

# Uptake of genetic counselling services by patients with cystic fibrosis and their families

Macaulay S, BSc, BSc(Hons), MSc(Med), MSc(Med) (Genetic Counselling)  
Gregersen N, MB BCh, FCPaed(SA), Cert(Medical Genetics), MSc(Med) (Genetic Counselling)  
Krause A, BSc, BSc(Hons), MB BCh, PhD  
Division of Human Genetics, School of Pathology  
University of the Witwatersrand, and the National Health Laboratory Service, Johannesburg  
Correspondence to: Shelley Macaulay, e-mail: shelley.macaulay@nhls.ac.za  
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## Abstract

**Background:** Although cystic fibrosis (CF) is a common genetic condition, genetic counselling services appear to be underutilised by affected families. The aim of this study was to determine the uptake of genetic counselling and mutation testing for CF by relatives of affected individuals, and the impact of introducing hospital-based genetic counselling services.

**Method:** The files of 153 families seen for genetic counselling for CF by staff of the Division of Human Genetics, School of Pathology, University of the Witwatersrand, and the National Health Laboratory Service (NHLS) in Johannesburg, were retrospectively reviewed from 1990 to 2006, the year when hospital-based genetic counselling services were introduced.

**Results:** Parents of CF probands were the largest single group (35%) of counselees. Most individuals (66%) attended genetic counselling to gather information. Most had been referred by medical specialists (56%). Only 10% of referrals originated from general practitioners. On average, from 1990-2005, six families received genetic counselling annually, whereas in 2006, 58 families were seen. In 140 unrelated families, 1 991 relatives with carrier risks of  $\geq 25\%$  were identified. Only 11% of these relatives underwent mutation testing, and eight per cent received genetic counselling through our division over the review period.

**Conclusion:** Overall, referrals of family members (of affected CF individuals) to genetic counselling, by general practitioners, are poor. Uptake of genetic counselling services is greater when such services are integrated into hospital-based CF management clinics, than when offered elsewhere. The low uptake of mutation testing and genetic counselling by at-risk relatives is a concern, since these relatives are at high risk of having affected children, if their partners are CF carriers. Education of affected individuals, their close relatives, and medical practitioners, should be prioritised. This will ensure referral to genetic counselling for discussion about the risks of and available testing for CF, and other genetic conditions.

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## Introduction

Cystic fibrosis (CF) is a chronic, inherited disorder that affects the respiratory tract, pancreas, gastrointestinal system, exocrine sweat glands, and genital tract. In its classic form, CF involves the accumulation of thick mucus secretions that obstruct the respiratory tract and exocrine glands.<sup>1</sup> The condition is inherited in an autosomal recessive manner. It is caused by mutations in the cystic fibrosis transmembrane regulator (*CFTR*) gene.<sup>2</sup> It is most common amongst individuals of north-west European descent, but has been described in almost every ethnic group.<sup>3</sup> In South Africa, carrier frequencies for CF have been estimated as 1 in 20 for the white population, 1 in 55 for the coloured population, and approximately 1 in 34 for the black

population.<sup>4,5</sup> However, further studies are required to verify the frequency for the latter group. The Molecular Genetics Laboratory of the Division of Human Genetics, School of Pathology, University of the Witwatersrand and the National Health Laboratory Service (NHLS), Johannesburg, perform a large portion of the country's CF genetic testing, and started offering testing to all patients with CF and their family members, soon after the *CFTR* gene was cloned in 1989.<sup>2</sup> At present, this laboratory tests for 30 common CF-causing mutations in individuals from the white, coloured and Indian populations, and one common mutation in the black population. The state covers the costs of genetic testing for patients at state hospitals. Testing costs for private patients are either covered by their medical aid schemes, or themselves. As more than 1 900 CF-causing mutations have

been identified worldwide, full *CFTR* mutation screening is not practical.<sup>6</sup> Thus, testing for the most common mutations in each population is used. Therefore, it is important to know the patient's ethnicity.

Parents of an affected individual are obligate carriers, but many relatives, including aunts, uncles, cousins and healthy siblings of probands (affected individuals), are also at risk of being carriers. Healthy unaffected siblings are at the highest risk (67%). Genetic counselling serves an important role in educating such individuals about the condition, their genetic risks, and the available testing options, as well as providing psychosocial support to families, and facilitating testing and feedback.<sup>7</sup>

Since 1975, the genetic counsellors and medical geneticists of the Division of Human Genetics, School of Pathology, University of the Witwatersrand, and the NHLS, have been offering genetic counselling to individuals with CF and their families in general genetic counselling clinics. Referrals originated from doctors treating affected patients in and around Johannesburg, in both the state and private hospital sectors. However, at the beginning of 2006, a new specialist genetic counselling clinic was established within the paediatric and adult CF clinics at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). Over the years, the nature of the genetic counselling service has remained the same. However, with time, more trained individuals have become available to see patients, allowing us to allocate a dedicated staff member to the CF clinics at CMJAH.

In South Africa, genetic counselling for CF has not been the subject of much research. Therefore, the aim of the present study was to gain information on following topics: the uptake of genetic counselling services and mutation testing by families with a member with CF, the number of at-risk relatives per family needing such services, and the impact of introducing a new service at the CMJAH CF clinics on affected families.

## Background

The present study was descriptive and retrospective. Ethics approval for the study was granted by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (reference number: M060943).

The sample included all individuals from families with a member with CF, and those who were confirmed CF carriers, counselled at the genetic counselling clinics of the Division of Human Genetics, University of the Witwatersrand and the NHLS, Johannesburg, from the beginning of 1990 until the end of 2006.

A total of 170 records with the diagnosis of CF were available for this 17-year period. Altogether 153 out of 170 (90%) files were located. Of the 153 families, 13 (8%) were related to other families in the series, and 140 (92%) were unrelated. Where families were related to each other, information pertaining to the number of at-risk relatives, as well as those who had undergone CF mutation testing, was recorded once only per extended family during data collection.

## Method

Information was gathered from the 153 files, and entered onto specifically constructed data collection sheets. Counselees were only included in the analysis if they were 12 years of age, or older. In general, each file contained the personal details of the counselees, a family pedigree, molecular genetics reports, notes made by the genetic counsellor or medical geneticist regarding the counselling session, and a copy of the comprehensive case summary written to the referring doctor.

Particulars collected on each family included the number of counselees present at an initial genetic counselling session, their relationships to the proband (e.g. CF probands themselves, parents, or specific relative, or partner of proband), their ages, and ethnic group. Information gathered pertaining to the counselling session included the session venue, the reasons for attendance, the referring person, and number of follow-up consultations. Pedigree analysis involved assessing whether consanguinity was present, and determining the number of at-risk relatives. At-risk relatives were defined as blood relatives of a proband, each of whom had a minimum carrier risk of 1 in 4 (25%). Individuals with lower risks were not included, and any individuals who were associated with a proband through marriage or adoption, were also excluded.

Although biological parents of probands are obligate carriers for CF mutations (100% risk), they too were included in the at-risk relatives group. Grandparents, who are at 50% risk of carrying a CF-causing mutation, were excluded from this study in order to focus on the generations for whom carrier status would have reproductive implications. Data were also collected on family members who had pursued CF mutation analysis, and on their test results.

The data were divided into those obtained for the years prior to 2006, i.e. 1990-2005, and those for 2006. Although it may not be ideal to compare data collected over a period of 16 years, to data collected over only one year, these two time periods were used in order to assess the impact of introducing the genetic counselling service in 2006 at the CMJAH CF clinics.

Most of the data generated were quantitative, and expressed as frequencies. Means and standard deviations were calculated using the statistical analysis functions in the Microsoft Office Excel computer programme. The chi-square test was used to calculate p-values, and these were considered significant if they were  $< 0.05$ .

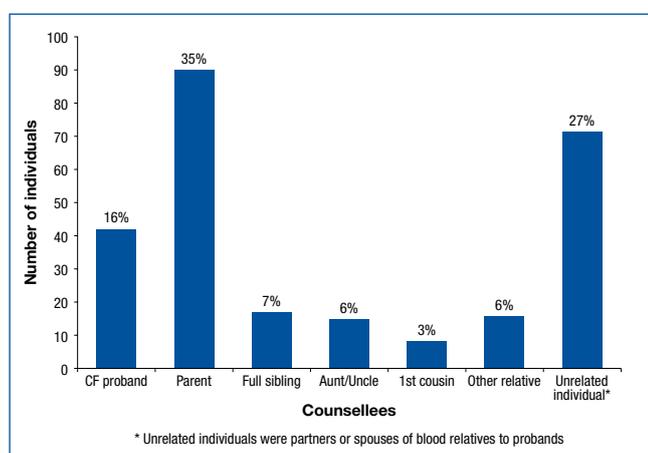
## Results

A total of 271 individuals from the 153 families, attended an initial genetic counselling session over the 17-year period. Among the 271 counselees, there were significantly more females (157, 58%) than males (114, 42%);  $p$ -value  $< 0.009$ . Ninety-five families received genetic counselling from 1990-2005, averaging six families per year, (range two to 13), and a further 58 families were counselled during 2006 alone.

The age of the counselees ranged from 12-66 years, with a mean of 30 years. Consanguinity was present in five (4%) of the 140 families. The clinic venue where these families were counselled changed three times over the years. However, in 2006, 90% (52 out of 58) of all CF genetic counselling sessions took place at CMJAH CF clinics.

The majority (93%) of counselees were from the white population (Table I). However, the small numbers from the black and coloured populations doubled in 2006, compared to the numbers over the previous 16 years.

The data for the counselees using the service were analysed in terms of whether they were the proband, or related to the proband (Figure 1). The largest single group of counselees were parents of CF probands (93 out of 271, 35%), followed by unrelated individuals (74 out of 271, 27%), and then the probands (44 out of 271, 16%). In almost all cases, an "unrelated individual" was the partner of a blood relative to a proband. Only a small number of siblings (18 out of 271, 7%) sought genetic counselling.



**Figure 1:** Relationship of counselees to probands (n = 271) attending clinics for genetic counselling

**Table I:** Ethnicity of individuals attending genetic counselling sessions for cystic fibrosis from 1990-2005, and in 2006

Ethnicity	Number and percentages of counselees		
	1990-2005	2006	Total
	n (%)	n (%)	n (%)
White	170 (97)	83 (88)	253 (93)
Black	2 (1)	5 (5)	7 (3)
Coloured	2 (1)	6 (6)	8 (3)
Indian	2 (1)	1 (1)	3 (1)
<b>Total</b>	<b>176 (100)</b>	<b>95 (100)</b>	<b>271 (100)</b>

Over half of the referrals originated from medical specialists (86 out of 153, 56%), particularly paediatricians (49 out of 86, 57%) and physicians (10 out of 86, 12%). The remainder of referrals derived from the CF probands (28 out of 153, 18%) themselves and other individuals, such as nurses (20 out of 153, 13%), general practitioners (15 out of 153, 10%), and relatives of affected individuals (4 out of 153, 3%). Specialist referrals increased considerably during 2006 (a total of 41 out of 58, 71% referrals), compared to the previous 16 years (a total of 45 out of 95, 47%, mean of 2.8 referrals per year).

The reasons why counselees attended their first genetic counselling session are given in Table II, and the numbers for 1990-2005 are compared with those for 2006. In one case, noted in Table II, the family had CF carrier testing performed by a private laboratory without prior genetic counselling, and they sought genetic counselling to have their results explained to them.

**Table II:** Reasons why families (n = 153) attended an initial genetic counselling session

Reason	Number of families		
	1990-2005	2006	Total
	n (%)	n (%)	n (%)
Information gathering	45 (47)	56 (97)	101 (66)
Prenatal counselling	35 (37)	2 (3)	37 (24)
Planning a family	14 (15)	0 (0)	14 (9)
Result-giving session	1 (1)	0 (0)	1 (1)
<b>Total</b>	<b>95 (100)</b>	<b>58 (100)</b>	<b>153 (100)</b>

Approximately half of the follow-up genetic counselling sessions involved result-giving (20 out of 41, 49%). The number of follow-up sessions increased greatly during 2006. A total of 41 follow-up sessions took place over the 17-year period, 29 (71%) of which occurred during 2006.

Examination of the pedigrees of the 140 unrelated families showed that there were 1 991 relatives with a carrier risk of 25% or more (Table III). Exclusion of the obligate carriers (n = 271), resulted in a sub-total of 1 720 at-risk relatives being identified in 140 families, averaging 14 non-obligate

**Table III:** At-risk individuals, with carrier risks of 25-100%, in 140 unrelated families, and the results of those tested

Carrier risk (%)	Total number of at-risk individuals	At-risk individuals tested	Tested individuals found to be carriers	Tested individuals found to be affected
	n	n (%)	n (%)	n (%)
100	271	99 (37)	86 (87)	0 (0)
67	123	48 (39)	35 (73)	1 (2)*
50	662	53 (8)	29 (55)	3 (6)**
33	53	2 (4)	1 (50)	0 (0)
25	882	15 (2)	8 (53)	0 (0)
<b>Total</b>	<b>1991</b>	<b>217</b>	<b>159</b>	<b>4</b>

\*One sibling, supposedly unaffected, but found to have two mutations (phenotypic variability between affected individuals)

\*\*Foetuses diagnosed by prenatal testing

potential carriers per family. Of these, 1 720 at-risk relatives, 118 (7%) were known to have undergone CF mutation testing through the NHLS, and 73 out of 118 (62%) were found to be carriers. Individuals at higher risk were more likely to be tested.

According to the counselling records and analysis of the pedigrees, a total of 168 out of 1 991 at-risk relatives, including obligate carriers, presented for genetic counselling. Therefore, eight per cent of relatives with a carrier risk of 25% or higher, received genetic counselling within our service.

## Discussion

The largest single group of individuals who attended genetic counselling clinics were parents of children with CF. This finding is expected, as parents of affected children are most in need of psychosocial support, an understanding about recurrence risks and their prenatal testing options, medical and genetic information, and referral to appropriate services.

According to our findings, the majority of counselees were in their thirties, and were from the white population. Considering that most individuals who are known to have CF are from populations of European extraction, and that the prevalence of CF is highest in these populations, this finding is not unexpected.<sup>4</sup> However, it was necessary to analyse the data by ethnic group because a carrier frequency of 1 in 34 has been estimated for the South African black population.<sup>5</sup> Therefore, one would expect that a substantial number of affected black families would be referred. In this study, although only 3% of all counselees were from the black population, there was an increase in referrals from this group once hospital-based genetic counselling clinics were set up in 2006. Given the fact that the specific CF-causing mutation in the South African black population has only been known since 1996, and that CF was previously considered to be rare in this ethnic group, it is likely that CF is still under-recognised and under-diagnosed in black

children.<sup>8</sup> There is a need for medical practitioners to consider this diagnosis in black patients, and refer them for genetic counselling. Furthermore, mutation detection in affected individuals from the black, coloured and Indian populations is often problematic. Only a few mutations have been identified in these populations, and other common mutations have not yet been investigated.

CF probands were the third largest group to attend genetic counselling. This is encouraging, as a previous study showed that half of South African CF probands were unaware of the inheritance pattern of their disorder.<sup>9</sup> This finding suggests that the in-hospital service may be effective in meeting the needs of the CF probands and their parents. It also indicates that as a result of improved medical treatment, CF probands are living through to, and beyond, adolescence, and planning relationships and families.

A finding that caused concern was the small proportion (22%) of siblings and extended family members, at significant risk of being carriers, who sought genetic counselling sessions (Figure 1). With respect to healthy siblings (at 67% risk), one would expect more than the seven per cent (Figure 1), found here, to have attended a genetic counselling consultation. Interestingly, 39% (Table III) had undergone genetic testing, mostly without expert genetic counselling. This finding echoes the lack of knowledge amongst siblings of CF probands regarding the condition and its inheritance, as reported by Henley and Hill.<sup>9</sup> Another South African study found that the lack of knowledge among unaffected siblings could also be associated with the guilt expressed by parents who realised they may have passed on the affected gene to their normal children, and who may therefore have found it difficult to discuss this matter with them.<sup>10</sup> The low uptake of genetic counselling by non-nuclear family members may be due to the fact that CF is often viewed as a nuclear family problem, which does not necessarily encompass the extended family.<sup>11</sup> In addition, it has been reported that the main reason why people do not present for genetic counselling is because they are not aware of

its existence.<sup>12</sup> They may not have been informed of their risk status, the related implications, and how a genetic counselling session would benefit them. Primary health care personnel, such as general practitioners and nurses, may have the best opportunities to promote referral to genetic counselling clinics. With only 10% of genetic counselling referrals originating from general practitioners, it is essential that the awareness of the genetic counselling service is promoted among these doctors. General practitioners are often the key clinicians involved in the overall management and care of the affected individual, and also the rest of the family.

“Information gathering” was the reason why half the individuals attended genetic counselling over the 17-year period. This is in keeping with the findings of Veach et al.<sup>13</sup> This suggests that even where a diagnosis of CF has been known for many years, families have a specific need to understand the genetic component of the condition. This need should be met by genetic counsellors and medical geneticists. It is unlikely that treating physicians will provide genetic counselling themselves. This is supported by our finding that most counselees attended a genetic counselling session to obtain more information about their condition, which had obviously not previously been communicated to them in a manner that they could understand. Many patients said they were grateful for the information as they had not received a formal genetic explanation from their treating doctors.

Our findings show that when a genetic counselling service is incorporated into the hospital-based clinical care of CF patients, the uptake increases. Collins et al also found that, through the integration of the genetic service into the care programme, uptake was more likely to be favourable.<sup>12</sup> When genetic counselling is available within the clinic where an individual is being treated, utilisation of the service is far greater than when it is offered elsewhere, and requires referral, and the attendance of patients at another venue. Convenience, low costs, and familiarity with the clinic and its staff are positive factors associated with the incorporation of the genetic counselling service into treatment clinics. In addition, the large numbers of follow-up sessions, and the increase in attendance of those from ethnic groups other than white, which occurred in 2006, reflects the usefulness of having the genetic service readily available and accessible.

Each family in this study had an average of 14 at-risk relatives, in keeping with a previous study that found 15 at-risk relatives per family.<sup>14</sup> However, only 8% (168 out of 1 991) of all such relatives attended genetic counselling. Since no other genetic counselling service is available in

Johannesburg at the time of this study, it is unlikely that they received expert genetic counselling elsewhere, regardless of whether or not they were private or state hospital sector patients. Furthermore, only a small group (7%) of at-risk relatives, excluding obligate carriers, used the available CF mutation testing facilities.

In this study, the under-utilisation of the genetic counselling service by at-risk relatives requires consideration. It may result from lack of communication among family members, or be due to inaccurate carrier perceptions among relatives. According to the World Health Organization (WHO), it is the ethical duty of an individual who is aware of a genetic condition in his or her family to inform other blood relatives that they may be at genetic risk.<sup>15</sup> The WHO does not recommend that genetic professionals make direct contact with the relatives, but rather that they act as mediators, by instilling a feeling of duty and responsibility in the counselees towards relatives.<sup>15</sup> South African genetic counsellors and medical geneticists follow this protocol. The use of an appropriate information letter or pamphlet addressed to the at-risk relatives, and given to counselees at clinics to pass on to their relatives, motivating and inviting them to attend a genetic counselling session, would hopefully increase awareness among family members.

Other reasons influencing the decision to determine one's genetic status may relate to the fact that knowledge of carrier status can potentially threaten one's self-concept, as stated by some researchers.<sup>16</sup> It is possible that some at-risk relatives chose not to pursue carrier testing due to fear of a positive result, leading to social harm and discrimination, particularly with regard to loss of insurance or employment.<sup>17</sup> They may also have been ignorant about their genetic risks. Of all the non-obligate at-risk relatives who were tested in the present study, 62% (73 out of 118) were CF carriers (Table III). These positive test results raise concern about the large number of untested at-risk relatives who are unaware of their genetic status. If they marry, or are in a relationship with, a CF carrier, they are at-risk of having children with CF. Therefore, it is essential for medical practitioners and other health professionals to encourage cascade testing within families who are affected by CF.

## Conclusion

Based on the results of the current study, the 2006 introduction of the genetic counselling service at the CMJAH CF clinics has been worthwhile. The number of referrals, uptake of counselling sessions and follow-up consultations, increased considerably during that year, compared to previous years. The results pinpoint an obvious lack in referrals from general practitioners and family members of

affected individuals. This may be due to poor promotion of the genetic counselling service and its benefits. Genetic counselling is an essential part of the diagnosis and care of any genetic disorder. This study highlights the benefits and value of the service, particularly within the specialist clinics, and will hopefully result in ongoing appropriate referrals from healthcare professionals and the general public. In addition, through increased interaction and involvement with other health professionals at treatment clinics, genetic counsellors and medical geneticists will hopefully become accepted and established members of the multidisciplinary team caring for patients with genetic conditions.

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