CLINICAL GUIDELINES FOR GENETICS SERVICES

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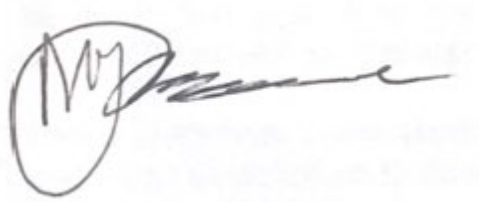
Foreword

In order to achieve the 2030 Sustainable Development Goals (SDGs), South Africa aims to reduce institutional neonatal mortality and stillbirths by 50 per cent by 2030 (as stated in the Maternal, Perinatal and Neonatal Health Policy). In alignment with and to achieve this, the country needs to expand and strengthen genetic service interventions to include the prevention, early identification, early diagnosis, referral, treatment, care, management and notification of congenital disorders. This involves strengthening access to genetic services at all levels of care.

Congenital disorders are one of the top five contributors to neonatal mortality in South Africa. Through the implementation of the ministerial committees' recommendations, the country has put in place interventions to reduce the institutional neonatal death rate from 12,7 per 1 000 live births in 2016 to the current level of 12 per 1 000 live births which have remained stagnant for the past three years (District Health Information System). Further, these interventions have resulted in the reduction of the infant mortality rate from 29 (2014) to 25 (2018) per 1 000 live births and children-under-five mortality rate from 42 (2014) to 34 (2018) per 1 000 live births respectively (Rapid Mortality Survey, 2018).

Currently, genetic services are not offered comprehensively or equitably across all of South Africa's nine provinces. To address this, the National Clinical Guidelines for Genetic Services detail standards to guide the establishment of regional and specialised genetic services units to improve access.

The challenges with the prevention and management of congenital disorders are that they are multifaceted and are not age specific as some may appear later in life. Therefore, the approach of this guideline is to detail standards and considerations according to the life cycle and across the continuum of care. Due to continuous technological advancements and developments in genetics and genomics, the guidelines further highlight current and future interventions aimed at improving service delivery. Implementation of this guidelines by healthcare providers at all levels of care will ensure that patients and their families are offered comprehensive, integrated, patient-centred genetic services.



Dr MJ Phaahla, MP
Minister of Health
Date: 02/11/2021

Preamble

Genetics services continue to evolve with improved knowledge and advancements in technology and genetic testing. To keep up with trends and improvements, the national Department of Health set out to review the Policy Guidelines for the Management and Prevention of Genetic Disorders, Birth Defects and Disabilities (2001). The current status of maternal, neonatal, child and reproductive health in South Africa motivated for a paradigm shift in the provision of genetic services due to their significant impact on outcomes. To optimise this impact, genetic services must be integrated into maternal, neonatal, child and reproductive health and other public health programmes across the continuum and levels of care, ranging from community to tertiary and quaternary services.

The primary focus of the guidelines are to promote the prevention, screening, diagnosis (clinical and laboratory) and management of congenital disorders, including genetic counselling and palliative care services where necessary. The secondary focus is the reduction of morbidity and mortality due to congenital disorders and improving the quality of life of affected individuals. Patient-centred care is a core principle of service provision in these guidelines, ensuring that care is accessible, coordinated and integrated, respects patients' values, preferences and expressed needs, offers emotional support, involves family and friends and offers continuity and transition. Care is further expanded to include the patient's experience of care including informed decision making, consent and confidentiality.

The best available evidence was used to support the development of these guidelines despite the paucity of data and the lack of comprehensive genetic services' guidelines globally and locally for benchmarking.

The guidelines are aimed at all healthcare workers involved in the planning, management, delivery, monitoring and evaluation, and research of genetic services. Genetic services cuts across all health programmes, which involves healthcare services provided at primary healthcare facilities and hospitals. This includes healthcare workers in areas such as reproductive and sexual health; maternal and neonatal health; child and school health; adolescent and youth health; mental health; communicable and non-communicable diseases; including all services provided by allied health workers. The guidelines are also aimed at laboratories, academics, researchers, civil society, and communities with an interest in genetic services.

These guidelines were developed in extensive consultation with various stakeholders. A core writing team was established to develop the initial draft which was shared with stakeholders (in person and electronically) for inputs, including medical geneticists and genetic counsellors, laboratories, obstetricians and gynaecologists, neonatologists, paediatricians, academics and civil society.

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Definition of terms

Advocacy: A combination of individual and social actions designed to gain political commitment, policy support, social acceptance and systems support for a particular health goal or programme (WHO, 2000). This may involve speaking up for those without a voice and providing support.

Ante-natal care (pre-natal care): Care from healthcare professionals throughout pregnancy, from confirmation of pregnancy through to birth. It includes regular check-ups to prevent, identify and treat pregnancy complications, promote healthy lifestyles and to optimise the health of the mother and baby.

Autosomal recessive: Inheritance is a way a genetic trait or condition can be passed down from parent to child. A genetic condition may occur when the child inherits one copy of a mutated/changed gene from each parent. The parents of a child with autosomal recessive condition usually do not have the condition/are unaffected. The unaffected parents are called carriers because they each carry one copy of the mutated gene and can pass it to their children. In a carrier, the effect of the abnormal recessive gene is usually not seen, and the individual appears normal.

Behavioural change: Efforts put in place to change people's personal habits and attitudes, to prevent disease and improve individual and population health. Behaviour change in public health is also known as social and behaviour change communication.

Carrier screening: Is a type of genetic testing performed on people who display no symptoms of congenital disorders, but may be at risk for passing on a congenital disorder to their children or are at risk of developing the disease later in their life. A carrier for a genetic congenital disorder has inherited one normal and one abnormal allele for a gene associated with the disorder. A child must inherit two abnormal alleles in order for symptoms to appear.

Civil society: A range of formal and informal organisations that are outside the state and the marketplace – non-governmental organisations (NGOs) and/or non-profit organisations (NPOs), including social movements, volunteer organisations, mass-based membership organisations, faith-based groups, and community-based organisations, as well as communities and citizens acting individually and collectively.

Chromosomal disorders/abnormalities: Chromosomal disorders (or abnormalities) are due to errors in cell division occurring before conception that result in a gain or loss of genetic material, either through the addition or loss of a whole chromosome (trisomy or monosomy) or part of a chromosome (duplication or deletion).

Communication: The process of sending and receiving messages through verbal or non-verbal means, including speech, or oral communication; writing and graphical representations (such as infographics, maps, and charts); and signs, signals, and behaviour.

Complex disorders: Multifactorial in aetiology, resulting from a genetic predisposition interacting with environmental factors. They usually manifest later in life but can be seen in childhood. Common complex disorders are systematic and involve different organs and systems e.g. cancer, cardiovascular disease, diabetes, hypertension, mental disorders and stroke.

Congenital disorders (also known as birth defects): Any potential pathological condition present at or before birth, including all disorders caused by environmental, teratogens, genetic or unknown factors, whether they are evident at birth or manifest later in life (e.g. Huntington's Disease, Lynch syndrome). Serious congenital disorders can cause death or disability in the absence of care.

Congenital anomalies: Macroscopic morphological (structural) anomalies present at birth. Many are multifactorial in origin with genetic and environmental risk factors. Congenital anomalies include a sub-set of congenital disorders/birth defects only and exclude functional birth defects including non-syndromic, congenital disability (intellectual, physical, visual, and auditory disability and epilepsy), common single gene disorders (e.g. haemoglobin disorders, G6PD deficiency, cystic fibrosis, spinal muscular atrophy and inborn errors of albinism), and many teratogen induced birth defects (congenital syphilis, congenital rubella syndrome and iodine deficiency.

Consanguinity: Refers to a reproductive union between two related individuals (second cousins or closer).

End-of-life care: End-of-life or terminal care addresses the needs of the patient and family when the patient is dying. It is the last phase of palliative care and is usually given during the last weeks or days of life focusing on symptom management, comfort and dignity. The aim is not to prolong life but to help achieve a "good death".

Epidemiological transition: The change in population health statistics and pattern of diseases of a country or region, consequent on change in socioeconomic, education, infrastructure and healthcare development.

Family: A social unit including one or more adults (usually one or more parents), children, extended family considered as a group whether dwelling together or not. They may be related by birth, marriage, adoption or via guardianship.

Family history: Screening health information about a person and his or her close relatives obtained by asking questions about three generations of relatives (children, siblings, parents, aunts and uncles, nieces and nephews, grandparents, and cousins). Taking a family history and drawing a family tree helps to identify those with an increased risk of having a child with a congenital disorder. A positive family history increases the risk of an inherited congenital disorder.

Genetic counselling: A professional interaction (or conversation) between a healthcare provider with specialised knowledge of genetics and an individual patient or family. This may include determining whether a condition may be genetic and estimates the risk of recurrence for subsequent children or other relatives/family members being affected and interpreting genetic tests that may help estimate the associated risk. The aim is to share relevant information to address concerns of the patient/family, inform reproductive choices and provide psychological counselling to help families adapt to their condition or predicted risk.

Genetic counsellor: A registered healthcare provider who provides genetic counselling, including risk assessment, education and support for individuals and families at risk of, or diagnosed with, a variety of genetic conditions and other congenital disorders. Genetic counsellors also interpret genetic testing, provide supportive counselling, and serve as patient advocates.

Genetic disorder: It is a disorder that is caused by one or more abnormalities in a person's deoxyribonucleic acid (DNA). It can be caused by a change or mutation in a single gene.

Genetic disposition or susceptibility: An individual who may not be born with a congenital disorder, but may be at high risk of developing a particular disease due to the presence of one or more gene mutations, and/or a combination of alleles and environmental triggers.

Genetic risk: The chance of a person inheriting a specific genetic disease or condition.

Genetic services: Interventions to prevent, detect and care for those affected by or at risk of a congenital disorder. Genetic services aim to reduce the suffering of those affected by offering care to enable them to live and reproduce as normally as possible and to improve overall health by preventing congenital disorders.

Genomics: The study of the organisation, structure and functioning of an organism's genome (all the genetic material in an organism).

Genomic medicine: An emerging medical discipline that uses an individual's genomic information as part of their clinical care (e.g. for diagnostic or therapeutic decision-making) and to measure health outcomes.

Healthcare provider (HCP): People "providing health services in terms of any law", including the National Health Act, 2003 (Act 61 of 2003); Allied Health Professions Act, 1982 (Act 63 of 1982); the Health Professions Act, 1974 (Act 56 of 1974), the Nursing Act, 1978 (Act 50 of 1978); the Pharmacy Act, 1974 (Act 53 of 1974);, and the Dental Technicians Act, 1979 (Act 19 of 1979).

Major congenital disorders (also known as serious birth defects): Are structural changes in one or more parts of the body, they are present at birth, can have a serious, adverse effect on the health, development or functional ability of the baby. They have significant medical, social or cosmetic consequences for the affected individual and typically require medical intervention. Examples include cleft lip/palate, spina bifida and congenital heart defects.

Malformation: A structural congenital disease which develops during the first trimester and is caused by failure of the embryo to develop normally. Malformations may be caused by chromosomal, single gene, multifactorial factors or teratogens. Malformations may be mild such as an abnormally shaped ear or severe such as a neural tube defect.

Management of disease: This includes diagnosis through appropriate investigations and providing the patient and family with best possible ongoing medical/surgical interventions for the condition, genetic counselling, and psychosocial support.

Medical genetics: A medical speciality applying knowledge of human genetics to health and disease of individuals and communities, including the prevention, diagnosis, counselling, management of genetic, familial, and other congenital disorders in individuals, families and communities.

Medical geneticist: A registered medical practitioner with an appropriate specialist qualification and registration with the Health Professions Council of South Africa (HPCSA) in the speciality of medical genetics. Medical geneticists are trained and expert in genetics, inherited diseases and congenital disorders - and guide the request and interpretation of genetic/other tests and the impact of genetic risks and diagnosis on individuals, families, communities and society. Medical geneticists are part of the multidisciplinary team of professionals that care for patients and families with congenital disorders.

Minor congenital disorder: Structural changes that pose no significant health problem and tend to have limited social or cosmetic consequences for the affected individual. Although minor, they are more prevalent in the population. Examples include single palmar crease and clinodactyly.

Multi-disciplinary team: A group of healthcare providers who are members of different disciplines, who oversee and ensure coordinated care of patients.

Multifactorial inheritance: An inherited trait or disease that is caused by interaction of genes with each other and the environment.

Newborn screening: Population screening for selected inherited (and other) diseases shortly after birth. testing babies in their first days of life for certain disorders and

serious conditions that progress quickly and affect normal development, typically performed before the baby leaves the hospital or within the first few days of life (three to six days).

Non-communicable diseases (NCDs) (also known as chronic diseases): Medical conditions or diseases which, by definition, are non-infectious and cannot be passed from person to person. NDCs tend to be of long duration and progress slowly and may be the result of a combination of genetic, physiological, environmental and behaviours factors.

Obstetric history: Any information that relates to the process of pregnancy, childbirth and post-natal period. This includes any medical conditions that develop due to pregnancy or childbirth.

Palliative care: Is a multidisciplinary approach to the holistic care and support for patients and families facing a life-limiting illness, improving quality of life while maintaining dignity from the time of diagnosis until death. For children, the spectrum of illness includes life limiting illness/conditions which may progress to death or may be severely disabling. Palliative care should be available to all patients as needed from birth or diagnosis until death and should be accessible at all levels of healthcare services. Palliative care cuts across all health programmes.

Perinatal: The period of time from conception up to seven days after birth.

Pre-conception care: Interventions to optimise the health or knowledge of women before conception.

Preimplantation genetic testing: A technique used to identify genetic defects in embryos through in vitro fertilisation (IVF) before pregnancy. Refers to the set of techniques for testing whether embryos (obtained through IVF) have chromosomal abnormalities or single gene disorders, especially where there is a positive family history.

Pre-symptomatic and predictive test: Tests to identify genetic changes that increase a person's risk of developing a genetic disorder or congenital disorder. These may be undertaken before or after symptoms appear.

Proband: A person being studied or reported and the first person in a family to provide information or receive genetic counselling and/or testing for a suspected hereditary risk. A proband may or may not be affected with the congenital disorder in question.

Psychosocial support: Support to address the ongoing emotional, social and spiritual concerns of those affected (directly or indirectly) by congenital disorders. This may include mental health counselling, education, spiritual support, group support,

and other services provided by a range of healthcare providers, allied healthcare providers, clergy and established patient support groups**.**

Rehabilitative care: Care to enable people affected by congenital disorders, including those living with disability, to reach and maintain optimal physical, sensory, intellectual, psychological and/or social function. Rehabilitative care encompasses a wide range of activities to improve the quality of life, including rehabilitative medical care, physical, psychological, speech, and occupational therapy and support services.

Regional Genetic Service Unit: A primary or secondary level facility with adequate staffing and equipment to render the essential packages of services for the prevention identification, early diagnosis and management congenital disorders.

Single gene disorder: Are caused by DNA changes in one particular gene, and often have predictable inheritance patterns.

Social mobilisation: *Advocacy* to influence policy changes and sustain political and financial commitment; two-way *communication* between the care providers and affected people, including communities, to improve knowledge of relevant health policies, programmes and services; and *social mobilisation* to engage society and all allies and partners in the campaign to encourage healthy choices.

Specialised Genetic Service Unit: A tertiary or quaternary level facility that has specialists, equipment and staff to provide specialised packages of genetic services and genetic testing, specialist genetic assessment, confirmation of diagnosis, genetic counseling, management and care, rehabilitation and palliative care, outreach to primary or secondary level of care and to conduct training of medical geneticists and genetic counsellors and other healthcare providers.

Teratogen: Any agent that causes an abnormality following foetal exposure during pregnancy. Teratogens include medicinal and recreational drugs (e.g. alcohol, warfarin), maternal infections (e.g. syphilis, toxoplasma gondii, rubella, cytomegalovirus, herpes simplex, and other infections), maternal illness (e.g. diabetes mellitus) and exposure to physical agents (radiation) and environmental chemicals (e.g. lead, methyl mercury).

X-linked disorders: In X-linked disorders**,** the defective gene causing the trait, or the disorder is located on the X chromosome. Genes on the X chromosome can be recessive or dominant and their expression in females and males is not the same.

Abbreviations and acronyms

AMA	Advanced maternal age
ANC	Ante-natal care
CD	Congenital disorder
CHW	Community health worker
CBO	Church-based organisations
CVS	Chorionic villus sampling
FASD	Foetal alcohol spectrum disorder
FAS	Foetal alcohol syndrome
GP	General practitioner
GC	Genetic counsellor
HCP	Healthcare provider
IEM	Inborn errors of metabolism
IVF	In vitro fertilisation
MDT	Multidisciplinary team
MGEP	Medical Genetic Education Programme
NCD	Non-communicable diseases
NDoH	National Department of Health
NDP	National Development Plan
NHI	National Health Insurance
NT	Nuchal translucency
NGO	Non-governmental organisation
NIPT/(S)	Non-invasive prenatal testing/(screening)
NPO	Non-profit organisation
PGT	Pre-implantation genetic testing
PGT-A	Pre-implantation genetic testing - aneuploid
PGT-M	Pre-implantation genetic testing - monogenic
PHC	Primary healthcare
PPIP	Perinatal Problem Identification Programme
RGSU	Regional Genetics Service Unit
RTHB	Road-to-Health Booklet
SA	South Africa
SDG	Sustainable Development Goals
SGSU	Specialised Genetic Service Unit
SHN	School health nurses
SRH	Sexual reproductive health

STORCH	Syphilis, toxoplasma gondii, rubella, cytomegalovirus, herpes simplex, and other infections
TOP	Termination of pregnancy
TTTS	Twin to Twin Transfusion Syndrome
WBOTS	Ward-based outreach teams
WHA	World Health Assembly
WHO	World Health Organization

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Introduction

Genetic services span all public health and clinical disciplines in the lifetime of a patient - from pre-conception throughout the lifespan. These services provide preventive measures, risk assessment, diagnostic, therapeutic and management options for those affected, who, if diagnosed early, may have many of their symptoms prevented, cured or mitigated (1). Healthcare providers working in areas other than genetics, across the levels and continuum of care, need to be trained on how to recognise, manage and refer the patient for genetic services and also request relevant tests given the vast scope of the discipline and its rapidly evolving nature.

Congenital disorders affect an estimated one in 15, or seven per cent, of live births every year in South Africa (2). Of these 70 000 affected births, some are diagnosed at birth, while others only manifest across the lifespan or may present as sudden death course (3). The majority (80.5 per cent) of congenital disorders are genetic/partially genetic in cause while 19.5 per cent are caused by teratogens (2). The latter is more than the 10 to 15 per cent expected in South Africa, owing to the high prevalence of foetal alcohol syndrome (FAS) (2,4). The aetiology of many complex disorders and non-communicable diseases (NCDs) are multifactorial, making individuals genetically predisposed to developing the disease (e.g. cancer, cardiovascular disease, diabetes etc). Though there is a lack of data on familial cancers in South Africa, it is estimated that approximately 12 per cent of women and four per cent of the general population will be affected by breast and colorectal cancer respectively (5,6). According to data from the national Department of Health, the prevalence of blindness and childhood blindness in South Africa is estimated to be 0.75 per cent and 0.47 per 1 000 for children under five respectively (7).

With access to relevant, optimal lifesaving medical and/or surgical interventions, therapeutics and rehabilitation, 70 per cent of congenital disorders can be prevented or disability ameliorated (1). Accurate empiric data on congenital disorders is lacking in South Africa, with current national surveillance reporting only two per cent of the estimated congenital disorders (8), leading to underreporting and an underestimate of the congenital disorder burden of disease.

Serious congenital disorders are usually life threatening and contribute significantly to the burden of disease, including both child morbidity and mortality in South Africa. The provision of equitable and accessible genetic services plays a crucial role in reproductive decision making and can improve maternal, foetal, neonatal and children-under-five outcomes. As the country transitions epidemiologically, the proportion of child mortality attributed to congenital disorders is expected to rise and emerge as a leading cause of death in children under five (2). This is in keeping with the trend experienced by high-income countries where congenital disorders emerged and remain the leading cause of death in children today, accounting for 28 per cent of infant deaths alone (9).

This growing health burden remains hidden under the parallel burden of communicable disease and NCDs in South Africa, although data is beginning to emerge. The 2014-2016 Perinatal Problem Identification Programme (PPIP) data listed congenital disorders as the fourth most common cause of neonatal death in neonates weighing more than 1 000g (10).

There has been a steady increase in the proportion of mortality in neonates more than 1 000g due to congenital disorders from 10.5 per cent to 11.8 per cent between 2002 and 2016 respectively (11; 10). In the Western Cape, congenital disorders have overtaken infection and are ranked as the third cause of early neonatal death in neonates weighing more than 500g and more than 1 000g (12); It is expected that if all congenital disorder causes of death were reported, the resulting proportion of neonatal deaths due to congenital disorders would be much higher (12).

Purpose

The Department of Health aims to ensure that all patients survive, thrive and transform. The purpose of these guidelines are to provide guidance to healthcare providers to enable prevention, early recognition, screening, diagnosis, and prompt referral and care of patients requiring these services, in order to improve outcomes.

Goal

To prevent, diagnose, provide care for and improve the quality of life of patients with a congenital disorder across the lifespan.

Strategic objectives

- To prevent congenital disorders through community awareness and education of communities and healthcare providers to enable those affected or at risk to make informed reproductive choices.
- To improve early detection of congenital disorders by screening and diagnosing individuals at risk and/or reducing the occurrence/recurrence of congenital disorders throughout the continuum of care.
- To strengthen clinical genetic and laboratory services to promote early and accurate diagnosis of congenital disorders to reduce morbidity and mortality.
- To set standards for optimal care and management of patients and families with congenital disorders to improve the quality of life of those affected, including access to rehabilitative and palliative care.
- To strengthen referral pathways focusing on patient-centred and coordinated care.
- To develop an effective and sustainable surveillance and monitoring and evaluation system.

Guiding principles

Global framework

- The Global Strategy for Women's, Children's and Adolescents' Health (2016-2030) is aligned to the Sustainable Development Goals (SDGs). The genetic services guideline is aligned to this strategy's objectives of ending preventable deaths (survive), ensuring health and well-being (thrive) and expanding enabling environments (transform) (13).

- South Africa recognises the United Nations' Resolution 70.1 adopted by the General Assembly on 25 September 2015: Transforming our world: the 2030 agenda for sustainable development. The development of these guidelines are thus guided by SDG 3: "Ensure healthy lives and promote well-being for all at all ages" and specified 2030 targets (14).

- The 2014 World Health Assembly (WHA) Resolution 67.19 on palliative care, called for countries to improve access to palliative care, to improve the quality of life of affected patients, with a special focus on primary healthcare (15).

- The 2012 United Nations Resolution 67.81 on universal healthcare adopted in December 2012 urges countries and governments to provide affordable, quality healthcare services in order to achieve international development goals (16).

- The 2010 WHA resolution 63.17 recognised the importance of congenital diseases as a cause of stillbirth and neonatal mortality, and their significant contribution to under-five mortality and many other considerations affecting maternal, neonatal and child health. WHA 63.17 urged Member States to address the impact of congenital disorders on under-five mortality by setting relevant priorities, raising awareness, committing resources, increasing prevention strategies, strengthening registrations and surveillance, developing expertise and building capacity (17).

- The Global Strategy for the Prevention and Control of Non-Communicable Diseases (NCDs) was developed as a recommendation of the 2000 WHA Resolution 53.14. The overall goal of the strategy is to reduce the burden of morbidity, and premature mortality related to NCDs through surveillance, promotion of health, prevention, and the management of NCDs (18).

National frameworks

- South Africa is in the process of introducing the National Health Insurance (NHI) 2019, in line with the National Development Plan (NDP). The NHI aims to ensure that all South Africans have access to affordable, quality health services, based on health needs, rather than socioeconomic status (19).

- In recognising that the health and development of the country are integrally linked, health reform in South Africa is firmly embedded in the country's National Development Plan (NDP) 2030 *Our Future – make it work*. The NDP aims for inter-connectivity with the World Health Commission on the Social Determinants of Health which are considered key in any equitable health service delivery platform and includes the need to: improve the conditions of daily life, tackle inequitable distribution of power, money and resources and measure the problem, evaluate actions and expand the knowledge base (20).

- The National Health Act, 2003 (Act 61 of 2003) (NHA) sets out the legal provisions regarding healthcare and genetic services specifically. It stipulates the rights of patients, including the right to confidentiality and the right to consent for treatment. Together with its regulations and amendments, the NHA is the overarching legislation regarding healthcare services in South Africa (21).

- The Children's Act, 2005 (Act 38 of 2005) consolidates the rights of children under South African law and is an important consideration regarding the provision of genetic services (22).

- The Constitution of the Republic of South Africa, 1996 (Act 108 of 1996) provides the legal foundation for the existence of the Republic, sets out the rights and duties of its citizens, and defines the structure of the government. Access to healthcare services, and more specifically genetic service, falls within the ambit of the right to health under the Constitution (23).

Legislation

The genetics services guidelines are aligned to the following legislation:

- Children's Act, 2005 (Act 38 of 2005)
- National Health Act, 2003 (Act 61 of 2003)
- The National Health Laboratories Service Act, 2000 (Act 37 of 2000)
- Constitution of the Republic of South Africa, 1996 (Act 108 of 1996)
- Choice on Termination of Pregnancy Act, 1996 (Act 92 of 1996)
- Inquests Act, 1959 (Act 58 of 1959)
- National Public Health Institute of South Africa Act, 2020 (Act 1 of 2020)
- Medicines and Related Substances Amendment Act, 1965 (Act 101 of 1965 – including 14 of 2015)
- Health Professions Act, 1974 (Act 56 of 1974 - including Amendment Act 29 of 2007)
- Mental Health Care Act, 2002 (Act 17 of 2002 – including Amendment Act 12 of 2014)
- Nursing Act, 2005 (Act 33 of 2005)
- Social Assistance Act, 2004 (Act 13 of 2004)

Strategic plans, policies, guidelines and programmes

This genetic services guideline is aligned to the following, strategic plans, policies, guidelines, and programmes:

- Maternal, Perinatal and Neonatal Health Policy 2021.
- National Guideline for Breast Cancer Control and Management 2019.
- National Clinical Guidelines for Safe Conception and Infertility 2019.
- National Guideline for Implementation of the Choice on Termination of Pregnancy Act; 2019

- Guideline for the Prevention of Mother-to-Child Transmission of Communicable Infections (HIV, Hepatitis, Listeriosis, Malaria, Syphilis and TB) 2019.
- Standard Treatment Guidelines and Essential Medicines List for South Africa. Primary Health Care Level 2018.
- Breast Cancer Prevention and Control Policy 2017.
- National Adolescent and Youth Health Policy 2017.
- Maternity Care Guideline 2016.
- Newborn Care Charts. Routine Care at Birth and Management of the Sick and Small Newborn in Hospital. Guidelines for the Care of all Newborns in District Hospitals, Health Centres and Midwife Obstetric Units in South Africa 2014.
- Strategic Plan for the Prevention and Control of Non-Communicable Diseases 2013-2017
- Integrated School Health Policy 2012.

KEY AREA 1: GENETIC SERVICES IN PRECONCEPTION

STANDARD 1.1

Provide information and advocacy on genetic services to all individuals of childbearing age including the risk of exposure to teratogenic substances.

Considerations:

- Family history of genetic problems (previous child with congenital disorder)
- Antenatal and birth history (maternal factors, foetal factors, labour/delivery and early neonatal period, newborn factors and past medical history)
- Teratogenic exposure (chronic medication, maternal illness, maternal infection, environmental exposure: **See Standard 1.2**)
- Carrier screening for common autosomal recessive and X-linked conditions.

Box 1: Examples of information/education to be shared include

- What is a congenital disorders?

Also known as birth defects, congenital disorders are any potential pathological condition present at or before birth, including all disorders caused by environmental, teratogens, genetic or unknown factors, whether they are evident at birth or manifest later in life. Serious congenital disorders can cause death or disability in the absence of care.

- What are the risk factors?

All women have a risk of delivering a baby with a congenital disorders. The risk increases when:

- there is a family history of a congenital disorders
- there is alcohol and/or drug use including smoking during pregnancy
- women are of advanced maternal age (AMA), above 35 years
- a woman has untreated infections including sexually transmitted infections (STORCH: syphilis, toxoplasma gondii, rubella, cytomegalovirus, herpes simplex, and other infections)
- women with existing maternal medical conditions and/or use of high-risk medication e.g. diabetes, epilepsy, cardiac conditions
- parental consanguinity

- How to reduce the risk of having a baby with a congenital disorder?
  - Knowledge of family history (fertility, pregnancy and neonatal).
  - Use of contraceptives until planning to become pregnant.
  - Taking folic acid before conception and during pregnancy.
  - Optimise diet before conception and during pregnancy.
  - Avoid alcohol, drugs and tobacco before conception and during pregnancy.
  - Avoid over-the-counter medication and only use medication prescribed by a HCP.
  - Avoid or minimise environmental exposures.
  - Manage pre-existing conditions (e.g. diabetes, epilepsy) before conception and during pregnancy. Optimise drug doses to the lowest viable dose and least harmful drug to maintain maternal health but also reduce the risk to the foetus.
  - Treat all infections before conception and during pregnancy.
  - Book early for antenatal care (first visit before 14 weeks) and attend all antenatal visits.

- Not all congenital disorders can be prevented but the interventions outlined above can reduce the risk of having a baby with a congenital disorder.

- Some conditions (with known family history) may require testing preferably during preconception and prenatally to allow for early intervention.
- Couples with a family history of congenital disorders and other risk factors must be referred for genetic counselling. The mother and/or her family must be referred for genetic counselling once a congenital disorder is suspected.
- Promote use of B-Wise and Mom-Connect platforms for extra info.

Box 2: Taking a genetic family history

Taking and drawing a genetic family history may involve asking for information about many family members or may be targeted to specific individuals to detect a family pattern of a particular condition, depending on the clinical question. The basic approach is the same for both and involves collecting information about relatives and their partnerships in one generation before moving up or down a generation.

Key questions about family members:

1. Do you have any concerns about diseases/conditions that seem to run on either your side or your partner's side of the family?
2. Does anyone in your family have a major medical, physical or mental problem?
3. Has anyone in your family ever needed treatment in hospital?
4. Has anyone in your family ever had any serious illnesses or operations? How old were they when they were diagnosed?
5. Have any adults, children or babies in your family died? How old were they and what was the cause of death?
6. Have there been any miscarriages or babies who were stillborn in your family?

See **Annexure A** for a detailed example of a family history collection form to assist drawing of a pedigree.

Adapted from NHS, UK guideline

Box 3: Considerations when taking a comprehensive antenatal care and birth history

1. Maternal factors
    a. Maternal age at conception
    b. General health and nutrition
    c. Outcome of previous pregnancies (e.g. multiple, miscarriage/stillbirths)
    d. Length of gestation
    e. Maternal weight gain
    f. Pregnancy complications
    g. Screening test results
    h. Use of assisted reproductive technology
2. Foetal factors
    a. Foetal growth (soft markers/foetal abnormalities)
    b. Foetal movement
3. Labour/delivery and early neonatal period
    a. Antepartum condition (e.g. evidence of foetal distress, fresh meconium in amniotic fluid)
    b. Labour (length of labour, progress, drugs used)
    c. Presentation (e.g. breech, persistent abnormal foetal lie-hydrocephalus) and type of delivery (vertex or assisted delivery and reason)
    d. Placenta and cord weight (check for abnormality)

4. Newborn factors
    a. Newborn baby condition
    b. Neonatal progress
5. Past medical history of previous child with a congenital disorder
    a. General health (previous medical illnesses and surgical operations)
    b. Growth (plot weight, height/length, head circumference), development (appropriate to age), behaviour.

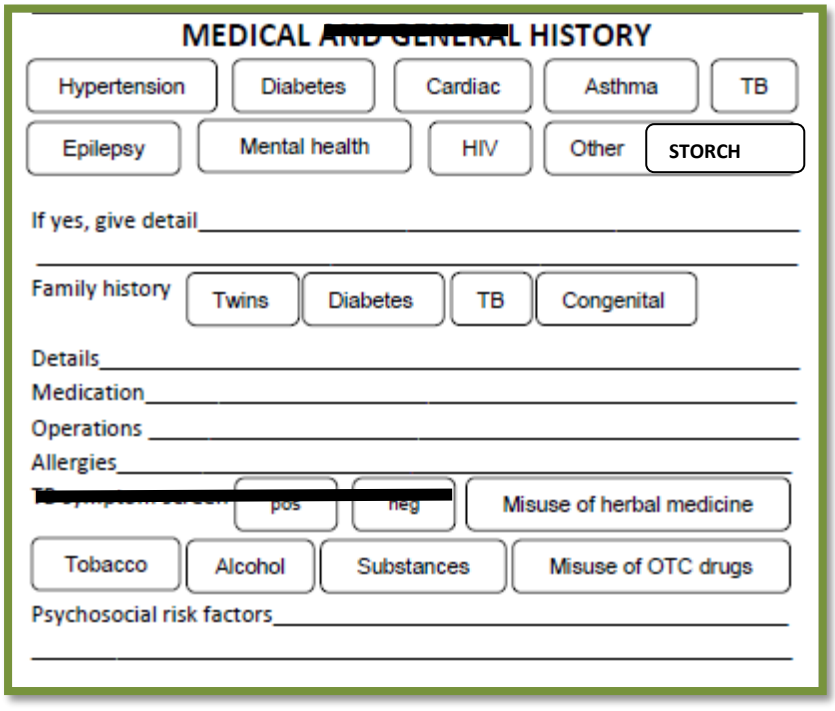
STANDARD 1.2

Optimise women's health by identifying the risk of exposure to teratogenic substances to women at reproductive age and manage the risk where possible across the levels of care.

Considerations:

- Maternal illness (e.g. epilepsy, diabetes)
- Chronic medication exposure (e.g. warfarin, valproate)
- Maternal infection (e.g. syphilis, rubella)
- Environmental exposure (e.g. pesticides)

Figure 1: Questions to ask when taking medical history



Extracted from Maternity case record, NDOH.

STANDARD 1.3

Offer/refer women with an increased risk of a genetic disorder (indicated by a positive family history) pre-conception genetic counselling to enable informed decision making in reproductive choices.

Considerations:

- Maternal age
- Repeated previous miscarriage or stillbirth
- Previous pregnancies affected by a congenital disorder
- Positive family history i.e. other family members affected (children/parents, grandparents, cousins etc.)
- Consanguineous unions (if degree of kinship is first cousins or closer)
- Informed decision making and family planning
- Exposure to teratogenic substances

Box 4: Pre-conception/pre-natal counselling

- Take a genetic family history
- Draw family tree
- Identify carriers and affected family members (proband and partner)
- Risk analysis- probabilities of having affected child and recurrent risks
- Share information on suspected condition

STANDARD 1.4

Optimise access and use of multiple micronutrient supplementation (MMS) to all women planning a pregnancy and those who are pregnant. (See National Clinical Guidelines for Safe Conception and Infertility and the Maternity Care Guidelines 2019).

Considerations:

- MMS (refer Maternal Neonatal and Perinatal Health Policy)
- Diet

Box 5: Recommended micronutrient supplementation

Promote an adequate general diet e.g. with sufficient proteins, calories and iron. As per the regulations relating to the fortification of certain foodstuffs, 2003, wheat flour, maize meal and bread are fortified with various micronutrients namely Vitamin A, Thiamine, Riboflavin, Niacin, Pyridoxine, Folic acid, Iron and Zinc. All women of reproductive age are encouraged to use iodised salt to prevent iodine deficiency disorders. The women are further encouraged to use staple foods fortified with folic acid to prevent NTDs and other malformations.

To supplement, all pregnant women must be given the following (Maternity Care Guidelines, 2016)

- ferrous sulphate tablets 200 mg daily, to prevent anaemia
- calcium tablets 1000 mg daily, to prevent complications of pre-eclampsia (e.g. calcium carbonate (168 mg) two tablets orally, three times daily with food. this is best taken four hours before or after iron supplements

- folic acid tablets 5mg daily

KEY AREA 2: GENETIC SERVICES IN PREGNANT WOMEN AND NEONATES

STANDARD 2.1

Provide information and advocacy on genetic services to pregnant women at first antenatal visit, ideally before 14 weeks.

Considerations:

- Genetic family history (previous child with congenital disorder)
- Antenatal and birth history (maternal factors, foetal factors, labour/delivery and early neonatal period, newborn factors and past medical history)
- Teratogenic exposure (chronic medication, maternal illness, maternal infection, environmental exposure: See **Standard 1.2**)
- Basic antenatal care

STANDARD 2.2

All pregnant women must be assessed and/or examined to identify if the pregnancy is at increased risk (see **Box 1**) and must be managed according to the identified risk. It is advisable to diagnose and treat foetal problems from as early in the pregnancy as possible from both a management and psychological perspective for the mother and family.

Considerations:

- Increased risk
- Assessment and examination
- Following initial management of identified high risk pregnancies; women must be referred to a next level of expertise for further assessment and management.
- Possible referral for genetic counselling and investigation

Box 6: Assessment to identify women at increased risk

- Take a genetic family history, if positive, classify pregnancy as high risk (Box 2)
- Take an ANC and birth history, if positive, classify pregnancy as high risk (Box 3)
- Identify women of AMA, over the age of 35
- Identify women with medical conditions and manage them according to their risk (e.g. epilepsy, diabetes)
- Identify women who are on chronic medication (e.g. warfarin, valproate) and manage according to their risk
- Identify women with maternal infections (e.g. syphilis, rubella) and treat according to relevant treatment guidelines
- Identify women who have been exposed to environmental toxins (e.g. pesticides)
- Identify women who use alcohol, tobacco and recreational drugs.

REFER WOMEN IDENTIFIED AS HIGH RISK FOR FURTHER INVESTIGATION AND MANAGEMENT

STANDARD 2.3

All women identified as high risk must have prenatal screening and diagnosis before 20 weeks. For early detection, counselling and management of congenital disorders, women should be given an earlier return date for results. Where possible, prenatal diagnosis must be confirmed before maximum 24 weeks and/or in accordance with institutional guidelines and Choice on Termination of Pregnancy Act, 1996 (Act 92 of 1996) and all its amendments, accompanied by genetic counselling.

Considerations:

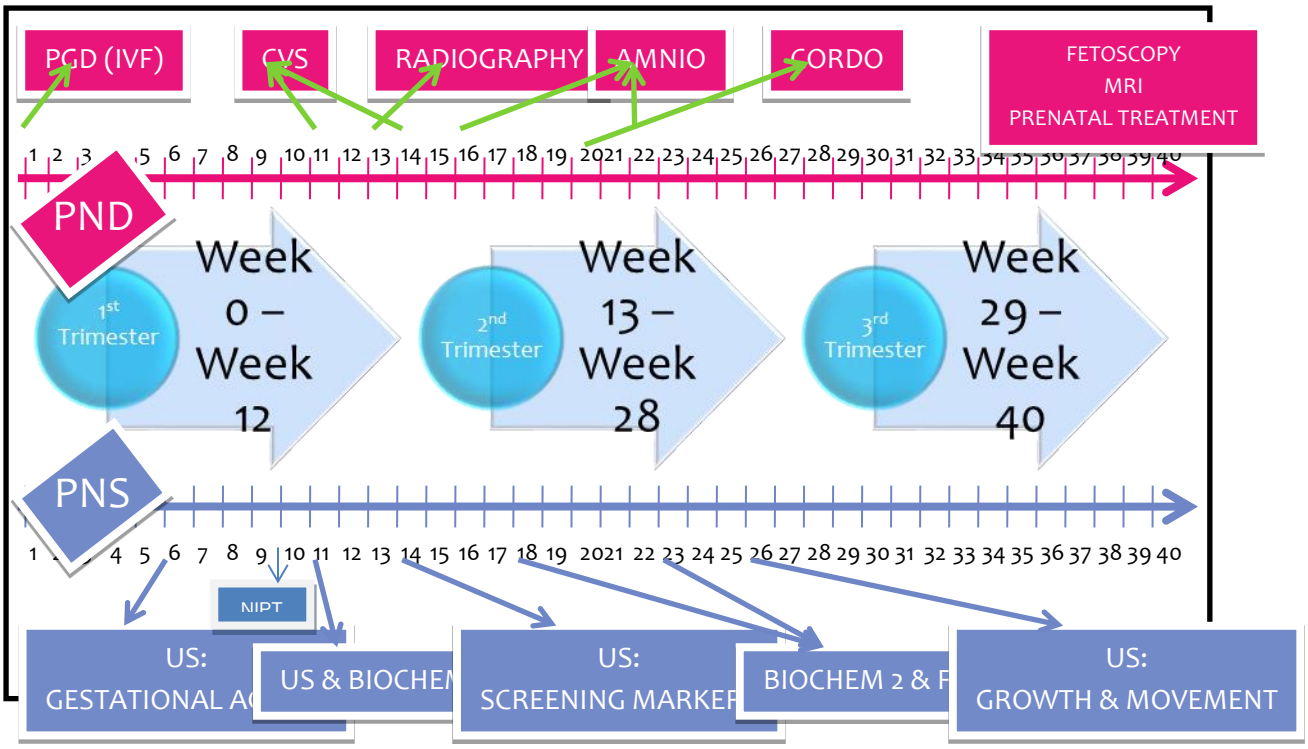
- Where possible, all investigations should be aligned to the eight basic antenatal care visits.
- Women are permitted two ultrasounds, a compulsory initial sonar at nine to 12 weeks but before 14 weeks and an additional intervention related sonar at the next level of expertise where indicated.
- Prenatal screening options:
    1. History taking and obstetric examination
    2. Foetal ultrasound (nuchal translucency): ideally performed at 11 to 13.6 weeks
    3. Foetal anomaly scan: ideally performed at 20 weeks when indicated
    4. Biochemical testing: first trimester testing at 11 to 13.6 weeks and second trimester at 16 to 20 weeks.
- Prenatal diagnosis:

Provide invasive diagnostic testing, where indicated in women with foetal abnormalities suspected as genetic conditions

Table 1: Prenatal diagnosis tests

	Chorionic villus sampling	Amniocentesis	Cordocentesis
Weeks when test is performed	11-13.6	16-22	≥ 18 weeks
Risk of miscarriage	1-2%	0.7-10%	2-3%
Contraindications	Unsuppressed viral load	Unsuppressed viral load (Pt not on HAART) Active PV bleeding Bleeding disorders Threatened preterm labour	Unsuppressed viral load
TOP services	TOP is easier as foetus is smaller	TOP more complex as foetus is older	TOP more complex as foetus is older

Figure 2. Overview of prenatal screening and testing options



Box 7: Progression of prenatal screening and diagnosis

1. Non-invasive prenatal testing (NIPT):
   - Offer NIPT to women of AMA for detection of chromosomal abnormalities.
   - This should be offered at tertiary level to women whose history and ultrasound risk is above 1:300. If screening is not available, then diagnostic testing is indicated. NIPT is done from 10 weeks with follow-up invasive testing if necessary. NIPT is used to identify women with foetuses at high risk for chromosome abnormalities.
   - Women at significantly increased risk of aneuploidy as a result of maternal age, previous child or family history of chromosomal trisomy or a positive ultrasound and/or maternal serum screen results screen should be offered invasive testing or more accurate refinement of risk with NIPT where available.
   - Pregnancies identified as high risk by biochemical tests should be offered NIPT before an invasive testing is performed.
   - Positive NIPT must be followed up with a confirmation invasive test and extensive counselling.

2. Pre-implantation genetic diagnosis (PGD)-IVF
   - Offer PGD to women of advanced maternal age and women with recurrent pregnancy losses for detection of single gene and chromosomal abnormalities during in vitro fertilisation (IVF).
   - PGD is undertaken on embryos up to five days old.
   - Genetic counselling must be offered before and after a PGD test.

3. Foetal medicine
   - Foetal therapy: A therapeutic intervention for the purpose of correcting or treating a foetus abnormality or condition. E.g. anaemic foetuses can be transfused, foetal shunting procedures can be instituted for foetal pleural effusion or bladder outlet

obstruction and foetal intracardiac procedures to prevent evolution of lethal foetal cardiac abnormalities such as foetal hypoplastic left heart syndrome.

- Fetocide is offered in situations where the diagnosis of a severe congenital disorder is made after 24 weeks gestation. Two sub-specialities must agree that the birth of the neonate will result in a child with severe physical/mental disability in compliance with the Choice of TOP Act. It should only be offered at tertiary level in consultation with the sub-speciality foetal units. Genetic counselling must be offered before and after fetocide.
- Fetoscopy is an endoscopic procedure performed during pregnancy to allow access to the foetus, the amniotic cavity, the umbilical cord and the foetal side of the placenta. It is done after 18 weeks of gestation and is used to treat Twin to Twin Transfusion Syndrome (TTTS), amniotic band syndrome and congenital diaphragmatic hernia.

STANDARD 2.4

Offer counselling and available options in case of definite diagnosis of severe congenital disorders.

Considerations

- Access to termination of pregnancy and further reproductive options.
- Allow mother to make informed choice on planned delivery, timing and site options that will provide optimal care to both the mother and neonate, including medical, surgical and palliative care.

Box 8: Therapeutic abortion

- Therapeutic abortion is defined as the termination of pregnancy (TOP) in order to preserve maternal health. In its broadest definition, therapeutic abortion can be performed to
  (1) save the life of the mother
  (2) preserve the health of the mother
  (3) terminate a pregnancy that would result in the birth of a child with defects incompatible with life
  (4) terminate a pregnancy when a foetus is affected with a genetic condition that has severe morbidity
- Therapeutic abortion must be performed according to the latest National Termination of Pregnancy Guidelines and must be accompanied by pre/post TOP genetic counselling.
- Pre TOP genetic counselling involves discussion of investigation findings and facilitates informed decision making and further discusses the TOP procedure.
- Post TOP genetic counselling focuses on discussions of the investigations performed, coping mechanisms, recurrence risks and future pregnancies.

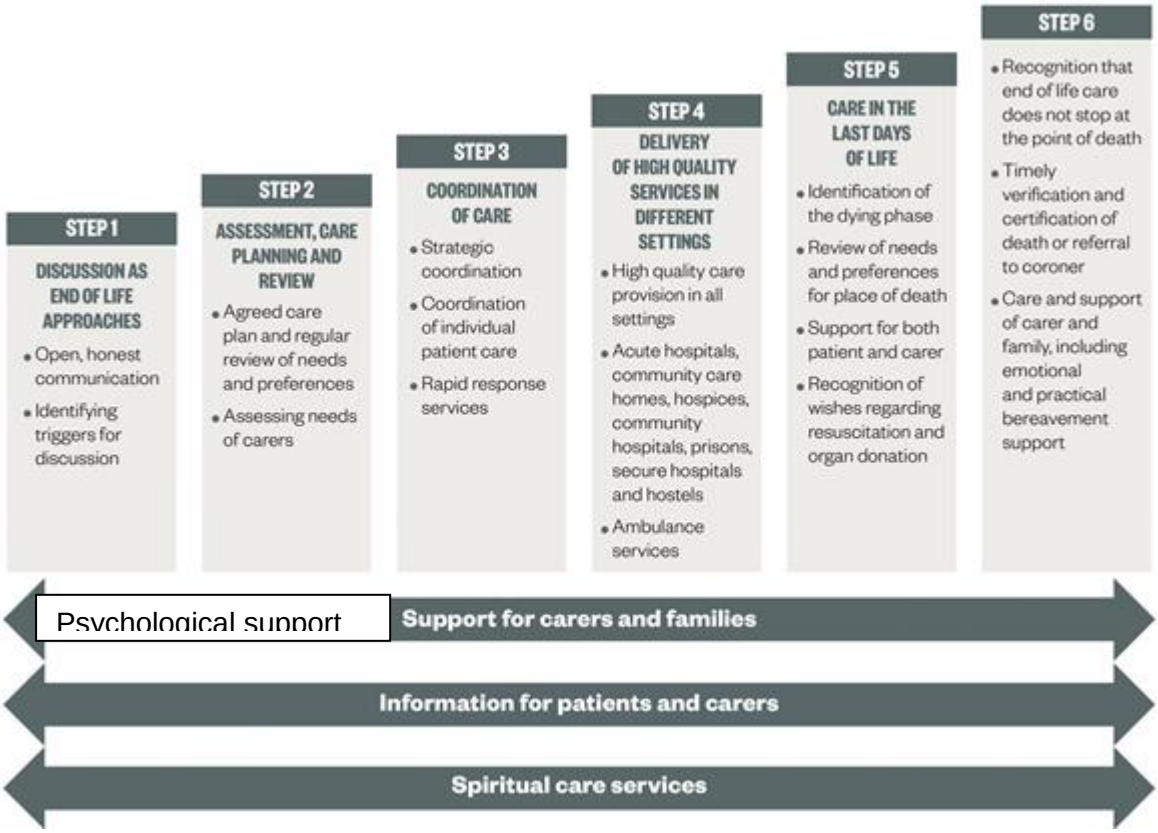
STANDARD 2.5

Despite the possible severity of the congenital disorder, every mother is entitled to a dignified and compassionate birth experience and should be given the right to choose the option most appropriate for her and her family.

Considerations:

- Allow woman to continue with pregnancy if that is her choice
- Counselling to allow closure in case of the loss of the baby
- Provide post-partum care including contraceptives of choice and counselling on the risk of recurrence

Figure 3. End-of-life care pathway



Adapted from: Department of Health. End of Life Care Strategy – promoting high quality care for all adults at the end of life (2008) United Kingdom.

STANDARD 2.6

All newborns must undergo a comprehensive head to toe physical examination at birth and before discharge to identify any dysmorphic features (See examination checklist in Maternity Case Record). Outliers to the parameters (considerations) should serve as an indication for further investigations and referral to genetic services

Considerations:

- Growth parameters
  - Weigh the baby; consider if foetus is small for gestational age - use a neonatal percentile chart.
  - Weight <2kg or >4kgs at full term, with deviation depended on gestational age
  - Length of <45cm or >55cm
  - Head circumference of <32cm or >38cm
  - Apgar score <8 at five minutes
- Check oxygen saturation within 24 hours, 89 to 97 per cent.
- Dysmorphic features including those suggestive of a known genetic condition (e.g. Down syndrome, trisomy 18) /multiple congenital abnormalities.
- Asymptomatic newborns at birth e.g. congenital syphilis where the mother never received a single dose of benzathine
- All stillbirths with obvious structural abnormalities must undergo further assessment and investigations.

Figure 4: Newborn examination checklist

FIRST EXAMINATION OF NEONATE (includes examination of stillborn babies)

Baby allowed to be placed skin to skin ☐ Time _____

General	Well	Sick			Comment*
Appearance	Well nourished	Obese	Wasted	Dysmorphic	
Behaviour	Responsive	Lethargic	Irritable	Jittery	
Cry	Normal	Hoarse	High-pitched	Absent	
Colour	Pink	Blue	Plethoric	Pale	
Skin	Intact	Jaundice	Rash / Purpura	Bruising	
Temperature	36-37°C	Hypothermic	Hyperthemic		
Odour	Normal	Offensive			
Head shape	Normal	Asymmetrical	Caput	Haematoma	
Fontanelles	Normal	Bulging	Large		
Sutures	Mobile	Overriding	Widened	Fused	
Face	Symmetrical	Asymmetrical	Abnormal		
Eyes	Normal	Infected	Small / Large	Slanting	
Ears	Normal	Abnormal	Low position		
Nose	Patent	Blocked			
Mouth	Normal	Smooth philtrum	Cleft lip		
Palate	Intact	Cleft soft	Cleft hard		
Tongue	Normal	Lip-tie, tongue tie	Large	Protruding	
Chin	Normal	Small			
Neck	Normal	Swellings	Webbed		
Apex beat	120-160/min	Tachycardia	Bradycardia		
Chest - Nipples	Normal	Accessory			
Chest – clavicles	Intact	Swelling	Crepitus		
Chest movement	Symmetrical	Asymmetrical	Shallow		
Chest indrawing	Absent	Costal	Sternal		
Respiratory rate	40 – 60 pm	Fast	Slow		
Breath sounds	Quiet	Grunting	Noisy		
Arms	Normal	Not moving	Fracture L/R		
Palmar creases	Normal	Single			
Fingers	Normal	Polydactyly	Syndactyly		
Abdomen	Normal	Distended			
Umbilicus	Normal	Moist	Flare	Bleeding	
Hips	Normal	Dislocated	Dislocatable		
Legs	Normal	Not moving			
Toes	Normal	Polydactyly	Syndactyly		
Feet position	Normal	Position Deformity	Clubbed		
Back	Normal	Meningocoele	Dimple / Hair tuft	Scoliosis	
Anus	Patent	Imperforate			
Femoral pulses	Present	Absent			
Genitalia: Male	Testes down	Undescended L/R	Hydrocoele	Inguinal hernia	
Genitalia: Female	Normal	Ambiguous			
Muscle tone	Normal	Hypotonic	Hypertonic		
Moro reflex	Present & equal	Asymmetrical	Weak	Absent	
Grasp reflex	Present	Weak	Absent		
Suck reflex	Present	Weak	Absent		
Urine	Passed	Not passed			
Meconium	Passed	Not passed			
Assessment:					
Examined by:				**Time and Date:**	
Checked by:				**Time and Date:**	

STANDARD 2.7

All newborns must have follow up a post-natal examination (three to six days postnatal) to identify congenital disorders missed at birth or discharge. See examination checklist in Maternity Case Record.

Considerations:

- Hearing and vision assessments
- Check oxygen saturation within 24 hours, 89 to 97 per cent, to detect congenital heart disease
- Growth and development
- False positive/negative assessment at birth

Box 9: Progression of newborn examination

1. Biochemical newborn examination
    a. Perform biochemical newborn screening on all newborns and stillbirths within three to six days postnatal.
    b. Perform newborn screening for congenital disorders where newborn screening prevents significant and irreversible morbidity and/or mortality
    c. More studies are needed to determine which congenital disorders must be include in the programme, however an initial screening programme should at minimum include congenital hypothyroidism, congenital adrenal hyperplasia, cystic fibrosis, classical galactosemia, glutaric aciduria type 1 and propionic acidemia.
    d. Neonates that screen positive need to be referred for confirmation of diagnosis, genetic counselling and management.

2. Pulse oximetry reading
    a. Check oxygen saturation within 24 hours, 89 to 97 per cent, to detect congenital heart disease
    b. Pulse oximetry reading of less than 80 per cent up to one hour of life is a pointer for further investigation. Consider false positives.

STANDARD 2.8

Offer information and specific counselling to every mother with a neonate with a suspected or known congenital disorder. It is the responsibility of every trained HCP to ensure that parents/families receive pre and post diagnosis counselling (and information on congenital disorders) and where necessary, refer the mother to a genetic counsellor (See **Box 10** for pointer questions).

Considerations:

- Information/preliminary counselling (provided by trained HCP and not only limited to genetic counsellors)
    - General, supportive, information sharing
    - Pre diagnosis counselling
    - Procedures and investigations to be done

- Risks

- Condition specific counselling (Provided by HCP with genetics background and genetic counsellors)
  - Based on diagnosis
  - Prognosis- possible loss of the child
  - Causes of congenital disorder and aetiology
  - Recurrence risk
  - Management of condition
  - Management of future pregnancies

Box 10: Example of condition specific counselling (Down syndrome)

Recommendations for delivering a diagnosis of Down syndrome

- Tell the parents about the diagnosis as soon as possible, even if the diagnosis is suspected but not yet confirmed. If the diagnosis has not been confirmed by karyotype, explain what physical features or medical concerns are suggestive of the diagnosis.
- Ideally, the diagnosis should be delivered in person, by a healthcare professional with sufficient knowledge of the condition. Healthcare providers should coordinate the message to ensure consistency in the information provided to the family.
- Whenever possible, meet with both parents together, or arrange a telephone call at a time when both partners will be present. If only the mother is available, ask to make arrangements to speak with her partner at a later time. If an initial face-to-face visit is not possible, the couple should be offered an office visit as soon as possible. The plan for discussing results should be agreed upon between patient and counselor during the pretest counseling session.
- The family should be informed of the diagnosis in their preferred language. If possible, a professional medical interpreter should be present at the time of disclosure.
- Discuss the diagnosis in a private, comfortable setting, free from interruptions. Allow time for questions and make plans for a follow-up conversation.
- Parents should be provided with accurate and up-to-date information. Information should be given with a balanced perspective, including both positive aspects and challenges related to Down syndrome.
- Provide the information in a sensitive and caring, yet confident and straightforward manner, using understandable language that is clear and concise.
- Use neutral language and avoid using value judgments when starting the conversation, such as "I'm sorry" or "Unfortunately, I have bad news".
- Use sensitive language and avoid outdated or offensive terminology. In the newborn setting, the baby should be present, and should be referred to by name. Use person-centric language, emphasizing that this is a baby who has Down syndrome, rather than a "Downs baby" or a "Down syndrome child."
- Allow time for silence and time for tears. Do not feel that you need to talk to "fill the silence". Offer the family time alone.
- Assess the emotional reactions of the parents, and validate these feelings. Use active listening and empathic responses to support the parents.
- Informational resources should be provided, including contact information for local and national support groups, up-to-date printed information or fact sheets, and books. The opportunity to meet with families who are raising a child with Down syndrome, those who have chosen to create an adoption plan, and/or those who have terminated a pregnancy should be offered. When appropriate, referrals to other specialists may also be helpful (e.g., medical geneticists, genetic counselors, cardiologists, neonatologists, etc.).

Sources: Cooley 1993; Dent and Carey 2006; Helm et al. 1998; Krahn et al. 1993; Powell 1991; Skotko 2005a, b, c; Skotko and Bedia 2005; Skotko et al. 2009; Skotko et al. 2009

Essential information for the initial discussion of a diagnosis of Down Syndrome

- Down syndrome (DS) is caused by extra genetic material from chromosome 21. DS may be suspected based on physical findings, but the diagnosis is confirmed by chromosome analysis.
- Individuals with DS have a variable range of intellectual disability from mild to moderate.
- Babies with DS have delays in achieving developmental milestones and benefit from early intervention including physical, occupational and speech therapy.
- 80% of babies with DS will have hypotonia.
- 50% of babies with DS have one or more congenital abnormality: 40–60% of babies with DS have a heart defect and 12% have a gastrointestinal defect that may require surgery. Assistance with referrals to specialists is appropriate for identified complications.
- Children with DS are more like other children than they are different.
- Raising a child with DS may involve more time commitment than typical children.
- Individuals with DS can participate in community sports, activities, and leagues.
- Individuals with DS can learn in a special education class or may be included in regular classes, and most can complete high school.
- Individuals with DS can be employed competitively or in a workshop setting.
- Individuals with DS can live independently or in a group home.
- Individuals with DS have friends and intimate relationships.
- Life expectancy extends into the 50s or 60s.
- Information on local support groups, advocacy organizations, early intervention centers, printed material, fact sheets, books, specialist referral(s) as needed, and the option to contact a family raising a child with DS should be offered.
- A personalized recurrence risk for future pregnancies should be offered.

Source: Sheets et al. 2011

STANDARD 2.9

Develop a specific follow-up plan for all neonates suspected to have congenital disorders even if there was no final diagnosis on discharge. Assess and classify the possible congenital disorders suspected identified in Standards 2.6 and 2.7 to enable early and accurate clinical diagnosis of congenital disorder, including investigation and genetic testing where relevant.

Considerations:

- Diagnosis:
  - Determine if isolated congenital disorders vs. multiple congenital disorders vs. syndromic to inform referral and management
  - For recognisable syndromes (e.g. trisomies), test to confirm diagnosis and follow management guidelines
  - Not all congenital disorders will be obvious or diagnosable at birth but all encounters should be used to assess babies further
  - A negative family history does not exclude a neonate from further investigation
  - Depends on level of specialist package available at facilities e.g. foetal medicine
  - Further investigations (e.g. X-ray, blood tests)
  - Genetic testing per level of care

Box 11: Clinical classification of congenital disorders

How to determine if a congenital disorder is isolated vs. multiple congenital disorders (MCD) vs. syndromic:

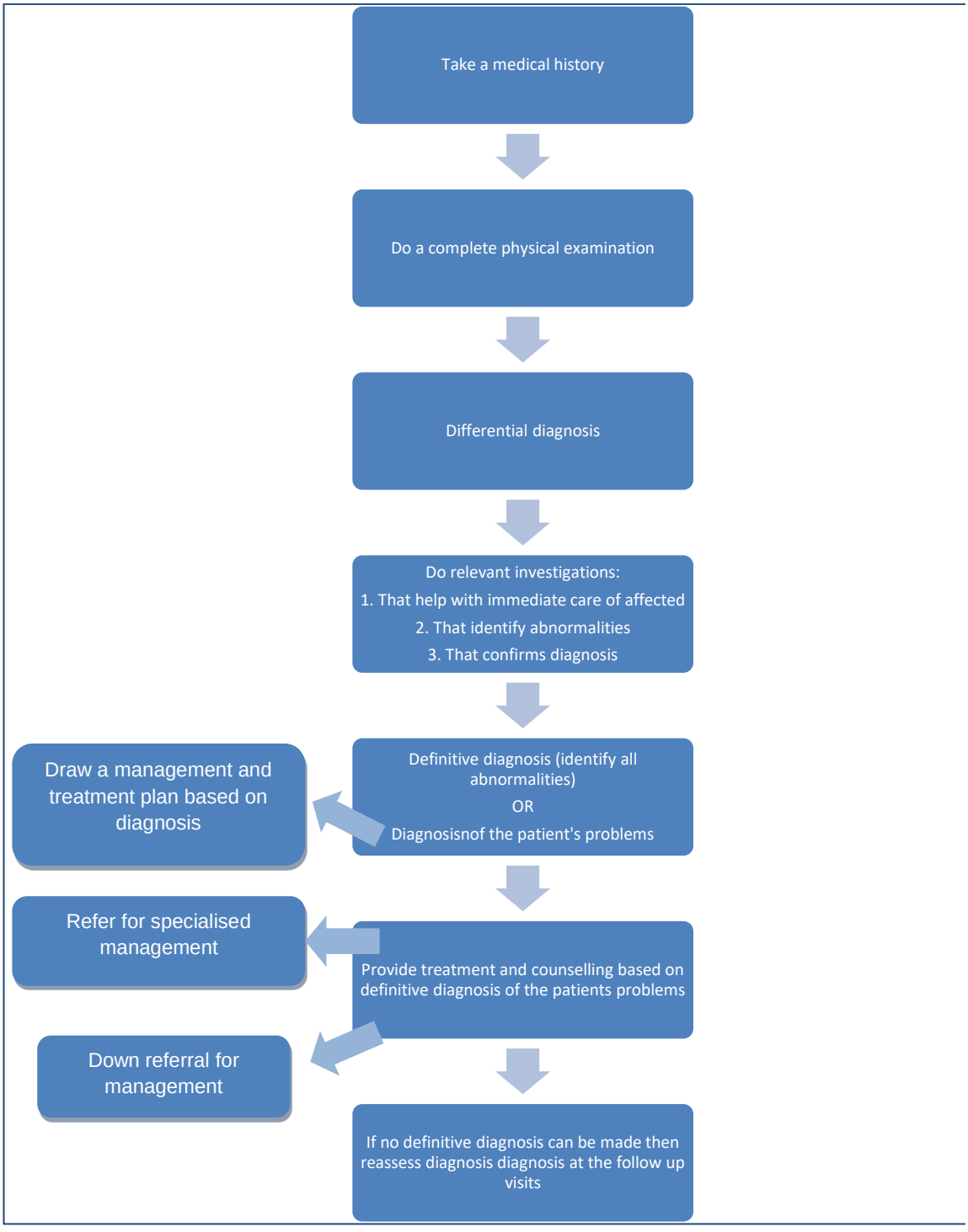
Key questions to classify cases:

1. Does the case have only one major malformation?
   If yes = isolated.
   If no, answer point 2

2. Are the two or more major anomalies related?
   If yes = isolated (sequence: a pattern of cascade anomalies explained by a single localised initiating event with secondary defects in other organs).
   If no = MCD or syndrome.

3. Is there a defined cause for the major anomalies?
   If yes = syndrome (e.g. chromosomal disorders, single gene disorders, teratogenic exposure)
   If no = MCD.

Box 12: Clinical diagnostic pathway and follow-up plan.



STANDARD 2.10

Develop a clear management plan for all neonates diagnosed with a congenital disorder. The plan must be patient-centred and focus on quality clinical care and management. The plan must be comprehensive to include psychosocial support. See **Annexure B** for management guides of various congenital disorders.

Considerations:

- Refer to Regional Genetic Services Unit
- Management according to defined protocol
- Medical management e.g. anti-failure drugs, anti-epileptics
- Surgical interventions such as cardiothoracic, gastrointestinal tract and renal
- Allied health: rehabilitation, splinting, and clefts feeding
- Referral to appropriate level of expertise
- Palliative care and end-of-life care
- Down referral once diagnosis and management plan is in place
- Multidisciplinary approach/team to ensure coordinated care
- Psychosocial support
    - Genetic counselling
    - Counselling
    - Linkage to patient support groups
    - Social services referral where necessary

Box 13. Treatment modalities for congenital disorders

Medical treatment
Some clinical manifestations of congenital disorders are amenable to treatment.

Examples:
- Antibiotics for recurrent infections
- Bronchodilators
- Sunscreen for oculocutaneous albinism
- Cardiac failure treatment
- Blood transfusion for anaemia
- Factor VIII or IX for haemophilia
- Anti-convulsant medicines for epilepsy
- Anti-D for rhesus incompatibility
- Phototherapy for neonatal jaundice
- Treatment of some inborn errors of metabolism, e.g. congenital hypothyroidism

Surgical treatment
Ease symptoms, reduce complications and improve quality of life.

Examples:
- Surgery for neural tube defects
- Gastroschisis and omphalocele
- Congenital heart defects
- Orthopaedic manipulation and surgery for club foot
- Removal of congenital cataracts
- Surgery for cleft lip and/or palate

Neurodevelopmental therapy and rehabilitation
Assist people with congenital disorders to overcome their disabilities and to integrate into society (occupational and speech therapy and physiotherapy).

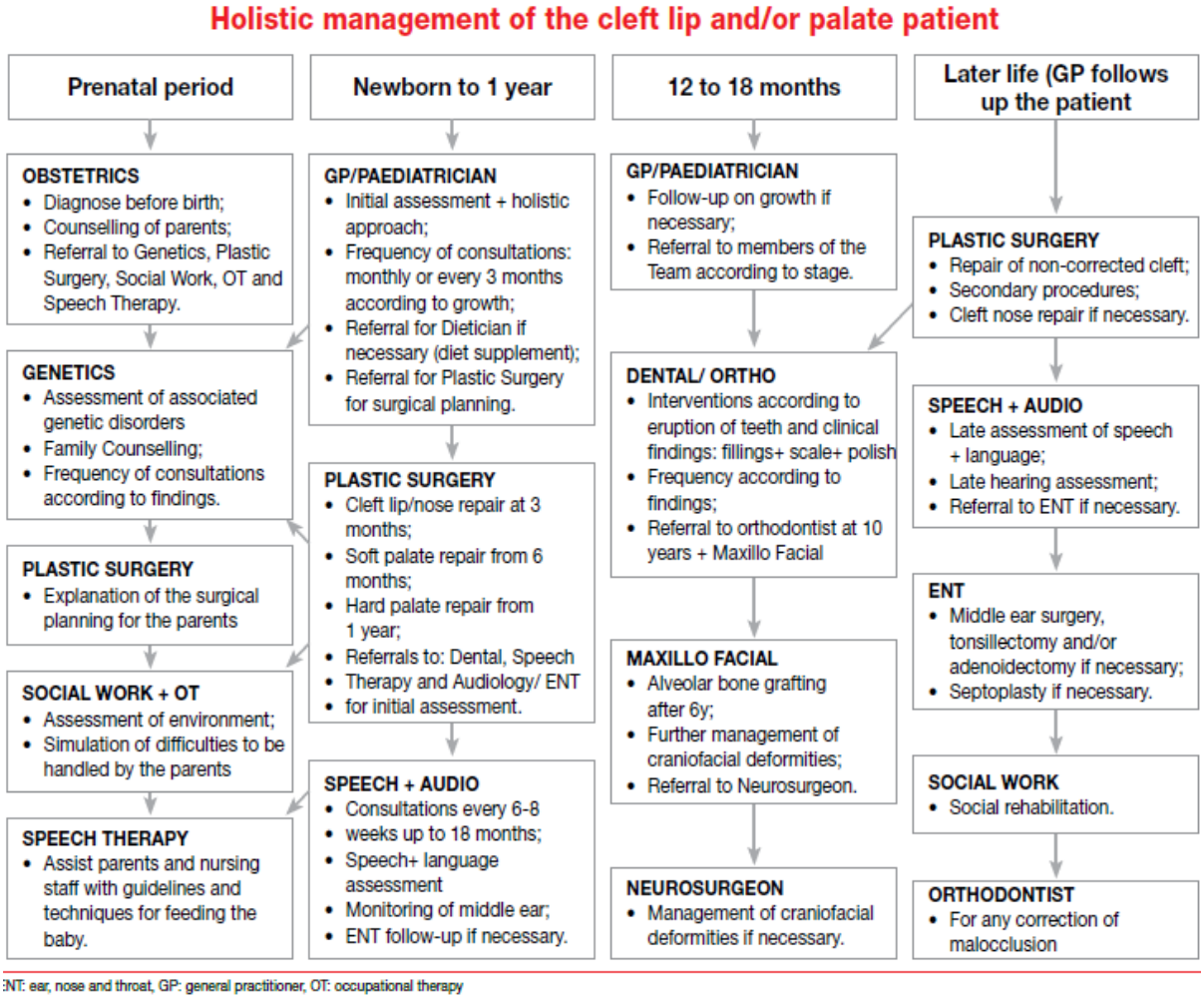
Examples:
- Stoma therapy for individuals with repaired meningomyelocoele who are incontinent
- Speech therapy to assist with techniques for feeding a baby with cleft lip and/or palate
- Speech therapy for speech in individuals with Down syndrome
- Physiotherapy of joints for individuals with haemophilia
- Occupational and neuro developmental therapy-strengthen weakened muscles (muscle atrophy)

Genetic counselling and psychosocial support
Increase the family's understanding about a genetic disease(s), the risks and benefits of genetic testing and disease management, and available options to make informed decisions.

Palliative care
An approach that improves the quality of life of patients and their families facing life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

Adapted from Bettercare: Care, prevention and counselling

Box 14 Example of comprehensive management for cleft lip and/or palate



Adapted from Giaquinto-Cilliers et al. MGC,S Afr Fam Pract 2013 533 Vol 55 No 6

KEY AREA 3: GENETIC SERVICES FOR INFANTS AND CHILDREN UNDER 6 YEARS

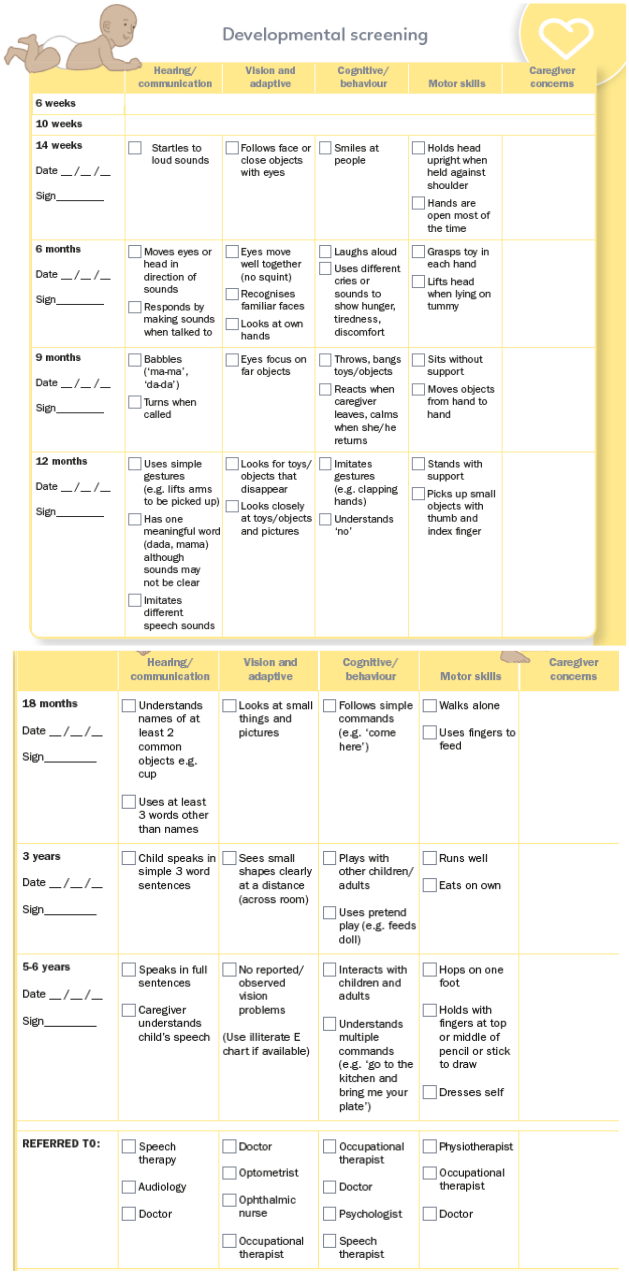
STANDARD 3.1

Every infant/child must undergo a comprehensive physical examination at birth and subsequently at each well baby visit to identify any unusual features which require further assessment or referral (six weeks, 10 weeks, 14 weeks, six, nine, 12, 18, 24 months) and every six months until six years

Considerations:

- Observe milestones and growth parameters according to the Road-to-Health Booklet. If infant does not meet one or more of the milestones or the stage targets, then refer for clinical and neurodevelopmental assessment.
- Red flags:
    - Obvious congenital disorder at birth
    - Failure to thrive with no other explanation
    - Not reaching developmental skills/milestones
    - Parental concerns about hearing and vision difficulties
    - Increased head circumference or head looks large
    - Asymmetry or increased/high (spasticity) or decreased/low (floppiness) muscle tone
    - Not communicating through speech or gestures at 18 months
    - Unexplained medical conditions (e.g. recurrent infection, recurrent hospital admissions)
- Refer for further investigations and diagnosis or genetics services based on red flags, enable early and accurate clinical diagnosis of congenital disorders, including investigation and genetic testing where relevant.
- Not all congenital disorders will be obvious or diagnosable at birth but all encounters should be used to assess babies further.
- A negative family history does not exclude a child from further investigation

Figure 5: Road-To-Health book development screening



Developmental screening

	Hearing/ communication	Vision and adaptive	Cognitive/ behaviour	Motor skills	Caregiver concerns
6 weeks					
10 weeks					
14 weeks Date __/__/__ Sign_____	☐ Startles to loud sounds	☐ Follows face or close objects with eyes	☐ Smiles at people	☐ Holds head upright when held against shoulder ☐ Hands are open most of the time	
6 months Date __/__/__ Sign_____	☐ Moves eyes or head in direction of sounds ☐ Responds by making sounds when talked to	☐ Eyes move well together (no squint) ☐ Recognises familiar faces ☐ Looks at own hands	☐ Laughs aloud ☐ Uses different cries or sounds to show hunger, tiredness, discomfort	☐ Grasps toy in each hand ☐ Lifts head when lying on tummy	
9 months Date __/__/__ Sign_____	☐ Babbles ('ma-ma', 'da-da') ☐ Turns when called	☐ Eyes focus on far objects	☐ Throws, bangs toys/objects ☐ Reacts when caregiver leaves, calms when she/he returns	☐ Sits without support ☐ Moves objects from hand to hand	
12 months Date __/__/__ Sign_____	☐ Uses simple gestures (e.g. lifts arms to be picked up) ☐ Has one meaningful word (dada, mama) although sounds may not be clear ☐ Imitates different speech sounds	☐ Looks for toys/ objects that disappear ☐ Looks closely at toys/objects and pictures	☐ Imitates gestures (e.g. clapping hands) ☐ Understands 'no'	☐ Stands with support ☐ Picks up small objects with thumb and index finger	
18 months Date __/__/__ Sign_____	☐ Understands names of at least 2 common objects e.g. cup ☐ Uses at least 3 words other than names	☐ Looks at small things and pictures	☐ Follows simple commands (e.g. 'come here')	☐ Walks alone ☐ Uses fingers to feed	
3 years Date __/__/__ Sign_____	☐ Child speaks in simple 3 word sentences	☐ Sees small shapes clearly at a distance (across room)	☐ Plays with other children/ adults ☐ Uses pretend play (e.g. feeds doll)	☐ Runs well ☐ Eats on own	
5-6 years Date __/__/__ Sign_____	☐ Speaks in full sentences ☐ Caregiver understands child's speech	☐ No reported/ observed vision problems (Use illiterate E chart if available)	☐ Interacts with children and adults ☐ Understands multiple commands (e.g. 'go to the kitchen and bring me your plate')	☐ Hops on one foot ☐ Holds with fingers at top or middle of pencil or stick to draw ☐ Dresses self	
REFERRED TO:	☐ Speech therapy ☐ Audiology ☐ Doctor	☐ Doctor ☐ Optometrist ☐ Ophthalmic nurse ☐ Occupational therapist	☐ Occupational therapist ☐ Doctor ☐ Psychologist ☐ Speech therapist	☐ Physiotherapist ☐ Occupational therapist ☐ Doctor	

Box 15: When to refer

When, why and how to refer:

- Depending on identified red flags, refer child to next level of expertise for a diagnosis.
- If possible, classify diagnosed congenital disorder as isolated, multiple congenital disorders or syndromic as this will determine referral and management protocol.
- For recognisable syndromes (e.g. trisomies), test to confirm diagnosis and follow management guidelines
- Referral is dependent on the level of specialist package available at referral facilities.
- Refer for further investigation (e.g. X-ray) and genetic testing per level of care.

STANDARD 3.2

Develop a specific follow-up plan for all children suspected to have congenital disorders even if there was no final diagnosis on discharge. Assess and classify the suspected congenital disorder to enable early and accurate clinical diagnosis, including investigation and genetic testing where relevant (refer to **Standard 2.9**).

Considerations:

- Determine if isolated vs. multiple congenital disorders vs syndrome to inform referral and management.
- For recognisable syndromes (e.g. trisomies), test to confirm diagnosis and follow management guidelines.
- Not all congenital disorders will be obvious or diagnosable at birth but all encounters should be used to assess babies further.
- A negative family history does not exclude a child from further investigation.
- Depends on level of specialist package available at facilities e.g. Foetal medicine.
- Further investigations (e.g. X-ray, blood tests).
- Genetic testing per level of care e.g. (See **Table 3** in the guideline).

STANDARD 3.3

Offer information and specific counselling to every mother with a child with a suspected or known congenital disorder. It is the responsibility of every trained HCP to ensure that parents/families receive pre/post diagnosis counselling (and information on congenital disorders) and where necessary and refer the mother/parents to a genetic counsellor (refer to **Standard 2.8**).

Considerations:

- Information/preliminary counselling (provided by trained HCP and not only limited to genetic counsellors)
  - General, supportive, information sharing
  - Pre diagnosis counselling
  - Procedures and investigations to be done
  - Risks

- Condition specific counselling (provided by HCP with genetics background and genetic counsellors).
  - Based on diagnosis
  - Prognosis - possible loss of the child
  - Causes of congenital disorder and aetiology
  - Recurrence risks
  - Management of condition
  - Management of future pregnancies

KEY AREA 4: GENETIC SERVICES: SIX TO NINE YEARS (SCHOOL HEALTH)

STANDARD 4.1

Assess children aged six to nine years for congenital disorders through the school health programme or at opportunistic health facility visits.

Considerations:

- Red flags:
    - Family history of congenital disorders.
    - Not reaching developmental skills/milestones
    - Observe milestones for growth deficiency.
    - Unexplained medical conditions (e.g. recurrent infection, unexplained bleeding episodes, recurrent hospital admissions)

STANDARD 4.2

Develop a specific follow-up plan for all children suspected to have congenital disorders even if there was no final diagnosis on discharge. Assess and classify the possible suspected congenital disorders to enable early and accurate clinical diagnosis of congenital disorders, including investigation and genetic testing where relevant (refer **Standard 2.9**).

Considerations:

- Determine if isolated congenital disorder vs. multiple congenital disorders vs. syndromic to inform referral and management
- For recognisable syndromes (e.g. trisomies), test to confirm diagnosis and follow management guidelines
- Not all congenital disorders will be obvious or diagnosable at birth but all encounters should be used to assess babies further
- A negative family history does not exclude a child from further investigation
- Depends on level of specialist package available at facilities e.g. Foetal medicine
- Further investigations (e.g. X-ray, blood tests)
- Genetic testing per level of care e.g. (See **Table 3** in the guideline)

STANDARD 4.3

Offer information and specific counselling to every mother with a child with a suspected or known congenital disorder. It is the responsibility of every trained HCP to ensure that parents/families receive pre/post diagnosis counselling (and information on congenital disorders) and where necessary and refer the mother to a genetic counsellor (refer **Standard 2.8**).

Considerations:

- Information/preliminary counselling (provided by trained HCP and not only limited to genetic counsellors
  - General, supportive, information sharing
  - Pre diagnosis counselling
  - Procedures and investigations to be done
  - Risks

- Condition specific counselling (provided by HCP with genetics background and genetic counsellors)
  - Based on diagnosis
  - Prognosis - possible loss of the child
  - Causes of congenital disorder and aetiology
  - Recurrence risks
  - Management of condition
  - Management of future pregnancies

KEY AREA 5: GENETIC SERVICES FOR ADOLESCENT AND YOUTH 10-19 YEARS

STANDARD 5.1

Provide information and advocacy to adolescents and youth about the increased risk for congenital disorders associated with maternal age under 18 years.

Considerations

- Risk associated with unplanned and unintended pregnancies.
- Risk of teratogens including smoking, alcohol, prescribed and recreational drugs.
- Risks associated with seeking late antenatal care
- Assess adolescents for delayed growth and puberty milestones and referral for genetic testing if indicated (see **Box 16**).
    - Physical examination and general health status.

Box16: Red flags for further assessment and investigation in adolescents

- Positive past medical and genetic history
- Short stature
- Absent or delayed puberty
- Mental retardation
- Virilization in females
- Gynecomastia and small testes in males

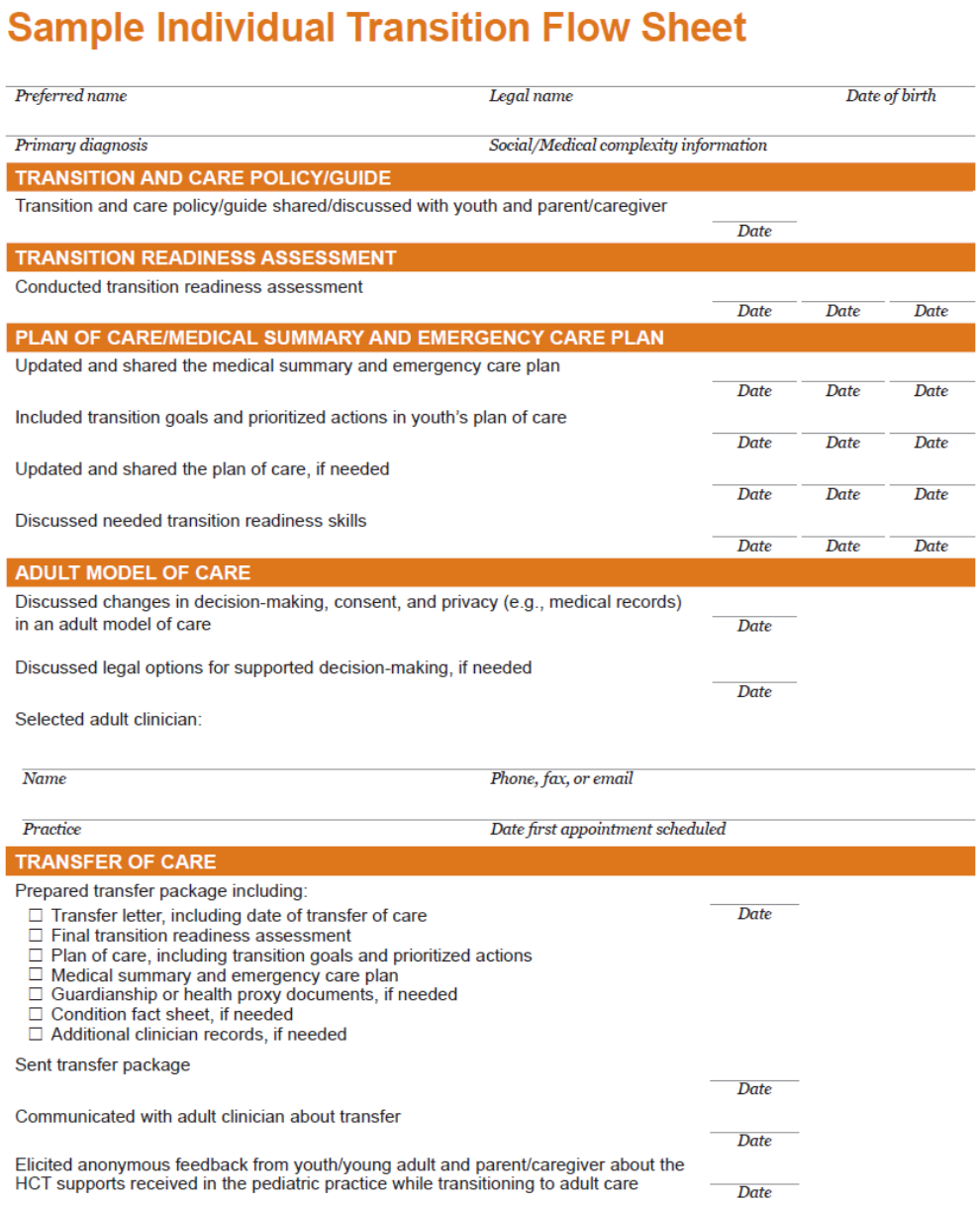
STANDARD 5.2

Provide adolescents and youth with a confirmed congenital disorder with comprehensive and coordinated care (see **Standard 2.10**) and prepare them for transition to adult healthcare.

Considerations:

- Management/treatment plan, follow-up plan, counselling and arrange with adult physician/clinician for transfer.
- A transition plan to adult healthcare services. Transition is the process of moving from child/family-centred model of healthcare to an adult/patient-centred model of healthcare with or without changing healthcare providers. Transitions assists adolescent and youth with special healthcare needs to manage their own healthcare and effectively use health services, and ensures an organised transfer of care, and integration into adult-centred healthcare.

Figure 6: Example of adolescent to adult healthcare transition plan



Sample Individual Transition Flow Sheet

Preferred name | *Legal name* | *Date of birth*

Primary diagnosis | *Social/Medical complexity information*

TRANSITION AND CARE POLICY/GUIDE

Transition and care policy/guide shared/discussed with youth and parent/caregiver — *Date*

TRANSITION READINESS ASSESSMENT

Conducted transition readiness assessment — *Date* | *Date* | *Date*

PLAN OF CARE/MEDICAL SUMMARY AND EMERGENCY CARE PLAN

Updated and shared the medical summary and emergency care plan — *Date* | *Date* | *Date*

Included transition goals and prioritized actions in youth's plan of care — *Date* | *Date* | *Date*

Updated and shared the plan of care, if needed — *Date* | *Date* | *Date*

Discussed needed transition readiness skills — *Date* | *Date* | *Date*

ADULT MODEL OF CARE

Discussed changes in decision-making, consent, and privacy (e.g., medical records) in an adult model of care — *Date*

Discussed legal options for supported decision-making, if needed — *Date*

Selected adult clinician:

Name | *Phone, fax, or email*

Practice | *Date first appointment scheduled*

TRANSFER OF CARE

Prepared transfer package including: — *Date*

- ☐ Transfer letter, including date of transfer of care
- ☐ Final transition readiness assessment
- ☐ Plan of care, including transition goals and prioritized actions
- ☐ Medical summary and emergency care plan
- ☐ Guardianship or health proxy documents, if needed
- ☐ Condition fact sheet, if needed
- ☐ Additional clinician records, if needed

Sent transfer package — *Date*

Communicated with adult clinician about transfer — *Date*

Elicited anonymous feedback from youth/young adult and parent/caregiver about the HCT supports received in the pediatric practice while transitioning to adult care — *Date*

White P, Schmidt A, Ilango S, Beck D, McManus M. Six Core Elements of Health Care Transition 3.0. Washington, DC: Got Transition, The National Alliance to Advance Adolescent Health, July 2020

KEY AREA 6: GENETIC SERVICES FOR ADULTS 20 YEARS AND ABOVE

STANDARD 6.1

Identify adults with suspected congenital disorders and refer timeously for further assessment, investigation, diagnosis and management.

Considerations:

- Adults presenting with positive family history
- Past medical history (genetic family history)
- Clinical features suggestive of a congenital disorder (see **Annexure B**)
- Physical examination/assessment
- Investigations
- Risk analysis
- Referral for further management

KEY AREA 7: GENETIC SERVICES AND THE LEVELS OF CARE

STANDARD 7.1

The Regional Genetic Service Unit (RGSU) should meet the minimum standards to provide accurate screening, diagnosis (clinical and genetic) and management of congenital disorders. The RGSU must work together with district hospitals to ensure patients with congenital disorders receive ongoing management and support.

Table 2: Minimum requirement for RGSU and SGSU

Minimum staffing requirements	**Minimum equipment requirements**	**Minimum service delivery package**
• Medical officer • Obstetrician • Genetic counsellors • Registered nurses (with genetics training) • Paediatrician (access to) • Medical geneticist (access to) • Anaesthetist (qualified professional with diploma in anaesthesia) • Paediatric surgeons/general surgeon/access to orthopaedic surgeon • Radiographer (access to) • Advanced midwives/ paediatric nurses • Administration • Patient advocacy representation (under nurse supervision) • Allied health staff e.g. Occupational, speech/audiologist, physiotherapist (access to) • Forensic pathologist (access to)	• Ultrasound (spec) • Teleconferencing facility • X-ray • Digital photography/smartphone with internet (access to) • Laboratory services (access to) • Sensory screening equipment e.g. otoacoustic emissions and visual screeners (access to)	• Navigation • Outreach services • Genetic counselling • Diagnosis of common congenital disorders • Genetic testing • Follow-up session for step down referral • Minor surgeries • Provision of devices • Education/training of HCP • Palliative care (access to) • Campaigns
Specialised Genetic Service Unit (Tertiary hospital)		

• Medical geneticist • Paediatrician • Medical officer • Obstetrician • Foetal medicine specialist • Cardiologist • Neurologists • Endocrinologists • ENT • Genetic counsellors (genetic clinic coordination, gate keeping, outreach, navigation, education and training) • Anaesthetist (qualified professional with diploma in anaesthesia) • General surgeon/access to orthopaedic surgeon/paediatric surgeons, neurosurgeons, plastic surgeons • Opthalmology • Radiologist • Sonographer • Registered nurses (with genetics training) • Advanced midwives/paediatric nurses • Administration • Patient advocacy representation (under nurse supervision) • Allied health staff e.g. Occupational, speech/audiologist, physiotherapist • Forensic pathologist	• Ultrasound (spec) • Telemedicine facility • X-ray • CT/MRI • Laboratory service (access to) • Sensory screening equipment e.g. otoacoustic emissions and visual screeners (access to)	• Outreach services • Diagnosis of congenital disorders • Genetic testing • Genetic counselling • Specialist genetic assessment • Palliative care services • Training of medical geneticists and counsellors

STANDARD 7.2

The Specialised Genetic Service Unit (SGSU) should allow rapid referral and access for specialist genetic assessment (SGA) within one to 90 days according to referral triage. Open access is required at certain institutions; however as regional structures improve, appointments via referral pathways will be preferable. Nevertheless, patients should not wait longer than 90 days for a first comprehensive assessment.

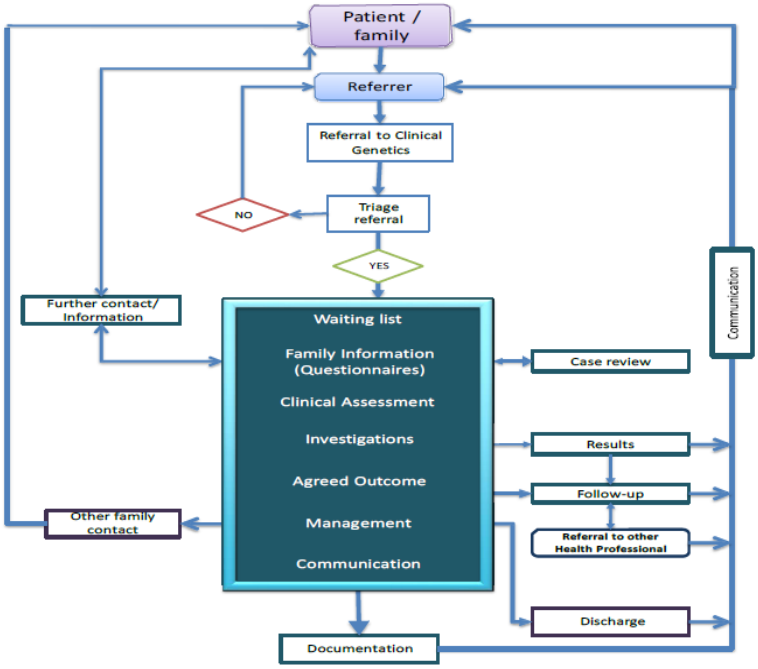
Considerations:

- Hub and Spoke System:
  Timely transition from screening and early detection to management is imperative for the survival of a patient suspected of congenital disorders. Patient care is jeopardised by the lengthy pathways for continuum of care. Hindrances to timely treatment are primarily due to, but not limited, the following:

- Shortage of qualified human resource (both specialised and support) for clinical assessment, diagnosis and counselling
- Limited availability and maintenance of medical devices and equipment
- Poor infrastructure
- Patient transport and accommodation
- Burdensome costs to the patient (and his/her loved ones)
- Disjointed referral requirements (repeated referrals for unnecessary tests, referrals to another facility or the same facility that causes an impasse, etc.)

- Given these limitations in the continuum of care, formal linkages must be established in the interim between RGSUs and SGSUs.
- An RGSU is a facility (primary or secondary) that has the adequate staffing and equipment to render the essential packages of services for secondary prevention and early diagnosis. Until South Africa can establish SGSUs (at the minimum) in each province, each RGSU must coordinate with an SGSU (tertiary or quaternary with multidisciplinary team (MDT) capabilities) for direct referrals. It is important to note that an RGSU-SGSU relationship is a contextual decision dependent on the services and capabilities available. The prerequisites for a direct referral must be agreed between the RGSU and SGSU. The aim is that patients who have been properly worked up and diagnosed are not overburdened or disadvantaged by the disjointed referral pathways (for any of the aforementioned limitations) as the disease progresses. Human resource capabilities should be maximised at all levels. It is envisaged that all these centres will require a designation process to ensure that they meet the minimum standards as specified in this guideline (or identify the level of support required to meet the standard).

Figure 7. Example of patient referral pathway



Amended from Human Genetics Society of Australia. Clinical Genetics Services Standards Framework. 2013

KEY AREA 8: GENETIC TESTING ACROSS THE LEVEL OF CARE

STANDARD 8.1

Genetic screening and testing should be done at the appropriate level of care and should be requested by the appropriate personnel (see **Table 3**). It should be used where it provides information contributing to the improvement of health through the prevention or management of congenital disorders. Genetic testing should always be accompanied by appropriate genetic counselling and management.

Considerations:
Genetic tests and indications for use:

- Newborn screening: Test newborns for congenital disorders that are not apparent at birth e.g. metabolic disorders.
- Diagnostic testing: Confirm or rule out known or suspected congenital disorders in a symptomatic individual.
- Predictive or pre-symptomatic testing: Offered to asymptomatic individuals to refine their risk of developing a condition later in life.
- Carrier testing: Identify individuals who carry autosomal or X-linked recessive mutations, and who may be at risk of having children with a genetic disorder.
- Prenatal or pre-implantation testing: Performed prior to or during a pregnancy to assess the health status of a foetus or embryo.

Table 3. Genetic testing per level of care ***Introduce as a pilot first before full implementation**

	PHC	DISTRICT HOSPITALS	REGIONAL HOSPITALS-HIGH RISK CLINIC	RGSU	SGSU
Preconception screening	• Infections: – STORCH • Check blood for: – Rhesus status – Full blood count – Fasting/random – Blood glucose	• Infections: – STORCH • Check blood for: – Rhesus status – Full blood count – Fasting/random – Blood glucose			• Carrier screening for common recessive disorders • Pre-implantation genetic diagnosis
Pre-natal screening and testing	<u>Prenatal screening</u> • Maternal infections – STORCH • Test blood for: – Rhesus status – Full blood count – Fasting/random – Blood sugar	<u>Prenatal screening</u> • Maternal infections – STORCH • Test blood for: – Rhesus status – Full blood count – Fasting/random – Blood sugar	<u>Prenatal screening</u> (for at risk pregnant women): • Ultrasound: Nuchal Translucency measurement • Ultrasound evaluation to exclude CDs • *Non-invasive prenatal testing (NIPT)	<u>Prenatal screening</u> (for at risk pregnant women): • Ultrasound: Nuchal Translucency measurement • Ultrasound evaluation to exclude CDs • *Non-invasive prenatal testing (NIPT)	<u>Prenatal screening</u> (for at risk pregnant women): • Ultrasound: Nuchal Translucency measurement • Ultrasound evaluation to exclude CDs • *Non-invasive prenatal testing (NIPT)

		• Maternal Serum Screening for chromosomal abnormalities, Neural tube defects • Ultrasound evaluation to exclude CDs	<u>Prenatal testing</u> • Chorionic villus biopsy • Amniocentesis	<u>Prenatal testing</u> • Chorionic villus biopsy • Amniocentesis	<u>Prenatal testing</u> • Chorionic villus biopsy • Amniocentesis • Cordocentesis
Newborn Screening and testing	*Newborn screening for metabolic and biochemical CDs at birth.	*Newborn screening for metabolic and biochemical CDs at birth.	*Newborn screening for metabolic and biochemical CDs at birth.	• Newborn screening for metabolic and biochemical CDs at birth*. • Investigations for stillbirths. • Confirmatory testing for abnormal newborn screening results. • Rare IEMs tests	• Newborn screening for metabolic and biochemical CDs at birth*. • Investigations for stillbirths. • Confirmatory testing for abnormal newborn screening results. • Rare IEMs tests
Childhood-Adolescent screening and testing				• Carrier screening for common recessive disorders • Rare IEMs tests and other late-onset type conditions such as, cardiomyopathy and others.	• Carrier screening for common recessive disorders • Rare IEMs tests

Adult screening and testing		• Familial cancer genetic testing • Carrier screening special emphasis on late onset CDs	• Familial cancer testing • Carrier screening for late onset CDs

KEY AREA 9: SURVEILLANCE AND MONITORING AND EVALUATION

STANDARD 9.1

Monitoring and evaluation of guideline implementation must be continuous to improve access to genetic services and quality care. **Table 3** shows indicators to monitor access to genetic services and quality care. An independent evaluator must be sought to run a formal evaluation of the guideline at the midterm and final points.

Table 4: Indicators to monitor implementation

Guideline component	Indicator/ data element	Numerator	Denominator	Source and frequency
Knowledge and information sharing	Proportion of CD awareness campaigns/ information sessions conducted per district	Number of CD awareness campaigns/ information sessions conducted per district	Total number of districts	Quarterly
	Proportion of community health workers (CHW) trained on CD prevention and care	Number of CHW trained on CD prevention and care	Total number of CHW	CHW register-Quarterly
	Genetics training coverage	Number of facilities with trained nurses on the prevention, care and management of CDs	Total number of facilities	Training register-Quarterly
Screening	Proportion of ANC clients at increased risk for CDs	Number of ANC clients at increased risk for CDs	Total number of ANC clients screened for CDs	ANC register/Tick register-Monthly
	Proportion of high risk ANC clients who had prenatal screening and	Number of high risk ANC clients who had prenatal screening and diagnosis < 20 weeks	Total number of ANC clients at increased risk for CDs (high risk)	ANC register/High risk register-Monthly

	diagnosis < 20 weeks			
	Proportion of high risk ANC clients, diagnosed < 20 weeks who opted for TOP	Number of high risk ANC clients who opted for TOP	Total number of high risk ANC clients diagnosed < 20 weeks	TOP Annexure - Monthly
Diagnosis, treatment and management	Proportion of live births with a CD referred for further management	Number of live births with a CD referred for further management	Live births with a CD	Neonatal admission register/ISNAR-Monthly
Identification	Proportion of live births with a CD	Number of live births with a CD	Live births (>500g) in facility	Birth register-Monthly
	CD case fatality rate	Number of neonatal deaths due to CDs	Neonatal deaths	Neonatal admission register/ISNAR-Monthly
	Proportion of regional hospitals notifying CDs (sentinel sites)	Number of regional hospital notifying CDs	Total number of regional hospitals	Congenital disorders notification system (CDNS)-Quarterly
Access to genetic services	Number of RGSU established per province	-	-	New-Quarterly
	Number of SGSU established per province	-	-	New-Quarterly

STANDARD 9.2

Develop a surveillance system for the ongoing collection, analysis, interpretation, dissemination and use of CD data for genetic service planning and implementation. See **Annexure C:** Congenital disorders notification form.

Considerations:

- Population vs. sentinel site surveillance system
- Case ascertainment: Passive vs. active data collection.
- Resources available including funding, workforce and data collection, validation and analysis tools.
- Surveillance champions.
- Reporting must be timeous, accurate and complete and disseminated.

ANNEXURE A: FAMILY HISTORY COLLECTION FORM

Example of family history collection form

Please complete the form below, giving as much information as possible about your immediate (blood) relatives. If there is any information that you do not know, perhaps someone in your family will be able to help you, otherwise write "don't know". You may find it easier to start on the row that refers to your mother and complete all boxes relating to her before you start on the next member of your family. An example of how to fill a row on the form is shown below.

Relative	First names and surname	Previous surnames e.g. at birth	Sex Male (M) or Female (F)	Address	Date of birth or approx year if unknown	Alive Yes or no	Date of death or approx year if unknown	Name of condition	Age at diagnosis	Hospitals where treated or town/city if unknown
Example	*Lilly Potter*	*Hooper*	*F*	*1 The Avenue, Warley, WR5 7JU*	*01/08/1952*	*Yes*	*-*	*Diabetes*	*32*	*General Hospital, Birmingham*
Your details										
Your children (or write none) 1										
2										
3										
Your sisters (or write none) 1			F							
2			F							
3			F							
Your brothers (or write none) 1			M							
2			M							
3			M							
Your mother			F							
Your father			M							

Relative	First names and surname	Previous surnames e.g. at birth	Sex Male (M) or Female (F)	Address	Date of birth or approx year if unknown	Alive Yes or no	Date of death or approx year if unknown	Name of condition	Age at diagnosis	Hospitals where treated or town/city if unknown
Your mother's mother			F							
Your mother's father			M							
Your father's mother			F							
Your father's father			M							
Your mother's brothers and sisters (or write none) 1										
2										
3										
Your father's brothers and sisters (or write none) 1										
2										
3										

Are you aware of any relative who is married to, or a partner of, a cousin, second cousin or other relative?
Please circle their names on the form and give details below. If both relatives are not listed here, please give their details on an additional sheet

.....

.....

We appreciate that space on this form is limited, so please continue on an additional sheet if necessary

Adapted from: https://www.bsgm.org.uk/healthcare-professionals/taking-and-recording-a-family-history/

ANNEXURE B: EXAMPLES OF MANAGEMENT GUIDE

	Congenital disorder	Clinical features	Diagnosis	Treatment and care
Autosomal Recessive disorders	Albinism	• Lack of pigment in the skin, hair and retina • Skin and eye hypersensitivity to sunlight • Increased risk of skin cancer • Reduced visual acuity and nystagmus	• Clinical diagnosis	• Treat skin infections • Sunscreen • Surgery for skin cancer • Glasses for reduced vision • Advise on skin and eye care and coverage with clothes and wide brimmed hats • Psychosocial support • Genetic counselling
	Cystic fibrosis (including adult onset)	• Recurrent chest infections and wheeze • Clubbing of fingers • Chronic diarrhoea • Malabsorbtion • Failure to thrive	• Sweat test • DNA diagnosis	• Aggressive treatment of respiratory infections (antibiotics, bronchodilators, physiotherapy) • Pancreatic enzyme replacement • Gene therapy in the future • Psychosocial support • Genetic counselling
	Congenital hypothyroidism	• Feeding problems • Decreased activity • Constipation • Macroglossia (large tongue) • Hypothermia and dry skin • Umbilical hernia • Intellectual disability/deafness	• Thyroid function tests – Thyroid stimulating hormone (TSH) • Free thyroxine (T3 and T4) • Neurodevelopmental/ psychometric assessment • Audiological testing (Pendred syndrome – have deafness)	• Growth monitoring • Thyroxine • Neurodevelopmental therapy/ community-based rehabilitation including psychosocial support • Genetic counselling
Autosomal	Huntington's disease	• Adult onset (average age 35 years)	• DNA diagnosis • Pre-symptomatic testing possible • Brain scan	• No effective treatment • Diagnosis to death averages 15 years

		• Progressive involuntary movements (chorea) • Progressive dementia and psychiatric symptoms • Weight loss		• Psychosocial support • Genetic counselling
	Achondroplasia	• Skeletal dysplasia with asymmetric short stature (short limbs) • Macrocephaly (head circumference above 97th centile) • Trident hand. May develop hydrocephalus and spinal cord compression	• Clinical diagnosis • DNA diagnosis available	• Surgery when indicated and if available • Avoid contact sports • Genetic counselling • Psychosocial support • Medical assistive devices
	Myotonic dystrophy	• Presents usually in young adults • Progressive muscular weakness • Myotonia and frontal baldness • Cataracts\cardiac conduction defects • Hypogonadismongenital form (gene inherited from mother) severe hypotonia, facial diplegia, ptosis, arthrogryposis, cataracts	• Electromyography (EMG) • DNA diagnosis	• Supportive • Genetic counselling • Psychosocial support • Medical assistive devices
X-linked disorders	Haemophillia A and B	• Spontaneous bleeding disorder • Variable clinical expression • Haemarthrosis	• Prolonged partial thromboplastin time • Decreased factor VIII (A) or IX (B) in blood • DNA diagnosis available	• Replace factor VIII (A) or IX (B)* • Pain relief • Splinting and other assistive devices • Physiotherapy/CBR • Genetic counselling • Psychosocial support

	Duchenne muscular dystrophy	• Clinical onset three to five years of age • Gait abnormalities • Weakness of the pelvic girdle • Gower sign • Pseudohypertrophy of the calves • Tightening of the Achilles tendons • Lumbar lordosis • Progressive muscle weakness and atrophy of muscles • Loss of ability to walk by nine to 16 years • Cardiomyopathy/heart failure • Respiratory failure • Death by 25 years	• High creatine phosphokinase (CPK) • DNA diagnosis	• Physiotherapy • Surgery if indicated • Cardiac failure treatment • Treatment of respiratory infection • Wheel chair and other assistive devices • Genetic counselling • Psychosocial support

Chromosomal disorders	Down Syndrome	• Hypotonia • Intellectual disability • Craniofacial: brachycephaly, flat face, up-slanting palpebral fissures, epicanthic folds, flat nasal bridge, small, low set ears, squint, relative macroglossia, Brushfield spots (Caucasians) • Short stature • Brachydactyly, single palmar creases, 5th finger clinodactyly and hypoplasia mid-phalanx • Sandal gap between first and second toes, plantar creases Small penis/hypogonadism • Congenital heart disease • Duodenal atresia • Recurrent infection, especially of the respiratory tract	• Chromosomal/ FISH analysis/QR-PCR • Trisomy 21 – 95 per cent • Mosaicism – 2.5 per cent • Translocation – 2.5 per cent • Thyroid function tests • Neurodevelopmental/ psychometric assessment • Cardiac assessment • Audiology	• Growth monitoring • Surgery when indicated and available • Treatment for cardiac failure • Treatment of infections • Thyroxine if indicated • Neurodevelopmental therapy/ community-based rehabilitation including psychosocial support • Genetic counselling
	Trisomy 18	• Decreased foetal movement • Prenatal growth deficiency • Severe developmental delay • Hypertonia with weak cry, poor sucking • Craniofacial: Bifrontal narrowing, prominent occiput, microcephaly, low set malformed ears, short	• Chromosomal/ FISH analysis/QR-PCR	• Supportive/palliative care • Genetic counselling • Psychosocial support

		palpebral fissures, small chin and mouth, cleft lip/palate • Clenched hands, overriding fingers • Rocker-bottom feet, clubfeet • Congenital heart disease • Genital hypoplasia • Neonatal or early infant death		
	Trisomy 13	• Prenatal growth deficiency • CNS malformations • Hypertonia/hypotonia with severe developmental delay • Craniofacial: Microcephaly/ sloping forehead, microphthalmia, anophthalmia, abnormal ears, cleft lip/palate, micrognathia • Polydactyly, camptodactyly, convex hypoplastic finger nails, cryptorchidism • Congenital heart disease • Neonatal or early infant death	• Chromosomal/ FISH analysis/QR-PCR	• Supportive/palliative care • Genetic counselling • Psychosocial support
	Turner syndrome	• Female phenotype • Short stature • Congenital heart disease (aortic stenosis/coarctation of aorta) • Renal anomalies • Ovarian dysgenesis/infertility • Learning difficulties	• Chromosomal/ FISH analysis/QF-PCR • Monosomy XO/Turner mosaics • Neurodevelopmental/ psychometric assessment • Cardiac assessment	• Growth monitoring • Surgery when indicated and if available • Ovarian hormone replacement therapy • Prevention of osteoporosis • Neurodevelopmental therapy/ community-based rehabilitation including psychosocial support

				• Genetic counselling • Discuss future fertility
Multifactorial disorders	Spina bifida	• Spinal lesion with paraplegia/ incontinence • Hydrocephalus and developmental delay	• Clinical diagnosis • Brain ultrasound/CAT scan • Urological assessment • Neurodevelopmental/ psychometric assessment	• Surgery when indicated and if available • Incontinence care • Neurodevelopmental therapy/ community-based rehabilitation including psychosocial support/palliative care • Medical assistive devices
	Anencephaly	• Incomplete development and closure of the skull and development of the brain • Incompatible with life	• Clinical diagnosis	• Palliative care • Genetic counselling • Psychosocial support
	Encephalocele	• Incomplete closure of the skull without-pouching containing neural tissue • Microcephaly • Developmental delay • Seizures	• Clinical diagnosis • Brain scan • Neurodevelopmental/ psychometric assessment	• Surgery when indicated and if possible • Neurodevelopmental therapy/ community-based rehabilitation including psychosocial support • Seizure control • Genetic counselling • Psychosocial support
	Cleft lip/palate	• Cleft lip and/or palate • Feeding problems • Speech difficulties	• Clinical diagnosis • Audiology	• Surgery • Feeding plate in infancy • Neurodevelopmental therapy/ community-based rehabilitation including psychosocial support • Genetic counselling
	Talipes equinovarus (clubfoot)	• Fixed equinovarus deformation of the foot (feet) • X-rays	• Clinical diagnosis	• Manipulation and plaster of Paris casts • Surgery when indicated • Genetic counselling

Teratogens disorders	Foetal alcohol syndrome	• Pre- and postnatal growth deficiency • Microcephaly • Intellectual disability • Behaviour disorder • Craniofacial: Short palpebral fissures, short up-turned nose, smooth philtrum, thin vermillion borer. • Joint anomalies • Congenital heart defects	• Clinical diagnosis	• Neurodevelopmental/psychometric assessment • Cardiac assessment • Growth monitoring • Surgery when indicated and if available • Neurodevelopmental therapy/ community-based rehabilitation including psychosocial support • Neuro-behavioural management • Genetic counselling • Psychosocial support
	Foetal rubella syndrome	• Growth deficiency • Microcephaly • Intellectual disability • Sensori-neural deafness • Cataracts, chorioretinitis, microphthalmia, squint • Congenital heart disease (PDA, septal defects, peripheral pulmonary stenosis) • Hepatosplenomegaly • Thrombocytopenia, anaemia	• Clinical diagnosis • Serum IgG and IgM for rubella • Identify virus in urine • Neurodevelopmental/psychometric assessment • Visual assessment • Audiology • Cardiac assessment • Full blood count	• Growth monitoring • Surgery when indicated and if available • Auditory and vision management. Neurodevelopmental therapy/ community-based rehabilitation including psychosocial support • Genetic counselling • Psychosocial support
	Congenital syphilis	• Early findings of early congenital syphilis (< 2 years) • Prematurity and low birth weight (10-40 per cent of infants) • Hepatomegaly with or without splenomegaly (33-100 per cent) • Skin rash (40 per cent)	• Clinical diagnosis • Laboratory investigations	• Asymptomatic neonates born to RPR-positive women: 50 000 units/kg of benzathine penicillin (single intramuscular dose) • Symptomatic infants: intramuscular or intravenous aqueous crystalline penicillin G at a dose 50 000 units/kg every 12 hours for the first seven days of life and then every eight hours for

		• Bone changes seen on X-ray (75-100%) • Pseudoparalysis (12 per cent of neonates, 36 per cent of infants) • Respiratory distress (34 per cent of neonates, 57 per cent of infants) • Bleeding (10 per cent), fever (16 per cent) • Positive maternal serology result		three days or intramuscular procaine penicillin G at a dose of 50 000IU/kg as a single dose for 10 days.
	Familial cancers: • Breast cancer • Epithelial ovarian cancer • Metastatic prostate cancer • Colorectal cancer • Exocrine pancreatic	• Affects both female and male • Presence of a positive family history of cancer • No family history but a personal diagnosis of an aggressive cancer type at a younger age compared to the normal population • Personal diagnosis of more than one cancer type • Al individuals with any blood relative with a known pathogenic/likely pathogenic variant in a cancer susceptibility gene • All patients that tested negative with previous limited testing (e.g. founder testing or single testing) • Gemline testing for patients with pathogenic/likely	• Targeted genotyping for recurrent/founder variants (depending on ethnicity) where available. • Comprehensive screening of causative genes using a targeted NGS cancer gene panel (for breast cancer – a minimum of three genes as stipulated by the latest guidelines (2019) including BRCA1, BRCA 2 and Yp53	• Most patients will be candidates for multiple lines of systemic therapy to palliative advanced breast cancer guided by the ER, PR and Her2 status of the tumour. • At each reassessment, clinicians should assess the value of ongoing treatment, the risks and benefits of an additional line of systemic therapy, patient's performance status and patient preferences through a shared decision-making process • Discuss preventative measures such as prophylactic mastectomy/ oomphorectmy • Genetic counselling • Psychosocial support

		pathogenic identified during tumour profiling.		

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Case ID _____

DEPARTMENT OF HEALTH
CONGENITAL DISORDERS (CD) NOTIFICATION
Please mark applicable areas with an X

GENERAL INFORMATION

Province:	District:	Name of Hospital/Facility:	Name of person notifying:	Date:
		Facility Contact No.:	Signature:	y y y y / m m / d d

PARTICULARS OF MOTHER

Surname:	Name:	Date of birth:	Age of mother:
		y y y y / m m / d d	

Maternal Conditions:

Pre-existing diabetes	Gestational diabetes	Epilepsy	Syphilis	TB	Cardiac Conditions	Hypertension	HIV

Maternal medication (cover the counter):

Gravida & Parity:

PARTICULARS OF PATIENT

Surname:	Name:	Date of birth:	Gender:		
		y y y y / m m / d d	Male	Female	Unspecified

Population group:

African	White	Indian	Coloured	Other	Specify:

Pregnancy outcome:			Diagnosed prenatally:						
Live Birth	Still Birth	Termination of Pregnancy	Yes	No	If Yes:	Ultrasound	Chorionic Villus Sampling	Amniocentesis	Cordocentesis

Birth weight:					Gestational age:		BANC 1st visit (weeks):	BANC total visits (number):
<1000g	1000-1499g	1500-1999g	2000-2499g>	≥2500g	<37 weeks	≥37 weeks		

INVESTIGATIONS REQUESTED

Chromosome/cytogenetic	Biochemical/metabolic	DNA/molecular	No investigation necessary	Other diagnostic or screening procedure

Specify:

COUNSELLING GIVEN (BY)

Clinical geneticist	Medical Doctor	Registered Nurse	Genetic counselor	No counseling given	Genetic Training received:	Yes	No

PATIENT STATUS/OUTCOME

Alive:	Inpatient	Outpatient	Discharged	*Unit/Clinic/Ward name*	Dead:	Date of death if deceased:	y y y y / m m / d d

Referral:

Referred to another Hospital?	Yes	No	Referred from Hospital?	Yes	No	If yes, name of that Hospital:

DIAGNOSIS

Skull	Face	Chest	Heart	Abdomen	Gastrointestinal Tract	Genitals	Arms	Legs	Hands	Feet	Skin

Description:

Diagnosis: **ICD 10 code:**

Diagnosed by (If different than person notifying):	Doctor	Registered Nurse	Genetic Training received:	Yes	No

Name: **Contact No.:**

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