copy of this ethics clearance certificate prior to commencing with the study hrec-medical.researchoffice@wits.ac.za

Principal Investigator Signature

06/09/2024

Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix C: Approved research protocol

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Ms Sandra Munesar
E-mail: Sandra.munesar@wits.ac.za

13 August 2024
Person No: 2305138
PAG

Ms AM Tshwane
Private bag x745
Pretoria
0001
South Africa

Dear Ms Asante Tshwane

Master of Science in Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *A retrospective review of the prenatal genetic counselling services in state healthcare hospitals of Johannesburg, South Africa* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Ms Sandra Munesar
Faculty Registrar
Faculty of Health Sciences

Appendix C: Approved research protocol

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

CANDIDATE'S SURNAME:	FIRST NAME/S:	STUDENT NUMBER:
Tshwane	Asante	2305138

CURRENT QUALIFICATIONS: BSc (Hons) Molecular Biology and Human Genetics

TEL: N/A	CELL: 060 786 3129	E-MAIL: 2305138@students.wits.ac.za	FAX: N/A

DEGREE FOR WHICH PROTOCOL IS BEING SUBMITTED: MSc (Med) Genetic Counselling

PART-TIME OR FULL-TIME: Full-time

FIRST REGISTERED FOR THIS DEGREE:	TERM: 1	YEAR: 2024

DEPARTMENT: Human Genetics

TITLE OF PROPOSED RESEARCH: A retrospective review of the prenatal genetic counselling services in state healthcare hospitals of Johannesburg, South Africa

CANDIDATE'S SIGNATURE:	DATE: 27/05/2024
SUPERVISOR 1 (NAME & SURNAME): Elzette Gilfillan	% Supervision 60%

SUPERVISOR'S QUALIFICATIONS MSc (Med) Genetic Counselling

SUPERVISOR'S DEPARTMENT Human Genetics

SUPERVISOR'S ADDRESS / TEL / E-MAIL: elzette.nienaber@nhls.ac.za

SUPERVISOR 2 (NAME & SURNAME): Barry Shingwenyana	% Supervision 40%

SUPERVISOR'S QUALIFICATIONS MSc (Med) Genetic Counselling

SUPERVISOR'S ADDRESS / TEL / E-MAIL: Barry.Shingwenyana@nhls.ac.za

SUPERVISOR 3 (NAME & SURNAME):	% Supervision
SUPERVISOR'S QUALIFICATIONS	
SUPERVISOR'S ADDRESS / TEL / E-MAIL:	

SYNOPSIS OF RESEARCH:*(Brief summary of proposed research project; between 200-300 words only; with sub-headings: an introduction and justification for study, aim/s, proposed methodology and expected outcome/s)*

[Use reverse side of this page if more space is required]

Introduction and justification for study

Congenital disorders (CDs) contribute significantly to the global burden of disease, with a larger impact on middle to low-income countries. In South Africa, CDs are the fourth most common contributor to early neonatal death. While CDs with genetic origins cannot be prevented, earlier identification efforts, such as prenatal screening and prenatal diagnosis, have been an effective medium of intervention and care.

Screening outcomes are used to determine the need for further diagnostic testing, which can confirm the presence of an anomaly or genetic condition in an unborn child. Thus, prenatal genetic counselling services are a vital component of antenatal care as they assist in patient education and information giving regarding findings, outcomes, prognosis, and options going forward. However, there is still limited data detailing these services in the South African context, particularly in Johannesburg. Thus, it is necessary to conduct research that provides insights into the prenatal clinical services provided by genetic counsellors in these settings.

Aim:

To evaluate the prenatal genetic services provided by genetic counsellors at several State tertiary hospitals in Johannesburg over a five-year period.

Methodology:

This study is a retrospective file review, involving an audit of genetic counselling clinic records from the University of the Witwatersrand/NHLS affiliated state hospitals in Johannesburg. The Division of Human Genetics Research Electronic Data Capture (REDCap) will be accessed to retrieve clinical data about patient demographics, gestational age, reason for referral, ultrasound screening findings, uptake of invasive testing, genetic diagnosis, and decision regarding pregnancy. Statistical analysis will be performed to describe the anonymised data and to decipher trends seen in the prenatal genetic counselling services offered in Johannesburg state hospitals.

Expected outcomes:

This research will highlight factors from the local population that both practicing counsellors and prospective counsellors should consider when offering counselling services. Additionally, findings may serve as a foundation for future studies into the prenatal genetic services provided in the Johannesburg state healthcare system.

WITS ETHICS NOT REQUIRED: Yes (No) WITS ETHICS PENDING: (Yes) No WITS ETHICS APPROVED: Ues No (circle appropriate symbol)* *Please note the final human ethics clearance certificate or animal ethics certificate must be available prior to starting research	IF U SUPPLY ETHICS CLEARANCE CERTIFICATE AS ATTACHMENT AND INCLUDE ETHICS NUMBER HERE:

As supervisor/s, I/we confirm that I have read the protocol which has been submitted for assessment.		
SIGNATURE OF SUPERVISOR/S:	…….	B. SHINGWENYANA
SIGNATURE PG OFFICE STAFF ……..	REGISTERED YES….. NO…..	STAMP

SYNOPSIS OF RESEARCH CONTINUED

11 March 2019/MP

A retrospective review of the prenatal genetic counselling services in state healthcare hospitals of Johannesburg, South Africa

Asante Tshwane

2305138

MSc (Med) Genetic Counselling

Supervisor 1:

Mrs Elzette Gilfillan

MSc (Med) Genetic Counselling, Genetic Counsellor

Division of Human Genetics, School of Pathology, Faculty of Health Sciences,

University of the Witwatersrand

Supervisor 2:

Mr Barry Shingwenyana

MSc (Med) Genetic Counselling, Genetic Counsellor

Division of Human Genetics, School of Pathology, Faculty of Health Sciences,

University of the Witwatersrand

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Asante Tshwane (Student number: 2305138) am a student registered for the degree of MSc(Med) Genetic Counselling in the academic year 2024 .

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.

- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.

- I have followed the required conventions in referencing the thoughts and ideas of others.

- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.

- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: _____ Date:_____27/05/2024_____

1. Background literature analysis and critique

1.1. Introduction

Congenital disorders (CD), or birth defects, are structural or functional abnormalities that develop between conception and birth (WHO, 2023). CDs may be detected prenatally, at birth, or later in life. Additionally, they are a major component of the global disease burden with a greater degree of impact on middle to low-income countries (WHO,2023; Christianson et al. 2006). A large proportion of CDs cannot be attributed to a specific cause. However, the known possible causes may fall within three categories, namely genetic (15%), environmental (7% to 10%), and multifactorial (20% to 25%) (EUROCAT, 2004). Multifactorial causes manifest from the interaction of genetic and environmental factors. In South Africa, CDs are the fourth most common contributor to early neonatal death (Rhoda et al. 2018). Yet, the extent to which these cases can be attributed to specific causes is unclear due to the paucity of research in this area. It is reported that 70% to 85.3% of CDs can be prevented or mitigated by appropriate care (Czeizel, 2005; Christianson et al.2006). While CDs caused by genetic factors cannot be prevented, earlier identification efforts have been an effective medium of intervention and care. This is largely attributed to improvements in prenatal screening and prenatal diagnosis for high-risk pregnancies (Christianson et al. 2006).

1.2. Indications of a high-risk pregnancy

A pregnancy is classified as high-risk when the mother, the unborn child, or both are at an elevated risk of adverse outcomes, before or after birth. Common referral criteria for prenatal genetic consultations include advanced maternal age (AMA), consanguinity, soft markers and abnormalities detected on ultrasound, known or suspected family history of genetic conditions, history of pregnancies with genetic or structural abnormalities, parents with a chromosomal rearrangement, multiple miscarriages, and exposure to teratogens during pregnancy (Aalfs et al. 2004). AMA, referring to pregnant women older than 35 years of age, has been the most popular referral indicator for prenatal testing since the 1970s due to an increased risk of having children with common aneuploidies (Smith-Bindman et al. 2001; Lampret et al. 2008). Aneuploidy refers to an abnormal number of chromosomes within a cell. Among women of AMA, the most common aneuploidies are Trisomy 13,18, and 21 (Lampret et al. 2008). In each of these genetic conditions, fetal abnormalities arise from an extra copy of the related chromosome.

1.2.1. Clinical features of common aneuploidies

Trisomy 13 and 18 have extremely poor prognoses and are associated with an elevated risk of mortality, shortly after birth. Most cases result in intrauterine death while survival beyond the first year of life is

reported in only 5% - 10% of cases (Kroes et al.2014). Goel et al. (2019) reported a mean live birth prevalence of 0.55/10 000 and 1.07/10 000 for Trisomy 13 and 18, respectively. Trisomy 13, also called Patau Syndrome, typically presents with renal and cardiac malformations, polydactyly, holoprosencephaly, along with facial malformations such as cleft lip and palate, hypotelorism, as well as microphthalmia (Kroes et al. 2014). Trisomy 18, or Edwards Syndrome, also exhibits congenital heart and renal malformations in addition to clenched hands with overlapping fingers, club or rocker bottom feet, low-birth weight, low-set ears, diaphragmic hernia, microcephaly, micrognathia, and failure to thrive (Kroes et al. 2014; Goel et al. 2019). Trisomy 21, commonly referred to as Down Syndrome, presents in one out of 800 births (Driscoll and Ross, 2009). Some characteristic clinical features of Trisomy 21 are brachycephaly, decreased muscle tone, flat nasal bridge, small mouth, ears, and eyes, congenital heart malformations and cognitive delay. Children with Trisomy 21 have a better prognosis and subsequent higher life expectancy than those with Trisomy 13 and 18(Driscoll and Ross, 2009).

1.3. Prenatal screening

High-risk pregnancies can be identified during both the first and second trimester as part of the prenatal screening process. Prenatal screening aims to identify pregnancies that are at a higher risk of adverse outcomes and is available to pregnant women of all ages. In 1984, Merkatz et al. discovered an association between low second-trimester maternal serum alpha-feto protein (AFP) and chromosomal anomalies. Subsequently, biochemical testing has been incorporated into the prenatal screening process during the first two trimesters of pregnancy. During the first-trimester, levels of pregnancy associated plasma protein -A (PAPP-A) and maternal serum free β-human chorionic gonadotropin (β-hCG) are measured while levels of β-hCG and AFP are assessed in the second trimester. Utilisation of these biochemical markers has improved aneuploidy detection rates (Nicolaides et al. 2011; Lildballe et al. 2014). This is done in combination with fetal ultrasounds, first-trimester non-invasive prenatal testing (NIPT), obstetric examination, and family history taking (Nicolaides et al. 2011).

Fetal ultrasounds are a routine part of antenatal care. The nuchal translucency (NT) scan is a first trimester scan conducted between 11 to 14 weeks of gestation which also looks at fetal growth, presence of the nasal bone, and risk of pre-eclampsia. Nuchal translucency thicker than 3mm are associated with an increased risk of a variety of cardiac, skeletal, and genetic abnormalities such as Trisomy 21 (Kroes et al. 2014; Zhang et al. 2019). This is accompanied by the fetal anomaly (FA) scan, which is performed between 18 to 21 weeks, in the second trimester of pregnancy. This scan screens for major structural malformations as well as soft markers. Ultrasonographic soft markers are minor, observable findings known to be predictive of aneuploidies. Common detected soft markers are hypoplasia of the nasal

bone, choroid plexus cysts, short long bones, echogenic intracardiac focus, and echogenic bowel (Smith-Bindman et al. 2001; Papp et al. 2008).

1.4. Prenatal diagnosis

Diagnostic genetic testing is necessary when screening outcomes indicate an increased likelihood of a fetus with aneuploidy or other chromosomal abnormalities. There are three common prenatal diagnostic procedures performed under continuous ultrasonographic guidance and sterile conditions. Chorionic Villus sampling (CVS) can be performed as early as 11 to 14 weeks. In this procedure, a sterile needle is inserted into the placenta to obtain a sample of the chorionic villi. Amniocentesis involves the extraction of a small volume of amniotic fluid from the amniotic cavity, between 16 to 22 weeks of pregnancy (Practice Bulletin No.162, 2016). Lastly, a cord blood sample is obtained through cordocentesis, between 16 to 24 weeks of gestation. This procedure entails the insertion of a gauge spinal needle into the umbilical cord (Wilson et al. 2015). However, these diagnostic procedures are invasive and may lead to negative pregnancy outcomes. When amniocentesis and CVS are performed by experienced operators, there is a 0.17-0.52% fetal loss rate (Bakker et al. 2016). Cordocentesis carries a 1.3% risk of fetal loss (Wilson et al. 2015). Other potential minor complications include vaginal bleeding, cramping and amniotic fluid leakage (Driscoll and Ross, 2009; Wilson et al. 2015). This conveys the importance of non-invasive procedures, prompting the implementation of NIPT for aneuploidy screening in clinical settings.

Samples obtained during these diagnostic procedures undergo cytogenetic analysis such as karyotyping, fluorescent in situ hybridisation (FISH), and chromosomal microarray analysis (CMA) to definitively confirm or exclude the presence of chromosomal abnormalities. Quantitative fluorescent polymerase chain reaction (QF-PCR) also serves as a faster and more cost-effective alternative for detecting aneuploidies involving chromosomes 13, 18, 21, X, and Y (Cottino et al. 2022).

1.5. Prenatal genetic counselling: considerations in the South African context

The 4th edition of Guidelines for Maternity Care, published in 2015 by the South African National Department of Health, proposed the implementation of genetic counselling services as a key feature of public hospitals. According to the National Society of Genetic Counsellors (NSGC), genetic counselling entails helping individuals to comprehend and adjust to the medical, psychological, and familial implications of genetic factors that contribute to disease (Resta et al. 2006). While genetic services were established in Johannesburg in the late 1960s, there continues to be a limited capacity (Kromberg et al.

2013). Early services included chromosomal studies which later diverted into genetic counselling. This also saw the establishment of prenatal diagnosis, particularly for women of AMA at risk of fetal chromosomal abnormalities and neural tube defects. This study also disclosed that only 10% of the national genetic disease burden was being addressed with most services solely accessible at tertiary hospitals in four of the nine provinces in South Africa. In addition, they also reported on the sparse number of registered genetic counsellors. In the prenatal setting, genetic counselling is a source of psychosocial support and guidance on appropriate testing and management choices, making it a vital aspect of antenatal care (Malope et al. 2023).

1.5.1. The prenatal genetic testing landscape

Healthcare in the South African context is represented by both the private and public sectors. Eighty percent of the population's health-related needs are met by the public sector while 20% of citizens access care in private settings (Cottino et al. 2022). Due to the scarcity of resources and limited funding, the option of invasive testing is only made available to high-risk pregnancies in some parts of the country (Bhorat et al. 2018). The South African Health policy maintains that all women who are of AMA should have access to amniocentesis but there is stunted utilisation in this regard. A retrospective analysis of patient records at Tygerberg Groote Schuur Hospital in Cape Town demonstrated inadequate attendance of AMA counselling services and of those receiving counselling, approximately 31% opted for amniocentesis (Urban et al. 2011). This value differed from the increased acceptance of amniocentesis for referrals based on abnormalities detected on ultrasound. These findings prompted them to conclude that maternal age as a screening criterion performed poorly in comparison to other indicators.

As previously mentioned, QF-PCR is a less time consuming and a more economical test than traditional karyotyping for the detection of aneuploidies. At the National Health Laboratory Service (NHLS) Braamfontein, this option has been available since 2001 for aneuploidy detection in both pre- and post-natal cases. While there is a reduced and unbalanced utilisation of this test in the country, QF-PCR has proven to be useful given the lack of resources due to aforementioned reasons (Cottino et al. 2022). CMA is an additional newer technology that is seemingly more favourable than karyotyping, based on its ability to uncover copy number variations in DNA (Zhang et al. 2019). In contrast to QF-PCR, this test is more appropriate for abnormalities not in keeping with common aneuploidies. The question remains whether further testing should be offered if the negative QF-PCR results do not align with what is phenotypically observable. In most first world countries, CMA is offered as a first line test for abnormalities detected on ultrasound. For developing countries, Zhang et al. (2019) recommend the utilisation of CMA in cases with enlarged fetal nuchal folds, should rapid testing yield negative results. CMA is not offered in South African state hospitals, but it remains an important consideration for genetic counsellors who would have to gauge patient willingness for more testing.

1.5.2. Decision making in pregnancy

The South African Choice on Termination of Pregnancy Amendment Act 1 of 2008 imposes strict guidelines on termination of pregnancy (TOP) at different stages of gestation. There are no conditions for a medical TOP (mTOP) in the first 12 weeks of the pregnancy. During 13 to 20 weeks of gestation, mTOP is dependent on a considerable risk of gross mental or physical malformation to the fetus. Following the 20th week of gestation, mTOP is permitted based on endangerment to the mother and the risk of injury and severe fetal abnormalities. At this stage, two medical practitioners must agree upon offering a mTOP. This procedure is less complicated when offered during the early stages of pregnancy (Todd et al. 2010). Following a prenatal diagnosis of a CD, parents have options regarding the management of pregnancy and can decide to continue the pregnancy or undergo a mTOP.

Although TOP has been legalised, it continues to be marked by considerable stigma. Often, the right of choice is negatively impacted by the fear of being shunned by the community (Harries et al. 2007). Moreover, prospective parents are tasked with making decisions that correlate with their moral, ethical, and religious beliefs (Scott et al. 2013). Many women view termination to be against their moral beliefs despite being knowledgeable about the TOP acts (Harries et al. 2007). As reported by Malope et al. (2023), religion emerged as the most impactful factor among various demographic, socioeconomic, life, and personality related- elements, in the consideration of mTOP for severe congenital anomalies. Most women found comfort and hope in the belief that everything was up to God's will. The evaluation of attitudes towards diagnosis and mTOP in parents of children with Down Syndrome, revealed themes depicting children as "precious" and blessings from a higher being (Scott et al. 2013). These sentiments informed negative attitudes towards the procedure.

There are psychological and financial strains in the decision to continue with a pregnancy where a CD was diagnosed. Mothers of children with CDs report experiences of emotional pain, guilt, denial, and disbelief. Depending on the severity of the CD, children may require life-long interventions. Some mothers must pause their educational endeavours in order to care for their children (Mazibuko et al. 2022). Furthermore, there is an economical burden related to frequent medical visits and loss of work opportunities (Dambi et al. 2015). Thus, the decision to terminate is complex and there are many factors that contribute to the choices that are made. There are also unique considerations in the provision of genetic counselling services in the South African context. However, there is still limited data detailing these services in the country, particularly in Johannesburg. This highlights the necessity of research that provides insights into the prenatal clinical services provided by genetic counsellors in these settings.

2. Aims and Objectives

2.1. Aim

To evaluate the prenatal genetic services provided by genetic counsellors at several state tertiary hospitals in Johannesburg over a five-year period.

2.2. Objectives

(1) To describe the demographics of prenatal cases seen for genetic counselling in the Johannesburg state healthcare system over a five-year period (2019-2024).

(2) To determine the main reasons for referral for genetic counselling.

(3) To assess the common soft markers and abnormalities detected on ultrasound scans during the first and second trimester.

(4) To analyse the uptake of invasive testing, types of genetic testing performed on diagnostic prenatal samples, and their outcomes.

(5) To assess the main contributing factors towards decision-making around uptake of invasive testing and pregnancy outcomes.

3. Methods

3.1. Study participants

The study cohort will comprise of an estimated 900 to 1000 prenatal genetic counselling files belonging to women who were seen by a genetic counsellor from the Division of Human Genetics at the National Health Laboratory Service (NHLS) and the University of Witwatersrand (Wits), between July 2019 and July 2024. These prenatal genetic counselling services are offered at fetal medicine clinics housed at Chris Hani Baragwanath Academic Hospital, Rahima Moosa Mother and Child Hospital, and Charlotte Maxeke Johannesburg Academic Hospital. Patient files of women of any age, ethnicity, and gestation will be included.

3.1.1. Inclusion criteria

1. Records of women seen in prenatal Genetic Counselling clinics in Johannesburg state hospitals.
2. Patients seen between July 2019 and July 2024.

3.1.2. Exclusion criteria

1. Patient records that are missing a substantial amount of information.

2. Patients seen in the private healthcare system.

3.2. Study design

This study is a retrospective file review, involving an audit of prenatal genetic counselling clinic records from Wits/NHLS affiliated state hospitals in Johannesburg. The Division of Human Genetics Research Electronic Data Capture (REDCap) (Harris et al. 2009) will be accessed to retrieve clinical data. An exhaustive search will be performed using pregnancy-related keywords. This will generate a report of all the prenatal genetic counselling files on REDCap. Each clinic record will be reviewed for patient demographics (maternal age, ethnicity, and home language), gestational age, reason for referral, ultrasound screening findings, uptake of invasive testing, genetic diagnosis, and decision regarding pregnancy. For confidentiality purposes, this data will be anonymised.

3.3. Data analysis

This study will comprise of continuous and categorical data. The analysis will be performed using Statistica software in which descriptive statistics will be used to describe the data. For the analysis of continuous data (maternal age and gestational age), parameters such as means and standard deviations with a 95% confidence interval will be used for descriptive purposes, given that the data is normally distributed. The Shapiro-Wilk test will be used to test for normality. Continuous data that does not meet normality will be represented by median and interquartile range values. Categorical data (reason for referral, ultrasound screening findings, uptake of invasive testing, genetic diagnosis, and decision regarding pregnancy) will be represented by percentages. Chi-square tests will be used to test for significance differences in the distribution of two or more categorical variables. Such as, to investigate whether there are significant differences in women who opted for invasive diagnostic testing, considering factors such as maternal age (AMA versus non-AMA), ultrasound screening findings (soft markers versus gross abnormalities), and timing of presentation (early gestation versus late gestation). Statistical significance will be set according to a p-value of < 0.05. Genetic counsellors typically note the rationale for opting for or rejecting invasive testing in the psychosocial aspects section of the REDCap record. This information will be reviewed to evaluate the factors that influenced the decision-making process around the uptake of invasive testing and to assess the resulting pregnancy outcomes.

4. Ethics

Submission to the Human Research Ethics Committee (Medical) of the University of the Witwatersrand was made on the 18th of April 2024. Ethical clearance will be awaited prior to the commencement of

data collection. The clinical data will be anonymised and coded. All data will be stored on a secure password protected computer. Furthermore, access to the identifying information will only be granted to the researcher and the supervisors. Permission has been requested from the clinical data gatekeeper.

5. Timing

	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Literature review											
Ethics application											
Protocol preparation											
Protocol assessment											
Data collection											
Data analysis											
Writing report											

Figure 1: A Gantt chart representing the proposed timeline of the study.

6. Funding

6.1. Predicted budget

Table 1: A table representing the predicted budget of the study.

Activity	Cost (R)
Wits Statistica Workshop	300
Wits data analysis workshop	300
Total	600

7. Study limitations

This study may be limited by inconsistencies in clinical data captured on the patient files. This includes missing genetic counselling records as well as omitted patient data. Thus, this may potentially lead to a small sample size since records missing a substantial amount of data will be excluded.

8. References

Aalfs, C., Mollema, E., Oort, F., De Haes, J., Leschot, N., & Smets, E. (2004). Genetic counseling for familial conditions during pregnancy: An analysis of patient characteristics. *Clinical Genetics*, *66*(2), 112–121. https://doi.org/10.1111/j.0009-9163.2004.00279.x

Bakker, M., Birnie, E., Robles de Medina, P., Sollie, K. M., Pajkrt, E., & Bilardo, C. M. (2017). Total pregnancy loss after chorionic villus sampling and amniocentesis: a cohort study. *Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology*, *49*(5), 599–606. https://doi.org/10.1002/uog.15986

Bhorat, D. I., Chauke, D. L., Coetzee, E., Geerts, L., Lombaard, H., Nicolaou, E., Pistorius, D. L., & Soma-Pillay, P. (2018). *Challenges and Controversies in Prenatal Genetic Screening in the South African Context*.

Christianson A, Howson CP, Modell B. (2006) *March of Dimes: Global Report on Birth Defects, the Hidden Toll of Dying and Disabled Children*.

Cottino, L., Sahibdeen, V., Mudau, M., Lekgate, N., & Krause, A. (2022). QF-PCR: A valuable first-line prenatal and postnatal test for common aneuploidies in South Africa. *Journal of Community Genetics*, *13*(3), 355–363. https://doi.org/10.1007/s12687-022-00587-y

Czeizel, A. E. (2005). Birth Defects Are Preventable. *International Journal of Medical Sciences*, 91–92. https://doi.org/10.7150/ijms.2.91

Dambi, J. M., Jelsma, J., & Mlambo, T. (2015). Caring for a child with Cerebral Palsy: The experience of Zimbabwean mothers. *African Journal of Disability*, *4*(1). https://doi.org/10.4102/ajod.v4i1.168

Driscoll, D. A., & Gross, S. (2009). Prenatal Screening for Aneuploidy. *New England Journal of Medicine*, *360*(24), 2556–2562. https://doi.org/10.1056/NEJMcp0900134

EUROCAT, W. (2004). A review of environmental risk factors for congenital anomalies. *EUROCAT, European surveillance of congenital anomalies: Newtownabbey, University of Ulster, Northern Ireland*.

Goel, N., Morris, J. K., Tucker, D., de Walle, H. E. K., Bakker, M. K., Kancherla, V., Marengo, L., Canfield, M. A., Kallen, K., Lelong, N., Camelo, J. L., Stallings, E. B., Jones, A. M., Nance, A., Huynh, M. P., Martínez-Fernández, M. L., Sipek, A., Pierini, A., Nembhard, W. N., Goetz, D., … Morgan, M. (2019). Trisomy 13 and 18-Prevalence and mortality-A multi-registry population based

analysis. *American journal of medical genetics. Part A*, *179*(12), 2382–2392. https://doi.org/10.1002/ajmg.a.61365

Harries, J., Orner, P., Gabriel, M., & Mitchell, E. (2007). Delays in seeking an abortion until the second trimester: A qualitative study in South Africa. *Reproductive Health*, *4*(1), 7. https://doi.org/10.1186/1742-4755-4-7

Harris, P. A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., & Conde, J. G. (2009). Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of biomedical informatics*, *42*(2), 377–381. https://doi.org/10.1016/j.jbi.2008.08.010

Kroes, I., Janssens, S., & Defoort, P. (2014). Ultrasound features in trisomy 13 (Patau syndrome) and trisomy 18 (Edwards syndrome) in a consecutive series of 47 cases. *Facts, views & vision in ObGyn*, *6*(4), 245–249.

Kromberg, J. G. R., Sizer, E. B., & Christianson, A. L. (2013). Genetic services and testing in South Africa. *Journal of Community Genetics*, *4*(3), 413–423. https://doi.org/10.1007/s12687-012-0101-5

Lampret, Julie, Lane, Tony, & Christianson, Arnold. (2008). QF-PCR for prenatal diagnosis of common aneuploides in women of advanced maternal age. *SAMJ: South African Medical Journal*, *98*(2),68-69. http://www.scielo.org.za/scielo.php?script=sci_arttext&pid=S0256-95742008000200004&lng=en&tlng=en.

Lildballe, D. L., Vogel, I., Petersen, O. B., & Vestergaard, E. M. (2014). Diagnostic performance of quantitative fluorescence PCR analysis in high-risk pregnancies after combined first-trimester screening. *PubMed*, *61*(11), A4964–A4964

Malope, M. F., Stewart, C., Fieggen, K. J., & Wessels, T.-M. (2023). The decision-making process of pregnant individuals offered termination of pregnancy for serious congenital abnormalities. *Patient Education and Counseling*, *112*, 107745. https://doi.org/10.1016/j.pec.2023.107745

Mazibuko, T. B., Ramukumba, T., & Ngwenya, N. (2022). The lived experiences of mothers who have children with congenital abnormalities in the Gert Sibande district. *Curationis*, *45*(1). https://doi.org/10.4102/curationis.v45i1.2250

Merkatz, I. R., Nitowsky, H. M., Macri, J. N., & Johnson, W. E. (1984). An association between low maternal serum alpha-fetoprotein and fetal chromosomal abnormalities. *American journal of obstetrics and gynecology*, *148*(7), 886–894. https://doi.org/10.1016/0002-9378(84)90530-1

Nicolaides, K. H. (2011). Screening for fetal aneuploidies at 11 to 13 weeks. *Prenatal Diagnosis*, *31*(1), 7–15. https://doi.org/10.1002/pd.2637

Practice Bulletin No. 162: Prenatal Diagnostic Testing for Genetic Disorders. (2016). *Obstetrics and gynecology*, *127*(5), e108–e122. https://doi.org/10.1097/AOG.0000000000001405

Papp, C., Szigeti, Z., Tóth-Pál, E., Hajdú, J., Joó, J. G., & Papp, Z. (2008). Ultrasonographic Findings of Fetal Aneuploidies in the Second Trimester – Our Experiences. *Fetal Diagnosis and Therapy*, *23*(2), 105–113. https://doi.org/10.1159/000111588

Resta, R., Biesecker, B. B., Bennett, R. L., Blum, S., Estabrooks Hahn, S., Strecker, M. N., & Williams, J. L. (2006). A New Definition of Genetic Counseling: National Society of Genetic Counselors' Task Force Report. *Journal of Genetic Counseling*, *15*(2), 77–83. https://doi.org/10.1007/s10897-005-9014-3

Rhoda, N., Velaphi, S., Gebhardt, G., Kauchali, S., & Barron, P. (2018). Reducing neonatal deaths in South Africa: Progress and challenges. *South African Medical Journal, 108*(3a), s9-s16. doi:10.7196/SAMJ.2017.v108i3b.12804

Scott, C. J., Futter, M., & Wonkam, A. (2013). Prenatal diagnosis and termination of pregnancy: Perspectives of South African parents of children with Down syndrome. *Journal of Community Genetics*, *4*(1), 87–97. https://doi.org/10.1007/s12687-012-0122-0

Smith-Bindman, R., Hosmer, W., Feldstein, V. A., Deeks, J. J., & Goldberg, J. D. (2001). Second-trimester ultrasound to detect fetuses with Down syndrome: a meta-analysis. *JAMA*, *285*(8), 1044–1055. https://doi.org/10.1001/jama.285.8.1044

Todd, C., Haw, T., Kromberg, J., & Christianson, A. (2010). Genetic Counseling for Fetal Abnormalities in a South African Community. *Journal of Genetic Counseling*, *19*(3), 247–254. https://doi.org/10.1007/s10897-010-9278-0

Urban, M. F., Stewart, C., Ruppelt, T., & Geerts, L. (2011). Effectiveness of prenatal screening for Down syndrome on the basis of maternal age in Cape Town. *South African Medical Journal*, *101*(1), 45. https://doi.org/10.7196/SAMJ.4188

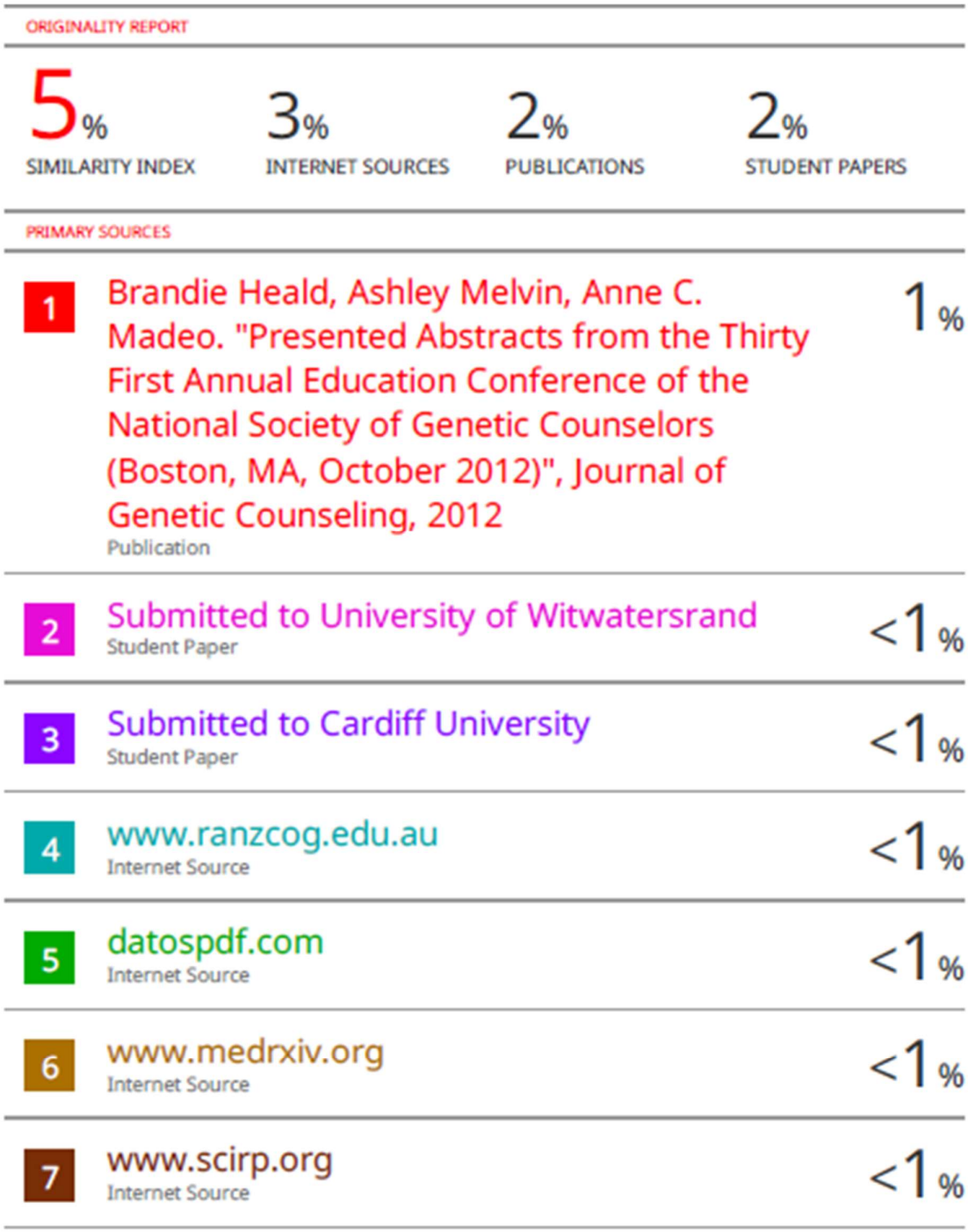
Watcham, S. J., Schön, S., & Christianson, A. L. (2007). Neglect in the care of pregnant South African women of advanced maternal age. *South African medical journal* ,*97*(11), 1064-1069

Wilson, R. D., Gagnon, A., Audibert, F., Campagnolo, C., Carroll, J., Wilson, R. D., Audibert, F., Brock, J.-A., Campagnolo, C., Carroll, J., Chong, K., Gagnon, A., Johnson, J.-A., MacDonald, W., Okun, N., Pastuck, M., & Vallee-Pouliot, K. (2015). Prenatal Diagnosis Procedures and Techniques to Obtain a Diagnostic Fetal Specimen or Tissue: Maternal and Fetal Risks and Benefits. *Journal of Obstetrics and Gynaecology Canada*, *37*(7), 656–668. https://doi.org/10.1016/S1701-2163(15)30205-X

World Health Organisation (WHO). (2023). Congenital Disorders. https://www.who.int/news-room/fact-sheets/detail/birth-defects

Zhang, Z., Hu, T., Wang, J., Li, Q., Wang, H., & Liu, S. (2019). Prenatal Diagnostic Value of Chromosomal Microarray in Fetuses with Nuchal Translucency Greater than 2.5 mm. *BioMed Research International*, *2019*, 1–9. https://doi.org/10.1155/2019/6504159

Appendix D: Turnitin report and plagiarism declaration



ORIGINALITY REPORT

5%	3%	2%	2%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Brandie Heald, Ashley Melvin, Anne C. Madeo. "Presented Abstracts from the Thirty First Annual Education Conference of the National Society of Genetic Counselors (Boston, MA, October 2012)", Journal of Genetic Counseling, 2012 Publication	1%
2	Submitted to University of Witwatersrand Student Paper	<1%
3	Submitted to Cardiff University Student Paper	<1%
4	www.ranzcog.edu.au Internet Source	<1%
5	datospdf.com Internet Source	<1%
6	www.medrxiv.org Internet Source	<1%
7	www.scirp.org Internet Source	<1%

8	Submitted to University of Sydney Student Paper	<1 %
9	link.springer.com Internet Source	<1 %
10	www.frontiersin.org Internet Source	<1 %
11	Dario Paladini, Paolo Volpe. "Ultrasound of Congenital Fetal Anomalies - Differential Diagnosis and Prognostic Indicators", CRC Press, 2024 Publication	<1 %
12	www.thespoiledmama.com Internet Source	<1 %
13	Peter A. Benn. "Expected performance of second trimester maternal serum testing followed by a 'genetic sonogram' in screening of fetal Down syndrome", Prenatal Diagnosis, 03/2008 Publication	<1 %
14	academic.oup.com Internet Source	<1 %
15	www.wits.ac.za Internet Source	<1 %
16	Submitted to Walter Sisulu University Student Paper	<1 %

17	healthandjusticejournal.biomedcentral.com Internet Source	<1%
18	Carlos Simón, Carmen Rubio. "Handbook of Genetic Diagnostic Technologies in Reproductive Medicine - Improving Patient Success Rates and Infant Health", CRC Press, 2022 Publication	<1%
19	mdpi-res.com Internet Source	<1%
20	www.medcraveonline.com Internet Source	<1%

Exclude quotes	Off	Exclude matches	Off
Exclude bibliography	Off		

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Asante Tshwane (Student number: 2305138) am a student registered for the degree of MSc(Med) Genetic Counselling in the academic year 2024.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: _____ Date: 20/06/2025

Appendix E: Author guidelines for the Journal of Genetic Counseling

Manuscript title

First name(s) Surname [1]| First name(s) Surname [1] | First name(s) Surname [1]

[1] Department, Institute/University/Hospital, City, (State,) Country

Short running title: less than 80 characters

Corresponding author:

Email address:

The following if applicable:

Conflict of interest statement

Ethics statement

Data availability statement

Funding statement

Patient consent statement

Permission to reproduce material from other sources

Clinical trial registration

Abstract

Unstructured, 300 words, including specific methodology used (e.g. cross sectional survey, RCT) and sample size. There should be one to two sentence responses to: (1) What is known about this topic and (2) What this paper adds to the topic.

1. Submission and Peer Review Process

Once the submission materials have been prepared in accordance with the Author Guidelines, manuscripts should be submitted online at https://www.editorialmanager.com/jogc/default.aspx.

For help with submissions, please contact: JOGC@Wiley.com. When necessary, the Editorial Office staff may refer questions to the Editor-in-Chief.

This journal does not charge submission fees.

Article Preparation Support

Wiley Editing Services offers expert help with English Language Editing, as well as translation, manuscript formatting, figure illustration, figure formatting, and graphical abstract design – so you can submit your manuscript with confidence.

Also, check out our resources for Preparing Your Article for general guidance about writing and preparing your manuscript.

Free Format submission

Journal of Genetic Counseling offers Free Format submission for a simplified and streamlined submission process.

Before you submit, you will need:

- Your manuscript: this should be an editable file including text, figures, and tables, or separate files—whichever you prefer. All required sections should be contained in your manuscript, including abstract, introduction, methods, results, and conclusions. Figures and tables should have legends. Figures should be uploaded in the highest resolution possible. If the figures are not of sufficiently high quality, your manuscript may be delayed. References may be submitted in any style or format, as long as it is consistent throughout the manuscript. Supporting information should be submitted in separate files. If the manuscript, figures or tables are difficult for you to read, they will also be difficult for the editors and reviewers, and the editorial office will send it back to you for revision. Your manuscript may also be sent back to you for revision if the quality of English language is poor.

- An ORCID ID, freely available at https://orcid.org. *(Why is this important? Your article, if accepted and published, will be attached to your ORCID profile. Institutions and funders are increasingly requiring authors to have ORCID IDs.)*
- The title page of the manuscript, including:
    - Your co-author details, including affiliation and email address. *(Why is this important? We need to keep all co-authors informed of the outcome of the peer review process.)*
    - Statements relating to our ethics and integrity policies, which may include any of the following *(Why are these important? We need to uphold rigorous ethical standards for the research we consider for publication)*:
        - data availability statement
        - funding statement
        - conflict of interest disclosure
        - ethics approval statement
        - patient consent statement
        - permission to reproduce material from other sources
        - clinical trial registration

Open Access

This journal is a subscription journal that offers an Open Access option. You'll have the option to make your article open access after acceptance, which will be subject to an APC unless a waiver applies. Read more about APCs here.

Preprint Policy

Please find the Wiley preprint policy here.

This journal accepts articles previously published on preprint servers.

Journal of Genetic Counseling will consider for review articles previously available as preprints. You may also post the submitted version of a manuscript to a preprint server at any time. You are requested to update any pre-publication versions with a link to the final published article.

Inclusive Language

An important element of the Journal of Genetic Counseling's commitment to diversity, equity, and inclusion is fostering authors' use of inclusive language in their manuscripts. To facilitate use of inclusive language we have compiled two excellent and comprehensive resources for authors' use:

CDC guidelines - https://www.cdc.gov/health-communication/php/toolkit/resources-style-guides.html

APA guidelines - https://apastyle.apa.org/style-grammar-guidelines/bias-free-language

Specific guidance:

1. Participant-reported demographic variables should be ascertained/used when reporting demographic information on participants.
2. Authors should explain the use of person-first or non-person-first language in the manuscript. For guidance, see https://apastyle.apa.org/style-grammar-guidelines/bias-free-language
3. For guidance on reducing stigma through use of terminology describing groups, see https://www.cdc.gov/health-communication/php/toolkit/resources-style-guides.html, and https://apastyle.apa.org/style-grammar-guidelines/bias-free-language
4. For guidance on use of terminology for sex and gender, see https://apastyle.apa.org/style-grammar-guidelines/bias-free-language
5. **Pedigrees:** Pedigrees should follow the recommendations for standardized nomenclature accepted by the National Society of Genetic Counselors. Authors should consult the following references for these recommendations:
    - Bennett, R. L. , Steinhaus, K. A., Uhrich, S. B., O' Sullivan, C. K., Resta, R. G. , Lochner-Doyle, D., Markel, D. S., Vincent, V., & Hamanishi, J. (1995). Recommendations for Standardized Human Pedigree Nomenclature. *Journal of Genetic Counseling,* 4, 267-279.
    - Bennett, R. L., Steinhaus French, K., Resta, R. G., & Lochner Doyle, D. (2008). Standardized Human Pedigree Nomenclature: Update and Assessment of the Recommendations of the National Society of Genetic Counselors. *Journal of Genetic Counseling,* 17, 424-433.
    - Bennett, R.L., Steinhaus, K.A., Resta R.G., Austin J. (2022). Practice resource-focused revision: Standardized pedigree nomenclature update centered on sex and gender inclusivity: A practice resource of the National Society of Genetic Counselors. *Journal of Genetic Counseling,* 31, 1238-1248.

Data Sharing and Data Availability

This journal expects data sharing. Review Wiley's Data Sharing policy where you will be able to see and select the data availability statement that is right for your submission.

Data Citation

Please review Wiley's Data Citation policy.

Data Protection

By submitting a manuscript to or reviewing for this publication, your name, email address, and affiliation, and other contact details the publication might require, will be used for the regular operations of the publication. Please review Wiley's Data Protection Policy to learn more.

Funding

You should list all funding sources in the Acknowledgments section. You are responsible for the accuracy of their funder designation. If in doubt, please check the Open Funder Registry for the correct nomenclature.

Authorship

All listed authors should have contributed to the manuscript substantially and have agreed to the final submitted version. Review editorial standards and scroll down for a description of authorship criteria.

Author Pronouns

Authors may now include their personal pronouns in the author bylines of their published articles and on Wiley Online Library. Authors will never be required to include their pronouns; it will always be optional for the author. Authors can include their pronouns in their manuscript upon submission and can add, edit, or remove their pronouns at any stage upon request. Submitting/corresponding authors should never add, edit, or remove a coauthor's pronouns without that coauthor's consent. Where post-publication changes to pronouns are required, these can be made without a correction notice to the paper, following Wiley's Name Change Policy to protect the author's privacy. Terms which fall outside of the scope of personal pronouns (e.g. proper or improper nouns), are currently not supported.

ORCID

This journal requires ORCID. Please refer to Wiley's resources on ORCID.

Reproduction of Copyright Material

If excerpts from copyrighted works owned by third parties are included, all sources must be credited within the manuscript. At minimum, the title and author should be provided.

The corresponding author is responsible for obtaining written permission to reproduce the material "in print and other media" from the publisher of the original source.

For more information, review Wiley's Guidelines for Obtaining Permission to Reproduce Material.

Title Page

The title page should contain:

1. A brief informative title containing the major key words. The title should not contain abbreviations (see Wiley's best practice SEO tips);
2. A short running title of less than 80 characters;
3. The full names of the authors;
4. The author's institutional affiliations where the work was conducted, with a footnote for the author's present address if different from where the work was conducted;
5. Acknowledgments.

Main Text File

Manuscripts can be uploaded either as a single document (containing the main text, tables and figures), or with figures and tables provided as separate files. The main manuscript file can be submitted in Microsoft Word (.doc or .docx) or LaTeX (.tex) format. Please use double line spacing.

Your main document file should include:

- A short informative title containing the major key words. The title should not contain abbreviations;
- The full names of the authors with institutional affiliations where the work was conducted, with a footnote for the author's present address if different from where the work was conducted;
- Abstract (unstructured), maximum 300 words;
- 1-2 sentence responses to:

What is known about this topic:

What this paper adds to the topic:

- Main body of paper. Sections may include Introduction (typically ~2 pages double line spaced), Methods (may include subsections such as: participants, instrumentation, procedures, data analysis, etc as appropriate), Conclusions;
- Author contributions;

- Acknowledgements;
- References;
- Tables (each table complete with title and footnotes);
- Figure legends: At initial submission, figures can be included in the manuscript or can be submitted in separate files. Should your manuscript reach revision stage, figures and tables must be provided as separate files (see below).

Author Contributions

Prior to submitting the manuscript all authors fulfilling the International Committee of Medical Journal Editors (ICMJE) criteria for authorship should be identified and should agree on the order in which their names will be listed in the manuscript.

ICMJE criteria are:

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

During the submission process you will be asked to select the contribution(s) made by each author from a pre-specified drop down menu.

Acknowledgements

Contributions from anyone who does not meet the ICMJE criteria for authorship should be listed in an Acknowledgements section. Financial and material support should also be mentioned in this section. Authors should list all funding sources and are responsible for the accuracy of their funder designation. If in doubt, please check the Open Funder Registry for the correct nomenclature: www.crossref.org/services/funder-registry.

If this paper is to be considered for the **Journal of Genetic Counseling Best Trainee Paper award**, please include a statement indicating that the research presented in the paper was conducted while the first author was in training or to fulfill a degree requirement of the first author. See the Best Trainee Paper Award tab above for more information about this award. Thanks to anonymous reviewers is not considered appropriate to include in Acknowledgements.

Reference Style

This journal uses APA reference style. Review your reference style guidelines prior to submission.

As this journal offers Free Format submission, however, this is for information only and you do not need to format the references in your article. This will instead be taken care of by the typesetter.

Figures and Supporting Information

Figures, supporting information, and appendices should be supplied as separate files. You should review the basic figure requirements for manuscripts for peer review, as well as the more detailed post-acceptance figure requirements. View Wiley's FAQs on supporting information.

Peer Review

This journal operates a single-anonymized peer review policy. Except where otherwise stated, manuscripts are peer reviewed by at least two anonymous reviewers and an Associate or Assistant Editor. Papers will only be sent to review if the Editor-in-Chief determines that the paper meets the appropriate quality and relevance requirements.

In-house submissions, i.e. papers authored by Editors or Editorial Board members of the title, will be sent to Editors unaffiliated with the author or institution and monitored carefully to ensure there is no peer review bias.

Wiley's policy on the confidentiality of the review process is available here.

Compliance with Ethical Standards

- ***Conflict of Interest Statement***

Journal of Genetic Counseling requires that all authors disclose any potential sources of conflict of interest. Any interest or relationship, financial or otherwise, which might be perceived as influencing an author's objectivity is considered a potential source of conflict of interest. These must be disclosed when directly relevant or directly related to the work that the authors describe in their manuscript. Potential sources of conflict of interest include, but are not limited to, patent or stock ownership, membership of a company board of directors, membership of an advisory board or committee for a company, and consultancy for or receipt of speaker's fees from a company. The existence of a conflict of interest does not necessarily preclude publication in the *Journal of Genetic Counseling*.

If the authors have no conflict of interest to declare, they must also state this in the manuscript. It is the responsibility of the corresponding author to review this policy with all authors and collectively to list in the manuscript under the subheading "Conflict of Interest" *all* pertinent commercial and other relationships.

The above policies are in accordance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals produced by the International Committee of Medical Journal Editors (http://www.icmje.org/).

The Conflict of Interest Statement should **mention each author separately by name.**

Submitting authors should ensure they liaise with all co-authors to confirm agreement with the final statement.

- ***Human Studies and Informed Consent***

Journal of Genetic Counseling requires that all appropriate steps were taken to obtain informed consent of all human subjects participating in the research reported in the manuscript submitted for review and possible publication, and statements to this effect must be included under this subheading. Participant anonymity should be preserved and all identifying information should be excluded in the manuscript unless the information is essential for scientific purposes and the study participants or patients (or parents or guardians) have provided written informed consent for publication. Images and information from individual participants will only be published where the authors have obtained the individual's free prior informed consent. Photographs need to be cropped sufficiently to prevent human subjects being recognized (an eye bar must not be used because of insufficient de-identification).

The editors reserve the right to reject manuscripts that do not comply with these requirements. The author will be held responsible for false statements or failure to fulfill these requirements.

For manuscripts reporting studies that involve human participants, a statement identifying the ethics committee that approved the study and confirmation that the study conforms to recognized standards is required, for example: Declaration of Helsinki; US Federal Policy for the Protection of Human Subjects; or European Medicines Agency Guidelines for Good Clinical Practice. It should also state clearly in the text that all persons gave their informed consent prior to their inclusion in the study.

Appeals and Complaints

Authors may appeal an editorial decision if they feel that the decision to reject was based on either a significant misunderstanding of a core aspect of the manuscript, a failure to understand how the manuscript advances the literature or concerns regarding the manuscript-handling process. Differences in opinion regarding the novelty or significance of the reported findings are not considered as grounds for appeal. To raise an appeal, please contact this journal by email, quoting your manuscript ID number and explaining your rationale for the appeal. The editor’s decision following an appeal consideration is final.

To raise a complaint regarding editorial staff, policy or process please contact the journal in the first instance. If you believe further support outside the journal's management is necessary, please refer to Wiley's Best Practice Guidelines on Research Integrity and Publishing Ethics.

AI Policy

Artificial Intelligence Generated Content (AIGC) tools—such as ChatGPT and others based on large language models (LLMs)—cannot be considered capable of initiating an original piece of research without direction by human authors. They also cannot be accountable for a published work or for research design, which is a generally held requirement of authorship (as discussed in the previous section), nor do they have legal standing or the ability to hold or assign copyright. Therefore—in accordance with COPE's position statement on AI tools—these tools cannot fulfill the role of, nor be listed as, an author of an article. If an author has used this kind of tool to develop any portion of a manuscript, its use must be described, transparently and in detail, in the Methods or Acknowledgements section. The author is fully responsible for the accuracy of any information provided by the tool and for correctly referencing any supporting work on which that information depends. Tools that are used to improve spelling, grammar, and general editing are not included in the scope of these guidelines. The final decision about whether use of an AIGC tool is appropriate or permissible in the circumstances of a submitted manuscript or a published article lies with the journal's editor or other party responsible for the publication's editorial policy.

Guidelines on Publishing and Research Ethics in Journal Articles

This journal requires that you include in the manuscript details IRB approvals, ethical treatment of human and animal research participants, and gathering of informed consent, as appropriate. You will be expected to declare all conflicts of interest, or none, on submission. Please review Wiley's policies surrounding human studies, clinical trial registration, biosecurity, and research reporting guidelines.

This journal follows the core practices of the Committee on Publication Ethics (COPE) and handles cases of research and publication misconduct accordingly (https://publicationethics.org/core-practices).

This journal uses iThenticate's CrossCheck software to detect instances of overlapping and similar text in submitted manuscripts. Read Wiley's Top 10 Publishing Ethics Tips for Authors and Wiley's Publication Ethics Guidelines.

2. Article Types

Article Type	Description	Word Limit	Abstract / Structure	Other Requirements

Original Articles (quantitative)	Manuscripts reporting on original quantitative research (incl. cross sectional surveys, pre-post design studies, RCTs etc)	6000 limit (excl. references)	Unstructured, 300 words, including specific methodology used (e.g. cross sectional survey, RCT) and sample size	Data Availability Statement Informed consent Please use the appropriate reporting guidelines STROBE for observational studies SQUIRE for quality improvement studies CONSORT for RCTs GCIRS for genetic counseling intervention and outcome studies
Original Articles (qualitative)	Manuscripts reporting on original qualitative research (incl. phenomenology, thematic analysis, narrative inquiry etc)	8000 limit (excl. references)	Unstructured, 300 words, including specific methodology (e.g. grounded theory, reflexive thematic analysis)	Data Availability Statement Informed consent Paradigm Level Guidelines: COREQ for (post)positivist qualitative research BQQRG for Big Q (e.g. constructivism/interpretivism) qualitative research Data Analysis Level Guidelines: RTARG for reflexive thematic analysis

Review Articles	Both systematic and scoping reviews are considered.	6000 limit (excl. references)	Unstructured, 300 words, naming review type (e.g. systematic, scoping)	Data Availability Statement PRISMA for systematic reviews PRISMA for scoping reviews
Brief Reports	Typically smaller/simpler studies or observations relevant to genetic counseling research that can be presented in a more concise way.	2000 limit (excl. references)	Unstructured, 300 words, including methodology if applicable	Data Availability Statement Informed consent
Case Studies	Manuscript addressing issues relevant to discipline and practice of genetic counseling by demonstrating and stimulating thought about	2000 limit	Unstructured, 300 words	Data Availability Statement Informed consent

	a difficult ethical, counseling, or genetic testing situation the author has encountered.			
Professional Issues	Manuscript reporting reflections by the author(s) on the discipline and practice of genetic counseling.	6000 limit (excl. references)	Unstructured, 300 words	Data Availability Statement Informed consent
Commentaries	Manuscript addressing matters of interest or controversy to the readership. Generally commissioned by the Editor-in-Chief.	2000 (excl. references)	None	

Practice Resource, Practice Guideline, Focused Revision	Manuscripts addressing specific areas of genetic counseling practice. Commissioned by the National Society of Genetic Counselors' Practice Guidelines Committee. Discuss with Editor-in-Chief.

3. After Acceptance

Wiley Author Services

When an accepted article is received by Wiley's production team, the corresponding author will receive an email asking them to login or register with Wiley Author Services. You will be asked to sign a publication license at this point as well as pay for any applicable APCs.

Copyright & Licensing

You may choose to publish under the terms of the journal's standard copyright agreement, or Open Access under the terms of a Creative Commons License.

Standard re-use and licensing rights vary by journal. Note that certain funders mandate a particular type of CC license be used.

Self-Archiving Definitions and Policies: Note that the journal's standard copyright agreement allows for self-archiving of different versions of the article under specific conditions.

Early View

Upon publication, articles are available as full text HTML or PDF in Early View prior to inclusion in an issue and can be cited as references using their Digital Object Identifier (DOI) number.

Proofs

Authors will receive an e-mail notification with a link and instructions for accessing HTML page proofs online/with their proofs included as a pdf. Authors should also make sure that any renumbered tables, figures, or references match text citations and that figure legends correspond with text citations and actual figures. Proofs must be returned within 48 hours of receipt of the email.

Article Promotion Support

Wiley Editing Services offers professional video, design, and writing services to create shareable video abstracts, infographics, conference posters, lay summaries, and research news stories for your research – so you can help your research get the attention it deserves.

Author Name Change Policy

In cases where authors wish to change their name following publication, Wiley will update and republish the paper and redeliver the updated metadata to indexing services. Our editorial and production teams will use discretion in recognizing that name changes may be of a sensitive and private nature for various reasons including (but not limited to) alignment with gender identity, or as a result of marriage, divorce, or religious conversion. Accordingly, to protect the author's privacy, we will not publish a correction notice to the paper, and we will not notify co-authors of the change. Authors should contact the journal's Editorial Office with their name change request.

Correction to Authorship

In accordance with Wiley's Best Practice Guidelines on Research Integrity and Publishing Ethics and the Committee on Publication Ethics' guidance, *Journal of Genetic Counseling* will allow authors to correct authorship on a submitted, accepted, or published article if a valid reason exists to do so. All authors – including those to be added or removed – must agree to any proposed change. To request a change to the author list, please complete the Request for Changes to a Journal Article Author List Form and contact either the journal's editorial or production office, depending on the status of the article. Authorship changes will not be considered without a fully completed Author Change form. [Correcting the authorship is different from changing an author's name; the relevant policy for that can be found in Wiley's Best Practice Guidelines under "Author name changes after publication."]