AN ASSESSMENT OF THE SUCCESSES AND SHORTFALLS OF THE CURRENT NATIONAL BIRTH DEFECTS DATABASE AND AN IMPROVED DATA COLLECTION METHOD FOR THE DATABASE

By

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Dedication

This thesis is dedicated to my husband, Golden Lebese and my beautiful children, Akani and Andzani Lebese. I could not have done this without your support.

Declaration

I **Vuyiswa Mtyongwe** declare that:

(i) The research reported in this dissertation, except where otherwise indicated, is my original work.

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Declaration of Publications

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The idea of this paper was first conceptualised by Professor Aldous. I analysed the data and drafted the paper as main author. Dr Malherbe assisted with elements of data analysis and the final editing and submission of the paper. Professor Aldous reviewed the paper and made inputs. All authors approved the paper before submission.

Summary

The Constitution of South Africa (SA) together with the National Health Act (63 of 1977) govern the provision of health services to the residents of the country. With a three-tier system of governance consisting of national, provincial and local (district) government, each tier functions autonomously, though in unison. The National Health Act outlines the health system whilst specifying services per level of governance. In this document, medical genetic services, amongst others, are included as a health issue that needs to be addressed as part of the functions of the National Department of Health (NDOH). At this level, these services form part of the Maternal and Child Health services. Although neglected, medical genetics services are important for the prevention and management of congenital disorders (CDs) in the community. These services are implemented through the development and implementation of policy guidelines. Data on CDs form the basis for policy development, decision making and planning for services. Without empirical data, services for this vulnerable group of individuals, cannot be adequately provided.

Collection of CD data was initiated in 1980, with multiple surveillance systems available in the country by the early 1990s. One system in particular (Birth Defects Surveillance System-BDSS) was successful, with its data (from 1992-2004) being submitted to the International Clearinghouse for Birth Defects Monitoring Systems (ICBDMS), whose functions include the exchange of CD birth prevalence among member countries and the promotion of epidemiologic studies. In 2006, the NDOH developed the standardized birth defect notification tool (BDNT), with the intention of substituting all existing CD surveillance systems with one notification tool and system for the entire country. The primary objective of this study was to measure the effectiveness of this system, taking into account the challenges experienced in the reporting period. This was done by analyzing the data and comparing it to other surveillance systems globally and locally. The secondary objective was to develop an improved surveillance system for the country.

Data from the BDNT was analyzed for a nine year period, 2006 until 2015. Analyzed data included the number of CDs reported per year, per province and per district. CDs of all pregnancy outcomes were included e.g. live births, stillbirths, terminated pregnancies and miscarriages. Birth prevalence was calculated based on aetiology, (whether the CD was genetically or environmentally determined), and per priority condition (This list of priority conditions was defined by the NDOH in their 2001 Birth defects policy guidelines. The number of priority CDs reported by doctors versus nurses was also determined). Priority conditions are, Down syndrome, fetal alcohol syndrome, neural tube defects, oculocutaneous albinism, orofacial clefts and talipes equinovarus.

A total of 17 761 notifications were received from across SA, of which 16 395 (92.13%) were CD notifications and 1 366 (7.69%) were zero notifications (these are notification tools that were completed by the health facility in months when no CDs were identified by the health

facility). Compliance was erratic with KwaZulu-Natal province reporting the most CDs, n=9 732 (59.36%), and Western Cape province reporting the least, n=389 (2.37 %). KwaZulu-Natal province's success is largely attributed to the good medical genetics services that were administered by Professor William Winship while he was alive. Overall, the districts where medical genetics facilities are located reported more CDs. When compared to modelled estimates, the BDNT surveillance system showed an underreporting rate of 98%. Malformations accounted for most of the reported CDs with a birth prevalence of 1.02 per 1 000 live births. Birth prevalence for CDs categorized by aetiology were: single gene disorders 0.07 per 1 000 live births; chromosomal disorders 0.13 per 1 000 live births; multifactorial disorders 0.09 per 1 000 live births; CDs caused by Rh (rhesus factor) incompatibility 0.00 (0.0032) per 1 000 live births and 0.01 per 1 000 live births for CDs caused by teratogens.

Birth prevalence for each priority CD was as follows: Down syndrome 0.12 per 1 000 live births, fetal alcohol syndrome 0.01 per 1 000 live births, neural tube defects 0.09 per 1 000 live births, oculocutaneous albinism 0.03 per 1 000 live births, orofacial clefts 0.10 per 1 000 live births and talipes equinovarus 0.10 per 1 000 live births. Over half (57.80%) of all reported CD cases were diagnosed by nursing staff.

Following analysis of data from the BDNT, a new surveillance system was developed containing the following factors: the types of CDs to be monitored, approaches to data collection, classification of collected data and the use of data received. Initially, the new CD surveillance system was going to be integrated into the national notifiable medical conditions surveillance system. In addition, an electronic system (with a backup paper-based notification system) was developed together with colleagues responsible for notifiable medical conditions surveillance and the National Institute for Communicable Diseases (NICD) which is yet to be piloted. Upon further research, certain elements were lacking in the system which could negatively impact upon implementation.

As a way forward, certain considerations were identified for future implementation of a CD surveillance system. These were categorized into mandatory and elective factors. The former includes political commitment to CDs as a health issue, legislation prescribing CD services including surveillance, vital registration of CDs at birth and death, and NDOH facilitating the coordination of CD surveillance systems in the country. The latter includes the use of a district based approach to data collection with specific personnel identified to collect data using an electronic system.

This study lays the foundation for national CD surveillance in SA. Various surveillance systems or patient registries are available, but none operate data at a national level. This study further identified the need for coordination between the different surveillance systems and/or patient registry data sets (e.g. non-governmental organisations and laboratories) which are not included in the BDNT. The national CD surveillance system could serve as a link between the various stakeholders (provinces, academic institutions, laboratories and non-governmental institutions), allowing each entity to have a system that is suitable to their

needs while collating data from these systems. The CD surveillance system should also follow patients from the point of diagnosis to treatment/management and/or death, allowing for the true burden of CDs to be measured.

Acronyms

AMA	Advanced maternal age
BANC	Basic antenatal care
BDNT	Birth defects notification tool
ChildPIP	Child Healthcare Problem Identification Program
CD	Congenital disorder
DHIS	District Health Information System
DHMIS	District Health Management Information System
FAS	Fetal alcohol syndrome
HCP	Health care provider
HIV/AIDS	Human immunodeficiency virus and acquired immune deficiency syndrome
ICD	International Classification of Disease
IDSR	Integrated Disease Surveillance and Response
LBW	Low birth weight
LMIC	Low and middle income countries
MGEP	Medical Genetics Education Program
NCR	National Cancer Registry
NDOH	National Department of Health
NGO	Non-governmental organization
NICD	National Institute of Communicable diseases
NMC	Notifiable medical condition
NMCSS	Notifiable medical condition surveillance system
NTD	Neural tube defects
OCA	Oculocutaneous albinism
OFC	Orofacial cleft
PER/BDS	Pregnancy Exposure Registry/ Birth Defects Surveillance
PPIP	Perinatal Problem Identification Program
RH factor	Rhesus factor
SA	South Africa
SANBS	South African National Blood Service
TOP	Termination of pregnancy

WHO	World Health Organization

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Chapter 1: Introduction

1.1 Introduction and problem statement

Public health surveillance is the ongoing systematic collection, analysis and interpretation of health data for public health purposes, as well the timely dissemination of public health information for assessment and public health response to reduce morbidity and mortality [1, 2]. In high income countries, congenital disorders (CDs) are the leading cause of infant and under five mortality rates accounting for 28% of under five deaths [3]. In the same setting, CDs are also the leading cause of death in the neonatal period at 0.52 per 1 000 live births [4]. Unfortunately, low-middle income countries (LMIC) lack accurate data for CDs [5]. With 7.9 million (6.8% of live births) children born annually with a serious CD and a lack of adequate medical genetics services experienced in LMICs, CDs are often misdiagnosed or undiagnosed, resulting in the true contribution of CDs to the disease burden not being accurately measured [2, 6].

The same is true for South Africa (SA). No empiric CD data is available at a national level. The data that is available is extrapolated from hospital-based studies undertaken by various academic institutions in the different provinces. Other data is derived from that estimated from studies worldwide and locally and modelled for the country. Observed data is important as it forms the basis for decision-making, planning and implementing of services for the prevention and care of CDs in the country. With the deteriorating medical genetics services in the country, data collection systems that provide quality data are becoming increasingly important for the revitalization of these services.

1.2 Background

A national birth defects surveillance system was implemented in 2006 in the form of the Birth Defects Notification Tool (BDNT). This was a standardized surveillance system that was introduced nationally with the intention of substituting the multiple surveillance systems that were in place at the time. The role of this system was to collect CD data in all provinces and on all CDs including six priority CDs specified in the National Department of Health (NDOH) policy guidelines [7]. Data from this surveillance system has yet to be analysed and compared and the effectiveness of this system post implementation (2006-2015) has yet to be determined.

1.3 Purpose of study

This study aims to address the issues raised above. The objectives of the study were to:

1. Evaluate the effectiveness of the BDNT surveillance system.
2. Document the successes and shortfalls experienced during implementation.
3. Develop an improved national CD surveillance system based on lessons learned from the BDNT surveillance system.

1.4 Outline of thesis

Chapter 1 - Introduction. This chapter highlights the importance of surveillance and gives a background on CD surveillance in SA. It also states the aims and objectives of the study.

Chapter 2 - Literature review. This chapter discusses in length all the factors that contribute and impact on CD surveillance including but not limited to, the epidemiological transition, CD surveillance in LMIC versus high income countries, terminology used during surveillance, calculation of birth prevalence and the coding of reported CDs.

Chapter 3 - Methods 1. This chapter gives detailed information on the BDNT and how it was used to collect CD data and the data collection process.

Chapter 4 - Methods 2. This second methods chapter details the processes that went into developing a new electronic CD surveillance system with a backup paper-based notification tool.

Chapter 5 - Results. All the results from BDNT data analysed are discussed in this chapter, including birth prevalence.

Chapter 6 - Discussion 1. This first discussion section compares data from this study to other surveillance systems globally and locally and also covers the challenges experienced during implementation of the BDNT.

Chapter 7 - Discussion 2. This chapter makes recommendations for an improved CD surveillance system for SA and details factors that must be taken into consideration when developing a CD surveillance system.

Chapter 8 - Conclusion. This chapter draws conclusions from the study results. It also makes recommendations on future research projects.

Chapter 2: Literature Review

2.1 Introduction

This chapter begins with a discussion on how congenital disorder (CD) surveillance historically began globally, nationally and regionally in different parts of the world. This is followed by a discussion on how the epidemiological transition influenced CD trends both in low and middle-income countries (LMIC) and developed countries. Post transition, the importance of surveillance and clarification of terms and definitions used during surveillance is highlighted. The different methods used during CD surveillance, the coding used and the contribution of CDs to child mortality rates are shared towards the end of this chapter.

2.2 Global history of CD surveillance

Public health surveillance (PHS) is the ongoing systematic collection, analysis, interpretation of health data for public health purposes, and the timely dissemination of public health information for assessment and public health response to reduce morbidity and mortality [1]. Epidemics were first recorded in 3180 B.C., but it was only in 1838 that William Farr developed a surveillance system, leading to him being dubbed the founder of modern concepts of surveillance [1, 8]. Communicable diseases were first reported in the United States of America in 1874 [9]. In 1964, the Director General of the World Health Organization (WHO) endorsed the strengthening of communicable disease surveillance [10]. This led to the development of an Epidemiological Surveillance Unit in the Division of Communicable Diseases at the WHO headquarters in Geneva in 1965 [10, 11]. This unit contributed to the WHO endorsing surveillance as an essential function of the public health practice [10, 11].

CD[1] reporting was initiated in the 1960s following the thalidomide tragedy [13]. The drug thalidomide was widely used in the late 1950s and early 1960s to treat nausea in pregnant women, but was withdrawn from use for this indication after thousands of babies were born with limb deficiency defects [14]. This tragedy stimulated the establishment of a number of initiatives to prevent this from recurring.

Nationally, in the United States of America (US) and the United Kingdom (UK), surveillance systems were developed to monitor and collect information on CDs [15, 16]. In the US, the Metropolitan Atlanta Congenital Defects Program (MACDP) was developed in 1967 [16, 17]. The MACDP, a population based surveillance system for CDs, was established by the Centers for Disease Control and Prevention (CDC) to monitor future increases related to preventable

[1] Congenital disorders are defined as abnormalities of structure or function, including the metabolism, that are present from birth 12. World Health Organization, *Management of Birth Defects and Haemoglobin Disorders. Report of a Joint who-March of Dimes Meeting. Geneva, Switzerland, 17-19 May 2006*, in *Human genetics programme, World Health Organization*. 2006, World Health Organization: Geneva. p. 1-27.

exposures and serve as an early warning system [13, 16, 18]. In the UK, the British Isles Network of Congenital Anomaly Registers (BINOCAR) was developed in the late 1990s [15]. This is a group of regional and disease-specific registers collecting information about CDs occurring in England, Northern Ireland, Scotland and Wales, with some of its registers forming part of EUROCAT [19]. BINOCAR monitors the frequency, nature and outcome of CDs in the British Isle population [19]

Globally, in 1974, the International Clearinghouse for Birth Defects Monitoring Systems (ICBDMS) was established at a meeting in Helsinki, Finland by representatives of malformation registries in 10 countries. The ICBDMS was established to encourage the exchange of data and collaborative research between its members, and for early detection of CD epidemics on a global level [17, 20].

On a regional level, the Commission of European Communities created the European Registry of Congenital Anomalies and Twins (EUROCAT) in 1979 with the aim of bringing together local registries with the same data collection methods [17]. The establishment of these various organisations, and the development of the Birth Defects Prevention Act of 1998 in the US, led to the acceleration of many other surveillance systems at global, regional and local levels which varied in their specific aims and coverages [2, 18]. As part of providing optimal medical genetics services, accurate data is important and so is surveillance [5, 21].

2.3 Epidemiological transition

Epidemiological transition is a term used to define changes in population health statistics and pattern of disease of a country or region as a result of changes in socioeconomic, education, infrastructure and health care development [2]. Omran details this transition in his three-stage model consisting of firstly the ‘age of pestilence and famine’, secondly the ‘age of receding pandemic’ and lastly, the ‘age of degenerative and man-made diseases’ [22]. In stage one, mortality rates are high and life expectancy at birth is low, with epidemics, famine and war as the main causes of death. In stage two, mortality rates decrease and is coupled with an increase in life expectancy. However, the level of communicable diseases remains high. In the last stage, life expectancy at birth continues to increase as mortality rates declines due to better control of communicable diseases, maternal and child health, and general improved healthcare [6, 22]. As a result, non-communicable diseases (NCDs) and degenerative diseases emerge in communities [6, 22]. Underlying deaths from CDs, especially in neonates, infants and children under five also emerge in stage three of transition, as deaths from communicable diseases are significantly controlled [2, 6, 23]. The epidemiological transition results in an increasing need for genetic services to improve individual patient outcomes and overall population health [23].

Developed countries are currently in stage three of the transition and followed Omran's classic model of epidemiological transition in the early 1950s and 1960s [2, 6, 22]. LMICs have not followed high-income countries through Omran's epidemiological transition [6]. In SA, the emergence of HIV/AIDS and the re-emergence of TB in the mid-1990s, halted the country from completing stage two of Omran's model of transition as mortalities increased due to these epidemics [6]. This caused the country to enter into an additional stage of transition known as the 'age of emergent and re-emergent infections' [6, 24]. Owing to strategies by the National Department of Health (NDOH), mortality rates from HIV/AIDS have significantly decreased resulting in increased life expectancy, thus returning the country into a positive epidemiological transition [6]. As SA continues to transition, CDs and other NCDs and degenerative diseases, are emerging.

2.4 CD surveillance in LMIC

CD surveillance is an important component of genetic services as resulting data can be used to advocate for prevention and care programmes and also to evaluate the impact of any interventions [5, 21, 25]. Without this empiric data, the contribution of CDs to the disease burden cannot be accurately evaluated. This leads to an underestimate of the health need and inadequate services being provided, resulting in the most vulnerable of society, children and those living with disability, not having access to the services they require [6, 26]. CD surveillance systems in LMICs are usually limited, despite over 90% of CD affected births and more than 94% of CD related deaths occurring in LMICs [23]. This lack of data results in barriers in estimating the true burden of disease of CDs [27]. Owing to underreporting, CDs in LMICs are underestimated. To close this data gap, data are either extrapolated from statistics in developed countries or are developed from hospital based studies [5, 28]. In 2006, the March of Dimes Global report on Birth Defects was released. This document provided modelled estimates of birth prevalence of genetic or partly genetic origin for 193 countries [2]. Modelling provides the expected numbers of CDs until surveillance systems are developed and improved to a level where modelling is no longer necessary.

2.5 Surveillance in developed countries

In parallel with the development of surveillance systems, other medical genetic services began to emerge in developed countries in the 1950s and 1960s [2]. The main purpose of medical genetic services is to assist people with a genetic disadvantage, those with a CD or at risk of having children with a CD, to live and reproduce as normally as possible [2, 28]. This is achieved through the implementation of prevention and care programmes including genetic counselling, clinical genetic services, prenatal diagnoses, genetic testing and screening [2, 27, 28]. This developed in response to the increasing proportion of child deaths due to CDs as a

result of epidemiological transition in these countries [2, 6, 23]. In these high-income countries, CDs remain the leading cause of infant death and lifelong disability [3, 4, 21]. And account for up to 28% of under-5 deaths (WHO 2015)

2.6 SA history of CD surveillance

CDs surveillance in South Africa (SA) was initiated in the 1980s through research on the teratogenic effects of water supplies undergoing new purification processes. This work was undertaken by the Water Research Commission through the University of Cape Town (UCT) [29]. A hospital based surveillance system was established in 1987 by the NDOH through UCT with the aim of providing information on the extent of disabling conditions in the community for the planning of a programme on prevention and rehabilitation [30]. This hospital based surveillance system, named the South African Birth Defects Surveillance System (SABDSS), applied for membership to the ICBDMS in 1992 and were approved in the same year [30, 31]. Data on CDs was routinely collected and submitted to the International Clearinghouse from 1992 through to 2004 [30-32]. In 2001, the SABDSS was further modified following the publication of the *Policy Guidelines for the Management and Prevention of Genetic Disorders, Birth Defects and Disabilities* [7]. This policy document introduced the birth defects notification tool (BDNT) which is currently being used, following revision in 2006, to collect CD data nationally. A study by Lebese *et al* demonstrated that there is 98% underreporting by the BDNT [29] (see appendix 3).

A secondary function of the SABDSS was to monitor priority CDs as defined by the NDOH with the aim of establishing birth prevalence's [30]. This came about following the fortification of foods with folic acid in 2003. Monitoring of the birth prevalence of neural tube defects (NTDs) before and after fortification was initiated to measure the impact of food fortification [30, 33]. Following fortification in 2003, of neural tube defects declined by 30.5% from 1.41 to 0.98 per 1 000 live births [33]. This study highlighted the importance of CD surveillance in any country.

2.7 Importance/Objectives of CD surveillance

The ultimate goal of a surveillance system is to prevent adverse effects and complications of the health issue being monitored [1]. CD surveillance is important for a number of reasons: Firstly, it is used to determine birth prevalence's in a population and to detect CD trends [7, 18, 21]. This is necessary for health service planning, development and implementation of prevention programs [5, 7, 34]. Secondly, CD surveillance is used to monitor the occurrence of defects in a specific area over time. This allows for early detection of emerging teratogens, and the assessment of any additional risk for fetal exposure [21]. Thirdly, it is used to inform the referral of affected babies to appropriate services [1, 13]. Fourthly, it can be used for

epidemiological studies, clinical research and community empowerment through education [5, 18, 21]. Lastly, CD surveillance data can be used to evaluate prevention programmes [1, 18, 35].

2.8 Terminology

Reliable epidemiological data monitoring requires consistent use of clearly defined categories of CDs [27]. These terms and definitions vary, including congenital anomalies, congenital defects, birth defects and congenital malformations. The use of clear and standard definitions is crucial to enable data comparisons between different surveillance systems.

The use of disparate definitions and terminology in CD surveillance systems has led to significant variation in data interpretation and reporting of CDs [36]. A large number of different terms are used to describe CDs leading to confusion [12, 17, 21, 28, 36]. Congenital malformations and congenital anomalies, are often used to define CDs [37]. The WHO defines congenital anomalies as macroscopic morphological anomalies present from birth [38]. Similarly, congenital malformations are defined as single or multiple defects of the morphogenesis of organs or body system identifiable at birth or during the intrauterine life [28, 39]. Both these terms explain structural abnormalities of prenatal origin and exclude functional abnormalities [40]. This makes these abnormalities only a portion of the totality of CDs. Some authors believe that congenital anomalies are the same as CDs and birth defects, while congenital malformations represent only structural abnormalities [21, 37, 41]. Similarly, chapter XVII of the *International Classification of Disease* (ICD) 10 codes, relates to congenital malformations, deformities and chromosomal abnormalities, which are all structural abnormalities [42, 43]. This means that all other functional and metabolic CDs are recorded elsewhere in the ICD-10 system, fragmenting CDs, leading to confusion around the correct terminology to be used [42].

In 2006, international consensus was reached by the WHO to use the terms congenital disorder and birth defects interchangeably [12]. Birth defects are defined as abnormalities of structure or function, including the metabolism, which are present from birth. Some are clinically obvious at birth while others manifest later in life. This includes CDs with genetic causes, partly genetic causes, teratogenic[2] and unknown causes [2, 12]. Comparably, CDs are defined as any potential pathological condition arising before birth, including all disorders caused by the environment, genetic and unknown factors, whether they are evident at birth or manifest later in life [27]. During the 2006 meeting, the WHO preferred the term congenital disorder while the March of Dimes preferred birth defects. Following deliberations, both parties reached consensus and agreed to use the terms synonymously [12]. Transient

[2] Teratogens are fetal environmental factors that cause CDs . They may be chemical substances, physical agents or infections.

disabilities present at birth due to hypoxia, trauma and infection are usually excluded from the definition of CDs.

Following this global agreed terminology and definitions, the continued use of different and non-equivalent terms continues. The continued use of all these different terms defeat overall efforts to compile and compare various data sets [42].

2.9 CD birth prevalence rates

Most diseases are measured in terms of incidence - the number of new cases entering or arising in a given population over a specified time period, and prevalence - the total number of existing cases in the population at a particular time [44]. However, with CDs, birth prevalence is used to indicate the frequency of CDs [17, 19, 45]. Birth prevalence is the number of babies affected in one or a defined collective group of CDs per 1 000 live births [2]. Measuring prevalence at birth allows comparison across populations and time and allows for the estimation of the human and financial toll of CDs [2, 45].

Other disease specific surveillance systems use population prevalence, which measure the number of affected individuals per 1 000 in a defined population [2, 44]. In CD surveillance, this number is lower than birth prevalence as serious CDs shorten life [2]. When estimating prevalence, it is important to accurately define your population with regard to live birth, still birth, miscarriages, terminated pregnancies due to prenatal diagnoses of CDs and late miscarriages [17, 19, 44, 45]. The causes of CDs can be divided into two categories: (1) genetic and partially genetic CDs which originate before conception and (2) non-genetic CDs which originate after conception but before birth [2]. The estimated birth prevalence of genetic and partly genetic CDs ranges from over 40 per 1 000 live births in high-income countries to 82 per 1 000 live births in LMIC [46]. In SA specifically, the birth prevalence of genetic and partly genetic CDs is 58.97 per 1 000 [2].

2.10 CD and child mortality rates

The March of Dimes defines a serious CD as one that is life threatening or has the potential to cause lifelong disability. More than 90% of all babies born with a serious CD are born in LMICs. Of this number, 95% die because of lack of adequate services for their care and management [2]. In developed countries, up to 30% of babies born with a serious CD die in infancy [2]. This results in a minimum estimate of 3.3 million deaths annually associated with a CD, mostly affecting children [2].

The WHO indicates that CDs are the leading cause of infant and under five mortality in developed countries, accounting for 28% of deaths [3]. In the US specifically, CD specific infant mortality rates have been as high as 1.63 per 1 000 live births [47]. In England and Wales, CDs

are the second leading cause of infant death with an infant mortality rate of 1.39 per 1 000 live births [4]. CDs are a more prominent cause of death in settings where overall mortality rates are lower, such as countries that have long since completed their epidemiological transition [2, 5, 6, 42].

2.11 Types of surveillance systems

Hospital based surveillance records CD data on births occurring in specific sentinel sites or health facilities [1, 13]. On the other hand, population based surveillance records data on all births (live births, still births and pregnancies terminated due to prenatal diagnoses of a CD) to mothers who reside in a designated area [1, 17]. This enables the estimation of the prevalence of defects in an entire population and its subgroups [16]. The latter form of surveillance is the more expensive but is preferred.

2.12 Electronic surveillance systems

Data collection is the foundation of public health surveillance. Many surveillance systems use paper-based questionnaires followed by manual input of the collected data into a computer database [48, 49]. This method of data collation is expensive, prone to errors and is time consuming [48]. All of these challenges can be solved by direct data input into a computer based application [48]. As part of electronic disease surveillance, the internet is also used as an effective tool for surveillance. Web-based applications improve reporting time, data quality, analysis, interpretation and dissemination of results [50]. This is due to better compliance by reporting facilities and more timely submission of reported cases. A study by Wang showed a 50% reduction in median days required for reporting by an electronic, web-based reporting system when compared to a manual, paper-based reporting system [51]. Paper-based reporting is more prone to errors, affecting data quality, Wang *et al* found that using an electronic reporting system resulted in increased completeness of data fields during data collection. This has been found to be the same in SA using mHealth, an initiative where mobile devices, e.g. mobile phones, are used to share information or to collect aggregate or patient data [52]. In KwaZulu-Natal province, electronic data collection methods, specifically mobile phone, have been proven to be feasible, acceptable, accurate and usable tools in surveillance [53].

2.13 Coding of a surveillance system

For the purpose of using, reporting on and exchanging data, it is customary to translate the data into codes [17]. Most CD registries use codes based on the WHO International Classification of Diseases (ICD) [17]. The ICD is the standard method for coding morbidity and

mortality data to monitor disease incidence, prevalence, and other health conditions [18]. Owing to the ICD not being sufficiently detailed for specialised purposes, some organisations have developed an extension of its codes, namely: British Paediatric Association (BPA), United States (US) Centers for Disease Control and Prevention (CDC) and the extension, for birth defects only, devised by EUROCAT [17]. Version 10 (ICD-10) is the most current version in use, with ICD-11 initially scheduled for release in 2017 but now postponed to 2018 [18, 54]. Like any other system, the ICD-10 has its limitations. Distinctions cannot be made between CDs among premature versus mature babies. Polydactyly, although common does not have a code to describe the position of the extra digit [18]. These limitations and others are sought to be corrected through the introduction of ICD-11.

2.14 Health care needs assessment

A health care needs assessment is a systematic approach to identifying problems and determining their extent. It further defines the target population to be served and the nature of services required by the population [55]. Health care needs assessments provide a rational, epidemiological-assisted approach for providing information to plan, introduce, and change health services to improve the health of populations [56]. The main aim is to identify unmet health needs and make changes to meet them [56]. With SA now on a positive epidemiological transition, CDs are gaining public health significance and are emerging as the next challenge [6]. Medical genetics services in SA are poor as funding and attention were diverted away from these services during the HIV/AIDS epidemic [6]. Because of limited epidemiological data and other reasons, health care needs assessments have not been undertaken in the field of CDs in the country. Even though there is a lack of empiric data, data exists in small pockets that can assist SA in determining health need for CDs, in order to revitalise medical genetic services and to prioritise CDs as per the World Health Assembly (WHA) Resolution WHA63.17 [2, 5, 6, 29].

Chapter 3: Methods 1

3.1 Introduction

The main aim of this study was to measure the effectiveness of the existing national CD surveillance system (introduced in 2006) by identifying the successes and the shortfalls, and to find an improved method of collecting data, thus enhancing CD surveillance. The objectives of the current CD surveillance systems were (i) to find out the birth prevalence of CDs; (ii) to determine priorities for intervention; (iii) to inform effective planning; (iv) to set objectives for prevention and care; and (v) data evaluation and provision of feedback to provinces, and health districts [7, 29]. This chapter discusses the current method used during CD surveillance while Chapter 4 discusses the methods used to develop a more refined, improved data collection system. Both sections will be discussed using the following sub-headings: case definition, case ascertainment, pregnancy outcomes and coding/classification.

3.2 Birth Defects Notification Tool

There were initially two methods of collecting CD data, the *Birth defects surveillance system (BDSS)* and the *Genetics postnatal congenital form*. The birth defects surveillance system collected data on priority CDs observable at birth while the genetics postnatal congenital form collected data at any age. Furthermore, some provinces had developed their own data collection tools. To standardise CD data collection in the country, the NDOH developed the standardised birth defects notification tool (BDNT) in 2006, which was also a recommendation of the *Policy Guidelines for the Management and Prevention of Genetic Disorders, Birth Defects and Disabilities* published in 2001 [7]. The BDNT, attached as Appendix 5, was developed by various stakeholders including Department of Health officials, Perinatal Problem Identification Program (PPIP) representatives, birth defects surveillance system representatives, academia, non-governmental organisations (NGOs) and officials from the Health System Research, and Research Co-ordination and Epidemiology (HSRRCE). This system is paper-based, with BDNT being completed at health facilities and submitted to NDOH via the district and provincial Department of Health. At NDOH, data is captured electronically, and a database is maintained (See Figure 3.1).

3.3 Case definition

A case definition is a set of criteria used to define the parameters for inclusion in the surveillance system. In CD surveillance specifically, this refers to an individual with characteristics that fit into the defined parameters [57]. The NDOH in their 2001 Policy Guidelines listed CDs to be monitored during surveillance [7]. These are CDs identifiable

within 24 hours of birth and are listed in Table 3.1. In 2005, the *National Guidelines for the Care and Prevention of the Most Common Genetic Disorders, Birth Defects and Disabilities* were published [58]. This document outlined priority CDs that are common in SA; these were added to the initial list for monitoring. Owing to the lack of skill and knowledge of health care providers (HCP) in identifying CDs, a section on reporting of identified abnormalities was incorporated into the BDNT. This section allowed for abnormalities to be reported even though a diagnosis could not be made. Any identified abnormalities were grouped according to their organs or body system e.g. skull defects, gastrointestinal defects, hand defects etc.

Table 3.1 CDs to be monitored according to NDOH 2001 and 2005 policy guidelines

CDs as per 2001 NDOH Policy guidelines
Neural tube defects (NTDs)
Down syndrome
Albinism
Microcephaly
Isolated cleft lip and/or palate
Hydrocephalus
CDs as per 2005 National guidelines
Talipes equinovarus
Fetal Alcohol Syndrome (FAS)
Congenital infections
Genetic deafness and blindness
Physical handicap
Mental retardation

3.4 Case ascertainment

3.4.1 Training

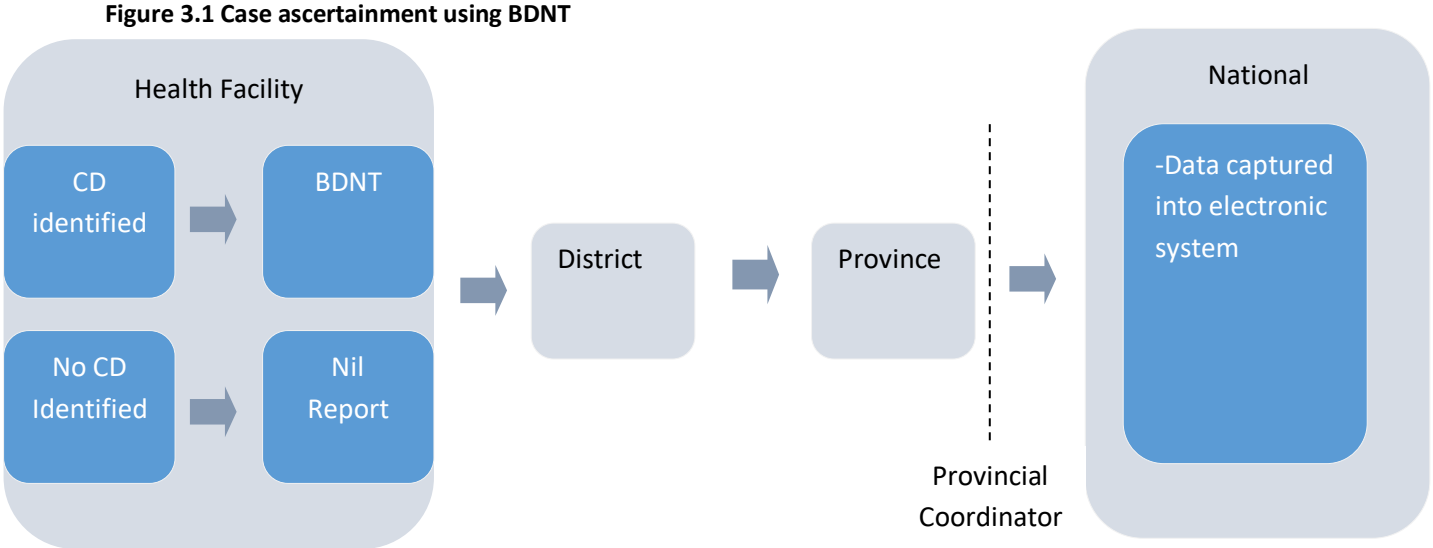
The BDNT was used by HCPs to notify CDs. HCPs include registered nurses, medical doctors, genetic counsellors or clinical geneticists, if available. Between 2006 and 2014, a total of 729 HCPs from all levels of care, from primary healthcare (PHC) to tertiary level in all districts, were trained in the Medical Genetics Education Programme (MGEP) [29]. MGEP is a postgraduate, distance learning course that equips HCPs with basic knowledge and skills to identify CDs, counsel patients and refer affected patients appropriately for further management [42, 59]. This training was done by NDOH in collaboration with the South African Inherited Disorders Association (SAIDA), recently renamed as Genetic Alliance South Africa (GA-SA) [59]. Following the development and implementation of the BDNT, basic knowledge on the use of the BDNT was given during MGEP. Training was aimed at labour and outpatients

ward staff, allowing for patients with CDs to be identified throughout the continuum of care. To improve surveillance, the use of the BDNT and sometimes data feedback, was presented at different conferences including the Priorities in Perinatal Care Conference, South African Society for Human Genetics (SASHG) and the Society of Midwives of South Africa Congress.

3.4.2 Data collection

Figure 3.1 below illustrates the data collection process followed from health facility to NDOH. Notification of CDs was done immediately following birth or within the first 24 hours of life. If undiagnosed within 24 hours, notification could be done at any age when the CD was identified. BDNTs were completed by hand, then submitted to the NDOH via the district and provincial Department of Health monthly. Provincial co-ordinators were responsible for the collation and analysis of provincial data prior to submitting to the NDOH. When no CDs were identified in a health facility, a zero notification (nil report) was completed and submitted to NDOH using the same method. One BDNT (marked zero notification) per facility is completed per month and submitted when no CDs are identified. Only identified (preliminary diagnoses) CDs were notified while laboratory and other investigations were undertaken for confirmation of the preliminary diagnosis.

Figure 3.1 Case ascertainment using BDNT



3.5 Pregnancy outcomes

CDs on all pregnancy outcomes were monitored, including live births, stillbirths, miscarriages and terminations of pregnancy (TOP). Definition of each pregnancy outcomes is detailed below:

- Live birth: any infant that shows signs of life after birth. These signs include breathing, beating of the heart, pulsation of the umbilical cord, and/or definite movement of voluntary muscles [52].
- Stillbirth: a fetus that had at least 26 weeks of intra-uterine existence, but showed no signs of life after complete birth as per the Birth and Registration Act, 51 of 1992 [58].
- Miscarriage: a fetus of less than 28 weeks gestation and where there is no evidence of life at delivery.
- Termination of pregnancy: the separation and expulsion, by medical or surgical means, of the contents of the uterus of a pregnant woman. This definition is according to the Termination of Pregnancy Act, 92 of 1996 [60]. The Act further states that a pregnancy may be terminated from 13 up to and including 20 weeks gestation if there is a substantial risk that the fetus would suffer from a severe physical or mental abnormality. TOP may further be performed after 20 weeks gestation if the medical practitioner is of the opinion that continued pregnancy would result in severe malformation of the fetus [60].

3.6 Coding/classification

The NDOH developed its own coding system, assigning each BDNT a unique identification code. All received BDNT were captured electronically using Microsoft Access and these data exported to Microsoft Excel. Numbers were assigned according to the sequence in which CDs were received in that year, e.g. the first reported CD for 2006 was coded as 001/06. The system was implemented from May 2006. This system of classification allowed for each case to have a unique identifier, avoiding the duplication of cases. However, this system is not aligned to the International Classification of Diseases (ICD).

Chapter 4: Methods 2

4.1 Introduction

In this chapter, a new approach to CD surveillance is discussed. The processes involved in developing a revised paper-based notification tool accompanied by an electronic version of this tool are discussed. Initially, the new approach was a joint surveillance system for notifiable medical conditions (NMC) and CDs. Following the development of the notification tool and electronic system, the joined surveillance system was separated. Recommendations regarding a way forward for CD surveillance for SA are discussed in Chapter 7: Discussion 2.

4.2 Integrated Disease Surveillance and Response

Countries are mandated to build capacity, allowing for the detection, assessment, notification and reporting of any health risks, especially infectious diseases, through the development of surveillance systems. This is according to the International Health Regulation (IHR) and the Global Health Security Agency [61, 62]. In SA, surveillance of notifiable medical conditions (NMCs) is mandatory as per the National Health Act and the regulations regarding communicable diseases [63]. Historically, the NMC surveillance system only reported on conditions prescribed by the National Health Act, No. 61 of 2003. These conditions were notified either within 24 hours[3] or seven days[4] of diagnosis [63].

In 2015, the NDOH and the National Institute for Communicable Diseases (NICD), embarked on the re-engineering of the current notifiable medical conditions surveillance system (NMCSS). The reasons for reengineering included the systems technology lagging behind and the system not being effectively utilized. The goal of the new NMCSS was to develop an integrated system with real time reporting, allowing for notifiable diseases to be detected early in order for a timeous public health response [64]. The new system further provided a coordinated and integrated approach to the collection, collation, analysis and dissemination of NMC data from both the public and private health sector. This reengineering process provided an opportunity for CD surveillance to partner with the national medical conditions surveillance system (NMCSS) with the intention of improving the CD surveillance system. In 2010, The Sixty Third World Health Assembly adopted a resolution which urges countries to develop registration and surveillance systems for CDs within the frame work of national

[3] Acute flaccid paralysis, Anthrax, Cholera, Crimean-Congo Haemorhagic Fever & other viral haemorhagic fevers, Food poisoning, Meningococcal infection, Plague, Rabies, Yellow fever

[4] Brucellosis, Congenital syphilis, Diptheria, Haemophilus influenzae type B, Lead poisoning, Legionellosis, Leprosy, Malaria, Measles, Rheumatic fever, Paratyphoid fever, Poisoning agricultural stock remedies, Schistosomiasis (Bilharziasis), Tetanus, Tetanus neonatorurn, Trachoma, Tuberculosis, Typhoid fever, Typhus fever (lice-borne), Typhus fever (ratflea-borne), Viral hepatitis, Whooping cough

health information systems [5]. In keeping with international trends, NDOH resolved to collaborate on CD and NMC surveillance.

The CD and NMC surveillance partnership led to the development of the Integrated Disease Surveillance and Response (IDSR). The IDSR is a strategy that was developed by the WHO African regional office in 1998 that aims to strengthen the availability and use of surveillance data for detecting, reporting, investigating, confirming, and responding to preventable diseases and other public health events [65]. The IDSR includes both an electronic and a paper-based approach to data collection. The electronic system uses the District Health Information System (DHIS), an information system that supports the information needs of health districts in the country [66]. The DHIS is a web-based, open source health management information system that is responsible for reporting, analysis and dissemination of data for all health programmes [67]. IDSR specifically uses DHIS2, a newer version of the DHIS and captures real time data using various devices including mobile phones, laptops, desktops and hand held devices [68]. This system has data entry forms, allowing users to capture data electronically. Data elements, indicators, charts and reports are also available, allowing users to easily analyse and manage data [69].

4.3 Objectives of the IDSR

The main objectives of the IDSR are to:

- Determine the birth prevalence of each CD (see Table 4.1).
- Determine the overall CD birth prevalence for conditions monitored.
- Quantify the contribution of CDs to child mortality, specifically neonatal mortality.

The details and specifics of the IDSR are outlined below.

4.4 Case definition

The World Health Organization (WHO) guidelines, *Birth Defects Surveillance a manual for programme managers*, were followed in selecting CDs to be monitored [1]. This guideline states that CDs that are readily identifiable and easily recognisable at birth or shortly after should be included for monitoring. Most CDs that were included in the IDSR were selected according to these criteria except for fetal alcohol syndrome (FAS), heart defects, haemophilia, cerebral palsy and Down syndrome. The latter CDs are mostly identified later in life except for Down syndrome. Table 4.1 illustrates the categories of CDs, namely, potentially preventable CDs that contribute to neonatal, infant and child mortality, those that negatively impact on the quality of life of the affected individual and lastly CDs that result from poor *intra partum* care. This categorization was introduced to initiate the integration of CDs into services for women's, maternal and child health. Prevention of CDs is implemented during peri-conception care which largely happens during the provision of women's health services

[7]. CDs that contribute to child mortality and those arising from poor intra partum care impact directly on maternal and child health services.

Table 4.1. CDs to be monitored via the IDSR

Categorization criteria	CD
Potentially preventable	- Fetal Alcohol Syndrome (FAS) - Neural tube defects
Contribute to mortality	- Anencephaly - Encephalocele -Spina bifida meningomyelocoele - Patau syndrome (Trisomy 13) - Edwards syndrome (Trisomy 18) - Heart defects
Impact quality of life Correctable	- Cleft lip &/or Palate - Club feet - Omphalocele/Exomphalos - Gastroschisis - Hypospadias
Manageable	- Albinism - Haemophilia - Spina bifida occulta - Ambiguous genitalia - Down syndrome - Spina Bifida meningocoele - Congenital Hydrocephalus - Reduction deformities, upper and lower limbs
Intra-partum care	-Cerebral palsy

4.5 Case ascertainment

4.5.1 Training

Training of Health Care Professionals (HCP) on the IDSR is scheduled to start in 2018. This training is aimed at HCP in the following areas:

- Labour ward staff in delivering facilities, and all Primary Health Care (PHC) staff offering Maternal Health services. This training is aimed at educating HCP to identify and report CDs at birth.
- Child Health services, specifically at Well-baby clinics, empowering them with the necessary skills required to identify and report CDs during scheduled immunisation visits.
- Early child development (ECD) centres (preschool phase). This training is aimed at identifying and reporting CDs missed at birth and during Well-baby clinic visits.

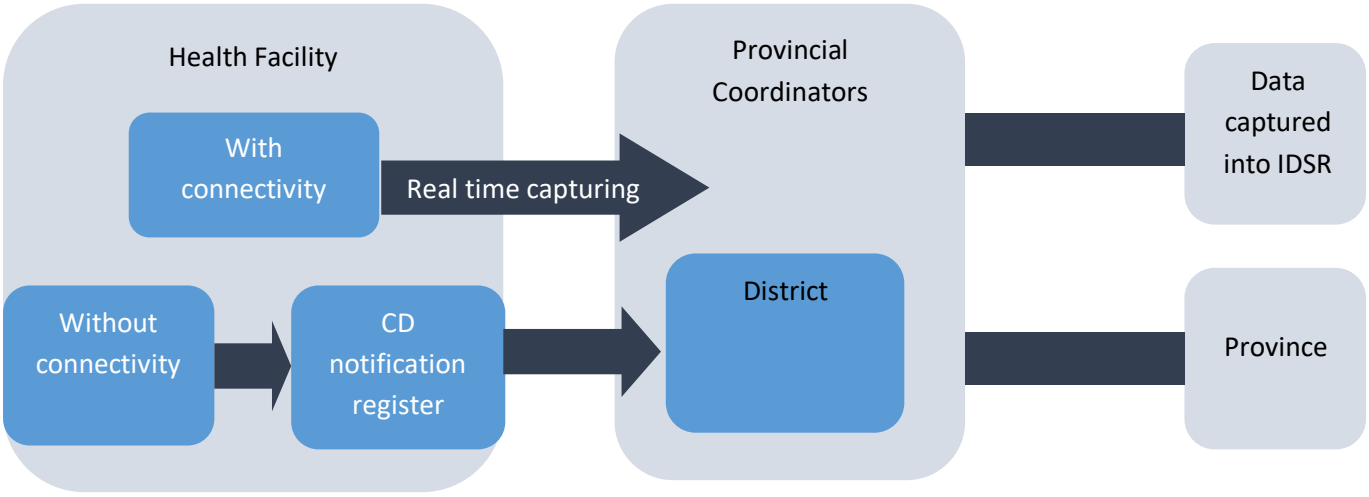
4.5.2 Data collection

Once identified, patients are registered using one of two methods. In health facilities with internet connectivity, the HCP would use their device of choice to register the patient electronically on the DHIS2 during or following consultation. DHIS2 captures data using various devices including mobile phones, laptops, desktops and hand-held devices.

Figure 4.1 illustrates the data collection process from health facility to NDOH using the IDSR. In facilities with no connectivity, experiencing downtime, or lacking devices, a paper-based method of registration is used. Following identification, the HCP completes the CDs notification register at the health facility. This is a triplicate copy register, with white, blue and pink copies. The completed top (white) copy is sent to the sub-district/district office for capturing. The middle (blue) copy is attached to the patient file or to the patient's referral letter. The bottom (pink) copy remains in the register and serves as the health facilities record. The NDOH and provincial Department of Health have equal access to the data captured by the district offices. As with the BDNT surveillance system, only preliminary diagnoses will be notified e.g. diagnosis at initial observation.

Both methods of registration capture the same information including patient demographics, type of CD, type of laboratory investigations performed to confirm diagnosis and details of the HCP notifying the patient. Most of the notifiable CDs mentioned in Table 4.1 are observable at birth and are notified as such. However, fetal alcohol syndrome (FAS), cerebral palsy and haemophilia may not be evident or diagnosed at birth. Consequently, all CDs are eligible for notification until five years. In particular, the target notification period is at birth, during scheduled immunization visits and during the ECD phase [70, 71].

Figure 4.1. Case ascertainment using Integrated Disease Surveillance and Response



4.6 Pregnancy outcomes

CDs on the following pregnancy outcomes will be monitored: live births, stillbirths and terminations of pregnancy (TOP). Miscarriages are excluded as they are difficult to report in SA. The same definitions as in Chapter 3 (see 3.2.3), pregnancy outcomes were used.

4.7 Coding/classification

The IDSR, specifically DHIS2, uses the 10th revision of the International Classification of Disease (ICD) for coding and data with other surveillance systems. With the expected release of ICD 11 in 2018, the IDSR will not be updated to comply with ICD 11 as there are no immediate plans to review the system.

4.8 Data dissemination and utilisation

Data from the BDNT has been collected since 2006 to date. These data are disseminated to the provinces for their verification and use. However, until a report by Lebese in 2016, the data has not been published or used to inform policy development because of its many challenges [29]. The ultimate goal of the IDSR is twofold: 1) to inform policy development on the prevention and care of CDs and 2) to develop a patient registry for the management and care of affected individuals, thereby improving service delivery.

4.9 Consultation

Following development of the new notification tool, the paper-based notification tool was converted into an electronic version for data collection by the HCP. Prior to this, inputs and feedback was sought from various stakeholders regarding the practicality of the tool and the usefulness of data field contained in the tool. The tool was sent to two technical advisers within the NDOH, one a child health specialist and the other a neonatal specialist. Their inputs were incorporated into the notification tool before the consultations were initiated in the provinces. Country wide consultation was undertaken in all nine provinces in SA. Sessions were held with Maternal, Child and Women's Health (MCWH) coordinators in the provinces together with HCP that are responsible for surveillance of NMCs in the provinces. All inputs from these sessions were incorporated into the new CD notification tool.

4.10 BDNT versus IDSR

Table 4.2 below summarises the differences between the BDNT and the proposed IDSR. The IDSR is intended to improve on the baseline data provided by the BDNT by capturing data electronically, over an extended notification period, using a system that is internationally recognized.

Table 4.2 BDNT versus the IDSR

BDNT	IDSR
Paper-based	Electronic
Data is captured monthly	Real time reporting
Collects data on all CDs, even those without a diagnosis	Only collects data on the CDs stated in Table 4.1
Notifies CD at any age	Notifies CDs until 5 years
Monitors all pregnancy outcomes	Excludes miscarriages as a pregnancy outcome
Not ICD compliant	ICD compliant (excluding update to ICD-11)
System only used by NDOH	Generic system that is used internationally

Chapter 5: Results

5.1 Annual Variation

Between May 2006 and December 2015, a total of 17 761 notifications were received across South Africa (SA), of which 16 395 (92%) were CD notifications and 1 366 (8%) were zero notifications (note these are only submitted one per month if no diagnosed CD). Implementation of the BDNT was erratic over the period with reporting at its lowest at the beginning of implementation in 2006 with only 648 CDs reported. Reporting peaked in 2012 with 2 577 cases reported, which was 3.13% of the expected number of CD cases based on modelled data [6, 72].

5.2 Provincial and District Variation

Table 5.2 summarises the distribution of reported CDs countrywide, excluding zero notifications. All nine provinces in SA implemented the BDNT over the nine-year study period. KwaZulu-Natal Province reported the most CDs with a majority proportion of 59.36% (n=9 732). The Western Cape Province reported the least with only 2.37 % (n=389) of cases reported countrywide (see Table 5.3). While all 52 districts countrywide reported CDs for at least one year during the study period, three specific districts in three different provinces - Xhariep (Free State), Sedibeng (Gauteng) and Central Karoo (Western Cape) did not report CDs for most of the study. Xhariep district only reported for one year during the period without submitting zero notifications (while Sedibeng and Central Karoo districts both reported twice). KwaZulu-Natal province, reported most consistently with eight of its 11 districts reporting annually from 2006 to 2015.

Table 5.1 CDs reported in SA for 2006 - 2015 compared with expected numbers based

Year	Live Births (n)	Zero notifications, (n)	CD notifications, (n)	Expected CD notifications*	Actual notifications as % of expected
2006	1 157 720	95	648	78 725	0.82
2007	1 186 149	93	1 338	80 658	1.66
2008	1 213 007	112	1 617	82 484	1.96
2009	1 221 737	135	1 879	83 078	2.26
2010	1 216 150	89	1 950	82 698	2.36
2011	1 207 511	387	2 405	82 111	2.93
2012	1 210 987	232	2 577	82 347	3.13
2013	1 212 947	119	1 420	82 480	1.72
2014	1 213 213	59	1 130	82 498	1.37
2015	1 212 055	45	1 431	82 420	1.74
Total	12 051 476	1366	16 395	819 500	2.00

**Based on modelled/estimated Figure of 6.8% of live births affected by CD per annual number of births*

Table 5.2 Distribution of CD notifications received between 2006-2015 from provinces and districts in South Africa

Province	District	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Total
Eastern Cape (746)	Alfred NZO	0	0	0	8	9	33	15	0	0	10	75
	Amathole	29	32	53	3	58	45	54	5	10	2	291
	Cacadu	0	0	5	0	1	24	20	14	14	0	78
	Chris Hani	4	1	2	0	2	42	13	2	4	0	70
	N Mandela Metr	0	0	3	7	21	2	27	12	0	0	72
	OR Tambo	1	4	9	5	5	25	31	20	0	0	100
	Joe Gqabi	1	1	0	1	2	23	21	11	0	0	60
	Buffalo City	0	0	0	0	0	0	0	0	0	0	0
Free State (895)	Fezile Dabi	0	0	0	14	7	19	6	6	1	0	53
	Lejweleputswa	41	45	23	28	4	26	109	45	27	0	348
	Motheo	0	0	0	13	88	108	81	34	11	131	466
	Thabo Mofutsanyane	0	0	4	8	2	5	3	5	0	0	27
	Xhariep	0	0	0	0	0	1	0	0	0	0	1
Gauteng (1836)	Ekurhuleni	2	0	9	0	5	46	36	12	0	0	110
	Johannesburg Metro	0	0	0	0	31	46	74	58	0	0	209
	Metsweding	0	0	1	9	7	16	0	0	0	0	33
	Sedibeng	0	0	0	0	0	7	7	0	0	0	14
	Tshwane	89	162	94	4	190	275	279	73	11	208	1 385
	West Rand	0	0	0	0	14	14	11	22	11	13	85
Kwa-Zulu Natal (9732)	Amajuba	26	61	53	45	48	71	40	8	12	10	374
	eThekwini	33	266	539	902	664	663	792	491	604	722	5 676
	iLembe	5	2	3	22	31	51	107	65	106	66	458
	Sisonke	17	15	25	13	29	20	9	6	4	7	145
	Ugu	8	46	26	28	56	50	19	36	9	0	278
	Umgungundlovu	0	24	56	92	114	125	51	65	67	50	644
	Umkhanyakude	4	13	12	25	35	42	27	14	14	5	191
	Umzinyathi	5	34	62	51	67	73	89	10	0	0	391
	Uthukela	20	95	69	57	49	23	0	0	0	0	313
	Uthungulu	90	121	107	134	118	136	167	101	0	1	975
	Zululand	24	52	8	52	105	37	0	0	10	0	288
Limpopo (572)	Capricorn	0	42	23	3	2	1	50	1	4	1	127
	Mopani	1	12	11	4	2	32	1	0	5	6	74
	Sekhukhune	0	0	5	29	1	32	13	1	1	0	82
	Vhembe	31	39	23	35	20	9	45	0	11	4	217
	Waterberg	0	12	10	10	0	14	0	9	0	17	72
Mpumalanga (864)	Ehlanzeni	50	16	6	47	18	34	36	106	36	4	353
	Gert Sibande	23	30	21	31	16	22	51	62	48	21	325
	Nkangala	26	27	0	15	0	16	62	35	5	0	186
North West (538)	Bojanala	20	6	41	33	7	18	22	0	0	0	147
	Dr Kenneth Kaunda	18	15	33	5	2	29	5	3	0	0	110
	Ngaka Modiri Molema	25	43	23	8	30	63	32	0	0	0	224
	Ruth S Mompati	15	17	16	7	2	0	0	0	0	0	57
Northern Cape (823)	Frances Baard	36	49	90	46	47	32	123	81	81	98	683
	John Taolo Gaetsewe	2	1	6	4	1	8	2	0	2	0	26
	Namaqua	1	5	3	0	1	1	11	0	4	0	26
	Pixley Ke Seme	0	0	4	5	7	3	3	0	4	1	27
	ZF Mgcawu	1	10	5	7	5	6	13	0	4	9	60
Western Cape (389)	Cape Winelands	0	18	25	7	0	1	0	2	0	0	53
	Central Karoo	0	0	3	1	0	0	0	0	0	0	4
	City of Cape Town	0	3	76	14	10	0	0	0	0	0	103
	Eden	0	0	13	25	13	26	10	4	10	38	139
	Overberg	0	19	13	10	0	2	4	1	0	3	52
	West Coast	0	0	4	12	4	8	6	0	0	4	38
SA Total		648	1 338	1 617	1 879	1 950	2 405	2 577	1 420	1 130	1 431	16 395

Table 5.3 Provincial data compared to expected CDs data based on population size and density

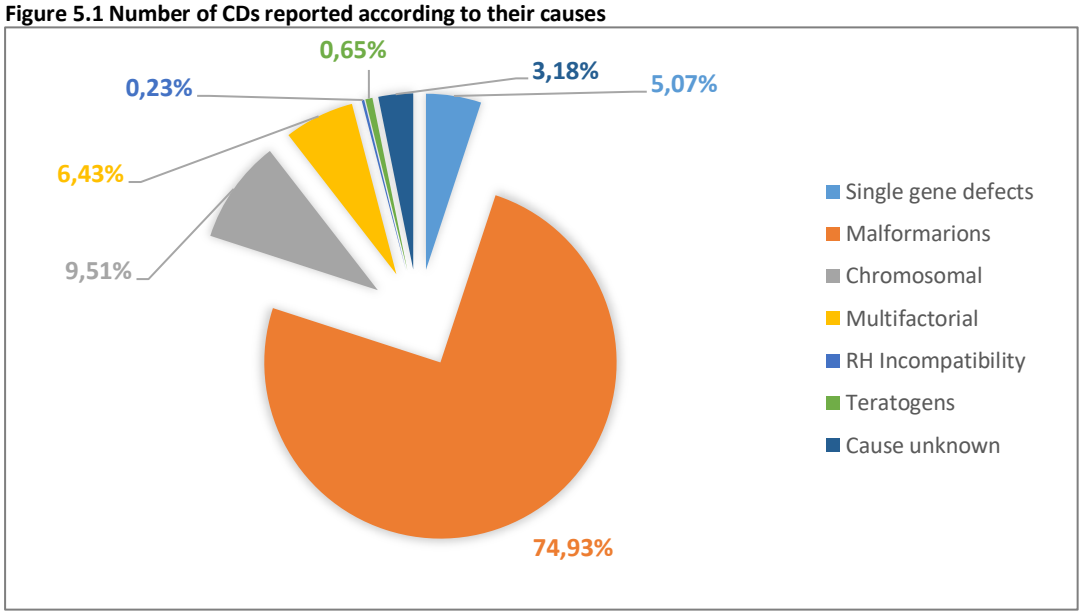
Provinces	CDs Notified (%)	CDs Expected* (%)	Geographical Area‡ (%)	Percentage Population (%)
Eastern Cape	4.55	12.58	13.8	3.91
Free State	5.46	5.13	10.6	2.06
Gauteng	11.2	24.02	1.40	69.68
KwaZulu-Natal	59.36	19.87	7.70	11.02
Limpopo	3.49	10.42	10.3	4.34
Mpumalanga	5.27	7.80	6.30	5.31
North West	5.02	2.16	8.70	3.39
Northern Cape	3.28	6.75	30.5	0.30
Western Cape	2.37	11.28	10.6	4.56

*Based on modelled/estimated Figure of 6.8% of live births affected by CD per annual number of births and population size
‡Data from StatsSA

5.3 CDs based on aetiology

Figure 5.1 below categorises notified CDs according to their aetiology. Both genetically and environmentally determined CDs were notified. Genetically determined CDs were in the majority with 96.2% of total CDs reported. This included single gene defects, malformations, chromosomal, multifactorial and CDs caused by RH incompatibility. The most reported of these were malformations (74.93%) and chromosomal CDs (9.51%). Environmentally determined CDs accounted for 0.65% of the total reported. These included CDs caused by alcohol use by the mother during pregnancy, maternal infections and an unfavourable maternal uterine environment. The cause of the remaining 3.18% CDs was unknown due to two reasons: Firstly, the abnormalities on the notification forms were not specified e.g. 'abnormal baby' written under diagnosis. Secondly, CDs associations were reported without a final/underlying diagnosis e.g. Down syndrome and spina bifida reported for a single patient.

Figure 5.1 Number of CDs reported according to their causes



5.4 Birth prevalence based on aetiology

Birth prevalence was determined for each of the CDs depending on whether they were genetically or environmentally caused. Examples of the commonly reported CDs per type of CD are listed below:

- Chromosomal abnormalities: e.g. Down syndrome, other trisomies, Turner syndrome
- Autosomal dominant: achondroplasia, Marfan syndrome, neurofibromatosis
- Autosomal recessive: oculocutaneous albinism (OCA), spinal muscular atrophy, Colloidion (Harlequin) baby syndrome
- X-linked- haemophilia, Aarskog-Scott syndrome, fragile X
- Multifactorial inherited abnormalities - neural tube defects (NTD)
- Teratogens – Fetal alcohol syndrome (FAS)
- Cardiovascular system malformations - heart defects
- Facial malformation - orofacial clefts (OFCs)
- Musculoskeletal system - polydactyly and talipes equinovarus

For certain conditions, inheritance patterns differ depending on the type of CD reported. In instances where the type was not specified, that case was categorised under 'more than one inheritance pattern'.

Birth prevalence's for each priority CD were calculated as follows:

$$\text{Birth prevalence} = \frac{\text{number of CD cases (live and still births, TOP)}}{\text{Total live births}}$$

In the formula above, the birth prevalence is calculated by combining the number of live births, stillbirths and terminated pregnancies (TOP) with a CD as a proportion of the total number of live births in the country [1]. The total live births reported between 2006-2015 were 12 051 476; this total number was used as the denominator to calculate birth prevalence for the different CDs.

Table 5.4 Birth prevalence of each category of CDs per 1 000 live births

Type of CD	Number of CDs	Prevalence/1 000 LIVE births
Single gene defects Sub-total	831	0.07
Autosomal dominant	188	0.02
Autosomal recessive	440	0.04
X-linked	76	0.01
Mutations	3	0.00
More than 1 inheritance pattern	83	0.01
Genetic type Unknown	41	0.00
Chromosomal	1 559	0.13
Multifactorial	1 055	0.09
Teratogen	106	0.01
RH Incompatibility	38	0.00
Malformations Sub-total	12 284	1.02
Cardiovascular system	1 274	0.11
Face	1 865	0.15
Gastrointestinal tract	1 275	0.11
Genital organs	452	0.04
Musculoskeletal system	4 129	0.34
Nervous system	1 366	0.11
Skin	53	0.00
Urinary system	143	0.01
Respiratory system	3	0.00
Multiple Malformations	1 692	0.14
Malformation not specified	32	0.00
Total	15 873	1.32

5.5 Priority CDs

A total of 5 649 priority CDs were reported from 2006 to 2015, see Table 5.5, accounting for 34.46% of the total CDs reported. The four most commonly reported CDs, in descending order, were Down syndrome (n=1 419), cleft lip and/or palate (n=1 204), talipes equinovarus (clubfoot) (n=1 188), and neural tube defects (NTDs) (n=1 024). The least reported priority CD was fetal alcohol syndrome (FAS) with 84 cases. Multiple priority CDs were reported on 352 notifications.

Table 5.5. Priority CD birth prevalence per 1 000 live births

Priority CD	Number of CDs	% of CD notified	Number/ 1 000	Population Group (n)					Gender (n)				Birth Outcome (n)					Weight (n)			Gestational age (n)		
				Black	White	Coloured	Other	Not Recorded	Ambiguous	Male	Female	Not Recorded	Live birth	Stillbirth	Miscarriage	TOP	Not Recorded	<2500g	≥2500g	Not Recorded	<37 Weeks	≥37 Weeks	Not Recorded
Down syndrome	1 419	25.12	0.12	1 238	14	68	33	66	17	647	691	64	1 239	50	1	3	126	414	827	178	319	749	351
OFCs	1 204	21.31	0.1	952	81	60	74	37	4	612	535	53	989	48	0	7	160	358	653	193	334	604	266
Talipes equinovarus	1 188	21.03	0.10	1 014	23	78	39	34	17	634	486	51	1 101	32	0	4	51	332	772	84	286	658	244
NTDs	1 024	18.31	0.09	879	14	64	34	33	16	496	463	49	738	176	2	30	78	429	489	106	385	436	203
FAS	84	1.49	0.01	38	0	41	0	5	1	44	36	3	80	0	0	0	4	53	18	13	29	33	22
Albinism	378	6.69	0.03	352	0	10	1	15	0	182	182	14	337	2	0	0	39	38	288	52	47	235	96
Priority CDs associations	352	6.23	0.03	306	3	25	3	15	9	190	138	15	283	50	5	3	11	137	196	19	115	181	56
Total	5 679	100	0.35	3 541	121	278	151	139	47	2 158	1 840	185	3 528	308	7	44	343	1 347	2 416	467	1 196	2 147	887
%				84.15	2.38	6.09	3.24	3.61	1.13	49.39	44.57	4.38	83.94	6.30	0.14	0.85	8.26	31.01	57.11	11.36	26.68	50.99	21.80

Table 5.5 includes data fields for each of the reported priority CDs namely population group, gender, pregnancy outcomes, birth weight and gestational age. Each of these data fields included data gaps and inaccuracies e.g. for population group, foreign nationals were marked as 'other' when the correct ethnicity is black. Empty data fields were marked as not recorded, although not all the data fields were applicable for each case e.g. for older patients, birth weight and gestational age were not relevant. The ethnicity for more than 80% of reported priority CDs was black. The other options were white, coloured and 'other'. For the 'other' data field, health care providers (HCP) were expected to specify the ethnicity of the patient if they did not belong to any of the previously mentioned groups. From the data, the 'other' data field consisted of Asian and Indian patients with the numbers approximately evenly distributed between the two. This trend was the same for all priority CDs except for FAS in which the majority of patients were of coloured descent. In terms of gender, the proportion of males with CDs was higher than that of females for most of the conditions. The two exceptions were Down syndrome and albinism, in which more females were reported to have Down syndrome than males while the number of male to female patients with albinism was similar. A majority (83.64%) of cases were born alive with mortalities highest in cases with NTDs diagnosed, followed by Down syndrome and patients with CD associations (when multiple abnormalities occur non-randomly and are not syndromes or sequences then they are referred to as associations). Results also indicated NTDs to have a higher proportion of low birth weight infants (i.e. less than 2 500g). The highest proportion of low birth weight infants however was found in FAS cases with 63% of cases under 2.5kg.

5.5.1 Down Syndrome

Table 5.6 demonstrates the number of Down syndrome cases reported for the period. Down syndrome was the greatest proportion of priority CDs notified though only a few cases were diagnosed prenatally. Only three (0.21%) cases from 2006-2015 were diagnosed prenatally and all the mothers opted for termination of pregnancy. The remaining cases were diagnosed at birth and throughout the continuum of care, with the oldest patient diagnosed at 29 years. Opportunities for diagnosis following delivery were sought at every contact between the mother and infant pair and the health facility including, six weeks' postnatal care, immunisations services and any acute illness services offered to children.

Table 5.6. Down syndrome cases reported from 2006-2015 including maternal age and age of diagnosis

Year	Number of DS cases	Maternal Age			Prenatal Diagnosis (TOP)	Age of Diagnosis			
		<35yrs	≥35yrs	Unknown		0-1 month	< 1 yr	1 -5 yrs	≥ 6-29 yrs
2006	72	19	25	28	0	28	22	13	5
2007	149	81	50	18	0	54	43	47	9
2008	125	60	42	23	3	56	31	32	4
2009	222	70	65	87	0	69	63	70	14
2010	187	69	64	54	0	63	48	58	9
2011	189	101	66	22	0	69	57	51	6
2012	170	89	73	8	0	76	25	50	9
2013	112	64	40	8	0	66	17	26	0
2014	90	51	31	8	0	25	27	29	4
2015	103	52	44	7	0	33	22	41	5
Total	1 419	656	500	263	3	582	355	417	65
%	100	46.23	35.24	18.53		41.01	25.02	29.39	4.58

5.5.2 Orofacial clefts (OFC)

Three categories of OFCs were notified, cleft lip, cleft palate and cleft lip and palate, with the majority of OFCs being the latter. Table 5.7 illustrates a combined total of OFCs and Table 5.7 the number of cases for each category specified above. Table 5.7 further details birth prevalence for isolated OFCs versus those forming part of a syndrome. The majority (78.07%) of OFCs cases were reported in the black population, 6.73% were reported in the white population, 4.98% in the coloured population and 6.14% in the Indian and Asian population combined. A percentage of 50.83% cases were males and 44.44% females; the remainder of the cases (0.33%) had ambiguous genitalia. Pregnancy outcomes for reported OFCs were: 82.14% livebirths, 3.99% stillbirths and 0.58% TOPs. Around 50% of reported cases were born after 37 weeks' gestation (≥ 37 weeks) with a birth weight above 2.5kgs (≥2.5kgs). Of the reported cases, 27.74% were born premature and 29.73% had a birth weight of under 2.5kgs.

Table 5.7 Birth prevalence for isolated and syndromic OFCs per 1 000 live births.

	Isolated OFCs	%	Number/1 000	Syndromic OFCs	%	Number/1 000
Cleft lip	248	20.1%	0.02	8	7.21%	0.00
Cleft palate	285	23.7%	0.02	42	37.84 %	0.00
Cleft lip and palate	671	55.7%	0.06	61	54.96%	0.01
Total	1 204	100.0%	0.10	111	100.0%	0.01

5.5.3 Talipes equinovarus (Clubfeet)

In Table 5.5, a total of 1 188 clubfeet cases were reported, which is a birth prevalence rate of 0.10 per 1 000 live births. More cases were reported in the black and coloured populations with 85.35% and 6.57% respectively. White, Indian and Asian populations combined

accounted for 5.22% of the reported cases. Similar to OFC more cases were reported in males (53.4%) than in females (40.91%). In 1.4% of the cases reported, the patients had ambiguous genitalia and no gender was specified in the remaining cases. Of the reported cases, 92.68% were livebirths, 2.69% were stillbirths and for less than 1% (0.33%)were terminated pregnancies. Approximately 55% of cases were delivered after 37 weeks' (≥ 37 weeks) gestation, while 24.07% were born before full pregnancy term. Most cases (64.98%) had normal and above average birth weight while 29.95% of cases had low birth weight.

5.5.4 Neural Tube Defects (NTDs)

Three types of NTDs were monitored: anencephaly, encephalocele and spina bifida. The combined total of NTDs reported was 1 024 as can be seen in Table 5.5. Birth outcomes of this total number: 20.3% of cases died, 17.2% were stillborn, 2.9% were terminated and 0.2% miscarried. Both the medical task force on anencephaly (established in 1990) and de Castro Santana *et al* documented the high mortality rates of anencephaly cases during pregnancy (65%) or soon after birth (90-95%) [73, 74]. Due to the high mortality rates of anencephaly cases in utero and after birth, the NTD birth prevalence including and excluding anencephaly were calculated to show the contribution of anencephaly cases to the total neural tube rate as some anencephaly cases would have been missed due to death during pregnancy and soon after birth (within the first week of life). These numbers are shown in Table 5.8 below.

Ethnic variation was as expected, with 85.84% of all reported NTDs cases found in the black population. This is expected as 86.18% of all reported CDs were found in the black population. NTDs reported in the white, coloured and Indian population together accounted for 10.94% of the reported cases. The gender distribution was fairly equal with 48.43% of cases being male and 45.21% female. A small percentage (1.56%) of cases had ambiguous genitalia. Most of the reported cases were live births with a percentage of 72.07%. NTDs had the highest stillbirth and termination of pregnancy rates of all the priority conditions with 17.18% and 2.93% respectively. A concerning number (37.60%) of NTD cases were born prematurely and others with low birth weight (41.89%).

Table 5.8 NTDs birth prevalence per 1 000 live births vs. birth prevalence excluding anencephaly

Type of NTD	NTDs including anencephaly	Number/ 1 000	NTDs excluding anencephaly	Number/ 1 000
Anencephaly	241	0.02	0	0.00
Encephalocele	134	0.01	134	0.01
Spina Bifida	647	0.05	647	0.05
NTD unspecified	2	0.0002	2	0.00
Total	1 024	0.09	783	0.07

5.5.5 Oculocutaneous Albinism (OCA)

A total of 378 OCA cases were reported from 2006-2015 as can be seen in Table 5.5. In terms of ethnic variation of cases, 93.54% black, 2.24% coloureds, 0.28% asian were observed. The gender ratio was equally split with both male and female cases being 48.1%. No gender was recorded in 3.7% of the reported cases. Most (89.15%) of all reported OCA cases were born alive, this is expected as this condition has a high survival rate. Only two (0.53%) stillbirths were reported with OCA and no pregnancy outcome was recorded in 10.32% of cases. Most of the reported cases were born full term (62.17%) and had normal or above normal (76.19%) birth weight. A small portion of cases were born prematurely (12.43%) and a few had low birth weight (10.05%).

5.5.6 Fetal Alcohol Syndrome (FAS)

A total of 84 FAS cases were reported from 2006-2015, the majority (48.8%) of which were from the coloured population. This number is higher than the 45.2% found amongst the black population as illustrated in Table 5.5. Table 5.9 below shows the distribution of cases according to the age of diagnosis and the provinces that notified the cases. No cases were reported from Limpopo and North West provinces. More males (52.38%) with FAS were reported than females (42.86%). A majority (95.24%) of FAS cases were reported as live births. No pregnancy outcome was recorded on the remainder of cases. A high number of FAS cases had associated low birth weight (LBW), 63.10% LBW cases were reported versus 21.14% for normal weight and the rest not recorded. Of all the FAS cases reported, 34.52% were preterm births while 39.29% were term births.

Table 5.9 FAS cases per province from 2006-2015 and the age of diagnosis

Province	Age of Diagnosis				Total
	0-1 month	< 1 yr	1-5 yrs	≥ 6 yrs*	
Eastern Cape	20	3	2	1	26
Free State	2	0	0	0	2
Gauteng	1	1	1	2	5
KwaZulu-Natal	10	3	5	2	20
Limpopo	0	0	0	0	0
Mpumalanga	1	0	0	0	1
North West	0	0	0	0	0
Northern Cape	7	0	0	5	12
Western Cape	4	7	4	3	18
Total	45	14	12	13	84

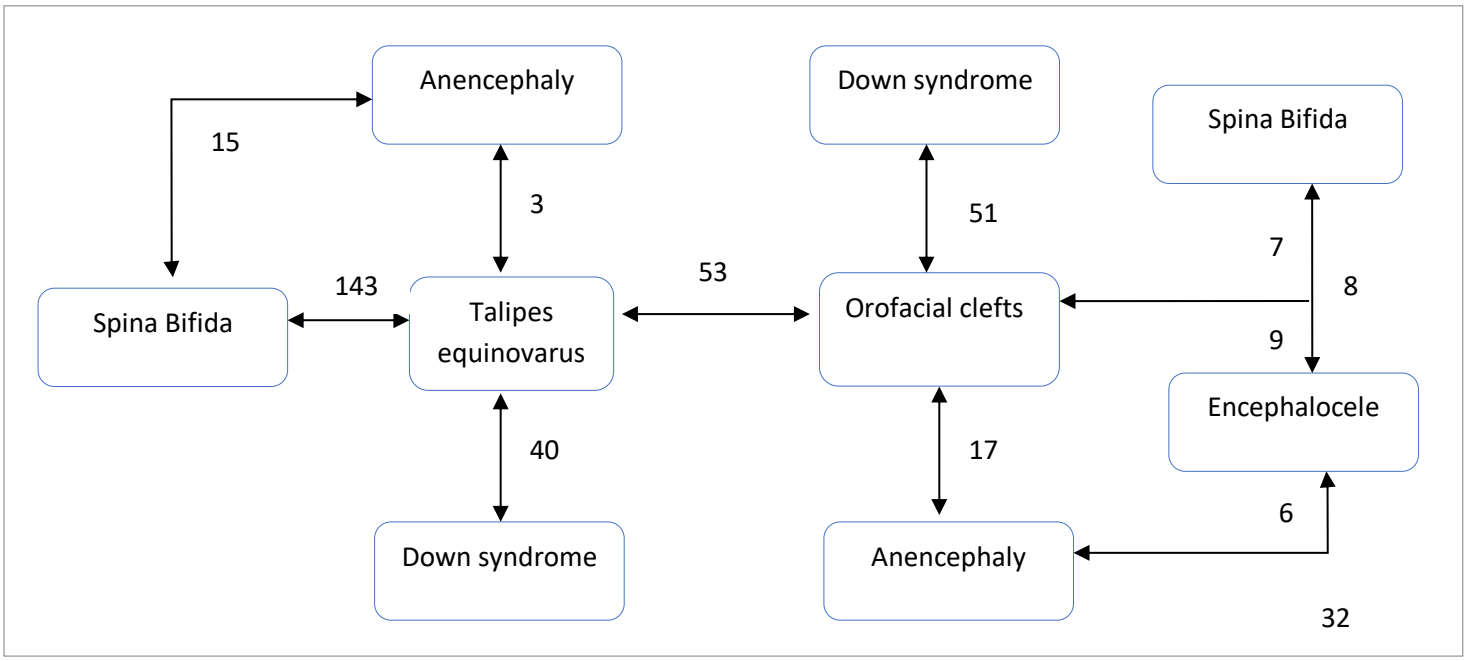
*this ranges from 6 years to 12 years

5.5.7 Priority CD association

In 352 cases, more than one priority CD was reported per patient. A combination of typical dysmorphic features in an individual is an indication of a syndrome [75]. If a diagnosis could not be made, those abnormalities the HCP observed had to be notified. In cases with multiple CD associations, 32.7% of infants were born preterm and 38.95% were born with low birth weight, less than 2,5kgs, as shown in Table 5.5.

Figure 5.2 shows various CDs associations observed. Most associations were between either clubfeet and other CDs, or OFCs and other CDs. The most reported association was spina bifida patients with clubfeet.

Figure 5.2 Schematic representation of association of CDs

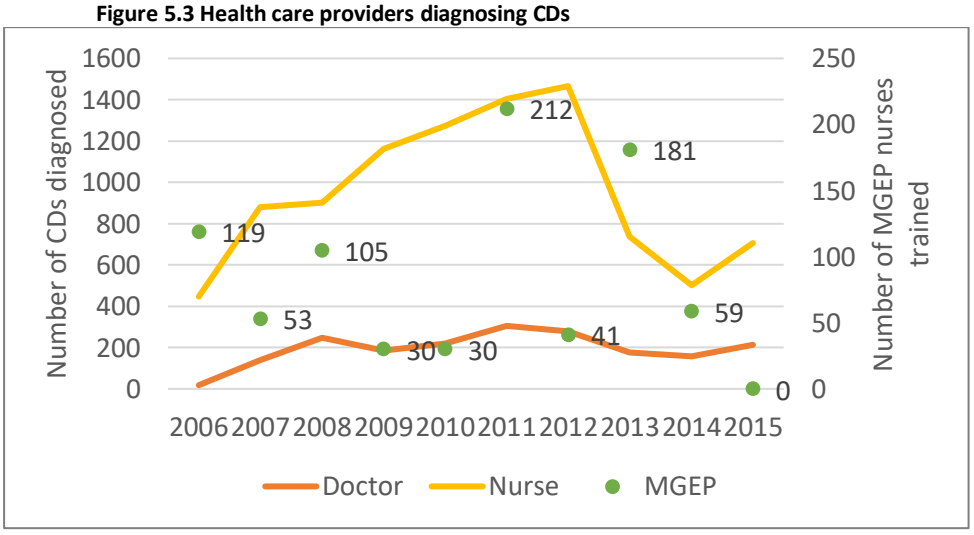


5.6 Diagnosis and reporting of BDNT

At primary health care (PHC) facilities, most patients with CDs are identified by nurses and at tertiary level facilities, by doctors. Doctors include both specialists (e.g. clinical geneticists, paediatricians) and medical officers. Figure 5.3 illustrates the trend of doctors versus nurses reporting cases, both priority CDs and OCDs.

The training of nurses in SA enables a level of clinical authority, allowing them to assess, diagnose, prescribe and dispense medication. Medical Genetics Education Programme (MGEP) training is offered to qualified nurses to improve their knowledge and skill with regard to the identification and reporting of CDs. MGEP training was conducted consistently from 2006-2014. For CD patients, nurses may make a preliminary diagnosis, and refer the patient for further management at the next level of care. Over half (57.80%) of all reported CD cases were diagnosed by nursing staff.

Figure 5.3 Health care providers diagnosing CDs

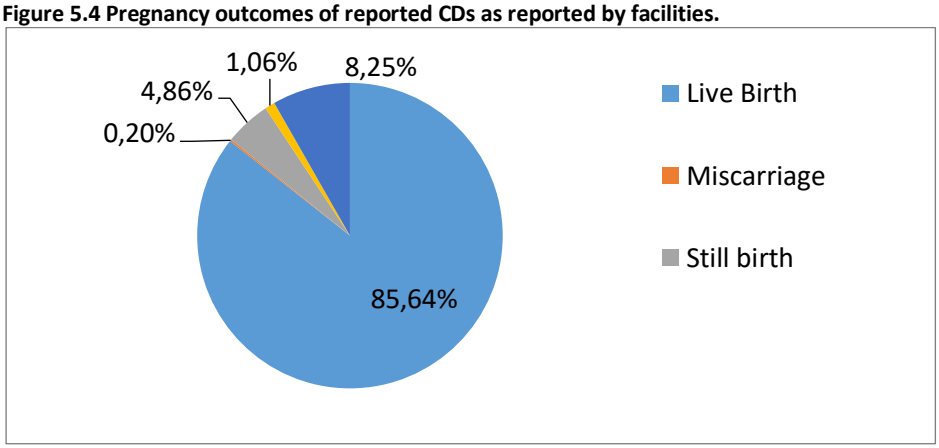


5.7 Pregnancy outcomes

CDs from all pregnancy outcomes were reported. These included live births, stillbirths, miscarriages and termination of pregnancies affected by a CD and are shown in Figure 5.4. Of the reported 16 395 CDs, the majority 14 041 were live births, 797 were stillbirths, 32 were miscarriages, 173 were elected terminated pregnancies. For 1 352 of reported cases the pregnancy outcome was not indicated. For this study, only infants affected by a CD and born within a health facility were notified. Similarly, only stillbirths, miscarriages and TOPs with a

CD that occurred in health facilities were notified. All infants delivered alive outside of health facilities and die outside of a health facility were excluded from this study.

Figure 5.4 Pregnancy outcomes of reported CDs as reported by facilities.



5.8 Preterm birth and low birth weight

Any infant born before 37 weeks (37 weeks and 0 days) but after 24 weeks of pregnancy is considered a preterm infant [52]. For this study, the only indication for preterm delivery was infants born before 37 weeks, regardless of whether they were born before or after 24 weeks. In addition to preterm delivery, the birth weight of infants born with a CD was also recorded. Infants were considered low birth weight if they weighed less than 2.5kgs at delivery. In this study, 26.40% of cases were reported as preterm births, while 29.98% of reported cases had low birth weight (see Table 5.10). Gestational age and birth weight were not applicable to all cases especially those that were identified at a much later age. Unfortunately, this limitation was not taken into consideration; HCP left the data fields empty, leading to an increase in cases not recorded.

Table 5.10 Number of CDs notified that were born preterm and those that were born with low birth weight.

Year	Birth weight			Gestational age		
	<2500g	≥2500g	Not Recorded	<37 weeks	≥37 weeks	Not Recorded
2006	192	379	77	131	357	160
2007	400	824	114	329	782	227
2008	482	852	283	430	772	415
2009	503	959	417	510	820	549
2010	615	1 157	178	507	1 031	412
2011	697	1 498	210	660	1 259	486
2012	723	1 633	221	609	1 352	616
2013	440	837	146	409	637	374
2014	390	595	146	329	373	428
2015	473	835	123	414	621	396
Totals	4 915	9 569	1 915	4 328	8 004	4 063
%	29.98%	58.37%	11.68%	26.40%	48.82%	24.78%

Chapter 6: Discussion 1

6.1 Introduction

The primary role of any surveillance system is to produce data that can be used for planning, implementation and evaluation of health strategies [1]. Accurate data is important for policy development and the delivery of health services. The importance of CDs surveillance was emphasized in the National Department of Health (NDOH) 2001 policy guidelines [7]. It was these guidelines that gave rise to the national birth defects notification tool (BDNT) surveillance system in 2006. This system has produced data, which to date has not resulted in any action in terms of the data being used for any CD prevention and/or management strategies. The purpose of this study was to measure the effectiveness and functionality of the national BDNT surveillance system.

The objectives of the study were to:

1. Evaluate the effectiveness of the BDNT surveillance system.
2. Document the successes and shortfalls experienced during implementation.
3. Develop an improved national CD surveillance system based on lessons learned from the BDNT surveillance system.

All the findings from the BDNT surveillance system detailed in Chapter 5 (Results) are compared with that of other systems globally and locally in this Discussion. The chapter ends by documenting the challenges of the BDNT surveillance based on the experience to date followed by recommendations for an improved CD surveillance system for South Africa (SA).

6.2 Annual Variation

From May 2006 – December 2014, 17 761 notification tools were received, including 16 395 reported CDs and 1 366 nil reports. Reporting peaked in 2011 and 2012, with 2 405 and 2 577 CDs reported respectively. A low number of 648 CDs was reported during the initiation year of the surveillance system, as expected since data was only received for eight months out of the 12 since the system was only implemented in May 2006. Annual reporting increased steadily from 2006 until 2012, and then decreased in the latter part of the reporting period. This suggests underreporting by the facilities as the number of lives births remained at an average of 1,2 million births annually from 2008 – 2015. Based on modelled data, 6.8% of live births are affected by a CD annually [6]. This implies that for this study period an estimated 819 500 (total) CDs should have been reported. This estimate is for all CDs, not just the obvious CDs diagnosable at birth as included in the BDNT. The BDNT reported 16 395 CDs for the total nine-year period. With only 2% of the expected numbers of CD cases reported, the BDNT surveillance system is underreporting CDs by 98% despite recording mostly CD diagnosable at birth.

6.3 Provincial and District Variation

Table 5.3 demonstrates the percentage of CDs notified versus the expected numbers using national demographic data. Since the CD expected percentage is calculated using live birth numbers per province, it is expected that the CD expected percentage per province is the same proportion as births per province. Based on the expected percentage of notifications per province, only the Free State province notified in the expected proportion, with 5.46% actual notifications compared versus 5.13% expected. The majority of CD notifications (52.07%) were reported in the Motheo district of the Free State, where both the Provincial capital, Bloemfontein and the medical genetics clinic are located. This clinic is operated by a medical geneticist who also runs outreach clinics in Northern Cape.

KwaZulu-Natal province reported more than its expected percentage, reporting 59.63% versus the 19.87% expected. Six of the 11 districts in the province reported consistently with the majority (58.32%) of CDs reported by eThekwini district. Similar to Motheo district in the Free State, the medical genetics clinic for KwaZulu-Natal province is based in eThekwini. This is an informal genetics clinic run by a paediatrician with an interest in CDs as there are no permanent posts for medical geneticists and genetic counsellors in the province. KwaZulu-Natal's significant provincial success may be attributed to i) continued Medical Genetics Education Programme (MGEP) training for HCP in the province - enabling increased recognition and identification of CDs, resulting in improved compliance in terms of completion and submission of notification tool, ii) the presence of an active provincial coordinator advocating for CD data collection and submission of notification tools to NDOH. Provincial coordinators are typically responsible for a combination of programmes, including: maternal, child and women's health and prevention of mother to child transmission of HIV/AIDS (Human immunodeficiency virus infection and acquired immune deficiency syndrome). Genetic services and the management thereof, are only one of many the coordinators duties. As a result, these competing priorities within the DOH result in poor co-ordination of genetic services, negatively impacting the co-ordination of HCP training and CD data flow from facilities to the NDOH via the province. The loss of KwaZulu-Natal's provincial coordinator in 2012, had a negative impact on the provincial and national reporting with a decline in data observed from 2013 to 2015.

North West Province reported 5.02% versus the expected 2.16% with most CDs reported from Ngaka Modiri Molema district (41.63%). Surprisingly, none of the districts in the province reported consistently, with CDs last reported by the province in 2013 (only three BDNT were received from Dr Kenneth Kaunda district). This province, like KwaZulu-Natal, had a very active coordinator who left the province in 2011 and without an individual coordinating the programme including CD surveillance, reporting dwindled from 2011 and eventually stopped

in 2013. Owing to the efforts of the coordinator prior to their departure, the province could report above expectation in five of the nine years of the reporting period.

Population density is not the only factor affecting the distribution of CDs countrywide. The rate of CDs is higher in people of a lower socioeconomic status, found in the more rural parts of the country [2]. More than half of the population in Limpopo, Northern Cape, Eastern Cape, Mpumalanga, North West and KwaZulu-Natal provinces are considered rural [76, 77]. Specific determinants influence health outcomes in these rural areas, including a) travelling distances to facilities, including transport costs b) quality of services rendered - influenced by a lack of human resources at rural facilities c) package of services available at the different levels of care, supported by a referral system allowing patients to access specialist services with outreach clinics held to supplement services [76]. These determinants directly impact upon the provision of medical genetics services in each province, including the reporting of CDs. The Eastern Cape, Limpopo, Mpumalanga and Northern Cape (all of which reported fewer CDs than expected) are mostly rural provinces, lacking medical genetics services (permanent medical geneticist and genetic counsellors) posts and capacity in those provinces except for limited outreach clinics. Of these mentioned provinces, only the Eastern Cape has an informal medical genetics clinic run by a paediatrician in Buffalo city district. Buffalo city was a part of Amathole district before being separated from it in 2011. Some of the cases for Buffalo city could be wrongly reported under Amathole district.

The Northern Cape province is especially vulnerable with the lowest population spread over the largest geographical area and the lowest population density, making it difficult for patients to access facilities due to the vast distances involved. The province reported half of the expected CD cases, with the majority (n=683, 82,30%) of the total 823 notifications reported in the Francis Baard district where the Provincial capital, Kimberley is located. Limited medical genetics services in the rural province are only available through outreach clinics provided by visiting specialists from the Free State Province.

Although in terms of population Gauteng and KwaZulu-Natal provinces are the largest and collectively have 43.9% of the population, KwaZulu-Natal is significantly larger in area and almost six times the size of Gauteng [72]. Despite the contrasting population densities, 69.68 p/m^2 in Gauteng and 11.02 p/m^2 in KwaZulu-Natal, these two provinces still have the highest CD provincial rates in the country and should notify the most CDs. Data from this study corroborates this premise, with both provinces collectively reporting 70.56% of the total CD notification in the reporting period.

Gauteng reported 1 836 CDs during the study period. While this ranked second overall, after KwaZulu-Natal, the 11.20% reported was less than half the 24.02% expected (See Table 5.3). Medical genetics services are available in two of the six districts in the province - Johannesburg metro and Tshwane districts. The majority of the notifications in the province

were reported by Tshwane district (75.44%) with a lesser contribution (11.38%) by Johannesburg metro. The low number of notifications in the province indicates lack of compliance by HCP resulting in underreporting. Owing to the large population density in Gauteng, more CDs should have been reported by the province. In addition, Johannesburg metro has medical genetic services including medical geneticist and genetic counsellors. Tshwane district has a medical genetics clinic run by a paediatrician with an interest in genetics. With services being available at facility level, and a provincial coordinator present at provincial level, two things can be attributed to the underreporting by the province: 1) Patients are seen in the medical genetics clinics but are not reported 2) patients are reported, but due to poor communication between the levels, notification forms are not reaching the national office.

The Western Cape is a mostly urban (with more than 80% of the provincial population living in a formal residential area) province with a population density of 44.98 people per square kilometer that accommodates 11.3% of SAs population [78, 79]. Urban areas generally have more health facilities and the population in those areas have better health outcomes than those in rural areas [76, 80]. Medical genetics services are available in the Western Cape province, however, these services are not translating into CDs being reported via the BDNT. Cape Town city hospitals and delivery facilities are linked to universities with good neonatal and genetic services where most newborns are examined by well trained staff. This suggests a serious defect in data collection, transfer or failure of the provincial co-coordinator to check on data transfer. The province reported the lowest number of notifications with only 389 CDs reported in the study period. This translates into a percentage reporting of 2.37% instead of the expected 11.38% for the province. Eden district was the most consistent district in the province in terms of reporting as they reported CDs in eight of the ten years of the study. The low percentage of CD notifications and the inconsistency in reporting indicates a lack of compliance by the HCP and poor communication between the different levels of governance.

6.4 Birth prevalence per CDs based on aetiology

The causes of CDs can be divided into two categories: (1) genetic and partially genetic CDs which originate before conception and (2) non-genetic CDs which originate after conception but before birth [2]. Most CDs originate before conception and are caused by abnormalities of the genetic material, which includes chromosomes and genes. Examples of these are single and multiple organ/system malformations, genetic syndromes and metabolic disorders [2, 23]. These are caused by single gene defects, chromosomal abnormalities (whole or part of chromosome lost or gained) and multifactorial abnormalities which arise from complex interactions between the genetic and environmental factors [23]. The most reported genetic CDs were malformations at 74.93%. This was followed by chromosomal CDs at 9.51% and single gene defects at 5.07%. These genetic and partially genetic CDs can be inherited or can

occur as isolated events. According to modelled data by Christianson and Modell [23], approximate birth prevalence for genetically caused CD is 36.5 per 1 000 live births for malformations, 3.8 per 1 000 live births for chromosomal CDs, 2.6 per 1 000 live births for genetic risk factor (RH incompatibility) and 12.3 per 1 000 for single gene defects [2, 23]. Genetic risk factors are common gene variants that cause problems relatively rarely. These include risk factors for late onset diseases and Rhesus negativity in the context of CDs. In this study, birth prevalence were much lower at 1.02 per 1 000 live births for malformations, 0.13 per 1 000 live births for chromosomal CDs, 0.00 per 1 000 live births for genetic risk factors CDs and 0.07 per 1 000 live births. Birth prevalence's from this study were much lower due to 1) the high underreporting rate by the BDNT, 2) data collected by the BDNT surveillance not being a true representation of SA as data is not received from all facilities in the public health sector and no data is received from the private health sector, 3) the poor diagnostic skill of HCPs, only preliminary diagnoses are reported, making data unreliable.

6.4.1 Malformation

This group of CDs is the largest group of genetically caused CDs [23]. While the birth prevalence of malformations in developing countries is reported as 29.3 per 1 000 in by Christianson and Modell, this study reports a much lower birth prevalence of 1.02 per 1 000 live births [23]. Birth prevalence for the congenital malformation was categorised according to the organ or system. Most common malformations reported in literature are those of the cardiovascular system with birth prevalence estimates of 7.9 per 1 000 in developing countries, 6.9 per 1 000 in Europe, 9.3 per 1 000 in Asia and 8 per 1 000 in the United States (US) (all calculated at per 1 000 live births) [23, 81]. Birth prevalence rates for congenital heart defects in SA are not available but it is estimated that 11 000 children are born annually with a congenital heart defect, of which 3 000 die or remain disabled due to untreated congenital heart defects [82]. Data from this study shows a birth prevalence rate of 0.11 per 1 000 live births with examples of congenital heart defects reported being patent ductus arteriosis, ventricular septal defect, atrial septal defect and tetralogy of Fallot. The most commonly reported malformation was that of the musculoskeletal system with a rate of 0.34 per 1 000 live births. The most commonly reported musculoskeletal malformation was talipes equinovarus (clubfoot). More on this condition is given below in section 6.5.3. Another commonly reported malformation is that of the face with an example being orofacial clefts (OFCs) also discussed below in section 6.5.2.

6.4.2 Single gene defects

This group of CDs consists of different categories including, dominant, recessive, X-linked and CD whose genetic type is unknown [2, 23]. Global birth prevalence's were all calculated at 1 000 live births, are estimated as follows: 7.0 per 1 000 for dominant, 7.4 per 1 000 for

recessive, 1.3 per 1 000 for X-linked and 1.2 per 1 000 for CDs with an unknown type. This study found low rates as follows: 0.02 per 1 000 for dominant, 0.04 per 1 000 for recessive, 0.01 per 1 000 for X-linked and 0.00 per 1 000 for genetic type unknown. As for the estimates from Christianson and Modell, this study found the most common single gene defects to be recessive inherited CDs, even with the underreporting experienced by the BDNT surveillance system.

6.4.3 Chromosomal

Christianson and Modell found Down syndrome to be among the most commonly reported chromosomal CDs [23]. Similar results were found in this study with other trisomies (including Edwards and Patau syndrome) also reported. More details on Down syndrome are shared in section 6.5.1 below.

6.4.4 Teratogens

CDs caused post-conception when the fetus has inherited normal genetic material are the result of teratogens [2]. Teratogens include altered metabolic states such as maternal diabetes mellitus and hypothyroidism, infectious agents, ingested substances like alcohol, illicit drugs and medications, hyperthermia, environmental pollutants and radiation [25, 83]. The most reported of these were CDs caused by alcohol use during pregnancy at 0.65%, with a birth prevalence of 0.01 per 1 000 live births. More on alcohol use during pregnancy and fetal alcohol syndrome (FAS) is discussed in section 6.5.6 below.

6.5 Priority CDs

6.5.1 Down syndrome

Of the total of 16 395 CDs reported nationally, 5 649 (34.46%) were priority CDs. Down syndrome is one of the common chromosomal disorders globally [84]. The World Health Organization (WHO) approximates the global birth prevalence of Down syndrome to between 1-10 affected births per 1 000 live births [85]. The birth prevalence of Down syndrome in low and middle income countries is estimated at 2-3 per 1 000 live births [2]. This rate is lower in developed countries (1.5 per 1 000 live births) because of the availability of prenatal screening and diagnostic services with the added option of termination of pregnancy coupled with increased access to family planning services and the use of contraceptives [2, 86, 87]. However, the population prevalence of Down syndrome is higher in developed countries because of increased survival rates of affected infants due to better care [86]. This was

demonstrated by Christianson *et al* [2] who stated that in SA, 65% of infants affected by Down syndrome died by the age of two years [87].

According to studies by Christianson, Urban and Willoughby, the average birth prevalence of Down syndrome in SA is 2 per 1 000 live births, with a lower birth prevalence observed in more urban settings [87-89]. Data collated in this current study indicated a birth prevalence of 0.12 per 1 000 live births. This is much lower than expected, and may be due to 1) overall low reporting rates as compared to estimated numbers based on known birth prevalence of established CD registries 2) Lower percentage of mothers of advanced maternal age (AMA) reported in this study 3) Lack of access to antenatal services including prenatal screening e.g. ultrasound 4) Challenges in diagnosing Down syndrome with the average chromosomal diagnosis of Down syndrome being over a year [89, 90].

Numerous peer reviewed studies demonstrate that birth prevalence of Down syndrome increases with advancing maternal age; at age 25 the average risk of a pregnancy affected with Down syndrome is 1 in 1 400 (11-13,15). This risk increases significantly to 1 in 350 at age 35 and 1 in 100 at age 40 [58, 86]. However, data in this study indicated that the majority of Down syndrome cases reported (n=656, 46%) occurred in mothers under 35 years. The NDOH *Guidelines for Maternity Care in South Africa* define the age for AMA as 37 years and older while the *Policy Guidelines for the Management and Prevention of Genetic Disorders, Birth Defects and Disabilities* defines AMA as 35 years and older [91]. This means that woman 35 and 36 years of age will not be referred to a specialist for health facility or a maternal fetal ultrasound for prenatal screening as specified in the Maternity Guidelines. This discrepancy in defining AMA could be the reason for the difference in data found in this study. Malherbe *et al* reviewed the Maternity Guidelines with relevance to CDs and discovered that particularly for women of AMA, current capacity in the medical genetics was inadequate to meet these women's needs [90].

Since 1997 and more recently in 2016, authors have reported difficulties encountered in diagnosing Down syndrome in Black infants [89, 92]. This results in missed opportunities for early intervention, with premature death as a consequence for many affected infants [2, 89]. This study confirms these diagnostic challenges, with only a third (37.98%) of the reported Down syndrome cases diagnosed and reported from birth until one month of age, 25.02% diagnosed under one year and the remaining 37% only being diagnosed after one year. Diagnosis of Down syndrome is mostly based on clinical identification of features, if the HCP performing a clinical examination of the infant does not have a trained eye (no medical genetics training), the probability of missing a Down syndrome diagnosis are very high. As the child grows, their features become more prominent, increasing the chances of a clinical diagnosis. This may explain why more Down syndrome diagnoses were made after one year.

6.5.2 Orofacial clefts (OFCs)

Cleft lip and/or palate or collectively referred to as orofacial clefts have a global birth prevalence of 0.7-1.47 per 1 000 live births [93]. In Africa, the rate ranges from 0.30 to as high as 1.65 per 1 000 live births [94, 95]. Variations in birth prevalence have been observed based on geographical areas and ethnic groupings, with lowest rates found in Africa and in the Black population. [93, 96]. In SA specifically, the birth prevalence ranges from 0.3 – 1.4 per 1 000 births depending on the ethnicity [97]. The data collated in this study indicated a rate of 0.10 per 1 000 live births. The most common reported orofacial clefts were cleft lip with a cleft palate with 671 cases, followed by isolated cleft palate and cleft lip with 285 and 248 cases respectively. This translates to birth prevalence of 0.02 for isolated cleft lip, 0.02 for isolated cleft palate and 0.06 for cleft lip and palate, all per 1 000 live births. The birth prevalence for isolated cleft lip of 0.02 per 100 live births in this study is lower than the 0.10 found by Kromberg in 1982 in the Black population. In this study, 79.07% of OFCs were found in the Black population, 6.73% in the white population, 4.98% in the coloured population and 6.15% in the Indian and Asian population combined. In 3.07% of reported cases, no ethnicity was indicated on the notification form.

In the literature, the reported occurrence of OFCs (including syndromic clefts) is three times higher in stillbirths than in live born infants [93, 96]. Of the total OFCs cases reported in this study, 3.99% occurred in stillbirth cases, a number significantly lower than expected. It is important to note that notification of CDs is done only for cases delivered in health facilities, as a result, stillbirths that are delivered outside health facilities are excluded, skewing the CD notification. In 13.29% of reported OFC cases, the pregnancy outcome was not recorded. These unspecified pregnancy outcomes could be stillbirths, and this missing data may contribute to the low number of OFC stillbirths found in this study. Poor data quality, exclusion of deliveries outside the health facility and underreporting affected the number of cleft lip and/or palate cases. It is also worth noting that the birth prevalence of isolated cleft palate is higher than isolated cleft lip. Owing to the obvious appearance of cleft lip it is expected that more of these cases would be reported versus cleft palate as these cases are visible at birth. This could be because more cleft palate cases were syndromic thereby having more abnormal features allowing for easier identification of cases. Reiter *et al* and Hanny *et al* found that cleft palate cases are often missed at birth and are diagnosed well after 30 days [98, 99]. Late diagnosis results in patients with multiple complications including feeding problems, malnutrition, nasal regurgitation and sometimes even death from aspiration [98]. Despite OFCs being correctable if diagnosed early and interventions implemented timeously, seven patients opted for termination of pregnancy. This could also be due to syndromic OFCs with poor outcomes but only reported as OFCs.

6.5.3 Talipes equinovarus (clubfeet)

Talipes equinovarus birth prevalence in the United States of America (US) and in Africa are 1 per 1 000 live births and 2 per 1 000 live births respectively [100, 101]. Evidence suggests that the frequency of clubfoot is generally higher in firstborn children and in males [100, 101]. Recent epidemiological data for SA is lacking, with a 1976 study by Meerdervoort *et al* indicating a birth prevalence range of 1.12-3.5 per 1 000 live births [102], decreasing to 1.55 per 1 000 live births by the 1980s as documented by Werler *et al* [94]. Data collated in this study indicated a low birth prevalence of 0.10 per 1 000 live births, with a higher occurrence (53.37%) of talipes equinovarus in male infants versus their female counterparts. Talipes equinovarus may be isolated or part of a known syndrome. High birth prevalence of talipes equinovarus and spina bifida occurring together (40.63% of reported CD associations) were reported in as indicated in Figure 5.2. In 1.43% cases, patients also had ambiguous genitalia [103]. In 4.29% of the reported talipes equinovarus cases, the gender of the infant was not recorded, demonstrating the continued challenges experienced regarding the quality of data received.

6.5.4 Neural Tube Defects

The total number of neural tube defects (NTD) cases included 23.54% anencephaly (241), 13.09% encephalocele (134), 63.18% spina bifida (647) plus two 0.20% unspecified NTDs cases. Prior to folate food fortification in 2003, NTDs prevalence's in SA ranged from 0.99 to as high as 6.13 per 1 000 births in varying parts of the country [33]. NTD prevalence using the BDNT is 0.08 per 1 000 births, considerably lower than 0.98 per 1 000 births observed by Sayed in 2008 post fortification [33, 104].

The underreporting of NTDs can be attributed to the following: 1) 65% of anencephaly cases die in utero and of those born alive 90-95% die within the first week of life [73, 74]. With this high mortality rate during pregnancy, a lot of these cases will be missed, remain undiagnosed and are not reported. 2) SA has a 'born before arrival' rate of 10%, where infants are born outside of health facilities with many home deliveries [105]. With 90-95% of anencephaly cases dying within the first week of life, many infants delivered at home with anencephaly may not be brought to health facilities and as a result are unreported.

6.5.5 Oculocutaneous Albinism (OCA)

OCA is a form of albinism where there is a lack of pigmentation in the eye, skin and hair [87]. OCA is a very common CD with a worldwide birth prevalence of 0.05 per 1 000 births [106]. There are four types of OCA with type 2 (OCA2) being the most common among the American

and Black populations [107]. The birth prevalence rate of OCA2 is 0.1 per 1 000 live births in American Blacks and 0.26 per 1 000 in South African Blacks [107, 108]. Between 2006-2014, 378 albinism cases were reported, resulting in a birth prevalence rate of 0.03 per 1 000 live births. This birth prevalence rate is closer to the global birth prevalence and lower than other rates found by other studies in SA. Previous OCA studies in SA have been hospital-based reporting live births of up to 30 000 [94, 104]. This study is a national study reporting on more than 12 million births over the nine-year period. The high number of births and the underreporting by the birth defects notification tool contributes to the low OCA birth prevalence reported. A majority (93.56%) of all reported OCA cases were from the Black population with no OCA cases reported from the white South African population.

Due to lack of melanin, complications from OCA may arise including visual impairment, squamous cell carcinomas and early mortality from skin cancer as a result of OCA patients being more susceptible to ultra violet rays [109]. Though OCA is a stable and manageable CD, it requires life-long management which is problematic in a resource limited LMIC such as SA. The incidence of squamous cell carcinomas in Africa is from 7.8-16%, the risk of this type of carcinoma in OCA patients is 1 000 fold higher [110]. Of all the reported OCA cases, 89.15% were livebirths. If not managed properly, patients may suffer high morbidity rates and in other instances early mortality.

6.5.6 Fetal Alcohol Syndrome (FAS)

FAS was the least reported priority CD with 84 cases reported between 2006-2015, indicating a birth prevalence of 0.01 per 1 000 live births. The global birth prevalence is estimated at 10 per 1 000 live births [111]. In SA, numerous studies on FAS birth prevalence have been undertaken in mostly two provinces, the Northern Cape and Western Cape with a few in Gauteng province [112-114], with the highest birth prevalence rate documented as 119.4 per 1 000 in Northern Cape [115]. In this study, the most FAS cases were reported in the Eastern Cape followed by KwaZulu-Natal, Northern Cape and Western Cape. Owing to the overall higher reporting level of CDs by KwaZulu-Natal Northern Cape, it is unsurprising that the province reported more cases than all other provinces. In addition, Northern Cape and Western Cape have previously been identified as high risk areas for FAS due to their ethnic variation [116]. The high number of FAS cases in Eastern Cape highlights the need for more FAS research in the province, which was initiated in 2016 [112]. The burden of FAS in SA seems to be increasing with high rates observed amongst children [113]. The rate of 0.01 per 1 000 is a fraction compared to other studies, this low number is unsurprising as the diagnosis of FAS at birth is challenging and requires a clinical examination of features by a trained and skilled HCP [29, 117]. Of the 84 cases reported, 44 were diagnosed at birth while 40 were diagnosed later in the continuum of care. With the focus of notification using the BDNT being

at birth, a lot of FAS cases will be missed, as evidence has shown that it is better and easier to identify FAS in school going children [113, 115].

6.5.7 CDs associations

The phenomenon of multiple CDs occurring per patient can be categorised into four groups, namely, monogenic syndromes, chromosomal syndromes, sequences and associations. When multiple abnormalities are due to single gene defects and are aetiologically related then it is a monogenic syndrome. This is different from a chromosomal syndrome in which there are structural and/or numerical chromosomal abnormalities. Sometimes these multiple clinical abnormalities are due to a single known structural defect and are known as sequences. When these multiple abnormalities occur non-randomly and are not syndromes or sequences then they are referred to as associations [118].

- A total of 352 cases with multiple priority CDs were reported. This consists of different combinations of the following CDs per patient: Down syndrome, OFCs, NTDs, clubfeet, FAS and albinism.
- A majority of the cases are OFCs associated CDs and non-idiopathic clubfeet (clubfeet that occurs in association with other neuromuscular and congenital disorders) [119].
- A diagnosis of the underlying condition associated with OFCs, clubfeet or any of the other CDs could not be done, resulting in them remaining unspecified either as syndromes or sequences but rather as associations.
- Of the total reported priority CD associations, 14.49% (51) were OFCs associated CDs, 52.84% (186) were non-idiopathic clubfeet cases, 15.06% (53) were cases with both OFCs and clubfeet. Of the remaining CDs, 8.24% (29) were CD associations among NTDs (e.g. patient with spina bifida and anencephaly) and 9.38% (33) were CD associations between all the other priority conditions including Down syndrome, FAS and various categories of NTDs.
- Of the 51 reported OFC associated CDs, the most reported were associations with Down Syndrome at 45.0%, followed by associations with anencephaly at 42.5% and associations with encephalocele at 22.5%.
- For non-idiopathic clubfeet cases (186), the most reported were clubfoot associated spina bifida cases with 76.88% and clubfoot associated Down syndrome with 21.5%. A study by Neto *et al* documented the frequency of clubfeet in spina bifida patients and found that 30% of all children born with spina bifida also have clubfeet [120].

6.6 Diagnosis and reporting of BDNT

In LMICs, all modalities of care are not always available, especially trained specialists and expensive drug treatments [23]. In SA, the lack of capacity within the medical genetics service has been widely documented [6, 42, 59]. Nurses, particularly those at primary health care (PHC), have been identified as the ideal alternative to supplement and progress medical genetics services in the country [59]. To support the latter, Medical Genetics Education Program (MGEP) training has been offered to nurses in all provinces to improve their knowledge and skill with regard to the identification of CDs [29, 42]. More than half (57.80%) of all reported CDs using the BDNT were diagnosed by nursing staff. This supports the premise of equipping nurses at PHC to identify and refer CDs as they are the first contact with patients at health facilities [23]. Proper management of CDs at this level ensures that diagnoses are made early, patients are referred appropriately and a suitable care plan may be implemented timeously.

6.7 Pregnancy Outcomes

Medical genetic services involve the diagnosis (which depends on clinical and family history, physical examination, ultrasonology and laboratory testing), option of termination of pregnancy (TOP), and genetic counselling with psychosocial support offered to the affected individual [23]. Early identification of CDs using prenatal diagnosis is an effective and important prevention strategy [2, 7]. It permits use of different approaches to the care and management of the affected fetus, including the option of TOP [2, 29, 58]. Of the 16 395 CDs reported, only 1.06% (n=173) were diagnosed prenatally and opted to terminate their pregnancies. Prenatal screening is most effective if the pregnant woman receives the service before 20 weeks gestation [2]. The *Guidelines for Maternity Care in South Africa* specifies that a woman should visit a health care facility as soon as she misses her first period to initiate basic antenatal care (BANC) [91]. However, in 2011/12 it was documented by the NDOH that only 40.2% pregnant women initiated basic antenatal care before 20 weeks [121]. With the challenges women face accessing services late, fewer options become available for the management of their affected pregnancies, including TOP which must be done under the prescripts of the TOP Act 92 of 1996 [60]. The notion of BANC plus for SA was developed by Hofmeyer in 2015 and was implemented in April 2017 with the aim of improving birth outcomes including maternal stillbirth and neonatal mortality rates [122]. The BANC plus strategy increases antenatal care contact days from four to eight visits, improving the monitoring of patients, allowing for pregnancy complications to be identified early. This could benefit the identification of CDs prenatally if HCPs are taught about the identification of high risk patients and prenatal diagnosis. However, implementation of this will require increased capacity both in terms of numbers of HCP and training to enable implementation.

6.8 Preterm birth and low birth weight

CDs are associated with an increased risk of preterm birth, and infants born prematurely have a higher probability of having a CD [123]. In pregnancy, the presence of structural CDs increases the risk of preterm birth, and this risk further increases in pregnancies affected by multiple CDs without a known aetiology [124]. The risk of preterm birth is between 5-15% higher in fetuses with multiple CDs, and risk greatest at earliest gestational age [124]. The risk of preterm birth is also dependent on the type of CD as different conditions differ in risk degrees [124, 125]. Mili *et al* found there to be an increase in preterm birth and low birth weight for infants born with a CDs affecting the central nervous system (e.g. NTDs) together with syndromes affecting the brain (e.g. trisomies) [126].

In this study 26.04% of priority CDs cases were preterm births (see Table 5.5 and 5.10). Some of the reported cases were identified later on in a patient's life, thus the gestational age and birth weight were not recorded on the BDNT. This limitation was not provided for and so non-applicable data was incorrectly captured as not recorded. This affected the data analysis, resulting in a high number of cases not recorded (24.78%). Infants born with NTDs, specifically anencephaly, are at high risk for preterm birth [125, 127]. This study corroborates this finding with 37,60% of NTDs being born preterm, which is the highest reported preterm percentage of all reported priority CDs. NTD also had the highest low birth weight percentage with 48.80% of all NTD cases. Infants born prematurely are often small for their gestational age or have low birth weight [128]. Mili *et al* showed a decrease in CDs for infants of a higher birth weight, the rate for CDs in infants weighing less than 1 500g is 16.2% compared to 3.2% for infants weighing 2 500–3 999g [126]. In this study, 29.98% of reported priority CD cases had low birth weight. Of all reported priority CDs, patients with FAS had the highest observed low birth weight rate with 63.09% of all FAS having low birth weight. Prematurity was found to be common in FAS cases with 34.52% of patients reported as being born prematurely. This aligns with work by Nembhard *et al* who reported the association between alcohol consumption during pregnancy with preterm birth and low birth weight [129].

6.9 Challenges of the BDNT

The success of the birth defects notification tool is influenced by the following factors:

6.9.1 Training of HCP

Medical genetics services in SA are not evenly distributed across the country. Some provinces do not have key components of this service including critical personnel, particularly medical geneticists and genetic counsellors [6, 59]. Budget constraints have also been implemented in laboratories providing medical genetic diagnostic services across the country [6]. With these restraints on services, alternate means of service provision have to be sought including

the training of HCP (nurses and doctors) in medical genetics. Training (mainly MGEP) is primarily aimed at capacitating HCPs in the recognition and identification of CDs [59]. Coupled with this, is the training of HCP in the notification of CDs and surveillance. These two trainings should occur concurrently, with the notification of CDs used as a measure of the effectiveness of training. Training is especially important in health facilities that deliver infants as CDs can be identified and reported at birth for obvious conditions. For late onset conditions, training is required for HCP that provides standard child health services including immunisations and school health services.

No training is offered in nursing teaching institutions causing nursing staff to enter the job market without the necessary skills and knowledge to identify CDs and report them. This increases the need for training of nursing staff already in the workplace. With competing priority programmes (e.g. HIV/Aids, non-communicable diseases, cancers) in the Department of Health, and accompanying funds allocated to these programmes, CDs and nurse genetic training has become neglected.

Furthermore, CD training, specifically training on CD surveillance is not integrated into maternal and child health programmes. If this is done, personnel dealing with women's, maternal, neonatal and child health programmes in health facilities will be equipped to identify CDs and report them. If training is provided to all these different categories of HCP, before and after they enter the job market, more CDs would be identified/diagnosed and consequently reported.

6.9.2 Compliance by HCP

Following MGEP training (which includes training on surveillance), HCP are expected to notify CDs as these notifications are used to measure the effectiveness of training. Notifications are expected to be submitted monthly with zero notifications (nil reports) submitted for months where no CDs were identified in a health facility. Notification of CDs is not mandated by law; the National Health Act 63 of 1977 specifies that only the Minister of Health after consultation may declare any medical condition as a notifiable medical condition (NMC) [130]. The reporting of all notifiable medical conditions is prescribed in the Communicable Disease Regulations making them compulsory [63]. This compels HCP to notify them, improving reporting rates. HCP are inundated with different reporting forms for different programmes and due to competing health needs and the huge burden of responsibilities on HCP, compliance to the BDNT suffered resulting in CDs not being notified and underreported. For example, on a monthly basis, HCP providing maternal and child health services have to report on 20 indicators in the Department of Health Annual Performance Plan 2016/17-2018/19 [131].

In addition to CD reporting not being compulsory, placement of trained HCP in the relevant facilities and/or wards is not guaranteed. Trained nursing staff in health facilities are rotated between wards, resulting in untrained staff then not reporting or notifying CD cases, with no overall ownership of this task in facilities.

6.9.3 Data flow

The District Health Management Information System (DHMIS) policy by Department of Health details the processes to be followed for data from the District Health Information system (DHIS) to move from the health facilities to NDOH [67]. The same data flow process was adopted for BDNT for consistency and ease of use by HCP. Following notification by the health facilities, the completed notification form is sent to the district, province and then NDOH for electronic capturing. All these offices in the different levels of governance make copies for their own reference before submitting the notification tool to the next level in the hierarchy. This process requires the physical presence of personnel in all tiers, for the successful relaying of the data from health facility to NDOH. If there is a lack of human capacity at any of these tiers, then the CDs reporting process halts. In addition, if computers, faxes or funding for courier services are unavailable then the reporting process also halts, leading to underreporting.

The DHMIS policy clearly states that submission of DHIS data to NDOH should occur within 45 days. The timeframe for reporting using the BDNT is monthly; however, this deadline was never enforced. As result, data is received at the national office late, making data analysis and feedback difficult. This also contributes to the underreporting rate as BDNT kept long in respective offices in the data flow process sometimes get lost and never makes it to the national office.

6.9.4 Paper-based notification

The BDNT is an A4 size paper form that is available in Microsoft Word and in pdf format. The former allows health facilities with computer facilities to capture and send the form electronically to the next level for capturing. The disadvantage of this method is the ability of health facilities to edit the form and submit forms that are different to the original BDNT. The pdf format avoids the ability of facilities editing the form as photocopies are made and HCP complete the form by hand. The first problem encountered with this method is the availability of photocopy machines in the different tiers of governance. Secondly, the illegibility of the completed forms results in data inaccuracies. Whether the Microsoft Word or the pdf method is used to complete the form, incomplete forms are submitted resulting in missing data fields and poor quality data.

6.9.5 Public sector reporting

The public health sector in SA serves more than 80% of the population [132, 133]. Despite this, 70% of doctors and specialists work only in the private health sector [133]. Medical genetic services in SA are available in both the public and private health sector, though they have deteriorated in the former [6, 42, 134]. Moreover, certain services e.g. neonatal metabolic screening, are only available in the private health sector [134]. The BDNT only collates data from public health facilities. No data is received from the private health sector though some patients access medical genetic service in the private health sector. This contributes to the underreporting of CDs by the BDNT.

Laboratory services, specifically medical genetic testing, are available through the National Health Laboratory Services (NHLS) and are utilised by both the public and private health sector [134]. The NHLS would be a good source of CD data for two reasons 1) they have information or data of the entire population, both private and public, 2) they have confirmed diagnostic results, allowing for the existence of a surveillance system with confirmed diagnoses, unlike the BDNT which only reports on preliminary diagnosis.

6.10 Conclusion

The BDNT was implemented in SA in 2006 to collect CD data in the country. The tool collects data on six priority CDs as specified by the national policy guidelines [7]. The tool further makes allowance for the reporting of CDs that are not specified as priorities and can also be used to report obvious CDs observed on infants during a clinic examination following delivery. The only requirement is a short description of the CD if a diagnosis cannot be made. HCPs are trained during MGEP training on the importance of data surveillance and on the use on the BDNT. Following the delivery of a infant identified as having a CD, HCPs in health facilities complete the BDNT and submit it to NDOH via the district and provincial Department of Health. It is important to note that not only CDs identified via live births are reported, but all other pregnancy outcomes are reported including miscarriages, TOP and stillbirths. At NDOH, the tool is captured electronically and forms part of the national CD database.

This study primarily focused on evaluating the effectiveness on the BDNT by analysing data obtained using the BDNT and comparing it with data from other studies globally, in Africa and locally. Results showed huge underreporting rates of 98% using this surveillance system albeit comparing against estimated numbers for all CDs. Of all the provinces, two reported above expected percentages, one reported as per expected and all others reported below the expected percentages. Similar to other studies, congenital malformations were the most reported genetically caused CDs. Other frequent genetically caused CDs were chromosomal CDs and single gene defects, the most common of which was recessively inherited

abnormalities. For CDs caused by teratogens, alcohol was the most reported. Of the six identified priority CDs, the most reported were Down syndrome, OFCs and clubfoot. Data from this study had similar findings for certain CDs but also had major differences for others. Most of the reported priority CDs were from the Black population; more cases were identified in live born male infants born full term with birth weights above 2,5kg.

Various challenges have been encountered throughout the implementation period, the main being the lack of training. Without the support of training on CDs, CD surveillance in SA will never improve. The public health sector functions with minimal doctors and specialists, with nurses serving as the back bone of service delivery [135]. These nurses need to be equipped with skills enabling them to identify and report CDs. Furthermore, due to competing priorities in the DOH, CDs are neglected at all tiers of governance. Despite this, data is received but it is of poor quality making analysis and utilisation of this data is difficult. Lastly, BDNT are only completed by HCP in the public health sector diminishing chances of collecting data from other data sources.

Based on the results, though small, these data demonstrate the need for strengthened genetic services in SA. Without adequate data, the true burden of CDs on the health system will not be quantified. This results in services for this group of patients continuing to deteriorate as they continue to not be prioritised by Department of Health, preventing them from receiving the necessary care. The importance of a functional CD surveillance system for decision making purposes regarding prevention and management of CDs has been highlighted by many, including the WHO. For SA, many components of medical genetics services need to be revived, surveillance being a key part of this process. Recommendations for an improved, new CD surveillance system are discussed in the next chapter.

Chapter 7: Discussion 2

7.1 Introduction

The current birth defects notification tool (BDNT) surveillance system in South Africa (SA) is under revision. This presents SA with an opportunity to reassess the current approach, take into consideration lessons learned since implementation and best practices from other surveillance systems, and implement an improved CD surveillance system. The primary role for implementing a surveillance system is to obtain data for decision making purposes, allowing the National Department of Health (NDOH) to efficiently plan for services. CD underreporting leads to a hidden burden of disease, resulting in neglected services for people affected by a CD and the family members. Section 27 (1)(c) of the Constitution of SA, states that everyone residing in the country has the right to access healthcare services, including reproductive healthcare [136]. The National Health Act (61 of 2003) clause 21(2)(b)(vii) which was developed based on the Constitution and other laws, further specifies genetic services as one of the health issues the NDOH must govern [130]. The Department of Health thus has a legal and ethical obligation to provide services to the people of SA, particularly for its most vulnerable citizens.

Following the development of the paper-based notification tool and the electronic data recording system, challenges were encountered regarding the final integrated electronic system that would be used to collect data from the various disease surveillance systems at NDOH. Solutions are currently being sought from the principals at NDOH regarding the way forward in this regard. During development of the Integrated Disease Surveillance and Response (IDSR), certain elements were highlighted as important factors to include in any CD surveillance system for implementation in SA. These factors are: political will (which includes the promulgation of CD legislation), vital registration, NDOH coordinating role, population-based approach to surveillance, active surveillance and the implementation of an electronic system. Two of these factors are essential - CD legislation and political will, serving as underlying factors that need to be addressed not only for surveillance but for the provision of medical genetics services in its entirety. The other three factors impacting on CD surveillance are optional depending on available resources but the implementation of all these issues will be to the benefit of the surveillance system.

7.2 Essential components of a revised surveillance system

7.2.1 Political commitment

Political commitment to health issues is required to improve services. An example of this is the government's commitment to reducing mortality resulting from cancer. Government support has been an important element in the successful implementation of the National

Cancer Registry (NCR). This was demonstrated through the introduction of legislation relating to cancer prevention and control including cancer surveillance [137]. This support was further demonstrated by the establishment of the National Advisory Committee on Cancer Prevention and Control and through support from the NDOH specifically. These acts demonstrate the impact of government commitment to cancer control and prevention.

Another example of the influence of political will upon the outcome of disease management is HIV/AIDS. The first case of HIV in SA was diagnosed in 1982 and by 2005, SA had the highest HIV/AIDS infection rate in the world with more than five million people testing positive for the disease [138]. The previous administration contributed to increasing infection rates by failing to roll out antiretroviral therapy (ART) and focusing on nutrition for HIV positive patients. Under the current Ministry of Health administration, the rate at which the population is being infected by HIV has been reduced from 1.9% in 2002 to 0.9% in 2017 [139]. The country is also now moving towards eliminating the transmission of HIV from mother to child with a target of <2% at six weeks decreased rates from 3.5% at 4 - 8 weeks of age in 2010 [140]. These advances in HIV/AIDS treatment and management highlight the role and impact political commitment and support plays in the success of disease management.

For both HIV/AIDS and cancer management, the role of civil society has been crucial in advancing the prevention and management of these conditions by advocating for the right of the patients to treatment.

These examples demonstrate that the same can be achieved for CD prevention and management if the government recognises the need and importance of CD services. Such will only be fully implemented if CDs are seen as a priority health issue. The government's commitment (political will) to CDs as a health care issue may be demonstrated by a number of factors including: a) the regulation of CD services; b) the provision of resources (financial and human capacity) towards service delivery, and c) establishment of a national committee on CDs advising the Minister on issues relating to CD prevention and management. Without political will and commitment, services for people with CDs will continue to be neglected.

7.2.2 Legislation

When comparing CD surveillance with surveillance systems for other medical conditions in SA, one component that differs is legislation regulating the notification of CDs. The National Health Act specifies the type of regulations the Minster of Health may publish relating to different conditions [130]. Two examples of this are the surveillance of notifiable medical conditions and cancers. Regulations for each were published by the Ministry of Health in 2008 and 2011 respectively [63, 141]. The existence of these regulations makes it mandatory for health care providers to notify diagnosed cases of notifiable medical conditions (NMC) and cancers, strengthening compliance to notification.

The development of legislation for the notification of CDs is recommended for SA. This should be done early on in the implementation of a surveillance system. A study by Schwab *et al* found an increase of up to 67% in the number of facilities reporting after introduction of mandatory reporting while the Health Protection Report reported an increase of 15% in the number of notifications with compulsory reporting [142, 143]. These are significant increases for consideration in the current context for CDs where underreporting is currently 98%.

Such regulations for CDs should specify details including:

- the type of CDs to be notified
- point of notification
- who must notify
- deadlines for submitting CD notifications and
- the notification tool to be used during notification

7.2.3 Vital registration

With advances in technology, it is now potentially possible to link vital records during surveillance. For CDs, this would allow for the tracking of affected children from their identification at birth through to them accessing services, leading to them being removed from the system post treatment (e.g. surgery) or upon death. This linking of birth and death certificates during surveillance, using the 'cradle to grave' approach.

7.2.3.1 Birth Registration

The use of birth certificates for CD surveillance purposes has been widely studied in the United States of America (USA) and Brazil and can be used in countries with minimal funding for CD surveillance as it is very cost effective and has a good population coverage rate [144, 145]. With a population of close to 56 million people and an average of 1.2 million live births annually, it is difficult to monitor the entire population in SA [72]. However, according to the Births and Deaths Registration Amendment Act (Act No. 18 of 2010), every birth must be registered within 30 days from the date of birth [146]. Birth certificates are an ideal means of collecting CD data as they are universal, standardised, have good population coverage rate and contain some medical information and details about the parents [13].

For SA, the first drawback to using birth certificates for CD surveillance is the need to amend it to include the presence of CDs identified at birth. Another drawback to this data collection method is the underreporting of CDs that is associated with this strategy [13, 144, 145, 147]. In Brazil, birth certificates have been found to underreport CDs by between 55%-88% mainly

because of incompleteness of forms and inadequate descriptions of CDs [13]. A further disadvantage is the poor completion of registration rates experienced in SA. Low completion rates of 7.8% (at its lowest) and 90.5% at the highest were recorded in SA while death registration had a lowest rate of 51.4% and a high of 97.1% [148]. A factor that contributed to low birth registration was the mother's age, with younger mothers having lower completion rates. For death registration, contributors include the age at death, with lower completion rate found among children under five years. With such high levels of underreporting by the current BDNT system (98%), a 55% underreporting rate would be an improvement. However, a system with higher standards should be sought to minimise underreporting and more accurately reflect the true situation. Poor data hides the true burden of CDs, obstructing the prevention, care and management of CDs from being prioritised [42].

7.2.3.2 Death Registration

Poor data masks the contribution of CDs to the burden of disease and under-5 mortality rates due to a number of specific issues: a) incorrect terminology used to define CDs; and b) misdiagnosed and undiagnosed cases, c) incorrect cause of death on death notification, d) lack of capacity, and the lack of infrastructure for diagnosis and treatment [42]. As countries move through the health transition, mortalities due to communicable diseases decrease while those attributed to CDs increase in proportion [6, 42, 149]. An efficient surveillance system should collect data not only on live births and stillbirths but also data on neonatal, infant and under-5 mortalities due to CDs. The current BDNT does not report on any mortality currently. Systems have been developed in the country to monitor death rates in children. The Perinatal Problem Identification Program (PPIP) and the Child Healthcare Problem Identification Program (ChildPIP) are death audit tools for participating facility-based deaths. PPIP monitors deaths in early neonates occurring during the first week after birth and ChildPIP monitors deaths in children aged from one month to 18 years admitted to paediatric/children's ward, in participating hospitals [150, 151]. Collectively these death audit programmes include 81.82% of child deaths in SA, since 44.2% of deaths occur in facilities in SA [150-153].

The revised CD surveillance system could potentially link up with data from the PPIP and the ChildPIP programmes, providing additional details on the reported CD deaths than those data currently available. It is important to highlight that there is a gap in data collection between one week and one month old infants for the PPIP and ChildPIP. This drawback should be taken into consideration for the revised CD surveillance system. An alternative option would be to a link all neonatal, infant and child mortalities reported via the District Health Information System (DHIS) to the CD surveillance system. The latter option may be more suitable due to 1) the PPIP and ChildPIP programmes only record deaths at participating hospitals, while the DHIS reports on all deaths occurring in health facilities and reporting is mandated by the Births and Deaths Registration Act (Act No. 51 of 1992) [146]. 2) Integrating CDs and PPIP and

ChildPIP has to date been challenging as CDs are not recognised as a major contributor to infant mortality despite the last Saving Babies report in which CDs had overtaken infection as the third leading causes of early neonatal mortalities for neonates above 1 000g [151]. A third option would be to implement both systems and use them as a mutual verification system.

As SA transitions epidemiologically, the importance of CD surveillance is heightened as empirical data is needed to demonstrate the true burden of CDs on the health system. This includes the reporting of CDs as a cause of death. Other strategies for CD surveillance should be explored including the use of birth certificates and registration of death due to CDs [13].

7.2.4 Coordinating role

There are various CD surveillance systems or patient registries in SA. Each of these systems addresses one or more of the following functions a) case detection b) reporting c) investigation and confirmation d) analysis e) action [154]. In general, following a case being notified, investigation ensures confirmation of the preliminary diagnosis, so that only confirmed cases are maintained in the surveillance database. Surveillance systems may have different data sources. For example, the NCR is a pathology based surveillance system which collates and analyses cancer cases diagnosed in pathology laboratories, both in the public and the private health sector [137, 155]. Pathology based surveillance, however, has its own limitations, particularly the underreporting of cases not diagnosed by histology or cytology [137]. To counteract these, the NCR is implementing a population based surveillance system in addition to the already existing pathology based registry [156].

The BDNT surveillance system is a single data source system reporting on the preliminary diagnosis of CDs and does not capture any test results to confirm diagnosis. Firstly, this implies that some of the reported CDs may be incorrectly diagnosed and secondly, data from the laboratories may be available but is not used by the BDNT surveillance system. The only information available on the BDNT is the type of laboratory testing undertaken to confirm diagnosis. This information can easily be linked to the laboratory data since barcode stickers are used to link patients, their files and laboratory results. To improve reporting, data from the laboratories should be included in surveillance. This could be done by either allowing for the tests results to be incorporated into the notification tool or by collecting CD data directly from the laboratories and feeding it into a different registry at the NDOH. This will result in an alternative data source, allowing for CDs to be reported by both the laboratories and by HCP. To allow for different systems to collect data on the same patient, each reported CD should be assigned a unique identifier linked to the individual's identification number. Another option is to perform a search function using the identification number before the case is captured electronically (notified). This allows for various components of information from different sources to be pooled together at the national level.

There are various CD registries run by non-governmental organizations (NGOs), private laboratories and provinces. Examples of these are the Pregnancy Exposure Registry/ Birth Defects Surveillance (PER/BDS) run by KwaZulu-Natal province, CD database from South African National Blood Services (SANBS), and CD specific databases run by patient support groups such as the South African Haemophilia Foundation and the Smile Foundation. The PER/BDS identifies CDs resulting from teratogens, particularly antiretroviral therapy (ART) and other medications during pregnancy that may have an adverse effect on the fetus. The SANBS cytogenetic laboratory undertakes all medical genetic testing for KwaZulu-Natal province, data from these tests are collated into an existing database [89].

Consideration should be given to the new surveillance system serving as a hub and coordinating centre for all the existing and diverse CD registries. Owing to the different needs and uses of the abovementioned systems, one population-based system for all stakeholders is not practical and may compromise the quality of data collected. Thus, the NDOH, through the national CD surveillance system, could coordinate the feeding of data from the various registries into the national surveillance system hub.

7.2.5 Training of health care providers

To improve the notification of CDs, training of HCP should be compulsory. Comprehensive training of HCP on CDs should start at nursing colleges and medical schools, allowing for nursing staff and doctors to enter the job market with the necessary skills and knowledge to identify CDs and report them. Currently, a lot of HCP in the workplace, do not have the required skills, necessitating in-service training. The Medical Genetics Education Program (MGEP) was introduced to close this gap. However, MGEP curriculum does not formally include a module on CD notification and data collection. This module needs to be developed and integrated into the program, compelling CD notification to be an expected outcome of training. Other than the formal MGEP training, other means of teaching/ improving knowledge should be promoted such as on-line training for HCP. An example of this is the Bettercare learning platform (http://bettercare.co.za/learn) where course books can be accessed on line.

7.3 Elective factors

7.3.1 Active surveillance

The BDNT surveillance system currently uses a passive approach to data collection whereby HCP working at health facilities identify a infant with a CD and report it via the BDNT. Within the current unregulated context of CD surveillance and neglect of medical genetics services [134], CD reporting is poorly undertaken, leading to underreporting.

While the NCR has seen an increase in reporting following legislation, levels are still considered to be too low with many patients remaining unregistered. As a result, the NCR is incorporating active reporting where personnel are specifically hired to visit health facilities and communities to collect data in conjunction with the laboratory [137].

Such a shift from passive to active reporting may also be an option for CD surveillance. With the lack of resources experienced by the country, it may not be feasible to hire personnel specifically for CD identification and reporting. However, individuals (already working at the health facility) or a team identified within participating sites in each reporting area, could be responsible for promoting or raising awareness around reporting of CDs and encouraging colleagues to report. These 'champions' have proven successful for NCR and the same approach can be adopted for CD surveillance [137]. This should ideally be those with an interest in CDs, as experience from the BDNT has shown that people that are active in data reporting are those that are self-motivated.

7.3.2 Population (district) based surveillance

The population included in a population-based surveillance system may be a city, region or district or the entire population of a country [1].When applied to CD surveillance, this may be defined as infants born with a CD to mothers residing in a defined catchment area within a defined timeframe [1]. This includes all births in that catchment area irrespective of birth place (whether born in a health facility or at home). The BDNT surveillance system collects data from the entire population which has proven to be difficult to implement.

A population-based approach, focusing on populations within a district or a combination of districts and then used to calculate the expected numbers in the rest of the country is preferable. This is a similar approach to the new NCR population-based registry. The NCR system is being implemented in four districts in the country, with the population in these districts representing the geographical and ethnic diversity of South Africa's population [137]. As the chosen districts have populations representative of the country, national birth prevalence can be estimated. This approach can then be upscaled nationally if implemented successfully in the chosen districts and infrastructure and staffing challenges have been resolved. This approach may work for CDs as there are only three provinces with genetic service facilities at tertiary level [134]. All other provinces refer patients to these facilities for services. For patients to receive the appropriate medical genetic services, strong referral pathways must exist between the health facilities and the provinces. These provinces (or districts) with the genetic service facilities can be used as district surveillance sites to run population-based surveillance system. Birth prevalence for SA can then be estimated based on data received from all the sentinel sites.

7.3.3 Electronic surveillance

Computer technology can be used to improve the quality, capacity and effectiveness of the BDNT surveillance system [11]. Computers, mobile phones and other handheld devices have successfully been used to collect surveillance data particularly in developing countries [49, 157]. The use of mobile phones for electronic data collection in SA has been proven feasible and workable [158]. As technological advancements progress, CD surveillance needs to keep pace and transition from the current paper-based data collection to an electronic format. Paper-based methods are prone to errors, resulting in poor quality of data received. Paper based methods also tend to be long and overly complicated, making them difficult to complete, resulting health facilities failing to comply with the request for data collection. Electronic data collection greatly improves data accuracy as the chances for human error are reduced. Furthermore, the flow of data for paper-based collection from the health facilities via the district and provincial health offices to NDOH introduces many opportunities for things to go wrong, resulting in delayed access to captured data. Electronic data collection may be real time or routine, resulting in captured data being immediately available to users and allowing for multiple access to data.

For the HIV/AIDS programme, when ART was scaled up in SA due to the HIV epidemic, the monitoring of all patients on ART became problematic. This gave rise to the development of TIER.Net, a three tier approach to monitoring which consists of, a paper-based system making up tier 1, an electronic version of the paper registry making up tier 2 and lastly a full electronic medical record (EMR) software making up the last tier 3 [159]. This system allows health facilities to implement one or more of the tiers depending on their resources but also allows for facilities to move from one tier to the next as resources become available [159]. This approach to surveillance could be adopted, with an initial introduction of a paper-based approach to data collection implemented, with the intention to evolve to the EMR phase.

7.4 Way forward

Different disease programmes have implemented surveillance systems successfully in SA with lessons that can be learned from each system (e.g. cancer, NMC and HIV/AIDS). Furthermore, the National Public Health Institute of South Africa (NAPHISA) bill which was promulgated in 2017 addresses the establishment of NAPHISA whose functions include the coordination, development and maintenance of surveillance systems to collect, analyse and interpret public non-communicable data, amongst others, in order to guide health interventions [160]. Taking into consideration the country's specific characteristics, a CD surveillance system for SA should adopt and adapt the best from international and other systems (including being managed by NAPHISA) to meet national needs. This makes it challenging as a balance has to be found between international versus local practice. The greatest obstacle for the success of many other programmes in health is the HIV/AIDS epidemic which has consumed a lot of

resources, resulting in many other services neglected in the process. Medical genetic services have suffered the same fate with services dwindling in the past decade resulting in poor reporting of CDs. Lack of trained HCP who can identify and report CDs has also contributed to poor reporting of CDs. With the country in the final stages of epidemiological transition, mortality due to degenerative conditions (e.g. cancers, CDs) is expected to rise. This has already begun to emerge with the high cancer mortality rates in the country.

Various components resulting in a successful CD surveillance system have been discussed above. In the journey to establishing this new system, many challenges are being encountered. Achieving one system for use by different stakeholders is problematic. A better approach may be to implement different systems (e.g. one for HCP, laboratories, NGOs etc.) by various stakeholders, tailored to their needs, but linked to and feeding a central point. This will result in more than one data source with one central national database/registry producing national birth prevalence for the entire country.

Chapter 8: Conclusion

8.1 Aim of the study

This study had two main aims, 1) to evaluate the current national CD surveillance system and 2) to develop an improved national surveillance system for future implementation. The objectives were as follows:

1. Evaluate the effectiveness of the birth defects notification tool (BDNT) implementation.
2. Document the successes and shortfalls experienced during implementation.
3. Develop an improved national CD surveillance system based on lessons learned from the BDNT surveillance system.

To achieve the primary objective, data from the BDNT was compared to other surveillance systems locally and globally. This was undertaken through the analysis of data received and calculating birth prevalence. This was followed by the documenting of challenges and achievements encountered throughout the implementation period. The Integrated Disease Surveillance and Response (IDSR) (both the electronic and the paper-based notification tool) was developed but could not be implemented due to problems encountered regarding joint implementation of the system for notifiable medical conditions and CDs. A separate notification system was developed (not yet implemented at time of writing) by the National Institute for Communicable Diseases (NICD) for the reporting of notifiable medical conditions. To meet the second objective, recommendations were made for the development and implementation of a CD surveillance system based on lessons learned from the BDNT surveillance system and best practices from other disease surveillance system both locally and globally.

8.2 Summary of main findings

8.2.1 Effectiveness of the BDNT

The BDNT was implemented in SA in 2006. Data from the BDNT was analyzed from 2006 to 2015. When compared to modelled data estimates, the BDNT surveillance system underreported CDs by 98%. Estimated data includes all CDs, while BDNT data includes mostly CDs diagnosable at birth and priority conditions as defined by the Policy guideline for the management and prevention of genetic disorders, birth defects and disabilities. Despite this, the trend of underreporting continued when provincial data from this study was compared to expected data as per the population size. Only one province reported as expected, with two provinces reporting above expectation and the remaining provinces reporting below

expectation. Overall, districts where medical genetics facilities are located reported more CDs.

Birth prevalence was calculated for the reported CDs in two categories, 1) based on aetiology 2) based on the list of priority conditions listed in the NDOH policy guidelines. All birth prevalence for this study were lower in comparison to other CD surveillance systems. As expected the most commonly reported CDs were those caused by genetic factors, specifically malformations of various systems/organs. In terms of the priority CDs, the most reported were Down syndrome, clubfoot and oculocutaneous albinism.

CDs were not only reported in live births but also in stillbirths, terminated pregnancies and miscarriages. Only a few terminations of pregnancy (TOP) cases were reported as prenatal services, particularly prenatal diagnosis of CDs, is lacking as most women initiate prenatal services after 20 weeks' gestation. An association between CDs and preterm births was observed in this study. Furthermore, an increased association was observed between NTDs, specifically anencephaly and preterm birth. Reported NTD cases also had the highest low birth weight rate of all reported priority CDs. This is also true for most preterm born infants as they are often low birth weight.

When compared to other studies, the BDNT generally underperformed showing very high underreporting rates. This demonstrates the inefficiency of the system and highlights the need for improvement. Low-middle income countries (LMICs) have inadequate medical genetics services particularly because CDs in these areas are not recognized or prioritized as a public health issue. Coupled with this is a lack of accurate data that can be used to inform decision making to remedy the situation. Results from this study can attest to this conclusion as genetic services in this country continue to deteriorate.

8.2.2 Challenges of the BDNT

The main challenges experienced during implementation were:

- Lack of trained HCPs which leads to undiagnosed and misdiagnosed CD which are not reported.
- Following training, HCPs, in this instance nurses, are expected to report CDs following identification of an individual with a CD. Data showed that nurses report more CDs than doctors. As reporting is currently voluntary, both nurses and doctors are not fully compliant with notification of CDs.
- The completed BDNT is submitted to NDOH via the district and provincial Department of Health. The lack of personnel in these offices results in notifications not reaching the NDOH and hence not being captured onto the national database.
- Paper-based notification has high rate of data inaccuracies. Thus many data fields are not being completed and are illegible.

8.2.3 Development of CD Surveillance system

A new notification tool was developed by NDOH incorporating an electronic system; however, challenges were encountered with regards to its implementation. To make this new system more efficient, the following recommendations were made based on best practices from other disease surveillances. Mandatory reporting of CDs through the promulgation of regulations on CD services and surveillance. This system should further serve as central hub, linking all registries and databases from other stakeholders and sources. These include public and private laboratories, NGOs and patient registries run by academic institutions and/or provinces. This national system should have the ability to track patients from point of diagnosis, starting from prenatal diagnosis, through to treatment until death if the CD cannot be corrected or treated. Owing to the large population in the country, surveillance may need to be limited to certain districts or a combination thereof with specific people responsible for championing surveillance of CDs in that area.

8.3 Possible explanations for the findings

Various factors contributed to the general underreporting of the BDNT surveillance system:

- CDs form part of the Maternal and Child Health (MCWH) cluster in the health system, making coordination and facilitation of the programme a responsibility of the MCWH coordinator. With competing health conditions, the coordination of CD services is often neglected, including surveillance.
- Modelled numbers include estimates for all CDs whereas the BDNT only includes observed data for a limited number of CDs that are obvious and easy to diagnose at birth.
- Insufficient training results in HCP, especially nurses not having the necessary skills to identify and report CDs.
- The lack of medical genetics facilities in six of the nine provinces contributed as services in these provinces are only supplied through outreach clinics in those areas. These clinics only happen at scheduled visits, often quarterly.
- Lack of coordination and communication between the health facility, district, province and NDOH is also an issue that needs to be strengthened. BDNT are submitted to NDOH through the various offices, giving opportunities for failure if each office does not submit to the next.

8.4 Limitations of the study

- Gross underreporting of CD data by health care providers.
- Analysis was limited to data received from May 2006 until December 2015.

- Only CDs notified by HCP in a health facility were reported.
- No data was included from the private health sector or other stakeholders.
- Data analysis was only possible where a clear diagnosis was recorded (e.g. limb malformation) and this was often lacking /not clearly indicated on the BDNT. In these instances, the reported CD was captured as an unspecified malformation and could not be included in data analysis.
- Information that was not applicable to certain cases was incorrectly documented as 'not recorded' instead of not applicable. E.g. CDs identified in older patients do not require birth weight and/or gestational age. Often this data field was marked as 'not recorded', adding to the number of data fields not recorded.

8.5 Factors that contribute to CD surveillance

- The government, through the Department of Health (DOH), needs to acknowledge the existence of CDs as a health issue and devote attention to these conditions.
- The Ministry of Health needs to make a commitment to improve medical genetic services coupled with adequate resource allocation. This includes the creation or filling of posts for medical geneticists and genetic counsellors.
- Improved prenatal services, which includes screening of pregnant women by ultrasound and prenatal diagnosis, (especially those of advanced maternal age) results in increased CD identification and reporting at birth or following termination of pregnancy, if chosen.
- Organize medical genetics services into primary health care (PHC). For ease of implementation, medical genetics services should be integrated into PHC as they are largely preventative in nature. These services should also be provided as a package of MCWH services.
- Health care providers and allied health professionals need to be educated on CD prevention and management.
- The contribution of CD to mortalities and morbidities, specifically neonatal mortality needs to be accepted.

8.6 Area of future research

- Different studies could be undertaken or investigated to depict birth prevalence for the different CDs. Data for some CDs date as far back as the early 1990s.
- Trends of CDs reported in the different provinces should be investigated.
- An investigation into the feasibility of integrating different disease surveillance systems.
- Studies to evaluate the success of future data collection systems.

8.7 Conclusion

This study is important for SA as medical genetic services in the country have diminished in the last decade. With the deterioration in medical genetics services and the stagnating neonatal mortality rates, the importance of CD surveillance is highlighted. In general, CDs are often underreported and thus underestimated in developing countries. This same trend was observed in this study with an underreporting rate of 98%. Various challenges are attributed to the under-reporting rate including the lack of trained health care providers leading to the misdiagnosis and undiagnosed CDs. If CDs are not diagnosed they cannot be reported, as a consequence, the burden of CD cannot be quantified. Medical genetics services will not be prioritized if the burden of CDs continues to be underestimated. This is unfortunate, as the burden of CDs on the population in developing countries, is greater due to inadequate services.

With other competing priorities in the Department of health, such as the HIV/AIDS epidemic, cancers and resulting mortalities, funds were rediverted to tackling these, further neglecting genetic services. The true burden of CDs needs to be quantified for services to be revitalised and CD surveillance provides this information. For medical genetic services to be strengthened, a health needs assessment needs to be undertaken. This requires data, e.g. birth prevalence of the different CDs in the country, trends and cluster investigation of the different CDs. With this current system, SA will not be able to quantify CDs, measure their contribution to mortality and morbidity and measure CDs contribution to the health system.

The Ministry of health's commitment to improving genetic services is required. Services need to be prioritized including the development of an improved CD surveillance system. This system should adopt international standards while meeting the countries needs and circumstances. With advancements in technology, a simple electronic system implemented initially in a few sites is recommended. This system may then be upscaled nationally if the facilities have the required infrastructure and human capacity. This allows for better support and control at the sites for better data collection and improved CD estimates that will reflect the true burden of CDs in SA.

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Appendices

Appendix 1: The Study Protocol

University of KwaZulu-Natal
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An Assessment of the Success and Shortfalls of the Current National Birth Defects Database and Improved Data Collection Methods for the Database

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EXECUTIVE SUMMARY

The global incidence of birth defects is between 2-3% of all live births. In South Africa, approximately 1 million infants are born annually. We therefore expect that 20-30 thousand infants born annually should have a birth defect. With this high number it becomes increasingly important that these infants are treated and managed appropriately. The National Department of Health (NDoH) have put in place interventions to ensure that infants born with birth defects are managed correctly, one of which is the collection of birth defects data countrywide and the development of a birth defects national database. The data for the database is collected through a notification tool that is completed at the health facilities and forwarded to National office. This tool was instigated in 2002 and is being implemented by several health facilities. Apart from some facilities not implementing the tool, other negative aspects of the national database include the quality of data received and the method used to forward the data (notification tools) to the NDoH offices. This project aims to study and improve the methods used to collect and forward data to NDoH.

A study is going to be conducted to look into the collection of birth defects data in South Africa. This study is going to look at both the strengths and weaknesses of the current national database. It is going to include an investigation into the method used to collect and forward data to the national office. An improved notification tool and method of forwarding data is going to be developed and piloted in one area in Kwa-Zulu Natal province. The effectiveness of the old and new approach will be weighed against each other and a suitable wayforward will be determined. Accompanying the improved notification tool will be a new data flow that will be developed and also piloted in the same area in Kwa-Zulu Natal province. The effectiveness of both the new notification tool and data flow method will be measured against the previous method/old approach and a suitable way forward will be determined based on the results of the study

The National Department of Health uses the notification tool as its only method of collecting birth defects data. An improvement to the national database will mean better collection of relevant data which could be used to influence better health care for people born with abnormalities. Moreover, the national database serves as a foundation for further research on birth defects in South Africa

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1. DEFINING THE RESEARCH PROBLEM

The National department of Health (NDoH) routinely collects data from the facilities for their national birth defects database. This national database has various challenges namely, lack of implementation of the notification tool by various health facilities, quality of data received and the method used to forward the data to the NDoH offices.

2. LITERATURE OVERVIEW AND MOTIVATION

In 2001 the University of Cape Town's School of Public Health and Family Medicine carried out a birth defects surveillance system (BDSS) through a three year tender awarded by the NDoH. Before then, information relating to birth defects was assembled at NDoH but was not collected in such a way that prevalence rates of birth defects could be established. When considering the epidemiology of birth defects it is necessary to distinguish clearly between birth prevalence and population prevalence. Birth prevalence is the number of infants who have or will develop a birth defect per 1000 live births while population prevalence is the number of affected people per 1000 of the whole population. Birth prevalence is the appropriate prevalence indicator as it makes comparisons between different populations, assesses changes with time and projects the health burden. (Christianson *et al, 2004*). Knowing the health burden, in this case of birth defects, forms the foundation for decision making in public health and empowers decision makers to lead and manage more efficiently by providing useful evidence (CDC, 2012). The health burden resulting from birth defects in developing countries is shadowed by the burden of infectious and chronic diseases. It is however the responsibility of national governments to assess and prioritize the health needs of their population (WHO, 2006).

The aim of the BDSS was to establish baseline prevalence rates of selected priority conditions as defined by NDoH from 1993-2004 (NDoH, 2001). Following the specified period, a final report was compiled but was not distributed publicly. It is this same report that influenced the development of the standardised birth defects collection tool (notification tool) in 2006 that is currently being used to collect birth defects data nationally.

A national birth defects database is important as it gives (should give) information regarding the incidence and prevalence rates of genetic conditions, it allows the NDoH to determine priorities for intervention, plan effectively and set objectives for care of individuals with birth defects and their families. Establishing a national database for monitoring of common birth defects was one of the recommendations made by the March of Dimes (Christianson *et al*, 2006) to allow for more robust evaluation of national interventions.

As previously stated, the NDoH has not published any data on birth defects. The only available information is the final report that was compiled following the tender reported prevalence rates for neural tube defects, down syndrome, albinism, and orofacial clefts.The previous study (birth defects surveillance system) employed a hospital based system of collecting data from only 11 hospitals (sentinel sites) in five provinces. A condensed form was used to collect both maternal and infant information for seven birth defects that were identifiable at birth or during the hopitalisation period following birth. Moreover, birth defects amongst stillbirths were excluded in the study, together with birth defects amongst miscarriages and therapeutic abortions.

Following the release of the final report, NDoH has gone back to routinely collecting birth defects data; however, no formal report has been compiled since or released. In addition, various challenges have been identified with the method used to collect and forward data to NDoH. The notification tool that is currently being used is completed by health care providers at the facilities and forwarded to NDoH. One of the major problems encountered is that health care providers do not complete the form correctly or completely, leading to poor quality data, this could be attributed to the simplicity vs. difficulty of the tool. The second challenge is the late reporting of the facilities. Notification tools take months to reach NDoH or they are not submitted at all, this proves the inefficiency of the method and reasons for the delay need to be determined.

The notification tool was developed with the aim of reporting all birth defects, whether they were amongst live births, still births or whether the patient opted for a therapeutic abortion. This will show a better representation of the incidence and prevalence rates of birth defects across South Africa. The notification tool forms the basis of the national birth defects database and hence has to be as comprehensive yet simple as possible.

3. AIM AND OBJECTIVES

Aims:

1. To ascertain the effectiveness of the current National Birth defects Database data collection strategy.
2. Identify some of the challenges surrounding data collection for the current national database for birth defects.
3. Introduce interventions to improve the database in terms of the information it holds as well as efficacy of data collection.
4. Evaluate the effectiveness of the interventions.

Objectives:

1. Audit the current database by examining the number of notifications received as well as the quality of data reporting across South Africa.
2. Design an improved data recording and forwarding method
3. Pilot and evaluate the interventions in one local area (district) of Kwa-Zulu Natal Province

4. METHODS

4.1. STUDY DESIGN

An observational retrospective study will be performed when auditing the current National Birth Defects database. The evaluation of the interventions (the improved data recording and forwarding methods) will be carried out prospectively.

4.2. SETTING

The National Birth Defects database will be audited at the National Department of Health together with the development of the new data recording and forwarding method.

The pilot and evaluation of the interventions to improve the database will be done at four district hospitals in Umngungundlovu district.

4.3. PATIENT/RESEARCH OBJECT SELECTION

The audit of the National Birth defects database will concentrate only on data received from the years 2006 to 2012. In this period, 12 754 birth defect notification tools were received by the National Department and will be analysed. However, the pilot study will be conducted in Umngungundlovu district and will only focus on data received from the district between 1 January 2015 and 30 June 2015.

4.4. MEASUREMENTS

For the audit, the variables from the Birth Defects Notification form will be described, along with the amount of missing data and numbers of forms submitted in a specific time period. To measure the effectiveness of the interventions, the completeness and accuracy of the filled out forms will be assessed along with the numbers and turnaround time from completion to arrival at the National Sub-directorate for Human Genetics.

4.5. DATA ANALYSIS

Ordinary descriptive statistics will be applied to the data and will be done in consultation with a biostatistician if required.

4.5.1. SAMPLE SIZE

Our study will focus on a single district in KwaZulu-Natal Province. Umgungundlovu district has four hospitals, and all have nurses who have received MGEP 1 training.

5. ETHICAL CONSIDERATIONS

There are no ethical considerations for this study as no patient information will be used at any point in the process. Only the number of reported cases will be discussed. Approval to utilize the data will be received from the National Department of Health.

6. TIME LINES AND PROJECT MANAGEMENT

Task	Start Date	End Date	Duration (Months)
Audit the national birth defects database	Oct-13	Jan-14	4
Write first article	Feb-13	Aug-14	7
Redesign data recording form and data forwarding method	Aug-14	Aug-14	1
Pilot new form and data method	Sept-14	Nov-14	3
Adjust instrument and method	Jan-15	Mar-15	3
Trial system	Apr-15	June-15	3
Write second article	Jul-15	Sep-15	3
Write third article	Oct-15	Dec-15	3

8. CONTRIBUTORS AND AUTHORSHIP

Name	Department	Contribution	Author or acknowledgement
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10. APPENDICES

Standardised birth defects notification tool (attached as Annexure A).

The old data collection form will be reviewed and updated to include the following information:

- Official Departmental logo
- Maternal conditions present during pregnancy
- Type of prenatal screening
- Top to toe examination form

Appendix 2: Biomedical Research Ethics Committee Approval

UNIVERSITY OF
KWAZULU-NATAL
INYUVESI
YAKWAZULU-NATALI
RESEARCH OFFICE
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Private Bag X 54001
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25 January 2018

Ms Vuyiswa Mtyongwe
P O Box 17424
Pretoria North
0116
vuyimtyongwe@gmail.com

Dear Ms Mtyongwe

PROTOCOL: An Assessment of the success and shortfalls of the current national birth defects database and improved Data Collection Methods for the database. REF: BE087/14

RECERTIFICATION APPLICATION APPROVAL NOTICE

Approved:	05 February 2018
Expiration of Ethical Approval:	04 February 2019

I wish to advise you that your application for Recertification received on **22** January 2018 for the above protocol has been **noted and approved** by a sub-committee of the Biomedical Research Ethics Committee (BREC) for another approval period. The start and end dates of this period are indicated above.

If any modifications or adverse events occur in the project before your next scheduled review, you must submit them to BREC for review. Except in emergency situations, no change to the protocol may be implemented until you have received written BREC approval for the change.

This approval will be **ratified** by a full Committee at its meeting taking place on **13 March 2018.**

Yours sincerely

Mrs A Marimuthu
Senior Administrator: Biomedical Research Ethics

X

Appendix 3: South African Congenital Disorders Data, 2006-2014

South African congenital disorders data, 2006 - 2014

V Lebese, BSc Hons; **C Aldous**, PhD; **H L Malherbe**, MSc

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Background. The National Department of Health in South Africa (SA) routinely collects congenital disorder (CD) data for its national CD surveillance system. The current system has been implemented since 2006, but no reports on the data collected, methodology, achievements or challenges have been published to date.
Objectives. To ascertain the effectiveness of the current national CD surveillance system and its implementation.
Method. A descriptive, retrospective study using an audit of the current database was undertaken to evaluate the number of notifications received, types of CDs reported and the quality of reporting across SA for data received from 2006 to 2014.
Results. A total of 14 571 notifications were received, including 13 252 CDs and 1 319 zero notifications, across all nine provinces. Commonly reported CDs included Down syndrome, cleft lip and palate, talipes equinovarus, neural tube defects and albinism.
Conclusions. The major challenges identified included erratic compliance by health facilities and a lack of healthcare providers trained in human genetics related to CDs. This has led to misdiagnosed and undiagnosed CDs, collectively resulting in under-reporting of cases by >98% during the review period. Owing to limited human and financial resources, it is recommended that the surveillance system be modified into an electronic format. This should be piloted alongside relevant training in specific sentinel sites, to improve data coverage and quality for further evaluation.

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Congenital disorders (CDs) or birth defects are defined as abnormalities of structure or function, including metabolism, that are present from birth.[1] Some are clinically obvious at birth, while others manifest later in life. CDs may be caused by genetic or partially genetic factors (preconception), non-genetic causes (post-conception), a combination of these or unknown factors.

Surveillance of CDs is essential to providing reliable information for decision-making and policy development relevant to their care and prevention.[2] Accurate data are required to demonstrate the true contribution of CDs to the burden of disease, which is imperative for any country.

CDs are the leading causes of infant and under-5 child mortality in high-income countries, accounting for up to 28% of deaths.[3] Surveillance systems in these countries, such as the National Birth Defects Prevention Network in the USA and the British Isles' Network of Congenital Anomalies, collate relevant data to determine the contribution of CDs to infant and child morbidity and mortality rates.[4,5] Relevant health policy is developed in response to these observed data.

Insufficient epidemiological data hamper the provision of quality health services for people with CDs. This is a common challenge among low- and middle-income countries (LMICs) including South Africa (SA), necessitating the use of estimates through modelling. With the birth prevalence of CDs in LMICs greater than or equal to that of high-income countries, this highlights the importance of quality epidemiological data from comprehensive surveillance, and a functioning health system.[6,7]

CD surveillance was initiated in SA in 1980 through research on the teratogenic effects of water supplies undergoing new purification processes. Work by the Water Research Commission through the University of Cape Town[8] provided the National Department of Health (NDoH) with the basis of a national CD surveillance system. This system aimed to provide information on the extent of disabling conditions, and to plan prevention and rehabilitation programmes.[8]

Following the publication of the *Policy Guidelines for the Management and Prevention of Genetic Disorders, Birth Defects and Disabilities*[9] in 2001, the national CD surveillance system was modified further by the NDoH with the introduction of the Birth Defect Notification Tool (BDNT) form. This article reports on the data emanating from the surveillance system implemented by the NDoH from 2006 to 2014.

Methods

Surveillance systems require clear goals and objectives to produce data that can be used to improve the general health of the public. The goals of the NDoH system were: (*i*) to find out the incidence and prevalence rates of CDs; (*ii*) to determine priorities for intervention; (*iii*) to inform effective planning; (*iv*) to set objectives for prevention and care; and (*v*) data evaluation and provision of feedback to provinces, health areas and health districts.[9] The specific methodology used is outlined under subsequent headings.[10,11]

Case definitions

The case definitions define the parameters for the surveillance system. Various definitions were considered, including maximum age of patient and types of CDs (minor, major or only specific CDs).[4,10,11] In 2001, the NDoH compiled a list of CDs (those that are identifiable or measurable within 24 hours of birth) to be monitored. These included neural tube defects (NTDs), Down syndrome, albinism, microcephaly, isolated cleft lip and/or palate and isolated hydrocephalus.[9] In 2005, the *National Guidelines for the Care and Prevention of the Most Common Genetic Disorders, Birth Defects and Disabilities* were published.[12] These outlined priority CDs that are common in SA and added talipes equinovarus, congenital infections and genetic deafness, blindness, physical handicap and mental retardation to the initial list of conditions for inclusion.

Case ascertainment methods

Between 2006 and 2014, a total of 729 healthcare providers (HCPs) from all levels of care, including primary healthcare (PHC) centres, were trained in the use of the BDNT (D Tshikedi, personal communication, 2015). This training was undertaken through the Medical Genetics Education Programme (MGEP) for labour ward and outpatient ward staff to maximise opportunities for identifying CDs throughout the continuum of care. Completed BDNTs were submitted to the NDoH via the district and provincial departments of health (DoHs) on a monthly basis. Provincial co-ordinators were responsible for the collation and analysis of provincial data prior to submitting to the NDoH. The identification and notification of the CD would preferably occur immediately following delivery, but, if undiagnosed within 24 hours of birth, notification could occur at any age, when the CD is identified. When no CD was identified at a specific facility within a reporting month, a zero notification tool was completed and submitted for the specific month using the same method. The BDNT was completed by various HCPs including registered nurses, medical doctors, genetic counsellors or clinical geneticists, if available. Only identified CDs were reported (preliminary diagnoses) while laboratory or other investigations were undertaken for confirmation.

Pregnancy outcomes

CDs on all pregnancy outcomes were to be monitored, including live births, stillbirths, terminations of pregnancy (TOP) and miscarriages.

Classification/coding

Although most countries opt to use the *International Classification of Diseases*, 10th revision (ICD-10), the NDoH developed a tailored coding system, capturing each CD using Microsoft Access and exporting the data to Microsoft Excel (USA). Each CD case was assigned a unique identifying number in the sequence received in that year, e.g. the first reported CD for 2006 was coded as 001/06. The system was implemented from May 2006.

Results

Implementation of the BDNT system by the health facilities was slow and erratic. The total number of notifications received from 2006 to 2014 was 14 571, of which 13 252 were CDs and 1 319 were zero notifications.

National reporting (Table 1) peaked in 2011 with a total of 2 401 cases reported, which was 2.92% of the expected number of CD cases based on modelled figures.[13,14] In 2014, the lowest number of CDs to date (612) was reported, indicating under-reporting of more than 99%.

Table 2 shows the distribution of CD notification tools received per province. KwaZulu-Natal (KZN) recorded the highest number of reported CDs for every year of the review period and in total, with 7 219 notifications (54.47%). The Western

Table 1. CDs reported in SA for 2006 - 2014 compared with expected numbers based on modelled estimates

Year	Zero notifications, *n*	CD notifications, *n*	Expected CD notifications,* *n*	Actual notifications as % of expected
2006	77	647	78 201	0.83
2007	109	1 338	79 020	1.69
2008	112	1 449	79 914	1.81
2009	135	1 854	80 829	2.29
2010	89	1 745	81 680	2.14
2011	387	2 401	82 349	2.92
2012	232	2 174	83 118	2.62
2013	119	1 032	83 821	1.23
2014	59	612	84 461	0.72
Total	1 319	13 252	73 3393	1.81

*Based on modelled/estimated figure of 6.8% of live births affected by CD per annual number of births.[13,14]

Table 2. CDs notified per province, 2006 - 2014, *n*

Province	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total
Eastern Cape	35	39	72	24	98	194	174	64	28	728
Free State	41	45	27	63	99	159	191	90	29	744
Gauteng	91	162	104	13	244	404	396	165	21	1 600
KZN	231	732	790	1 396	1 116	1 287	930	408	329	7 219
Limpopo	32	105	72	81	25	88	106	11	21	541
Mpumalanga	99	72	27	93	34	72	148	203	89	837
North West	78	81	113	53	41	110	59	3	0	538
Northern Cape	40	65	110	62	61	50	150	81	95	714
Western Cape	0	37	134	69	27	37	20	7	0	331
Total	647	1 338	1 449	1 854	1 745	2 401	2 174	1 032	612	13 252

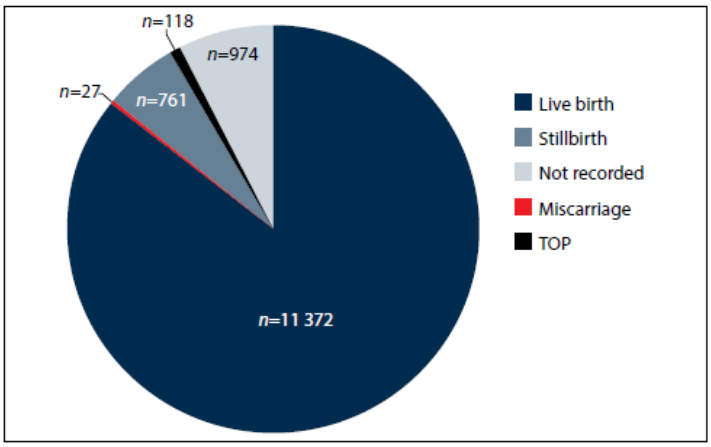

Fig. 1. Pregnancy outcomes of reported CDs as reported by facilities.

Cape reported the least notifications in total (*n*=331, 2.50%).

Pregnancy outcomes as reported by health facilities are shown in Fig. 1. Early identification and diagnosis are vital to enable appropriate care and management of the affected infant should the mother choose to continue with the pregnancy. Of the 13 252 reported CDs, 85.81% (*n*=11 372) were live births, 5.74% (*n*=761) stillbirths, 0.89% (*n*=118) TOP and 0.20% (*n*=27) miscarriages. For 7.35% (*n*=974) of notifications the pregnancy outcome was not indicated.

CDs may be identified prenatally or post delivery. Identifying CDs during pregnancy facilitates early identification of different approaches to management of the affected pregnancy, including choice of TOP.[9] The majority (85.81%) of infants affected by a CD in this study were born alive. However, the number of live births with a CD identified prenatally was only documented in 0.89% of cases, where patients opted for TOP following prenatal diagnosis.

During the review period, priority CDs[12] contributed 35.92% (*n*=4 760) of the total of 13 252 CDs reported (Fig. 2). The leading CDs reported were Down syndrome (*n*=1 236, 25.97%), talipes equinovarus (*n*=1 087, 22.84%), cleft lip and/or palate (*n*=943, 19.81%) and NTDs (*n*=787, 16.53%) (Table 3). Fetal alcohol syndrome (FAS) was the least reported, with 73 (1.54%) cases.

Other reported cases that were not common priority CDs were categorised as 'other congenital disorders' (OCDs). These totalled 8 492 (64.08%), of which only 1 497 (17.63%) were diagnosed. Where OCDs could not be diagnosed but clear abnormalities were observed, the abnormal organ/system was reported with a description. Abnormalities of the hands (mainly polydactyly) were the most commonly reported (*n*=1 775, 20.90%), followed by those of the skull (*n*=659, 7.76%) and the heart (*n*=574, 6.76%). Least reported were abnormalities of the skin with only nine cases (0.11%) that were only monitored from 2013. Abnormalities may be isolated or occur on multiple organs or structures. Multiple systems/structure CDs accounted for 1 360 (16.02%) of the reported OCDs.

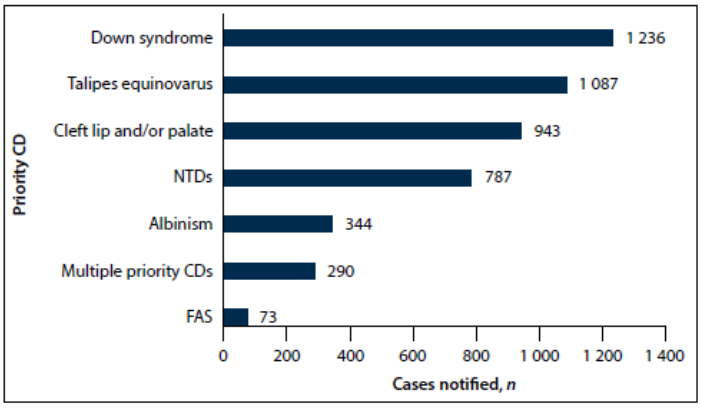

Fig. 2. Number of priority CDs notified, 2006 - 2012.

Discussion

The success of any congenital defects notification system or surveillance system depends upon three factors: (*i*) training of HCPs and their ability to apply the acquired knowledge; (*ii*) the presence of a local (provincial) co-ordinator; and (*iii*) the compliance of HCPs with the surveillance system. The provincial co-ordinators are pivotal in this process owing to their dual training and data collection and/or surveillance responsibilities.[9]

All nine provinces in SA should be implementing the BDNT, but current compliance is erratic and inadequate. The 13 252 CD notifications reported for the period 2006 - 2014 are only 1.81% of the expected total of 733 393, based on modelled estimates (Table 1).[13,14] This implies under-reporting by 98.19% during this 8-year period. In the last 2 years of the review period, reporting has dropped notably since implementation began in 2006, with the lowest figures reported in 2014.

KZN is the province with the second largest population in the country and reported an average of 54.47% of the total CD notification.[13] KZN's initial success can be attributed to the presence of an active provincial co-ordinator and consistent training of HCPs via MGEP. The national decline in data from 2012 may be attributed to the loss of a highly effective KZN provincial co-ordinator who remains unreplaced to date. This has impacted negatively both on the management of the provincial genetic services and on data flow for 2012 and subsequent years.

In the Western Cape, where the fewest CDs were reported, provincial co-ordinators are also responsible for other maternal and child health programmes. Although genetic services are available at different facilities, co-ordination is lacking. This negatively impacts on the co-ordination of HCP training and data flow from facilities to the NDoH via the province, evidenced by only 331 CDs reported in total for 2006 - 2014.

In Gauteng, the province with the largest population between 2002 and 2015, the number of CDs notified peaked in 2011 (*n*=404). However, with 200 443 births recorded in Gauteng in 2011,[15] modelled data indicate a minimum of 13 630 births (6.8%) with a CD in the province, with 3 571 of those identifiable within the first 24 hours of life.[14] This indicates significant under-reporting (97.04%) in Gauteng in 2011.

Of the total of 13 252 CDs reported nationally during the 8-year period of this study, only 35.92% (4 760) were common priority conditions. NTDs contributed the greatest single group of CDs (16.53%), including anencephaly, encephalocele and spina bifida. More than half (52.78%) of the reported CDs were undiagnosed. This highlights the importance of training HCPs in identifying, diagnosing and referring patients for appropriate CD management and care.

Table 3. Other CDs notified, 2006 - 2014

Other CDs	*n* (%)
Named diagnosis	1 497 (17.63)
Abdomen	461 (5.43)
Arms	88 (1.04)
Chest	81 (0.95)
Face	464 (5.46)
Feet	156 (1.84)
Gastrointestinal tract	498 (5.86)
Genitals	379 (4.46)
Hands	1 775 (20.90)
Heart	574 (6.76)
Legs	391 (4.60)
Skin	9 (0.11)*
Skull	659 (7.76)
Urinary system	100 (1.18)
Multiple systems/structure	1 360 (16.02)
Total OCDs	8 492 (100)

*Monitored from 2013.

FAS was the least-reported CD, with only 73 reported cases (1.53%). This is unsurprising as the diagnosis of FAS is extremely challenging, especially in the neonatal period, and requires clinical examination of features by a trained HCP.[16] Of the 73 FAS cases reported, 44 were diagnosed at birth and 29 were diagnosed later in the continuum of care. These data do not align with literature reporting FAS prevalence in SA as the highest documented globally, suggesting that FAS is grossly underreported via the BDNT.

Challenges

The provincial DoHs are guided by the NDoH but function autonomously. Nationally developed policies are implemented by the provinces in a top-down approach. The 2001 *Policy Guidelines* were developed in collaboration with the provinces and relevant stakeholders, but implementation of this policy, including the BDNT, has been problematic. Despite all provinces implementing the tool, erratic compliance by the districts is a challenge for data collection. Without a zero notification from a facility for a particular month, it is not known whether this is due to non-submission of forms or because no CDs were detected during that period.

By the end of 2012, although MGEP training had been conducted in every district in SA, only 46 of the 52 districts were submitting BDNTs. While some facilities lack a human genetics-trained HCP, there is also a lack of continued training for additional HCPs throughout the continuum of care with no relevant follow-up support provided. As a result, many CDs continue to be misdiagnosed or remain undiagnosed. This prevents a notification from being submitted and, more significantly, precludes the patient from receiving the appropriate care and treatment.

A further constraint is that only the public health sector is involved in national surveillance, with no notifications received from private healthcare. This further exacerbates the underreporting of CDs. The data collection process is also affected by the poor quality of the data received, including the submission of incomplete forms, illegibile handwriting and late submission. The greatest challenge is that the NDoH data capture system is not compatible with any other surveillance system, including the ICD-10 – preventing data comparison with other programmes.[9]

A well-functioning CD surveillance system could prove particularly useful when new pathogens appear. The Zika virus (ZIKV) has recently been implicated as a cause for microcephaly in newborns. The ZIKV vector is present in SA along the eastern seaboard, breeding in Strelitzia leaves, and there is anecdotal evidence that microcephaly has increased in incidence over the years. However, without accurate CD surveillance data, a possible link with ZIKV cannot be shown. ZIKV may have had a similar impact on CDs along the eastern reaches of SA as in Brazil, because of shipping routes east of Africa.[17] A comprehensive, functioning surveillance system would have identified any change in trend of microcephaly incidence and contributed to further research in this area.

Recommendations

Strengthening surveillance of CDs in SA requires the consideration of new avenues. The approach taken to date in SA is the use of a population-based surveillance programme, in which data are collected from an entire source population within a defined time period.[11] This approach is not working, because of limited resources (human and financial) and the current state of the medical genetic services in the country.[14] For the future, it is recommended that a hospital-based surveillance programme be implemented, similar to the Perinatal Problem Identification Program (PPIP) model, where data are collected from specific hospitals and facilities in a defined geographical area.[10,11] A revised BDNT should be developed using an electronic application (app)-based approach to collect data, eliminating the current paper-based method.

To improve the quality and collection of data, capacity building of HCPs in PHC settings should be reintroduced and strengthened. Health facilities responsible for the management and treatment of patients with CDs require improved support to enable them to notify CDs. Healthcare providers at these facilities are at the core of the system, reporting on confirmed diagnoses following further investigations.

Improved integration is required, and the NDoH, provinces, facilities and other roleplayers need to work together to improve CD data collection countrywide. The private healthcare sector should also be incorporated into the notification system. Laboratory services and their contribution to CD surveillance need improving and non-governmental organisations should be permitted to play a greater role in the collection of evidence-based data through patient registries, to more accurately reflect the true disease burden of CDs in SA.

Conclusions

The current national surveillance of CDs implemented through the BDNT is resulting in poor quality and quantity of data. This needs to be rectified to ensure a higher quality of CD observational data, to highlight the growing contribution of CDs to the disease burden in the country. Greater commitment is required to comprehensively collect and analyse CD data and apply these findings in policy development and implementation, by improving medical genetic services for those affected or at risk of CDs. Such improved surveillance would be an important step in response to World Health Assembly Resolution 63.17 of 2010.[2]

Acknowledgement. We thank the NDoH for their assistance in fast-tracking the data for this research.

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Accepted 1 August 2016.

Appendix 4: Birth Defects Notification Tool

☐ Full ☐ Zero

DEPARTMENT OF HEALTH
GENETIC SERVICES
BIRTH DEFECTS NOTIFICATION

Genetic reference number: .....
Code: .....

1. **GENERAL INFORMATION:**
   a. **Province:** ..... b. **District:** .....
   c. **Name of Hospital/Facility:** .....
   d. **Facility/Ward telephone number:** .....
   e. **Name of person notifying:** ..... f. **Date:** ..... / ..... / ..... (year / month / day)
2. **PARTICULARS OF MOTHER:**
   a. **Surname:** ..... b. **Name:** .....
   b. **Date of birth:** (mother) ..... / ..... / ..... (year / month / day) **Age:** .....

PLEASE TICK THE APPROPRIATE BLOCK

3. **PARTICULARS OF PATIENT:**
   a. **Surname:** ..... b. **Name:** .....
   c. **Gender:** ☐ Male ☐ Female ☐ Ambiguous d. **Date of birth:** (patient) ..... / ..... / ..... (year / month / day)
   e. **Population group:** ☐ African ☐ White ☐ Coloured ☐ Asiatic ☐ Other
   Specify: .....
   f. **Birth status:** ☐ Live Birth ☐ Still Birth ☐ Therapeutic Abortion ☐ Miscarriage
   g. **Birth weight:** ☐ <2500g ☐ >2500g h. **Gestational age:** ☐ <37 weeks ☐ >37 weeks
4. **PLACE OF BIRTH:**
   a. ☐ Urban Hospital b. ☐ Rural Hospital c. ☐ Clinic d. ☐ Home e. ☐ Born before arrival
   f. Referred to another Hospital? ☐ Yes ☐ No g. Referred from Hospital? ☐ Yes ☐ No
   h. If yes, name of that Hospital: .....
5. **DIAGNOSIS:**
   5.1 **PRIORITY BIRTH DEFECTS:**
   a. **Neural Tube Defects:** ☐ Anencephaly ☐ Encephalocele ☐ Spina Bifida
   b. ☐ Albinism c. ☐ Down Syndrome d. ☐ Talipes equinovarus/club feet e. ☐ Fetal Alcohol Syndrome
   f. **Clefts:** ☐ Cleft lip & palate ☐ Cleft lip only ☐ Cleft palate only
   Comments: .....
   5.2 **OTHER BIRTH DEFECTS:** (Other birth defects that have not been included in item 5.1)
   a. ☐ Skull b. ☐ Face c. ☐ Chest d. ☐ Heart e. ☐ Abdomen f. ☐ Gastrointestinal Tract
   g. ☐ Genitals h. ☐ Arms i. ☐ Legs j. ☐ Hands k. ☐ Feet l. ☐ Skin
   Description: .....
   Section 5 diagnosed by: ☐ Doctor ☐ Registered Nurse **Additional Genetic Training:** ☐ Yes ☐ No
6. **INVESTIGATIONS REQUESTED:**
   a. ☐ Chromosome/cytogenetic b. ☐ Biochemical/metabolic
   c. ☐ DNA/molecular d. ☐ No investigation necessary
   e. ☐ Other diagnostic or screening procedure **Specify:** .....
7. **COUNSELLING GIVEN (BY):**
   ☐ Clinical geneticist ☐ Medical Doctor ☐ Registered Nurse **Additional Genetic Training:** ☐ Yes ☐ No
   ☐ Genetic counselor ☐ No counseling given

Appendix 5: Integrated Disease Surveillance and Response Tool

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

IDSR 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: y y y y / m m / d d

PARTICULARS OF MOTHER

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

Maternal Conditions:

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

Maternal medication:	

PARTICULARS OF PATIENT

Surname:	Name:	Date of birth: y y y y / m m / d d	Gender:		
			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	2000-2400g>	≥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

Referral:

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

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

DIAGNOSIS

CDs/diseases of the circulatory system

- ☐ Q20.1-Double outlet right ventricle
- ☐ Q20.2-Double outlet left ventricle
- ☐ Q20.3-Discordant ventriculoarterial connection
- ☐ Q21.0-Ventricular septal defect
- ☐ Q21.1-Atrial septal defect
- ☐ Q21.2-Atrioventricular septal defect
- ☐ Q21.3-Tetralogy of Fallot
- ☐ Q22.0-Pulmonary valve atresia
- ☐ Q22.1-Congenital pulmonary valve stenosis
- ☐ I24.9-Cyanotic heart disease
- ☐ I51.7-Cardiomegaly
- ☐ Q22.4-Congenital tricuspid stenosis
- ☐ Q22.6-Hypoplastic right heart syndrome
- ☐ Q23.2-Congenital mitral stenosis
- ☐ Q23.3-Congenital mitral insufficiency
- ☐ Q23.4-Hypoplastic left heart syndrome
- ☐ Q24.0-Dextrocardia
- ☐ Q24-4-Congenital subaortic stenosis
- ☐ Q24.6-Congenital heart block
- ☐ Q25.0-Patent ductus arteriosis
- ☐ Q25.1-Coarctation of aorta
- ☐ Q25.2-Atresia of aorta
- ☐ Q25.5-Atresia of pulmonary artery
- ☐ Q25.6-Stenosis of pulmonary artery
- ☐ Q25.71-Coarctation of pulmonary artery
- ☐ Q26.2-Total anomalous pulmonary venous connection
- ☐ Q26.3-Partial anomalous pulmonary venous connection
- ☐ Q26.4-Anomalous pulmonary venous connection, unspecified
- ☐ Q24.9-Unspecified congenital malformation of heart

CDs/diseases of the nervous system

- ☐ Q00-Anencephaly
- ☐ Q01-Encephalocoele
- ☐ Q03-Hydrocephalus
- ☐ Q05-Spina Bifida
  - ☐ *Q05-Meningomyelocoele*
  - ☐ *Q05-Meningocoele*
  - ☐ *Q76.0-Spina bifida occulta*
- ☐ G80-Cerebral Palsy

CDs of the face

- ☐ Q35-Cleft palate alone
- ☐ Q36-Cleft lip alone
- ☐ Q37-Cleft lip and palate

CDs of the musculoskeletal system

- ☐ Q66-Talipes equinovarus
- ☐ Q71-Reduction deformity, upper limbs
- ☐ Q72-Reduction deformity, lower limbs
- ☐ Q79.2-Exomphalos/Omphalocele
- ☐ Q79.3-Gastroschisis

CDs of the genital organs

- ☐ Q54.9-Hypospadias
- ☐ Q56.4-Ambigious genitalia

Chromosomal CDs

- ☐ Q90-Down syndrome (Trisomy 21)
- ☐ Q91.3-Edward syndrome (Trisomy 18)
- ☐ Q91.7-Patau syndrome (Trisomy 13)

Other CDs

- ☐ D66-Haemophilia A
- ☐ D67-Haemophilia B
- ☐ D70.3-Albinism
- ☐ Q86.0-Fetal Alcohol Syndrome

Diagnosed by:	Doctor	Registered Nurse	**Genetic Training received:**	Yes	No	