



Capacity Building for the  
Transfer of Genetic Knowledge  
into Practice and Prevention



# GenTEE

**Genetic Testing in Emerging Economies  
An International Pilot Study**

## **Preliminary Report on South Africa**

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## INTRODUCTION

South Africa is a developing, middle-income country, and is one of the most advanced and successful countries on the African continent. Since 1994 it has had a fully democratic system of government, reversed much of the previously discriminating legislation, built more than a million houses and many new clinics, and increased access to clean drinking water, telephones and electricity (Benatar, 2004). However, the narrowing of the disparities in health care is a formidable challenge for the new government, especially in the context of the almost uncontrollable pandemic of the human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS), as well as the increasing prevalence of tuberculosis (TB). South Africa has one of the highest incidences and population prevalence of HIV/AIDS in the world and this is retarding the development of the country on many levels, affecting efficiency, work ethic, the maintenance of health and other services, as well as the provision of medical genetic services.

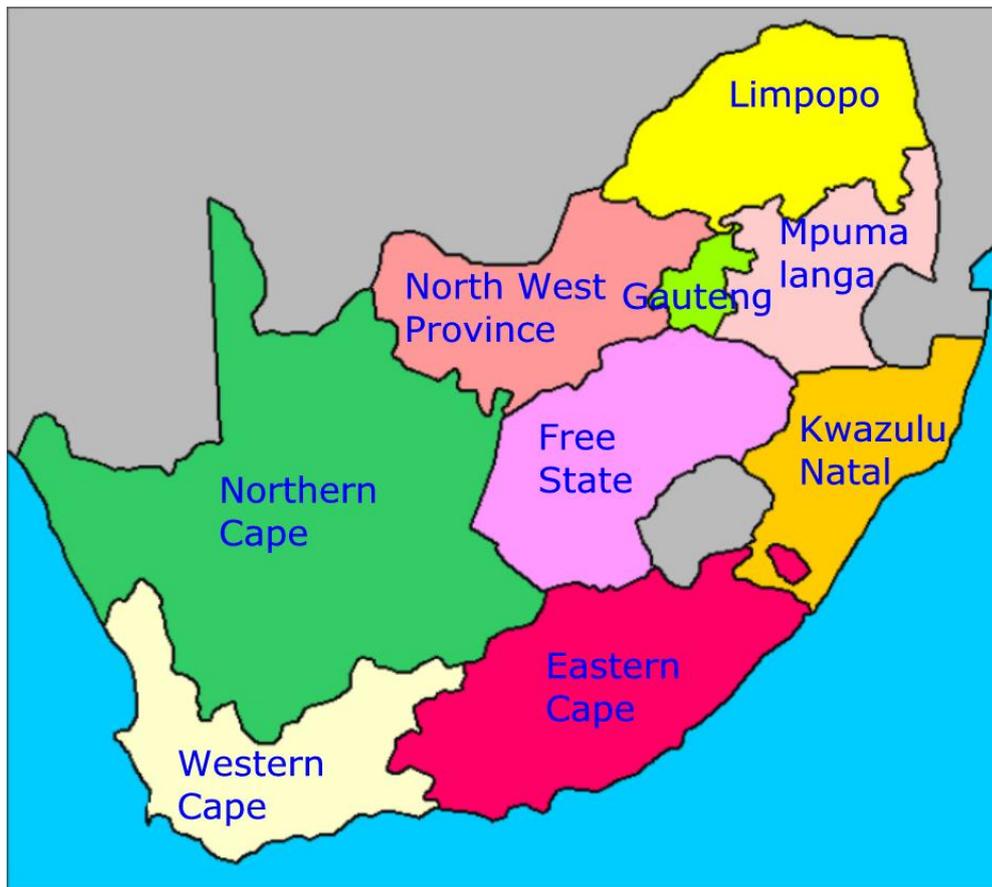
This report presents the data available on basic demographic statistics, health indicators, health expenditure as well as information on the genetic services and genetic testing available in the country. It follows the lay-out of the International Pilot Study protocol and uses the sources suggested in this protocol. These references include World Health Organisation (WHO) Health Statistics documents, Human Development Reports of the United Nations Development Program (UNDP), other United Nations statistics, and World Bank (WB) reports. In addition, some South African references are used such as Statistics South Africa (Stats SA), the Health Systems Trust (HST) Reports, Department of Health surveys, and the South African Institute of Race Relations (SAIRR) Annual Survey (this survey is considered to be a consistently reliable source of data, which are carefully checked for accuracy), as well as published articles on the local situation. These references are listed at the end of the report. The data presented below usually refer to the year specified in the protocol or to the latest year for which estimates are available. Comments have been made on the trends shown by the data and explanations have been given from published literature or the authors' experience, as suggested in the protocol. The AIDS epidemic has had and is still having a profound effect on the health data for South Africa, as will become evident below.

## PART 1: DEMOGRAPHY AND HEALTH INDICATORS

### 1.1. Total Population Size

The total population size of South Africa was listed as 49.32 million people at the last estimate from Statistics South Africa (StatsSA) in 2009. The 2006 estimate was 47.39 million, indicating an increase of almost two million people in three years.

The population is distributed in nine provinces of different sizes with widely differing population densities, as shown in Figure 1.1 below. The province with the greatest population is Gauteng (21.4%), followed by KwaZulu Natal (21.2%) and the Eastern Cape (13.5%). The Northern Cape, the largest province, is the most sparsely populated (2.3%) followed by the Free State (5.9%) (Health Systems Trust, 2008).



**Figure 1.1: Map showing the nine provinces of South Africa**  
 (From: [www.southafrica.to/provinces/provinces.htm](http://www.southafrica.to/provinces/provinces.htm))

#### **1.1.1. Rate of natural population increase (2005 – 2010)**

The rate of natural increase between 2005 and 2010 was given as 0.7% per annum by the Human Development Report (HDR, 2009), while the annual population growth rate for 2007-2008 was reported by Statistics SA (2009) as 0.82%.

#### **1.1.2. Immigration (% share of population)**

The percentage of the South African population made up of immigrants was estimated at 2.6% in 2005 (HDR, 2009). However, this figure might be an underestimate and may not fully include the many refugees, from other African countries, who enter the country for economic and political reasons.

#### **1.1.3. Percentage of total population living in urban areas**

The percentage of the population residing in urban areas in 2008 was 60.7%, according to the World Bank (2010a). This estimate is, however, higher than the 2008 estimate of 57.0% given in the Survey of the South African Institute of Race Relations (SAIRR, 2009)

#### **1.1.4. Percentage for the civil registration of births**

With regard to the registration of births, the World Health Organisation reported that 78% of all births between 2000 and 2007 were registered (WHO, 2009a).

### **1.1.5. Estimated population size in 2020**

It has been estimated that the population size of South Africa will have increased to 52.7 million by 2020, according to the HDR (2009).

### **1.1.6. Total fertility rate (births per woman)**

The total fertility rate, or number of births per woman, has been recorded by Stats SA as 2.38 children per women in 2009. This rate has decreased from 3.2 in 1998 (The United Nations Children's Fund, UNICEF, 2000), partly due to the availability of family planning services throughout the country, partly due to the high number of female household heads and bread winners in families, and possibly also due to the HIV/AIDS pandemic.

### **1.1.7. Maternal age at birth $\geq$ 35 years**

According to statistics from the United Nations (UN), in 2007 approximately 11.2% of live births were to women aged 35 to 39 years. A further 3.4% of births were to women aged 40 to 44 years, with 0.5 % of babies born to women aged 45 to 49 years. Women over the age of 50 years gave birth to approximately 0.08 % of live-born babies in 2007. In total, approximately 15.1% of all live births were to women over the age of 34 years.

## **1.2. Global Health Indicators**

### **1.2.1. Life expectancy at birth**

The average life expectancy of South Africans was estimated, in 2000, to be 58 years. This decreased to 54 years in 2007 (WHO, 2009a), and has further decreased to the most recent (2008) estimate of 51 years, according to the World Bank (WB, 2010a). Women have a slightly longer life expectancy of 53 years compared to 50 years for men (WB, 2010a). The decrease is mostly due to the HIV/AIDS pandemic, emerging TB epidemic and the associated problems with health service delivery.

### **1.2.2. Healthy life expectancy**

The healthy life expectancy of South Africans (in 2007) was 48 years for women and 47 years for men – an average of 48 years (WHO, 2009a). Healthy life expectancy has decreased in the last decade due to the HIV/AIDS epidemic and the high risk affected people have of developing tuberculosis and other serious infections.

### **1.2.3. Neonatal mortality**

The neonatal mortality rate is the number of deaths per 1,000 live births during the first 28 days of life. This was listed as 20 per 1,000 live births in 2008 (WHO, 2009a).

#### **1.2.4. Infant mortality**

Infant mortality – the probability of dying between birth and age one year – was estimated to be 46 per 1,000 in 2007 (WHO, 2009a). Males had a higher death rate of 48 per 1,000, while this rate was 44 per 1,000 for females. This is only slightly lower than the 1990 mortality rate of 49 per 1,000 (51 per 1,000 for males and 47 per 1,000 for females). The infant mortality rates differ by ethnic group and for 1980 they were estimated as 13, 20, 57 and 68 per 1,000 live births for White, Asian, Coloured (mixed ethnic group) and African children respectively (Nannan et al, 2007). The latest estimated average, across the population is 48 per 1,000 live births (World Bank, 2010a).

#### **1.2.5. Under-5 mortality**

The probability of dying by age five years (under-5 mortality rate) was 59 per 1,000 live births in 2007 (WHO, 2010a) and 67 per 1,000 in 2008 according to the World Bank (2010a). This rate was again higher for males (61 per 1,000) than for females (57 per 1,000) (WHO, 2010a). South Africa is one of only 12 countries in which mortality rates for children have increased since the Millennium Development Goals (MDGs) were set up in 1990 (Chopra et al, 2009). Although poverty and the AIDS epidemic are contributing factors, suboptimum implementation of the necessary interventions have had limited effectiveness and resulted in avoidable health system factors contributing to deaths.

#### **1.2.6. Adult mortality**

The term “adult mortality rate” is defined as the probability of dying between the ages of 15 and 60 years per 1,000 people in the population. The 2007 rate was given as 520 per 1,000, with women having a lower mortality rate (484) than men (557) (WHO, 2009a). The adult mortality rate has increased over recent years: in 2000 it was 386 per 1,000 (324 for females and 446 for males), while in 1990, it was 271 per 1,000 (190 for females and 345 for males) (WHO, 2009a). Again HIV/AIDS and its associated illnesses, such as tuberculosis, plus challenges in health care delivery are responsible for this situation, together with the problems in healthcare delivery.

#### **1.2.7. Maternal mortality**

The maternal mortality rate was given by both the WHO (2009a) and World Bank (2010a) as 400 per 100,000 live births in 2005. This rate has increased significantly, as it was only 230 per 100,000 women in 2000 (WHO, 2009a), again probably due to the failing health system and the shortage of doctors and nurses, as well as poverty and the AIDS epidemic. Maternal mortality has been shown to be nearly 10 times higher in HIV positive mothers than in those who are HIV negative (Patrick and Stephen, 2007). Again, South Africa is not meeting the Millennium Development Goal for a reduction in maternal mortality from 1990-2015 (Hogan et al, 2010).

#### **1.2.8. Summary of mortality rates**

In Table 1.1 below data from various sources for life expectancy and mortality rates for South Africa from 1980 to 2008 are summarised. According to Coovadia et al (2009), in the last two decades, the rate of child mortality has decreased in all but 12 countries– one of which is South

Africa. Many neonatal, child and maternal deaths, locally, are avoidable, particularly if HIV/AIDS-related deaths can be reduced (Chopra et al, 2009).

**Table 1.1. Life expectancy and mortality rates in South Africa**

	Life expectancy	Mortality Rate (per 1,000 live births)				
		Neonatal	Infant	Under 5	Adult	Maternal
<b>1980</b>	57 <sup>a</sup>		68 <sup>a</sup>	94 <sup>a</sup>		2.12. <sup>4ff</sup>
<b>1985</b>	59 <sup>a</sup>	23 <sup>e</sup>	54 <sup>a</sup>	71 <sup>a</sup>		
<b>1990</b>	63 <sup>b</sup>	19 <sup>e</sup>	49 <sup>b</sup>	64 <sup>b</sup>	271 <sup>b</sup>	2,3 <sup>d</sup>
<b>1995</b>	58 <sup>a</sup>	28 <sup>c</sup>	43 <sup>a</sup>	57 <sup>a</sup>		1,5 <sup>d</sup>
<b>2000</b>	58 <sup>b</sup>	20 <sup>d (1998 data)</sup>	56 <sup>b</sup>	74 <sup>b</sup>	386 <sup>b</sup>	2,3 <sup>b</sup>
<b>2005</b>	52 <sup>a</sup>		50 <sup>a</sup>	70 <sup>a</sup>	509 <sup>a</sup>	4,0 <sup>b</sup>
<b>2007</b>	54 <sup>b</sup>	14 <sup>d (2006 data)</sup>	46 <sup>b</sup>	59 <sup>b</sup>	520 <sup>b</sup>	
<b>2008</b>	51 <sup>a</sup>	20 <sup>b</sup>	48 <sup>a</sup>	67 <sup>a</sup>	544 <sup>a</sup>	2.4 <sup>f</sup>

<sup>a</sup> World Bank (2010a); <sup>b</sup> WHO (2009a); <sup>c</sup> Hyder et al (2003); <sup>d</sup> Health Systems Trust (2008)

<sup>e</sup> Department of Health, South Africa (1998); <sup>f</sup> Hogan et al (2010)

## PART 2: HEALTH EXPENDITURE AND FINANCING

### 2.1. Global Data

#### 2.1.1. Gross national income and Gini-index

South Africa's gross national income per capita was US\$5820 and International \$9790 in 2008 (World Bank, 2010a) The International Dollar "has the same purchasing power over GDP as a U.S. dollar has in the United States" (WB, 2010b) and is calculated using the purchasing power parity (PPP) exchange rate. PPP over gross domestic product (GDP) is "the ratio of the GDP of a country in national currency to its GDP in international prices" (UN, 2007b). This per capita income defines South Africa as a high middle-income country.

The Gini-index – which has values between 0 and 100 - represents income equality, higher values indicating greater inequality. The Gini-index for South Africa between 2000 and 2007 was listed as 57.8 by the World Bank (2010a) and the Human Development Report (2009). South Africa's Gini-index is increasing, with a value of 59.3 in 1994, 60 in 2003 and 65 in 2005 (Central Intelligence Agency Factbook, 2010; Landman et al, 2003).

#### 2.1.2. Health expenditure and financing

South Africa's per capita total expenditure on health in 2006 was given as International \$715 (WHO, 2009b) and in 2007 as US\$490 (World Bank, 2010a).

### Public expenditure on health

The per capita public expenditure on health in 2006 was Int\$1100. This accounted for approximately 9.1% of the total government expenditure in 2006 (WHO). This percentage increased to 14.1% in 2008/9 (HST, 2008), and was 11.6% in 2010, according to the South African Institute for Race Relations Survey (SAIRR, 2009).

As a percentage of the gross domestic product, total health expenditure (public and private) accounted for 8.0% in 2006 (WHO, 2009b), while a review by the Health Systems Trust (2008) proposed that by 2009/2010, funding for health services will likely exceed R200 billion – approximately 8.4% of the country's GDP (HST, 2008). The government health care budget funds all the health care needs of approximately 80% of the population who do not have health insurance, as well as all the healthcare training and education in the country.

Social security expenditure on health in 2006 was 4.3% of general government expenditure on health (WHO, 2009b). Social security expenditure is defined by the WHO as “expenditure on health by social security institutions...(which) are imposed and controlled by government units for the purpose of providing social benefits to members of the community as a whole, or to particular segments of the community” (WHO, 2007).

External Resources are defined by the WHO as “the sum of resources channelled towards health by all non-resident institutional units...(and) includes donations and loans, in cash and in-kind resources” (WHO, 2007). External resources (donor funding) accounted for 0.9% of the total expenditure on health in 2006 (WHO, 2009b), and approximately 2% in 2008 (HST, 2008).

### Private expenditure on health

Private expenditure on health accounted for 62.3% of total expenditure on health in 2006 (WHO, 2009b) and 57.1% in 2008/9 (HST, 2008).

Private sector healthcare expenditure has grown over the past 35 years and by 2004 approximately 9% of the GDP was spent on health care with 60% of this used for the private healthcare of the 18% of the citizens who had private insurance (Benatar, 2004). The same trend was evident in the deployment of doctors in the private sector, which grew from 40% in the 1970s to 66% in 2004.

Private pre-paid health insurance plans (called Medical Aid plans by many in South Africa) comprised approximately 77.7% of private expenditure on health in 2006 (WHO, 2009b), though only about 16% of the total South African population has private medical coverage (Econex, 2010). Out-of pocket expenses made up 17.5% of private expenditure on health (WHO, 2009b; 2006 Data), though this was estimated at between 10 and 14% in 2009, with most of this expenditure being for private health care provider consultations, rather than public sector services (Econex, 2010). In addition, it is interesting to note that 28.8% of the uninsured public used a private hospital in 2007 and about 54% consulted a private sector doctor, showing a preference for private services (Econex 2010).

Overall, the type of expenditure that would best describe the funding of health services in South Africa is a mix between private and public funding. Approximately 57% of the population use public medical services and 43% use private facilities (Econex, 2010). Many people use the private

health care services, while they are relatively inexpensive (e.g. general practitioners' visits) and public health care (e.g. for hospitalisation) when the costs increase.

## **2.2. Health Service Coverage**

Between 2000 and 2008, 92% of women had at least one antenatal care visit, with 56% having at least 4 visits (WHO, 2009b). Approximately 91% of births between 2000 and 2008 were attended by skilled health personnel (WHO, 2009b). The figures showed an increase from 84% in 1998 to 90% in 2003, according to the Health Systems Trust (HST, 2008). There is discrepancy between rural (where access to healthcare is more difficult) and urban areas, with rural rates listed as 85% and urban listed as 94% in 2003 (HST).

According to Coovadia et al (2009), South Africa has good policies in place to improve health care in South Africa. However, poor implementation and monitoring of these policies and poor management, has resulted in variable quality of care within the public health system.

## **PART 3: INDICATORS OF CONGENITAL AND GENETIC DISEASE BURDEN**

### **3.1. Availability of national surveys on genetic disorders prevalence, exposure to risk factors and availability of registries**

No national surveys on serious congenital disorders (defined as structural and functional disorders and abnormalities, present from birth, that can cause death or disability, WHO 2006) and genetic disorders have been performed and no registries on these disorders are maintained in South Africa. The Department of Health, Directorate: Maternal, Child and Women's Health encourages genetic nurses to complete notification forms in the case of congenital disorders. However, these forms are not being submitted systematically and routinely yet and the data arising from them has not been analysed. A programme called "The South Africa Birth Defects Surveillance System" (SABDSS) was started in 1988 and involved the routine, systematic collection of data regarding birth defects from 15 hospitals in the country. Such data collection ceased, however, in 2005 and currently only data for neural tube defects is collected (International Clearinghouse for Birth Defects, 2005).

### **3.2. Total birth prevalence of congenital/genetic disorders per 1,000 live births**

The total birth prevalence of serious genetic congenital disorders in South Africa is estimated to be 53.4 per 1,000 live births (March of Dimes, 2006). No data on the birth prevalence of teratogenic congenital disorders is available but one of the authors (AC) estimates that the birth prevalence of fetal alcohol syndrome in the country is about 14 per 1000 live births. Given that syphilis in pregnancy is also a problem (Delpont and Rothberg, 1992), it can be considered that the total birth prevalence of severe congenital disorders is in excess of 70 per 1000 live births.

### 3.3. Total birth prevalence of congenital disorders by cause per 1,000 live births

In Table 3.1 below the estimated prevalence rates for various congenital disorders, by cause, are summarised (March of Dimes, 2006). They are categorised by mode of inheritance, for the monogenic disorders, and information on the chromosome disorders and malformations is added. Also, the prevalence of conditions caused by two of the known risk factors, with the relevant references, is included in the Table.

Some congenital disorders are inherited in a multifactorial way and environmental and genetic factors play a part. These conditions include, for example the neural tube defects, cleft lip and palate, isolated hydrocephalus and talipes equinovarus. The prevalence of these conditions can vary in different ethnic groups (Kromberg and Jenkins, 1982b)

**Table 3.1: Estimated prevalence rates for congenital disorders by cause.**

Cause of Congenital Disorders	Prevalence (per 1,000 live births)	Reference
Dominant single gene defects	7	March of Dimes, 2006
X-linked single gene defects	1.3	March of Dimes, 2006
Recessive single gene defects	1.7	March of Dimes, 2006
Chromosomal defects	4.4	March of Dimes, 2006
Congenital malformations	37.3	March of Dimes, 2006
<b>Genetic risk factors</b>		
Glucose-6-phosphate dehydrogenase deficiency	0.5	Jenkins, 1990
Hypercholesterolemia	10	Delport, 2009

### 3.4. Birth prevalence of selected country specific "common" recessive single gene disorders

Some studies have been carried out on the common autosomal and X-linked recessively inherited disorders found in South Africa. Although these disorders are not necessarily country specific, they do occur at higher rates in certain sub-groups of the population. The population prevalence rates, estimated from the findings of the local studies, as well as the ethnic group most commonly affected, are presented in Table 3.2. The Afrikaans group refers to the members of a sub-group of the white population, most of whom are Afrikaans (a Dutch dialect) speaking and originated from the Netherlands, Germany and France, about four centuries ago.

The population prevalence rate of haemophilia, an X-linked recessive condition, is given in the table below, but the incidence rate is probably higher as it is suspected that severe cases of this condition have a high mortality rate in South Africa and probably die undiagnosed. One type of osteogenesis imperfecta, the recessively inherited Type III Sillence type, has been found to be more common in the black population than in other groups (Beighton et al, 1983). A comprehensive table showing inherited conditions of unusual prevalence among some southern African populations can be found in the paper by Jenkins (1990) (see Appendix A).

**Table 3.2: Prevalence of some common recessive and X-linked recessive disorders**

Disorder	Population prevalence	Ethnic/geographical group most commonly affected	Reference
Oculocutaneous albinism	1 in 3,900	Black	Kromberg and Jenkins, 1982a
Cystic fibrosis	1 in 3,000	White	Padoa et al, 1999
Fanconi's anaemia	1 in 26,000 1 in 40,000	Afrikaans, Black	Rosendorff et al, 1987 Morgan et al, 2005
Tay Sachs disease	1 in 3,000	Ashkenazi Jewish	Jenkins et al, 1977
Thalassaemia	<1 in 10,000	Greek ( $\beta$ ), Indian ( $\alpha$ and $\beta$ )	WHO, 2010a
Sickle cell anaemia	<1 in 10,000	Black immigrants	WHO, 2010a
Duchene muscular dystrophy <sup>a</sup>	1 in 14,000	Indian	Ballo et al, 1994
Galactosemia	1 in 18,000	Black	Manga et al, 1999
Gaucher disease	1 in 1600	Ashkenazi Jewish	Morar & Lane, 1996
Polycystic kidney disease: autosomal recessive type	1 in 26,000	Afrikaans	Lombard et al, 1989
Spinal muscular atrophy	1 in 2,000 <sup>b</sup>	Black	Labrum et al, 2007

<sup>a</sup>These disorders are X-linked recessives; prevalence rates reflect the prevalence among males;

<sup>b</sup>Birth incidence

### 3.5. Distribution of single gene disorders in ethnicities/geographical clusters.

Table 3.3 below shows the prevalence rates of a few common single gene, dominantly inherited, disorders and the ethnic group most often affected, in South Africa (rates for some of the recessive and X-linked conditions in ethnicities are shown in Table 3.2 above).

**Table 3.3. Prevalence of common single gene, dominantly inherited disorders**

Disorder	Prevalence	Ethnic/geographical group most commonly affected	Reference
Porphyria	3 per 1,000	Afrikaans	Hift and Meissner, 2005
Hypercholesterolemia	10 per 1,000	Afrikaans	Delpont, 2009

### 3.6. Birth prevalence of selected common chromosomal disorder

Estimates of the birth prevalence of certain common chromosomal disorders are present below in Table 3.4. The birth prevalence of Down Syndrome in the black population was high due to the high percentage of pregnant African women of advanced maternal age. In a rural area it was documented as 2.1 per 1000 live births and in urban Soweto 1.8 per 1000 live births (Christianson, 1996). Parrot (1997) estimated the birth prevalence in the South African Caucasian population as 1.6 per 1000 live births. This gave an estimated 1.9 per 1000 live births for the whole population. However, the rate of Down syndrome is possibly decreasing, at present, as the numbers of older women giving birth has decreased, with the AIDS epidemic.

**Table 3.4: Prevalence of common chromosome disorders**

Disorder	Prevalence	Reference
Down syndrome	~1 in 525*	Christianson (personal communication)
Fragile X	1 in 4,000 males	Goldman et al, 1997
Trisomy 18	1 in 10,000	Parrott, 1997
Trisomy 13	1 in 25,000	Parrott, 1997

\*An estimate for the total population

### 3.7. Birth Prevalence of Neural Tube Defects

The average birth prevalence of neural tube defects is 2.4 per 1000 live births, but this varies from up to 1 per 1000 live births in urban areas to as high as 6 per 1000 live births in rural areas (March of Dimes, 2006; Robertson H-L et al, 1997).

### 3.8. Prevalence of "late-onset" disorders

Various disorders that have a genetic component only become apparent later in life. Although little data are available on these conditions, locally, Table 3.5 below shows the prevalence of a few such disorders, in South Africa.

**Table 3.5: Prevalence/incidence of some common late-onset disorders**

Disorder	Prevalence/Incidence (per 100,000)	Reference
Breast Cancer <sup>a</sup>	Male: 0.88; Female: 31.16	National Cancer Registry South Africa, 2001
Colorectal Cancer <sup>a</sup>	Male: 8.72; Female: 5.48	National Cancer Registry, South Africa, 2001
Huntington disease	4 – 8	Warby et al, 2007

<sup>a</sup> Prevalence rates were not available for these disorders, so the available incidence rates are presented instead.

### 3.9. Percentage of all infant deaths due to congenital/genetic disorders

There are no figures available in the country on the percentage of infant or under 5 year deaths due to congenital disorders.

### 3.10. Percentage of paediatric hospital admissions

No studies have been undertaken on the numbers of children with congenital and/or genetic disorders in South African hospitals and no data are available.

### 3.11. Estimated potential for reducing the proportion of infant deaths due to congenital and genetic disorders (via known care and prevention strategies).

The addition of folic acid to staple foods (bread and maize meal) in South Africa started in October 2003. The result has been a 30.5% decline in the incidence of neural tube defects from 1.41 to 0.98 per 1,000 births (Sayed et al, 2008) in the sentinel sites surveyed, which were mostly in urban areas. Other than folic acid and iodine fortification of staple foods, and Tay Sachs screening in the high risk Jewish community, there are no universally and systematically applied preconception care and prenatal screening and diagnostic programmes for the prevention of congenital disorders in the country. Research is being undertaken to address the high rate of fetal alcohol syndrome in children in certain South Africa communities (between 20 and 40 per 1000 children, according to May et al, 2008).

The scope for the prevention of serious congenital disorders is therefore high and, if all preconception and prenatal modalities for prevention of congenital disorders were applied, it would be expected that the birth prevalence of these disorders would fall to less than 50 per 1000 live births, levels documented in industrialised countries.

### **3.12. Increased exposure to known risk factors that impact the prevalence of congenital/genetic disorders at birth.**

There are various factors known to increase the risk of a child being born with a birth defect. These include:

#### 3.12.1. Advanced maternal age

Advanced maternal age increases the risk of certain chromosomal abnormalities, particularly Down syndrome, but also trisomy 18 and 13 and Klinefelter syndrome. With approximately 15.1% of all live births in South Africa being to women over the age of 34 years (United Nations, 2007a), this is a risk factor that will impact on the birth prevalence of some of the common chromosome disorders.

#### 3.12.2. Consanguineous marriage

Consanguineous marriage used to be favoured by various ethnic groups (particularly the Sotho, Tswana and Swazi), in order to keep the power and/or the bride-price (often paid in cattle) in the family. Such marriages raise the risks for recessively inherited disorders in the off-spring. For example, 42%, 27% and 33% of the parents of children with oculocutaneous albinism in the Tswana, South Sotho and Swazi ethnic groups, respectively, were blood relatives (Kromberg and Jenkins, 1982a). In a small older study in the general Tswana community 7.2% had married their first cousins (Schapera, 1940).

#### 3.12.3. Migration

Certain single-gene defects have been introduced to the country due to migration. This is the case with porphyria (and probably hypercholesterolemia) which came to South Africa from the Netherlands due to emigration in the 17<sup>th</sup> century (Howson et al, 2008). It is now particularly common in the Afrikaans speaking population. Thalassaemia was also introduced into South Africa by immigrants from Greece and India. Recently, sickle cell anaemia is becoming more wide-spread in South Africa, due to many of the immigrants from West and Central Africa being carriers of this disorder (March of Dimes, 2006).

#### 3.12.4. Increased exposure to teratogens

One of the commonest teratogens identified in the country is alcohol, and about 5% of children born in the Cape Coloured community have fetal alcohol syndrome (May et al, 2008). Other teratogens, associated with birth defects, include syphilis, rubella infection (rubella immunisation is not included in the childhood immunisation programme), warfarin, and epilepsy medications. A study by Delpont and Rothberg (1992) showed that 2.5% of South African women had untreated syphilis at the time of delivery, with syphilis being the cause of up to 10% of stillbirths and 3% of neonatal deaths. Maternal rubella is also a problem in South Africa, with a study by Sellers et al (1976) reporting this to be the largest single cause of deafness among a sample of deaf school children. It is well known that maternal rubella also has teratogenic effects on the brain, eyes, and heart (Sellers et al, 1976).

#### **3.13. Estimate of how (increased) life expectancy, changes in life-styles etc. will impact the incidence of chronic diseases with a known genetic component**

Normal health transitions see a decrease in infectious diseases, resulting in people living to middle age. However, people may also move from rural areas to less healthy urban areas, increasing the exposure to risk factors and the prevalence of chronic disorders, such as hypertension.

This was the case in South Africa till around 2000, after which there has been a decrease in life expectancy, mostly due to an increase in HIV/AIDS and TB related deaths. This epidemic has significantly slowed the normal health transition, resulting in fewer people surviving to mid or later life. The consequence has been a decrease in the incidence of chronic diseases of later life (such as diabetes and hypertension) and a reduced prevalence of late onset disorders, such as, for example, Huntington disease, several types of cancers and forms of Alzheimer's and Parkinson's disease, which usually occur in older people. These diseases, however, once the HIV epidemic is overcome and the life expectancy increases, will again become evident.

## **PART 4: AVAILABILITY OF GENETIC SERVICES**

### **4.1. Description of the development of genetic services in South Africa**

Informal genetic counselling services started in Johannesburg and Cape Town in the early 1960s. A short time prior to that chromosome laboratory studies had been initiated and thereafter small genetics laboratories were opened in these two cities (for a detailed review of this early history see Jenkins, 1990 in Appendix A). Further development occurred in 1971 when the Department of Health and Welfare appointed a Director of Genetic Services to set up community oriented genetic services. The first two academic chairs of Human Genetics were established in 1972 in Cape Town and 1974 in Johannesburg and formal genetic counselling clinics were initiated.

The State department then, in 1974, employed about 15 genetic nurses (the first in Durban), in major centres across the country, and these nurses started offering a community genetics service, creating awareness, identifying patients and referring them to genetics clinics. Meanwhile the head-

office staff became involved in planning, policy-making and co-ordinating services. In 1977 the Minister of Health announced that Genetic Services were an integral part of the health system financed by the State, under the Health Act (Act 63 of 1977). The small diagnostic laboratory services were then extended and cytogenetic and biochemical testing became more readily available. Demand for prenatal genetic diagnosis increased rapidly (Kromberg et al, 1989) and community screening for conditions such as Tay Sachs disease was also initiated. The State provided some diagnostic tests free of charge, eg. for Haemolytic disease of the new-born, hereditary porphyria, chromosomal disorders, neural tube defects (in pregnancy), and hereditary metabolic disorders (in pregnancy). They also developed various community education and training programmes, as well as publishing and distributing supporting material, set up some epidemiological studies and assessment of people with intellectual disabilities in care centres (reviewed in Opt'Hof, 1985). These limited services however mainly benefited the white middle- and upper class communities.

At the same time the first two academic centres developed staffing, training and research increased. New services were set up at the universities in Pretoria (in the late 1980s, although this department was closed in 2001), Stellenbosch and Bloemfontein (in the early 1990s). In the 1980s research staff started to attain PhDs in Human Genetics, new initiatives led to the founding of molecular genetic laboratories, and new genetic tests were offered based on this expertise.

In the late 1980s the formal training of genetic counsellors began at the Master's degree level (two post-graduate programmes now exist, at the Universities of Cape Town and Witwatersrand) and genetic counselling services were expanded. In the early 1990s the Health Professionals Council of South Africa (HPCSA) set up registration for Genetic Counsellors and the profession became recognised and formalised. Similarly, the speciality of Medical Genetics was organised and recognised (in 1999). Initially, such specialists were required to have another specialisation first (eg Paediatrics), but recently this has changed and medical practitioners can proceed straight into a four year course to specialise in medical genetics.

In the 1990s a new approach to trying to offering medical genetic services to the public through primary health care was pioneered. This approach led to the National Ministry of Health accepting that basic clinical genetic services should be incorporated into paediatric care at primary health care level with links to secondary and tertiary care. A national task team to develop guidelines for this purpose was established. The Policy Guidelines for the Management and Prevention of Genetic Disorders, Birth Defects and disabilities were finalised and published by the Department of Health (2001) (See Appendix D).

Implementing the guidelines were to be the goal of the next decade. Initially there was some progress with the number of posts supported by the NHLS and provincial governments increasing in the late 1990s and early 2000s. These posts were mostly in Gauteng and supported by the NHLS, but there were also provincial government posts provided in the Cape Province, Bloemfontein, the Free State, and in Durban, KwaZulu Natal.

Generally, development in the field has slowed significantly in the last five years despite the National Department of Health recognising the need to strengthen medical genetics services in the country. This trend is due mainly to the AIDS epidemic and shifting Department of Health priorities. It is hoped that, with the recent recognition by the WHO that birth defects present major

health problems and therefore should become a global health priority, this perspective will change (WHO, 2010b)

#### 4.2. List of key genetic services

Table 4.1 below shows the key genetic services available in South Africa for different health purposes and in different settings. Genetic testing is available for many of the commoner genetic disorders, a complete detailed list of these conditions is available in Appendix B and further information appears in Diagnostic Genetic Tests, South Africa (2007) (Appendix C).

**Table 4.1: Availability of specific services in South Africa**

Type of service available	Setting					Availability in	
	Public domain			Private domain		Urban areas	Rural areas
	Primary care level	Secondary care level	Tertiary care level	Commercial	NGOs non-profit		
Pre-implantation genetic diagnosis	X	X	X	X	X	X	X
Prenatal genetic diagnosis	X	X	✓	✓	X	✓	X
Newborn screening	X	X	X	✓	X	✓	X
Genetic Screening	X	X	✓	✓	X	✓	X
Carrier testing	X	X	✓	✓	X	✓	X
Diagnostic testing	X	X	✓	✓	X	✓	X
Predictive testing	X	X	✓	✓	X	✓	X
Pharmacogenetic testing	X	X	X <sup>a</sup>	✓	X	✓	X
Molecular testing for viral infections	X	X	✓	X	X	✓	X
Genetic counselling services	X <sup>b</sup>	X	✓	X	X	✓	X
Abortion services	X	✓	✓	✓	X	✓	X

<sup>a</sup> This is beginning to be introduced for TB drugs.

<sup>b</sup> The effort to introduced basic clinical genetic services into primary health care\_has been very limited due to lack of resources.

#### 4.3. Provision of preconception care

Although family planning clinics and contraception are available throughout the country, there is very little genetic preconception care in South Africa. However, where there are consanguineous marriages and risks for recessive conditions are increased, some couples seek genetic counselling and genetic testing, prior to conception. Also, where risks for a specific genetic disorder are high, in a certain population group, members of that group might seek preconception testing. Examples include testing for Tay Sachs disease in Jewish couples, for beta thalassaemia in Greek couples, and cystic fibrosis in couples of European extraction, especially in cases of consanguinity. Salt is iodised and bread flour and maize meal are fortified with folic acid, reducing the risks for iodine deficiency disorders and neural tube defects respectively.

#### **4.4. Special care facilities available for affected children, such as medical care, social services, rehabilitation and education**

Some special care facilities are available for children with congenital disorders, mainly in the urban areas. Medical care and diagnostics are good if the child is referred to an academic, tertiary hospital. However, many rural children do not get to these centres and remain undiagnosed and untreated in their rural homes. Social services are inadequate due to the shortage of trained social and community workers. Nevertheless, disability grants are available for parents of severely affected children who are caring for them at home. Only limited rehabilitation facilities are available and this expertise is mainly sited in the cities. Some of the bigger rural hospitals do have the services of physiotherapists, occupational therapists and speech therapists, to assess disabled children and provide some appropriate community based rehabilitation services. Special education facilities, again, are accessible in most urban areas, but are few in other areas. However, the Education Department has a policy of mainstreaming affected children where possible and staff members are in the process of training teachers to cope with affected children in their classes. There are some special schools and some institutions that have boarding facilities, but these generally have long waiting lists and can only cater for <10% of the demand. A few holiday and respite care facilities are also available in some centres. None of these services are nearly adequate to meet the demand for special care.

#### **4.5. Total number of genetic service facilities in the different health care settings**

There were five genetic service facilities in South Africa in 2008. The largest was in Johannesburg (The NHLS/University of the Witwatersrand), there were two in the Cape, one each at the Universities of Cape Town and Stellenbosch, and services in Bloemfontein at the University of the Free State and in Durban at the University of KwaZulu Natal. The service in Durban has subsequently closed because of retirement and emigration of its medical geneticists. Services for children with congenital disorders are provided by paediatricians with a specific interest at the University of Pretoria and in Polokwane at the University of Limpopo.

The major academic departments also provide outreach services to some of the smaller cities and towns in the rural areas. Most of the genetic counselling services available are provided in the tertiary level public health care domain (88%), while the remainder is provided in private healthcare settings (Kromberg et al, 2009). One registered medical geneticist works in Pretoria, a retired medical geneticist offers a part time service in Cape Town and the University of the Witwatersrand offers a limited private practice service. A small number of nurses and doctors in primary healthcare settings have been trained, in short courses, to recognise birth defects, to offer basic treatment and counselling for the common disorders, and to refer patients appropriately when necessary. Due to lack of resources the number trained is limited and outreach services planned to support the programme has not materialised.

Laboratory services are offered mainly by the National Health Laboratory Service (NHLS), which is responsible for the provision of pathology services, including medical genetic laboratory services, for the public health service. The majority of the molecular genetic testing, at least 50% of the chromosome studies, and all metabolic testing are performed in these public healthcare laboratories. Six different private commercial companies, operating laboratories in four of the nine South African provinces, offer a limited number of genetic tests. Those genetic tests that require special expertise,

generally, are performed at the NHLS laboratories attached to an academic centre (mostly at the University of the Witwatersrand, but also at the Universities of Cape Town, Stellenbosch and Free State). Some rarer tests are centralised, and offered in one laboratory in the country where the necessary expertise is available, such as Tay Sachs disease gene testing (see Diagnostic Genetic Tests, South Africa, and Appendix A, regarding other tests available).

The only testing service offered by a non-governmental organisation is molecular testing for inherited retinal disorders, which is paid for by Retina (SA). This is done in conjunction with the Department of Medical Genetics, University of Cape Town. Other non-governmental organisations are offering some rehabilitation and educational services. A small number of nurses and doctors in primary healthcare settings have been trained, in short courses, to recognise birth defects, to offer basic treatment and counselling for the common disorders, and to refer patients appropriately when necessary.

Laboratory services are offered mainly by the National Health Laboratory Service (NHLS), who run 265 laboratories in cities and towns across the country. The majority of the molecular genetic testing, at least 50% of the chromosome studies, and most metabolic testing are performed in these public healthcare laboratories. Six different private commercial companies, operating laboratories in four of the nine South African provinces, offer a limited number of genetic tests. Those genetic tests that require special expertise, generally, are performed at the NHLS laboratories attached to an academic centre (mostly at the University of the Witwatersrand, but also at Cape Town University). Some rarer tests are centralised, and offered in one laboratory in the country where the necessary expertise is available, such as Tay Sachs disease gene testing (see Diagnostic Genetic Tests, South Africa, in Appendix C, and Appendix B, regarding other tests available).

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#### **4.6. Patients or samples sent abroad for testing or follow-up service purposes**

Rarely, when a test is not available locally, an overseas laboratory may be consulted and a sample might be sent away (patients are not sent abroad). Generally in such cases the expense is prohibitive and the work is only carried out if it can be done gratis, or if the patient is from the private sector with medical insurance which will cover the expenses (which situation is becoming more common). Fortunately, due to the good network of senior scientists in the country with collaborators in other countries, this matter can usually be negotiated. Most samples are sent to the United Kingdom, the Netherlands or the USA.

#### **4.7. Regular purchase by public providers of genetic services from abroad (export)**

Genetic testing services are not purchased from abroad through the public sector. However, in some cases, such services are purchased from other countries, if the patient can afford it (or has a Medical Aid Plan that covers testing expenses). For example, material for molecular prenatal diagnosis of a rare genetic disorder might be sent to an overseas laboratory with the necessary expertise.

#### **4.8. Provision of genetic testing services for health care services in other countries (import)**

Local laboratories provide genetic testing services for patients in other African countries, including the Central African Republic, Uganda and Kenya. This is mainly for the sickle cell anaemia. Chromosome analysis is requested for pre and postnatal diagnosis from Zimbabwe, Botswana and Namibia. Some patients also come from other African countries for prenatal and postnatal genetic diagnosis, since expertise is generally unavailable in other sub-Saharan African countries.

#### **4.9. Drivers of future development of medical genetic services in South Africa**

Development of medical genetic services, in the near future, will depend on the control and lessening of the HIV/AIDS epidemic. At present much of the funding for both health services and research is diverted to providing for, managing, understanding and finding solutions to this epidemic. However, attitudes at government level, as well as at the level of health professionals and the public, still need to be change if full use of the available services is to be made and if the services required in future are to be adequately funded and staffed. The universities are able to train students to a high level, but employment opportunities must be provided for the qualified professionals (or they may leave the country, as did a medical geneticist who qualified recently, but could not find employment). At present the available staff can only meet about 10% of the country's genetics needs. Further technological development (together with purchase of the necessary laboratory equipment) should be planned for, so that the South Africa can approach the level of developed countries. Both political will and financial commitment are required to move this enterprise forward. Pressure is being brought on key members of the health department by medical genetics professionals, as well as by genetic support group representatives, to respond to the basic genetic needs of South Africa, so that an adequate and appropriate medical genetic service can be developed which will benefit all the country's people.

### **PART 5: ACCESS TO GENETIC SERVICES**

#### **5.1. Costs and reimbursement systems for genetic services available in South Africa**

There appears to be a two-tier health care system in South Africa, which is now based on economic grounds rather than ethnic group, as was the case prior to 1994. Individuals who can afford private health insurance have access to, generally, better health care than those who cannot afford it, and who are reliant on public health services (Benatar, 2004).

Within the public health care system, there are different costing tiers depending on income. All pregnant and breastfeeding mothers, as well as children under the age of six years, receive free health care in South Africa, in public hospitals. Other patients have to pay a fee which is determined by a means test. The same applies to genetic services. There is no compulsory health insurance system in South Africa.

Those few patients, who access genetic services in private practice, generally have medical insurance and are reimbursed (depending on scheme and plan). For example, the cost of a genetic counselling session is set, approximately, at the accepted medical aid rate for such a consultation and therefore is fully refunded to the patient by the medical insurance. The details of services and costing are presented in Table 5.1. Prenatal genetic diagnosis services are only available in seven major academic hospitals, in the larger cities.

**Table 5.1. Costs and reimbursements for, and access to, various genetic services.**

Type of service available	Costs and reimbursement systems			Access		
	Public funding	Mix between public funding and private health insurance	Out-of-pocket funding	Self-referral	Referral by physician	Mandatory
Preimplantation genetic diagnosis	X	X	X	X	X	X
Prenatal genetic diagnosis	✓	✓	✓	✓	✓	X
New-born screening	X	X	✓	✓	✓	X
Genetic screening	✓	✓	✓	✓	✓	X
Carrier testing	✓	✓	✓	✓	✓	X
Diagnostic testing	✓	✓	✓	✓	✓	X
Predictive testing	✓	✓	✓	✓	✓	X
Pharmacogenetic testing	X	X	✓	✓	✓	X
Molecular testing to diagnose an infection (virus)	✓	✓	✓	X	✓	X
Genetic counselling	✓	✓	✓	✓	✓	X <sup>a</sup>
Abortion services	✓	✓	✓	✓	✓	X

<sup>a</sup>Genetic Counselling is only mandatory in certain instances, such as prior to predictive testing for diseases like Huntington disease. However, this is usually only enforced in the public sector and may not always be the case when testing is performed by private laboratories

## **5.2. Potential barriers to access to genetic services within South Africa**

There are several barriers to accessing genetic services; these include:

### **5.2.1. Financial barriers**

Sometimes finance can be a barrier, particularly where a genetic counselling session and/or tests are too costly for the patient, who either does not have a medical aid or where the medical aid will not cover the cost. However, such patients can be referred to the public hospital genetic clinics, in some cases. For poor patients the bus-fare to the hospital is sometimes prohibitive, especially where recurrent visits are necessary, and this may become a barrier.

Another financial barrier is caused by the budget that hospitals are given to cover the cost of all their pathology testing. Medical genetic tests may be perceived as expensive and hospitals therefore may either not allow or restrict such testing.

### **5.2.2. Geographical barriers**

The country is large and public transport to the cities, where genetic services are available, is sometimes not provided or too costly. Although comprehensive genetic services are not provided in the rural areas, genetic counselling teams for the Universities of the Witwatersrand and Cape Town do undertake outreach clinics and visit these areas periodically.

Distance and geographic isolation has also become a barrier for cytogenetic testing. Frequently the transport of blood for postnatal diagnosis of congenital disorders takes so long that the sample arrives in poor condition, the lymphocytes fail to grow and the test cannot be done. To overcome this barrier DNA based testing, using QF-PCR for aneuploidies, is offered now and, hopefully, CGH microarray testing, for children with intellectual disabilities and multiple congenital abnormalities, will become available in the future.

### **5.2.3. No timely access/lack of awareness**

The ignorance of both health professionals and the public regarding the available genetic services and their value, may present a barrier to access, since the benefits may not be understood and referrals may not be made appropriately or may be made late.

### **5.2.4. Other factors**

Other factors include cultural issues. For example, patients may have a fatalistic attitude to their health and pregnancy and therefore may not use genetic services (Kromberg and Jenkins, 1997). Also, many patients use both Western medical and traditional healer services and may choose, in certain situations, to use one or the other or both services; in the process they may reject genetic services. Further, the treatment of an AIDS related illness may require funds which, therefore, are not available to cover other health services, especially for those patients paying out-of-pocket.

### **5.2.5. Lack of political will and commitment**

Currently the health system in South Africa is in crisis for many different reasons. Principal amongst these are the effects of the HIV/AIDS epidemic but other issues include the high percentage of vacant posts for health professionals. In these circumstances medical genetic services have a low priority in the national and provincial departments of health. The situation at present is that the limited medical genetic services that had been developed have regressed in the last five years. This is probably the most significant barrier to care now and for the immediate

future.

### **5.3. Barriers to access because diagnostic tests, services and expertise are not available in South Africa and not accessible abroad.**

Diagnostic tests for the common genetic conditions, as well as services and expertise, are generally available and accessible in the main centres of the country. However, testing for rare conditions can be sought in other countries, if necessary, on a case by case basis. This may present a barrier if the costs of such testing are prohibitive.

### **5.4. Lack of available services in South Africa due to legal constraints (e.g. PGD, PND, etc)**

There are no legal constraints which reduce the availability of genetic services. The abortion law is quite a liberal one and so prenatal diagnosis (PND) can be performed at any time during pregnancy, if necessary. Preimplantation genetic diagnosis (PGD) is not available due to the lack of appropriate expertise and therefore legal constraints have not been considered yet.

### **5.5. Limitations of financial support for medical genetic services by public funds/social insurance in South Africa and its probable causes. Transparent evidence-based rationing and prioritisation of services in South Africa**

Financial support from public funds for genetic services is limited due mostly to the National and provincial departments of health having other health priorities particularly the HIV/AIDS and emerging TB epidemics. Financial support from public funds for genetic services is limited due mostly to the national and provincial departments of health having other priorities, particularly the HIV/AIDS and emerging TB epidemics. Also, there is still a large proportion of the population living in poverty and free treatment has been provided for pregnant women and children under the age of 6 years (which takes a large proportion of the annual health budget). However, there is also an element of ignorance regarding genetic services, and the many people who could benefit from them, were services better staffed and more widely available.

At present evidence-based rationing and prioritising of services processes are not well established in the country and, due to the shortage of health professionals, these processes are unlikely to become wide-spread in the near future. Some attempts are being made to approach evidence-based practice in some of the academic centres (such as the University of the Witwatersrand).

## **PART 6: STATE OF GENETIC SERVICES**

### **6.1 Human resources and training**

#### **6.1.1. Available health workforce (as defined in the World Health Statistics, WHO, 2009b).**

### Physicians

According to the WHO data for 2000-2007, there are 34,829 doctors in South Africa, which equates to a density of 8 doctors per 10,000 people in the population (WHO, 2009b). In 2008, the HPCSA recorded 33,534 registered doctors in the country. This number includes doctors registered in the country but practicing abroad. The latest estimate is that only about 24,147 doctors, general practitioners and specialists, were active in 2009 (Econex, 2010). According to the Health Systems Trust 34.9% of posts for medical practitioners in the public health service were vacant in 2008.

### Nursing and midwifery personnel

WHO 2000-2007 statistics reported that there were 184 459 nurses and midwifery personnel in the country – a density of 41 nurses per 10,000 people in the population (WHO, 2009b). However, according to Econex (2010), there are currently only 104,571 nurses who are active. According to Health Systems Trust reports 40.3% of professional nursing staff posts in the public health sector were vacant in 2008 (HST, 2008).

### Community health workers

Data regarding the number of community health workers in South Africa are not available, since this category is not yet a recognised entity. However, some universities are developing a new degree, a BSc in Health Sciences, which will qualify students in this field.

### Other health workers

The total number of other health workers, recorded between 2000 and 2007 (WHO, 2009b), was 71,850, equating to 16 per 10,000 people in the population.

The category “other health workers” includes pharmacists, laboratory health workers, environmental and public health workers, medical assistants, dieticians and nutritionists, rehabilitation therapists, operators of medical and dentistry equipment, optometrists and opticians, personal care workers, psychologists and others (WHO, 2009b).

### **6.1.2. Integration of medical genetics into the medical schools’ curricula**

In 2008 five medical schools in the country had access to medical genetics professionals (most are in NHLS or provincial posts and a few have joint appointments between the NHLS or province and the local University) to provide medical genetics teaching for medical students. This has subsequently been reduced to four. These four include the Universities of Cape Town and Witwatersrand (both have full Departments and Chairs of Human Genetics), Free State and Stellenbosch. At these medical schools medical genetics is integrated into the curricula at various levels and to a varying extent. Medical students are also trained at the Universities of Pretoria, KwaZulu Natal and Limpopo, but medical genetics teaching at these universities is limited and often falls to clinicians in various specialities, particularly paediatricians.

### **6.4.3. Medical genetics as a speciality in medicine**

Medical Genetics was initially recognised as a sub-speciality in 1999 (nine medical geneticists qualified under this system), but has recently (in 2007) been recognised as a primary speciality in medicine in South Africa. Specialist training towards a post-graduate MMed degree is offered at the Universities of Cape Town, Stellenbosch and the Witwatersrand. The students undertaking such training also have to take the College of Medicine (SA) Fellowship in Medical Genetics. Specialising in medical genetics involves a four year, full-time course, for doctors registered with the Health Professions Council of South Africa. The first group of five medical practitioners are presently in training.

In 2008 ten medical geneticists, registered with the HPCSA, were practising in academic medical centres and serving, mainly, the public sector. Subsequently, in 2009, two more medical geneticists were added to the register and one retired from academic practice. There are now 11 registered medical geneticists in academic practice. In addition, one medical geneticist works full time in private practice and another for a non-governmental organisation, involved with research on fetal alcohol syndrome, in 2008.

### **6.1.3. Post-graduate training programmes for biochemical, cytogenetic and molecular geneticists.**

Medical scientists can be trained in human genetics if they have a BSc (Honours) degree in a biological science and are registered as students with the HPCSA (2010). Such a degree is offered at the Universities of Cape Town, Free State, KwaZulu Natal, Limpopo, Pretoria, Stellenbosch, the Witwatersrand and the Walter Sisulu University (HPCSA, 2010). The degree is followed by a two year internship at one of three registered training centres (at the Universities of Cape Town, Free State and the Witwatersrand). Those students with Master's or PhD degrees in a biological science require only a six month internship. Students who complete their internships can then register with the HPCSA, as qualified medical scientists.

Medical technology students are required to register with the HPCSA prior to completing a three-year National Diploma or BSc degree in Biomedical Technology. This qualification can be obtained from a University of Technology. An internship for a minimum of 12 months, followed by an exit examination, then has to be completed, at either the University of Cape Town, Free State or the Witwatersrand before the candidate can qualify as a cytogenetic medical technologist.

### **6.1.4. Genetic counsellors as a recognised and registered profession.**

Genetic counselling in South Africa is a recognised and registered profession with formal post-graduate training at the Master's degree level (offered by the Universities of the Witwatersrand and Cape Town). The genetic counselling course involves two years of full-time formal teaching and clinical training, a research project, and a two year internship (one year of which overlaps with the second year of teaching). Registration with the HPCSA is required.

According to the HPCSA (2009), there were 15 registered genetic counsellors in South Africa in 2008. The majority were in full-time genetic counselling posts at the NHLS and University of the Witwatersrand. Other counsellors were in part-time provincial or university posts, with NGOs, private laboratories, or in private practice.

### **6.1.5. Education programmes in medical genetics and genetic counselling availability for non-genetic health professionals**

Since the early 1990s the Department of Health has provided limited finance for medical genetics education for nurses and doctors working in primary health care. In 2005 a standardised syllabus for this programme was developed by medical genetics professionals. This project was initially financed by a grant from the March of Dimes Foundation in the USA to the Division of Human Genetics, University of the Witwatersrand. The Medical Genetics Education Programme (MGEP) was trialed in several provinces and then accepted by the Department of Health, who continue to provide limited finance so that it can be offered in seven provinces (two provinces Western Cape and KwaZulu Natal fund their own MGEPs). A grant from the Lottery will cover funding for the course in the coming year. The programme consists of a four month distance learning section (using a specially compiled manual on Birth Defects), four contact days of lectures and tutorials, an examination. Candidates who pass the examination can then undertake four more training days on developing clinical skills, including dysmorphic examination, and counselling skills.

Medical geneticists and genetic counsellors give occasional lectures to non-genetic health professions students and qualified health professionals, such as medical specialists and registrars in various medical fields, general practitioners, physiotherapists, occupational therapists, speech therapists, social workers, pharmacists, and nurses, as well as medical insurance personnel.

### **6.1.6. Brain-drain/migration of health care personnel working in medical genetics**

The brain drain/migration of health care personnel working in medical genetics is a problem in the country. Of the nine medical geneticists trained in the country between 2000 and 2008 one has left the country, another is emigrating and one has left the profession. A further three are working part-time and no posts are available at present for future graduates.

Several genetic counsellors (probably about 15%) have also emigrated to the USA, UK, or Australia. One of the main reasons for this trend is the lack of job opportunities in South Africa, especially in the Cape and KwaZulu Natal provinces. Several counsellors are working in part-time positions, including all three who are working in the Western Cape.

Staffing NHLS laboratories in the public sector is problematic since medical scientists, once qualified, may leave to the private sector for better wages or emigrate. Vacated posts may then be frozen due to cost constraints. In this way the Division of Human Genetics, NHLS and University of the Witwatersrand in Johannesburg, between 2007 and 2010 lost 30% of its laboratory staff.

There are also no post-doctoral positions in the country which means that students who have gained PhDs have to find such positions overseas and often do not return after the post doctoral position is completed. The result is that the country is very short of trained personnel, staff numbers in the field are decreasing instead of increasing, and development in the field is being retarded. Medical scientists in research may also leave to gain experience overseas and many do not return.

### **6.1.7. Importing of specialists from abroad for the provision of medical genetics services**

Difficulties in obtaining registration with the HPCSA and poor salaries deters specialists from abroad from coming to work in the country and as a result none have been imported. However, one

medical geneticist from the Cameroon is working in the Department of Human Genetics at the University of Cape Town, but he is not registered with the HPCSA.

## **6.2 Workload**

### **6.2.1. Number, location and regional distribution of medical genetic departments/medical genetic units/centres in South Africa, including service networking activities, and coordination with other health services.**

There are now four academic medical genetics departments (previously five in 2008), which are regionally distributed throughout the country and three universities with no such department but offering a limited service for children with congenital disorders by paediatricians with an interest in the subject:

- The largest is the Division of Human Genetics, NHLS and University of the Witwatersrand in Johannesburg, Gauteng province. In 2008 the clinical unit staff included four medical geneticists, two experienced medical officers, and seven genetic counsellors. The head of department is also a medical geneticist but much of his time is taken up with administration.

There were also molecular, serogenetic and cytogenetic service laboratories with 18 15 registered medical scientists, 3 medical technologists and eight medical scientist and medical technologist interns working on diagnostic genetic testing for many different genetic conditions.

Six medical scientists were also involved purely on research. The departmental clinical and laboratory based research work was largely grant funded.

- The University of Cape Town, in the Western Cape, has a Department of Human Genetics that runs a large molecular research laboratory, doing mostly grant funded research work. Attached to the department is a NHLS cytogenetics laboratory (with a staff of seven medical scientists and technologists) and molecular laboratory (with two medical scientists), offering diagnostic genetic testing. There is also a clinical unit with two medical geneticists and one full-time and one part-time genetic counsellor, who are all provincial employees.
- The University of the Free State in Bloemfontein, Free State province, has a Division of Human Genetics comprising a medical geneticist in provincial government employ and a diagnostic service laboratory (cyto- and molecular genetics with two medical scientists and three medical scientist interns) that are part of the NHLS. This laboratory also does some grant funded research.
- At the University of Stellenbosch, also in the Western Cape, the provincial government employed, in 2008, a medical geneticist, part-time genetic counsellor, and laboratory staff for a small cytogenetic and molecular genetic NHLS laboratory (staffed by three medical scientists and a medical technologist).
- In KwaZulu Natal two medical geneticists (based in the Paediatrics department of the local university, in Durban) were employed by the province in 2008, but one emigrated that year and the other retired in 2009 (leaving 8 million people with no medical geneticist or genetic

counsellor and only one genetic trained nurse). The cytogenetic laboratory is run by the SA Blood Transfusion Service in Durban.

- The University of Pretoria, in Gauteng, employs a paediatrician, with an interest in medical genetics, to undertake genetics clinics at its academic hospitals. There is also a molecular laboratory based at the university undertaking some grant funded research, mainly on cancer.
- The University of the Limpopo (merger of the University of the North and the MEDUNSA campus) has a small NHLS cytogenetics laboratory that mainly serves Limpopo province. It had two medical technologists in cytogenetics in 2008.

Some informal networking occurs between all these departments, between all the provinces and with other health services. Some genetic testing is centralised, while some genetic counselling is provided by outreach programmes to underserved provinces and these clinics are staffed from the major centres. Networking also occurs between the academic departments, the NHLS, and the Department of Health. The Department of Health has a small section, in the Division of Maternal and Child Health, responsible for Genetic Services. There are four staff members and they have a budget to undertake community education, produce educational material and set up policies for Genetic Services; they work in collaboration with the academic departments of Human Genetics.

The workload in most academic units is heavy as most are short of qualified staff. The WHO suggests that two medical geneticist and four genetic counsellors are required to provide an adequate genetic service to every one million people. South Africa has 47 million people but is grossly understaffed in the field of medical genetics resulting in many unmet genetic health needs in local communities.

### **6.2.2. Extent of integration of genetic services targeted and designated for public health care into the health care system.**

Clinical genetic services, although limited, are integrated into the public health system, in and around the academic centres of the Universities of Cape Town, Free State, Stellenbosch, the Witwatersrand and formerly KwaZulu Natal. Most genetic counselling clinics are held in public hospitals, associated with academic hospitals and the genetic services are available through referral from other hospitals and clinics. The medical geneticists and genetic counsellors also undertake outreach visits both within and outside their provinces, although, with the limited resources, the majority of the population still remain underserved.

The universal systematised prevention of congenital defects is not presently possible in South Africa due to the limited medical and obstetric resources. Facilities for prenatal screening, prenatal diagnosis and genetic counselling are only available at the main academic hospitals. Limited screening, with ultrasound and prenatal diagnosis, is possible in other tertiary and some secondary care hospitals. In addition, local issues include poor uptake of prenatal diagnosis for high risk women, such as those of advanced maternal age, due to poor recognition of the problem in primary healthcare settings and the high rate of HIV/AIDS in pregnant women, which complicates decision-making (Bee, 2005).

However, the prevention of some congenital defects, with the fortification of bread and maize meal with folic acid, for the prevention of neural tube defects, has been successfully undertaken since 2004. This programme has resulted in a 30% decrease in the numbers of affected births (Sayed et al, 2008). The iodisation of salt to reduce iodine deficiency disorders was completed many years ago, but there have been no follow up studies to assess the success of this programme.

Community education of health care professionals, at many levels from primary healthcare to tertiary settings, is also undertaken in order to increase awareness and integrate the services into the healthcare system. Ideally, a full-time genetic education officer should be appointed in the major academic departments, to undertake this job more uniformly. SAIDA has employed a part-time genetic counsellor to undertake some educational tasks, since 2008. At present however, nurses in primary health care are receiving basic in-service training in medical genetics, and paramedical professionals, such as physiotherapists and occupational therapists, receive some teaching during their training. Educationalists', community, women's, and parents' groups are offered basic lectures on demand.

The integration of services for the care and prevention of birth defects, genetic disorders and disabilities, was mooted in the National Policy Guidelines published in 2001 (Department of Health, 2001) (See Appendix D). However, the effects on the health services imposed by the HIV/AIDS pandemic and other problems have severely limited the implementation of these guidelines. It is hoped that the recent recognition by the WHO of the need for developing nations to implement services for the care and prevention of birth defects, to assist them to attain their Millennium Development Goal 4, will stimulate government to give more attention and resources to medical genetic services.

### **6.2.3. Number of laboratories performing genetic testing services (laboratories specialised in genetics), service networking activities.**

Medical genetics diagnostic laboratory testing is undertaken, for public and private sector patients, mainly through the NHLS laboratories at the Universities of Cape Town, Free State, Stellenbosch and the Witwatersrand. The majority of the work is carried out at the University of the Witwatersrand/NHLS laboratories, where the largest variety of tests is offered. Samples for genetic testing sent to a local NHLS laboratory (265 such laboratories deliver pathology services to all public clinics and hospitals and operate in cities and towns across the country) will be transferred to the appropriate laboratory, if the local one cannot perform the test, so that the service is fully available, accessible and well integrated into the country's health system (National Health Laboratory Service, 2009). There is limited networking between the laboratories, but the NHLS is considering establishing a medical genetics expert committee to facilitate collaboration between its laboratories and the medical geneticists employed by the various authorities.

Some genetic testing is done in laboratories in academic departments other than human genetics, such as departments of Chemical Pathology or Haematology. Some of these laboratories are part of the NHLS and their tests are available to all clinicians and their patients throughout the country. Other tests are offered as part of a research programme, as is the case with the cancer genetics tests undertaken at the Department of Genetics, University of Pretoria, and the colon cancer and retinal disorders testing offered by the Department of Human Genetics, University of Cape Town. When the results of these tests become available the clinician, who referred the patient to the research laboratory, may use them for clinical purposes. The full range of medical genetic tests offered in the

academic and public domain is documented in Diagnostic Genetic Tests, South Africa (2007) (see Appendix C).

The 12 main laboratories, with academic affiliations, performing diagnostic genetic testing services, on a service basis, are listed in Table 6.1. In addition, the Western Province Cape Blood Transfusion Service performs paternity testing only, while the SA Blood Transfusion Services provide chromosomal testing in KwaZulu Natal as well as paternity testing countrywide. There are also various private laboratories, where some genetic tests are offered (cytogenetic, molecular and metabolic testing and postnatal screening), located around the country, mostly in the provinces of Gauteng, KwaZulu Natal, and the Western Cape. These services are used mainly by private patients covered by medical insurance. One such example is the private cytogenetics laboratory run by Lancet Laboratories in Johannesburg, which completed 3292 (1522 were amniotic fluid samples) tests in 2008 with three medical scientist staff and three medical technologists (Rosendorff, personal communication). However, no data are available regarding the genetic tests undertaken in most of these private laboratories.

**Table 6.1. Locations and affiliations of laboratories in South Africa offering genetic testing services** (Chr=Chromosomal, Bio=Biochemical/Metabolic, Mol=Molecular). Extracted from Appendix C.

Province	Laboratory	Affiliation	Types of tests performed		
			Chr	Bio	Mol
Free State	Division of Human Genetics	University of the Free State;	✓	✓	✓
Western Cape	Department of Chemical Pathology	University of Cape Town	✓	✓	✓
Western Cape	Division of Human Genetics	University of Cape Town	✓	✓	✓
Western Cape	Division of Lipidology	University of Cape Town		✓	✓
Western Cape	Department of Haematology	University of Cape Town	✓		
Western Cape	Division of Human Genetics	University of Stellenbosch	✓	✓	✓
Western Cape	Department of Haematology	University of Stellenbosch	✓		
Gauteng	Division of Human Genetics	University of the Witwatersrand	✓	✓	✓
Gauteng	Division of Genetics	University of Pretoria	✓	✓	✓
Gauteng	NHLS Ga-Rankuwa Tertiary Laboratories	Medical University of South Africa (MEDUNSA)	✓		
KwaZulu Natal	Department of Chemical Pathology	University of Durban/Westville			✓
North west	Department of Human Genetics	University of Limpopo		✓	

#### 6.2.4. Estimates of number of genetic tests performed in the country and observable trends in genetic testing activity.

The number of genetic tests performed in the country is very difficult to estimate, since testing is not centralised and many laboratories in various academic departments as well as in public and private settings, offer testing for various genetic conditions. However, in the four academic human genetics departments where genetic diagnostic laboratories were situated 15,720 tests were performed in 2008.

For example, in 2008, at the Division of Human Genetics laboratory at the NHLS and University of the Witwatersrand, Johannesburg (the biggest genetics laboratory in the country), 12,006 tests were carried out: 7,420 (paternities, molecular tests for common chromosome aneuploidies (using QF-PCR techniques) and biochemical tests eg. Screening for disorders common in the Jewish population) in the biochemical and molecular laboratory; 2,870 in the cytogenetics laboratory; 1,716 (eg. For fragile X, cystic fibrosis, spinal muscular atrophy) in the molecular laboratory.; There were about 18 registered medical scientists and technologists and 8 medical scientists interns. The laboratories are referral centres and samples for the rarer genetic disorders, and for tests not offered elsewhere, are received from all over the country. The numbers of tests in each of these four laboratories is increasing every year.

The University of Cape Town (UCT) Department of Human Genetics laboratory staff (one medical scientist and one medical technologist) processed 337 molecular diagnostic genetic samples through their UCT/NHLS Genetics laboratory in 2008 (however, this numbers does not include the molecular genetics testing undertaken for research purposes, for retinal diseases and colon cancer, but where results may be given to the referring doctor). These samples included: 81 for Spinal Cerebellar Ataxia, 58 for fragile X and 52 for Friedreich's ataxia. The UCT/NHLS cytogenetics laboratory, based at Groote Schuur Hospital, processed 1295 samples (793 were blood samples for chromosome studies or FISH analysis, 307 were amniotic fluid samples for culture or FISH analysis) with seven members of staff and one student intern.

At the University of Stellenbosch /Tygerberg Hospital Laboratory 931 genetic diagnostic tests were performed, in 2008, by three medical scientists and one medical technologist. These included 458 for prenatal cytogenetics (mostly amniotic fluid and cordocentesis samples and samples for FISH analysis) and 261 for postnatal cytogenetics (mostly blood karyotypes), and 212 for molecular genetics (mostly for DNA extraction to send elsewhere, but also for on-site DNA testing).

At the University of the Free State, Human Genetics laboratory 1151 genetic diagnostic tests were performed in 2008. The most common of these was for chromosome analysis (543 tests: 410 for post natal and 133 for prenatal testing), followed by haematological chromosome analysis (206), and breast cancer (104), Fanconi's anaemia (56), familial hypercholesterolemia (37) and other conditions.

The number and demand for tests, particularly on the molecular but also on the cytogenetic level, is increasing. However, expansion and new developments are being somewhat retarded by the training of too few medical scientist and technology students to meet the need (especially in cytogenetics laboratories across the country), by the resulting lack of experienced staff, poor job opportunities and career paths. The laboratories are also experiencing problems with maintaining and updating equipment.

#### **6.2.5. Most commonly tested ten conditions in South Africa and number of laboratories/centres performing the tests**

The 10 most commonly tested conditions appear to be: Paternity, chromosomes, aneuploidies (including Down syndrome), fragile X, Ashkenazi conditions screen, cystic fibrosis, spinal muscular atrophy, Duchenne and Becker muscular dystrophy, breast cancer, Huntington's disease. As an example, at the University of the Witwatersrand/NHLS molecular laboratory, the ten most commonly performed molecular tests included: fragile X, cystic fibrosis, spinal muscular atrophy, Ashkenazi Jewish carrier testing (including Tay Sachs and Gaucher's disease testing), Duchene muscular dystrophy, Fanconi anaemia, Huntington disease, Prader-Willi syndrome, Charcot-Marie-Tooth syndrome, and spinocerebellar ataxia. The next two most common tests performed were for haemophilia and alpha thalassaemia. However, about 22% of the molecular tests were one off tests, set up once for a specific condition.

Tests for the top ten conditions are normally only performed by one or more of the four academic/NHLS molecular genetic diagnostic laboratories (mentioned in Section 6.2.4 above) based in the academic centres of the major cities of South Africa. However, cytogenetics tests are offered in more laboratories, and a few private laboratories undertake a few of the molecular tests (eg. Cystic fibrosis).

The porphyrias are a common group of conditions (mostly inherited) found in South Africans, and the dominantly inherited porphyria variegata occurs mainly in those of Dutch descent, due to founder effect. One academic laboratory in the Department of Medicine at the University of Cape Town offers comprehensive testing for this condition for the whole country.

#### **6.2.6. Estimated workload of genetic consultations per health care professional/per year.**

The workload of genetic consultations per health care professional is difficult to estimate retrospectively, due to the variety of duties (which include teaching, research and administration, as well as consultations, which may involve screening children for diagnostic purposes at special schools or in depth hour long genetic counselling sessions) undertaken by genetics staff members, the many part-time workers, the staff turnover, and the consequent problems in establishing the actual numbers of full-time equivalent (FTE) staff members. If the consultations of the four academic units (medical geneticists and genetic counsellors full and part time) are summed the total is 7313 consultations performed by approximately 18.5 staff giving an estimated workload of 395 consultations per professional. However, genetic consultation workloads vary greatly in the different universities.

At the University of the Witwatersrand in 2008 in Johannesburg, 1837 genetic consultations were performed: medical geneticists (about 4.5) counselled 1168 cases and genetic counsellors counselled 669 (about 4.5) cases for genetic disorders. These figures represent an estimated workload of about 204 genetic consultations per FTE health professional per year. [Only full genetic consultations are undertaken in this unit; there is no screening.]

At The University of Cape Town in 2008 altogether 2201 patients were seen (1483 as new patients and 718 as follow-ups). The staff consisted of about two medical geneticists, two genetic counsellors and two genetic nurses, so the workload was approximately 367 consultations per professional.

At the University of Stellenbosch 2586 genetic consultations were performed by 2.5 staff members giving a workload of 1034 consultations per FTE professional.

At the University of the Free State 689 consultations were performed by one medical geneticist giving a workload of 689 per professional

Health professionals at another two universities offered some genetic consultations. At the University of KwaZulu Natal two medical geneticists (one on a session basis) working in Paediatrics, undertook genetic consultations regularly, but numbers are not available. Also in Paediatrics at the University of Pretoria one paediatrician, with an interest in medical genetics, offered genetic consultations, but there are no data on the numbers of cases seen.

### **6.3 Quality assurance of medical genetic services**

#### **6.3.1. Availability of quality assessment schemes and existing regulatory frameworks for genetic services**

Some quality assessment schemes are available and the academic departments of human genetics are exposed to regular peer reviews. The NHLS laboratories in academic and tertiary settings, doing genetic testing, are also monitored and accredited by the South African National Accreditation System (SANAS) so that they comply with international standards. However, this process is not mandatory. Private laboratories are not subjected to such scrutiny but tend to undertake it voluntarily. The NHLS laboratory at the University of the Witwatersrand participates in biannual quality assurance programmes and obtains accreditation for testing proficiency through the American College of Pathologists (CAP). It is in the process of moving into new accommodation and when this is complete it will undertake SANAS accreditation. Further, biological medical scientists follow a set syllabus and intern programme laid out by the HPCSA and only HPCSA registered medical scientists can work in the public and private sector laboratories.

#### **6.3.2. Documentation of process and outcome data**

The documentation of process and outcome data on medical genetics services takes place on the individual provider level and in individual academic departments and no national data are available. Each academic centre keeps the records and data they require for their internal assessments and/or annual report and there is no national policy or coordination of data for the whole country.

#### **6.3.3. Availability of national guidelines and recommendations for the provision of medical genetic services including ethical guidelines.**

National Policy Guidelines for the management and prevention of Genetic Disorders, Birth Defects and Disabilities (see Appendix D), were initially drawn up with contributions from all major stakeholders (from academic and government departments) and a document was published in 2001 by the Department of Health. The document provides recommendations for the provision of genetic services and has sections on general ethical guidelines for medical genetics (modified from the WHO Hereditary Disease Programme, 1995, document) and on ethical principles for genetic professionals (from Baumiller et al, 1996). This policy document is still available and it has not yet been superseded.

Some ethical guidelines, for genetic research purposes, were also drawn up, around the same time, by the Medical Research Council and a committee set up for the purpose. These guidelines appeared in a booklet entitled: Guidelines on Ethics for Medical Research: reproductive biology and genetic research (MRC, South Africa, 2002b). This booklet followed on from a booklet on the general principles of ethics for medical research (MRC South Africa, 2002a).

#### **6.4 National policies and legal frameworks**

##### **6.4.1. Existing national policies, guidelines and planning activities for the provision of medical genetic services including frameworks for the provision of medical genetic services and interventions such as surveillance, screening, provision of PND, PGD and abortion services**

In the existing national Policy Guidelines for the Management and Prevention of Genetic Disorders the priority medical genetic services are described (Department of Health, 2001, see Appendix D). These include services prior to conception, during pregnancy, at birth, in infancy and childhood, and in adolescence and adulthood. The way in which these services could be delivered at various levels from primary to tertiary health systems, is covered. Recommendations that medical geneticists' and genetic counsellors' posts should be provided urgently in every province in the country, in order to offer the services, have not yet been followed up, and some provinces have no posts at all.

The education of learners at schools and the training of health professionals, including medical students, genetic counsellors, nurses, medical scientists and technologists is also covered.

Interventions are described, including strategies for prevention, such as genetic counselling, preconception and prenatal methods of prevention (eg. prenatal diagnosis), postnatal diagnosis and population screening. There are recommendations regarding: medical genetics laboratory services and integrating these into the NHLS, which has been achieved; the composition (it was suggested medical genetics professionals as well as a lawyer should be included) and functions of a Medical Genetics Advisory Board; and evaluation of human genetics programmes.

International Conventions and Directives acknowledge that there are basic human rights for patients with genetic conditions and that everyone is entitled to basic health care (Convention of Human Rights, 1997). In line with these international standards the South African Constitution of 1996 provides not only for fundamental rights such as the right to life (section 11) and the rights to equality (section 9), dignity (Section 10) and privacy (section 14) but also provides in section 27 that everyone has the right to have access to health care, sufficient food and water and the right to social security. This section 27 right to health care and social security is a so-called socio-economic right and further states in section 27(2) that the State must take reasonable legislative and other measures, within available resources, to achieve the progressive realisation of each of these rights. This the State has done by providing a legislative framework to articulate these basic constitutional rights.

The National Health Act of 2003 (NHA) is arguably the most important of the Acts giving effect to the right of everyone to have access to health care services as guaranteed in section 27 of the Constitution. Section 4 of the NHA sets out who is entitled to free health care services in public health establishments and gives the Minister of Health, in consultation with the Minister of Finance,

discretion to prescribe conditions as to whom this free service is available taking into account the impact of any condition on access to health care services and the needs of vulnerable groups. Currently, the State is obliged to provide free health care services to pregnant and lactating women and to children under the age of six years, who are not members or beneficiaries of medical aid schemes. Furthermore free primary health care services must be provided to all those who are not members of medical aid schemes and to those persons entitled to compensation for occupational diseases. Section 4 also provides authority for women to have access to free termination of pregnancy, subject to the Choice on Termination of Pregnancy Act 92 of 1996.

The NHA has clear provisions in section 7 for consent to medical treatment and, with a few exceptions, a health care service may not be provided without informed consent. Section 6 of the NHA obliges a health care provider to inform the patients of their health status and the range of diagnostic procedures and treatment options as well as the benefits, risks, costs and consequences associated with each option. This section is also clear about a patient being informed in a language she understands, taking the literacy level of the patient into account. This constitutional right to have access to information and to the protection of personal information is given further articulation in sections 12-14 of the NHA where it is stated that all information must remain confidential and no information may be disclosed unless there is consent in writing, non-disclosure will result in a serious threat to public health or a court order requires disclosure. There is currently a Bill on the Protection of Information before Parliament and this legislation intends to balance the rights of access to, and protection of, information and as such is controversial.

Chapter 8 of the National Health Act of 2003 deals with the control of the use of blood products, tissue, and gametes and zygotes in humans and prevents the production of reproductive cloning of human beings. A person may not, in terms of this chapter, manipulate any genetic material of human gametes, zygotes or embryos. However, the Minister may permit, on written application, research on stem cells and zygotes that are not more than 14 days old. Some regulations in terms of this chapter have been published for comment but most sections of this chapter have not yet been promulgated and therefore the Human Tissues Act 65 of 1983 has not yet been repealed.

As mentioned above, the Choice of Termination of Pregnancy Act of 1996 provides the conditions and procedures to be followed for a person to obtain a termination of pregnancy. The Act provides that a woman may obtain a termination upon request in the first twelve weeks and thereafter, in consultation with a medical practitioner, where the health of the mother or the fetus may be at risk. Where the fetus is at risk, from 13-20 weeks there must be a substantial risk that the fetus would suffer from a severe physical or mental abnormality and after twenty weeks it should be shown that the continued pregnancy may result in a severe malformation of the fetus.

In addition to the legislation set out above there are Medical Research Council Guidelines (MRC, 2002a,b) for ethical research, including testing for fetal selection, and for confidentiality and privacy.

#### **6.4.2. Cultural and social issues pertaining to medical genetic services in South Africa**

There are a several specific cultural and social issues relating to genetic services in South Africa. These have been documented in an article by Kromberg and Jenkins (1997). The first issue is associated with systems of thought, prevailing fatalistic attitudes, communal decision-making, the indistinct line between life and death, and belief in the power of ancestral spirits. The second

concerns the beliefs and myths about the causes of genetic disorders. The third issue is the tendency, in the majority of people, to consult both Western medical health professionals and traditional healers. The fourth concerns the custom of consanguineous marriage, common practices and taboos, while the fifth issue is about language and communication, since in most local languages there are no terms for words such as genes and chromosomes. All these issues can affect the ways in which genetic services are delivered and received, the communication and interactions in genetic counselling sessions and the choices people make.

#### **6.4.3. Assessment of the attention given to medical genetic services by the national government/policy makers as compared to other health issues**

The national policy regarding medical genetic services was set out in the National Policy Guidelines (Department of Health, 2001). The policy was developed before the impact of the HIV/AIDS pandemic became apparent. As noted above, that and other problems including the increasing incidence of TB and difficulties in health service delivery, has resulted in medical genetic services having lesser priority than in the 1990s. It is hoped that the situation will improve consequent on the WHO recommendation this year that services for the care and prevention of congenital defects in developing countries should be prioritised (WHO, 2010b). However, given current circumstances, delineated in this document, it can be expected that improvement of medical genetic services will be slow in the short term.

## **PART 7: RESEARCH PRIORITIES IN GENETICS/GENOMICS**

### **7.1. Current national policies for funding research in genetics/genomics, priorities for funding and funding mechanisms**

There are no policies specifically covering funding for research in human or medical genetics/genomics. However, the government does fund some medical research, including research in the field of human genetics/genomics, through two bodies, the SA Medical Research Council (SAMRC) and the National Research Foundation (NRF). Through the NRF the National Department of Science and Technology (NDST) has a programme that financially augments certain research grants and this has aided medical genetics/genomics research. The NDST, through its biotechnology strategy has funded two Biotechnology Regional Innovation Centres (BRICS). These are high throughput genomics laboratories, namely the Life Lab at the University of KwaZulu Natal and Centre for Proteomics and Genomic Research at the University of Cape Town, in the Western Cape Province. In the former laboratory work is mainly on infectious diseases and in the latter contract research in the field of human genetics/genomics is undertaken. The NDST also funded the National Bioinformatics Network and, recently, has provided funding for 2010 and 2011 for Phase 1, the planning phase, of a National Human Genome Initiative.

The National Health Laboratory Service (NHLS) Research Trust funds research in Pathology, including medical genetics. Staff across of the NHLS received 367 research grants during the 2008-2009 year, valued at R124 million, with 21million coming from the NHLS Research Trust (NHLS Annual Report, 2008-2009). The amount awarded specifically for human genetics research is not available. However, projects in human genetics receive funding (on a competitive basis), every year, as well as some long-term funding.

## **7.2. Research funding by private parties**

Research funding is received from various private sources for short term projects (generally) on an ad hoc or regular basis. The Universities screen and fund acceptable research projects for their own staff and students. Further, several private donor research foundations (eg Richard Ward Foundation at the University of the Witwatersrand) held by universities have funded genetics projects from time to time. Some of the funding for human genetics projects at the University of Cape Town comes from genetic support groups, such as Retina South Africa who have funded research on inherited retinal disease, over many years, and the Muscular Dystrophy Foundation who fund various research projects in their field. Also, the Cancer Association of South Africa (CANSA) funds research on cancer at several universities.

## **7.3. Known co-operations with international funding agencies**

South African researchers in human genetics collaborate with international research teams and have received international funding from bodies such as the National Institute of Health (NIH, USA), Fogarty Foundation, WHO, Wellcome Trust, US Aid, Center for Disease Control (CDC), the March of Dimes (a USA non-governmental organisation), and the European Union through the Platform Frameworks. Also, the Genographic Project of the National Geographic Society has supported (2006-present) population genetic studies in the Human Genome Diversity and Disease Research Unit, at the University of the Witwatersrand.

## **7.4. Current centres of excellence in genetics/genomics research**

There are no centres of excellence in the field of Human Genetics at present. However, there are two prestigious MRC Units receiving 5 year funding grants (which can be renewed): the MRC Research Unit for Medical Genetics at the University of Cape Town and the Human Genome Diversity and Disease Unit at the University of the Witwatersrand.

## **7.5. Regulation of translation of new genetic tests into health care practice**

The translation of new genetic tests into health care practice is not regulated, at present.

# **PART 8: PATIENT ORGANISATIONS AND PUBLIC EDUCATION IN GENETICS**

## **8.1. The availability and structure of parent/patient organisations, including funding, objectives and provision of services.**

Parent/patient organisations and support groups for people with many different genetic disorders are available in South Africa. The Southern African Inherited Disorders Association (SAIDA) is an umbrella body for such groups. SAIDA is located in Johannesburg and is hosted by the Division of Human Genetics, University of the Witwatersrand. The Association and the groups gathered under

its umbrella are structured as non-governmental organisations and generally have an elected committee and members, consisting mainly of parents, family members, affected individuals and interested people. Some groups (eg. Cystic Fibrosis) also have a medical advisory board and a few have a fund-raiser. Most groups are small, with a small membership and budget, and a few essential activities.

The objectives of most of the support groups are very similar and, generally they aim to: raise awareness about the condition in the community; offer support, advice and literature to affected individuals and their families; support and stimulate relevant research (mostly in academic centres, eg. Retina SA) where possible; train support parents; gain support from interested medical experts and make appropriate referrals.

## **8.2. Parent/patient organisations for genetic disorders in South Africa**

Parent/patient groups for a number of the common genetic conditions are established in South Africa. Many were started in association with and with encouragement from SAIDA. This Association was initiated by a medical geneticist and genetic counsellor in 1975, in response to the request of a couple with a child with Tay Sachs disease. There are currently 25 groups who are members of SAIDA and a further 24 groups who have been members in the past. Most groups operate from the big cities and offer country-wide services to anyone affected by or interested in their specific disorder.

## **8.3. The main activities of these organisations**

The activities of the groups include:

### **8.3.1. Policy/lobbying/advocacy activities**

Some policy and lobbying activities take place, such as making contact with the Department of Health Genetic Services division to print brochures on specific disorders (eg Turners syndrome), or the Department of Education regarding inclusion and mainstreaming policies (eg. for children with Down syndrome), or the Department of Labour regarding employment for disabled people. Advocacy activities also occur (eg, self-advocacy courses for adults with Down syndrome), and empowerment activities (eg. affected individuals seeking free provision of sun-barrier cream for people with albinism at government hospitals).

### **8.3.2. Level and sources of funding**

Fund raising is generally undertaken in a limited way, unless a fund-raiser is employed or a member of the group undertakes this responsibility systematically (eg. Retina SA, who have a large budget and support research). Most support groups receive very little or no regular government funding (with the exception of the Cleft Pals group that has some Government funding) and fund themselves through membership fees and donations. Where fund-raising is undertaken, most funding comes from private businesses, corporate and individual donors, and in a few cases from international bodies (eg. the Haemophilia Foundation receives some support from the World Federation for Haemophilia) and grants from the national lottery (Lotto).

### **8.3.3. Services provided to individuals/families**

The services offered by the groups are generally appropriate to their objectives and include: providing literature on the condition and education for group members and the public; organising

support group meetings, providing psychosocial support, telephone consultations and an informative web-site (in some cases); raising funds for equipment to improve the quality of life of their members (eg. The Muscular Dystrophy Foundation SA provides wheelchairs for needy members); networking with relevant international organisations.

#### **8.3.4. Relationship with clinical genetics community/health service**

Many groups have communications with SAIDA and the SAIDA committee has office-bearers from the human genetics community. Clinical geneticists and genetic counsellors also keep in contact with the groups, leaflets on the conditions are often produced in collaboration with the support group, and referrals are made to and from group members. So the relationship between the groups and the genetics professionals is generally good and that between the groups and the health department appears to be fairly good, particularly when a special clinic is dedicated to management of a common condition in a tertiary public hospital setting (eg. the cystic fibrosis and haemophilia clinics).

#### **8.3.5. Volunteer involvement**

Most of the smaller groups function only with volunteer staff (mostly parents of affected children and their relatives), and they try to organise for a committee member who will do the secretarial work, a volunteer accountant/book keeper to act as treasurer and an auditor to audit the books annually, gratis.

#### **8.3.6. Number and categories of staff employed**

Some of the larger groups raise funds to support paid staff, particularly secretaries. For example Retina SA has 10 paid staff, the Down's association has two paid staff, including a secretary, and the Cystic Fibrosis group funds three staff members. The umbrella group, SAIDA, also funds a part-time secretary.

### **8.4. Availability of primary prevention of congenital/genetic disorders via concerted public and professional education programmes.**

Due to concerted lobbying, South Africa has had fortification of basic foods, such as bread and maize meal, for some years, and as a result the prevalence of neural tube defects has fallen by 30% (Sayed et al, 2008). Also, salt has been iodised for many years preventing most cases of postnatal iodine deficiency disorders and goiter (such disorders were, however, never very common in South Africa).

Public and professional education, covering recognition and prevention of congenital disorders, takes place at many levels. Health professionals, including nurses, receive some basic teaching in medical genetics during their degree and diploma studies, as well as in-service training when they are employed. Lay public groups, such as rotary clubs and women's groups, have talks from human genetics professionals when they request them. Genetic counsellors give educational lectures to a number of professional and lay groups (Kromberg et al, 2009) and compile leaflets for distribution on a number of common disorders (eg. Genetics of breast cancer), as well as on prenatal genetic diagnosis and genetic counselling services. SAIDA puts out an annual educational newsletter, which is distributed to many professional and lay groups.

Furthermore, SAIDA, with support funding from the Human Genetics sub-directorate, Department of Health, and more recently the national lottery, offers a short-term course on basic genetics for primary healthcare workers (MGEP). The course is directed at doctors and nurses working in primary healthcare clinics and covers aspects of basic genetics, including the identification, basic treatment and counselling (particularly breaking bad news) for affected children and their parents. The course consists of a combination of contact days, with lectures and workshops, as well as self-directed learning by using a provided text-book. In this manner, it is hoped that more patients and their families are reached and that earlier diagnoses can be made, as well as earlier intervention and care implemented. Nurses and doctors alike are participating in these courses, and it is hoped that a result will be more accurate reporting of birth defects, which will add to the epidemiological data for the country.

One day workshops are held, occasionally, for general practitioners in Johannesburg, and in some other urban areas of the country. However, due to the inadequate number of medical geneticists and genetic counsellors working in the country, availability of skilled human resources for the expansion of community education programmes remains a challenge.

## CONCLUSION

South Africa is a country in transition. However, the proportion of the global burden of disease borne by South Africa with a population of only 48 million is disproportionately high. The total disability adjusted life years for high burden diseases in South Africa is almost equivalent to that of Bangladesh, which has a population three times as large and living in much worse poverty (Lancet, paper 6, 2009). One of the greatest challenges facing post apartheid South Africa is the control of the concomitant HIV and TB epidemics. HIV is continuing to spread relentlessly and TB has been declared a national emergency. In 2007 South Africa, with 0.7% of the world's population, had 17% of the global burden of HIV infection, and one of the world's worst TB epidemics, compounded by rising drug resistance and HIV co-infection (Lancet, paper 3 abstract, 2009). South Africa is currently underperforming in its efforts to control HIV. The country has the resources and the capability to rise to these challenges, but has not been able to do deliver on the four priorities listed in the Strategic Plan for South Africa for HIV/AIDS (Lancet, paper 3, 2009). Since this is the background against which the medical genetics services are, presently, being developed and delivered, it is not surprising that the recommendations in the Policy Guidelines for the Management and prevention of genetic disorders (Department of Health, 2001, see Appendix D) have also not been met.

Nevertheless, a medical genetics service was developed in the country prior to the onset of the AIDS and TB epidemics. At present, this service provides an excellent base on which a more comprehensive service can be developed in the future. There are four academic departments of human genetics in four of the major universities situated in three provinces, which have already set up clinical services, compatible with any in developed countries, as well as laboratory services, which are capable of offering genetic testing services to the rest of Africa. They have also developed a research capacity that is involved in investigating local genetic disorders on many different levels. Two of these universities, in collaboration with the NHLS, have also established training for all the categories of expert staff required to run a sophisticated genetic service. When the time is right, and the political will is favourable, these services, though presently limited, could be expanded to meet the genetic health needs of the whole country.

Although expansion is difficult in the current circumstances, members of the South African medical genetics community are networking with interested people in the rest of Africa and, in 2011, the first combined congress will be organized by SA Society of Human Genetics (SASHG), in conjunction with the African Society of Human Genetics (AfrSHG), and held in Cape Town. At this meeting there will be international experts, as well as those from Africa, networking and sharing their needs, insights and knowledge.

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## REFERENCES

Ballo R, Viljoen D, Beighton P (1994). Duchenne and Becker muscular dystrophy prevalence in South Africa and molecular findings in 128 persons affected. *S Afr Med J*; 84(8 Pt 1):494-7.

Baumiller RC, Cunningham G, Fisher N, Fox L, Henderson R, Lebel R, McGrath G, Pelias MZ, Porter I, Seydel F, Wilson NR (1996). Code of Ethical Principles for Genetics Professionals. *Am J Med Genet*; 65: 177-183.

Bee J (2005). The influence of HIV status on women of advanced maternal age presenting for genetic counselling. MSc Research Report. Johannesburg, University of the Witwatersrand.

Beighton P, Spranger J, Versveld G (1983). Skeletal complications in osteogenesis imperfecta: a review of 153 South African patients. *S Afr Med J*; 64: 565-568

Benatar S. (2004). Health care reform and the crisis of HIV and AIDS in South Africa. *New England Journal of Medicine*. 351 (1): 81–92.

Central Intelligence Agency (2010). World Fact Book. Available from: <https://www.cia.gov/library/publications/the-world-factbook/>

Choice on Termination of Pregnancy Act 92 of 1996

Chopra M, Daviaud E, Pattinson R, Fonn S, Lawn JE (2009). Health in South Africa. Part Two: Saving the lives of South Africa's mothers, babies, and children: can the health system deliver? *Lancet*; 374: 835-846.

Christianson AL (1996). Down syndrome in sub-Saharan Africa. *J Med Genet*; 33: 89-92.

Christianson AL (2000). Community Genetics in South Africa. *Community Genetics*; 3: 128-131

Constitution of the Republic of South Africa Act 108 of 1996

Convention on Human Rights and Biomedicine of the Council of Europe (1997).

Coovadia H, Jewkes R, Barron P, Sanders D, McIntyre D (2009). Health in South Africa, Part One: The health and health systems of South Africa: historical roots of current public health challenges. *Lancet*; 374: 817-834.

Delport SD, Rothberg AD (1992). Congenital syphilis – now a notifiable disease. *S Afr Med J*; 81 (3): 288 - 289

Delport R (2009). Familial hypercholesterolaemia in South Africans: tracking findings and developments over time - with reference to: prevalence of hypercholesterolaemia in young Afrikaners with myocardial infarction. *Ischaemic heart disease risk factors; Cardiovasc J Afr.* 20 (1): 18-22.

Department of Health, South Africa (2001). Policy Guidelines for the management and prevention of Genetic Disorders, Birth Defects and Disabilities. Department of Health, Pretoria, South Africa.

Department of Health, South Africa (1998). South Africa Demographic and Health Survey. Chapter 6: Infant and Child Mortality. Available from: <http://www.doh.gov.za/facts/1998/sadhs98/chapter6.pdf>

Department of Health, South Africa (2007). Diagnostic Genetic Tests. Available from: [www.doh.gov.za/docs/index.html](http://www.doh.gov.za/docs/index.html)

Econex (2010). Financial Implications of a National Health Insurance Plan for South Africa. Available from: [www.econex.co.za/](http://www.econex.co.za/)

Goldman A, Krause A, Jenkins T (1997). Fragile X syndrome occurs in the South African black population. *S Afr Med J*; 87(4):418-20.

Health Professionals Council of South Africa (2009). Statistics. Available from: <http://www.hpcsa.co.za/statistics.og.2009>

Health Professionals Council of South Africa (2010). Professional boards. Medical technology. Available from: [http://www.hpcsa.co.za/board\\_medtech\\_education.php](http://www.hpcsa.co.za/board_medtech_education.php)

Health Systems Trust (2008). South African Health Report 2008. Available from: <http://www.hst.org.za/generic/29>

Hift RJ, Meissner PN. (2005). An analysis of 112 acute porphyric attacks in Cape Town, South Africa: Evidence that acute intermittent porphyria and variegate porphyria differ in susceptibility and severity. *Medicine (Baltimore)*; 84: 48-60.

Hogan MC, Foreman KJ, Naghavi M, Ahn SY, Wang M, Makela SM, Lopez AD, Lozano R, Murray CJL (2010). Maternal mortality for 181 countries, 1980-2008: a systematic analysis of progress towards Millenium Development Goal 5. *Lancet*; 375: 1609-1623.

Howson CP, Christianson AL, Modell B (2008). Disease Control Priorities Project. Controlling Birth Defects: Reducing the Hidden Toll of Dying and Disabled Children in Low Income Countries. Available from: [http://www.dcp2.org/file/230/dcpp-twpcongenitaldefects\\_web.pdf](http://www.dcp2.org/file/230/dcpp-twpcongenitaldefects_web.pdf)

Human Development Report (2009), Overcoming barriers: Human mobility and development. Available from: <http://hdr.undp.org/en/reports/global/hd2009/>

Human Tissues Act 65 of 1983

Hyder AA, Wali SA, McGuckin J (2003). The burden of disease from neonatal mortality: a review of South Asia and Sub-Saharan Africa. *Br J. Obstet Gynaecol*; 110: 894-901.

International Clearinghouse for Birth Defects (2005). Programme Descriptions. Available online at: <http://www.icbdsr.org/page.asp?p=12919&l=1#SouthAfrica>

Jenkins T (1990). Medical Genetics in South Africa. *J Med Genet*; 27: 760 – 779

Jenkins T, Lane AB, Kromberg JGR (1977). Tay-Sachs disease: screening and prevention in South Africa. *S Afr Med J*; 51, 95-98.

Kromberg JGR, Jenkins T (1982a). Prevalence of albinism in the South African negro. *S Afr Med J*; 61: 383-6.

Kromberg JGR, Jenkins T (1982b). Common birth defects in South African blacks. *S Afr Med J*; 62: 599-602

Kromberg JGR, Jenkins T (1997). Cultural Influences on the Perception of Genetic Disorders in the Black Population of Southern Africa. In Clarke A, Parsons E (eds). *Culture, Kinship and Genes*. London, Macmillan, 147-157.

Kromberg JGR, Bernstein R, Jacobson M, Rosendorff J, Jenkins T. (1989) A decade of mid-trimester amniocentesis in Johannesburg: prenatal diagnosis, problems and counselling. *S Afr Med J*; 76, 344-349

Kromberg JGR, Krause A, Wessels T (2009). Roles of Genetic Counsellors in South Africa. SA Society for Human Genetics 13th congress, 5-8 April 2009, Stellenbosch, South Africa. Book of Abstracts p36.

Labrum R, Rodda J, Krause A. (2007). The molecular basis of spinal muscular atrophy (SMA) in South African black patients. *Neuromuscul Disord*; 17 (9-10): 684-92.

Lancet Series (2009). Health in South Africa 1-6. Published online at <http://www.thelancet.com> on 15 August 2009

- Landman JP, Bhorat H, van der Berg S, van Aardt C (2003). Breaking the grip of poverty and inequality in South Africa: 2004 – 2014. Current trends, issues and future policy options. Available from: [www.ukzn.ac.za/ccs/files/P661-Povertyreport3b.pdf](http://www.ukzn.ac.za/ccs/files/P661-Povertyreport3b.pdf)
- Lombard EH, Kromberg JGR, Thomson PD, Milner LS, van Biljon I, Jenkins T. (1989). Autosomal recessive polycystic kidney disease. Evidence for high frequency of the gene in the Afrikaans-speaking population. *S Afr Med J.* 76(7):321-3.
- Manga N, Jenkins T, Jackson H, Whittaker DA, Lane AB (1999). The molecular basis of transferase galactosaemia in South African negroids. *J Inher Metab Dis;* 22, 37-42
- March of Dimes (2006). Global Report on Births Defects. Available online: [http://www.marchofdimes.com/professionals/871\\_18587.asp](http://www.marchofdimes.com/professionals/871_18587.asp)
- May PA, Gossage JP, Marais A-S, Hendricks LS, Snell CL, Tabachnick BG, Stellavato C, Buckley DG, Brooke LE, Viljoen DL (2008). Maternal Risk Factors for Fetal Alcohol Syndrome and Partial Fetal Alcohol Syndrome in South Africa: A Third Study. *Alcoholism: Clinical and Experimental Research;* 32 (5): 738-753.
- Medical Research Council, South Africa (2002a). Guidelines on Ethics for Medical Research: General Principles. MRC South Africa, Tygerberg
- Medical Research Council, South Africa (2002b). Guidelines on Ethics for Medical Research: Reproductive Biology and Genetic Research. MRC, South Africa, Tygerberg.
- Morgan NV, Essop F, Demuth I, de Ravel T, Jansen S, Tischkowitz M, Lewis CM, Wainwright L, Poole J, Joenje H, Digweed M, Krause A, Mathew CG (2005). A common Fanconi anemia mutation in black populations of Sub-Saharan Africa. *Blood;* 105 (9): 3542-3544
- Morar B, Lane AB (1996). The molecular characterisation of Gaucher disease in South Africa. *Clin Genet;* 50: 78-84.
- Nannan N, Timaeus IM, Laubscher R, Bradshaw D (2007). Levels and differentials in childhood mortality in South Africa, 1977 – 1998. *J. Biosoc. Sci;* 39. 613-632.
- National Cancer Registry South Africa (2001). Incidence of Histologically Diagnosed Cancers in South Africa. Available from: <http://www.nioh.ac.za/publications.php?main=list&item=6&back=1>
- National Health Act 61 of 2003
- National Health Laboratory Service (2009). Annual Report 2008-2009. Johannesburg, NHLS.
- Opt'Hof J (1985). Genetic Services for Congenital and Hereditary Disorders. Pretoria, Eng Enterprises.
- Padoa C, Goldman A, Jenkins T, Ramsay M (1999). Cystic Fibrosis carrier frequencies in populations of African origin. *J. Med. Genet;* 36 :41-44.

Parrott N (1997). A study of the three most common chromosome trisomies, 21 (Down syndrome), 18 (Edwards syndrome) and 13 (Patau syndrome). MSc Research Report, University of the Witwatersrand, Johannesburg.

Patrick M, Stephen C (2007). Saving children 2005: a survey of child healthcare in South Africa. Pretoria: MRC Unit for Maternal and Infant Health Care Strategies.

Promotion of Access to Information Act 2 of 2000.

Robertson H-L, Steyn NP, Venter Pa, Christianson AL (1997). Neural tube defects and folic acid- a South African perspective. *S Afr Med J*; 87; 928-931.

Rosendorff J, Bernstein R, Macdougall L, Jenkins T, Opitz JM, Reynolds JF (1987). Fanconi Anemia: another disease of unusually high prevalence in the Afrikaans population of South Africa. *Am J Med Genet*; 27 (4): 793-797.

Sayed A-R, Bourne D, Pattinson R, Nixon J, Henderson B (2008). Decline in the prevalence of neural tube defects following folic acid fortification and its cost-benefit in South Africa. *Birth Defects Research (Part A)*; 82: 211-216.

Schapera I (1966). Married life in an African tribe. London, Faber and Faber.

Sellers S, Groeneveldt L, Beighton P (1976). Aetiology of deafness in white children in the Cape. *S Afr. Med J*; 50: 1193-1197.

South African Institute of Race Relations (2009). South African Survey 2008/2009: Demographics. Geographical distribution and urbanisation. p35-39. Available from: <http://www.sairr.org.za>.

Statistics South Africa (2009). Mid-year population estimates. Mortality, expectation of life at birth, and fertility. p6-7. Available from: <http://www.statssa.gov.za/publications/P0302/P03022009.pdf>

United Nations Children's Fund: UNICEF (2000). The State of the Nations Children. Statistical Tables: Demographic indicators. Available from: <http://www.unicef.org/sowc00/stat7.htm>

United Nations (2007a). 10. Live-births by age of mother and sex of child and live-birth rates by age of mother: latest available year, 1998-2007.

Available from: <http://unstats.un.org/unsd/demographic/products/dyb/dyb2007.htm>

United Nations (2007b). Handbook of the International Comparison Programme.

Available from: [http://unstats.un.org/unsd/methods/icp/ipc7\\_hm.htm](http://unstats.un.org/unsd/methods/icp/ipc7_hm.htm)

Warby SC, Graham RK and Hayden MR (2007) Huntington Disease. Available from: <http://www.genereviews.org/servlet/access?db=geneclinics&site=gt&id=8888891&key=bfdRsMPZOTngl&gry=&fcn=y&fw=y7PM&filename=/profiles/huntington/index.html>

World Bank (2010a). Country Classification Table. Available from: <http://data.worldbank.org/country/south-africa>

World Bank (2010b). World Development Indicators Database.

Available from: [http://siteresources.worldbank.org/DATASTATISTICS/Resources/GDP\\_PPP.pdf](http://siteresources.worldbank.org/DATASTATISTICS/Resources/GDP_PPP.pdf)

World Health Organization (2006) Management of Birth Defects and Haemoglobin Disorders: Report of a joint WHO-March of Dimes meeting, Geneva, Switzerland, 17-19 May 2006. Available from: <http://www.who.int/genomics/publications/WHO-MODreport-final.pdf>

World Health Organization (2007). Glossary English.

Available from: <http://www.who.int/nha/Glossary%20English.pdf>

World Health Organization (2009a). World Health Statistics 2009. Part 4: Mortality and burden of disease. p35-45. Available from: <http://www.who.int/whosis/whostat/2009/en/index.html>

World Health Organization (2009b). World Health Statistics 2009. Part 7: Health Expenditure. p107-117. Available from: <http://www.who.int/whosis/whostat/2009/en/index.html>

World Health Organization. (2010a). Genes and Human Disease: Monogenic diseases. Map of global distribution of haemoglobin disorders.

Available from: <http://www.who.int/genomics/public/Maphaemoglobin.pdf>

World Health Organization (2010b). Sixty-Third World Health Assembly. Provisional agenda item 11.7. April 2010. Available from: [http://apps.who.int/gb/ebwha/pdf\\_files/WHA63/A63\\_10-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_10-en.pdf)