The prevalence of infection related death at Salt River Mortuary for the years 2013 and 2014

by

MARIA MAGDALENA KRUGER

KRGMAR035

SUBMITTED TO THE UNIVERSITY OF CAPE TOWN

In partial fulfilment of the requirements for the degree
MPhil (Biomedical Forensic Science)

Faculty of Health Sciences
UNIVERSITY OF CAPE TOWN

Date of submission: 21 October 2016

Supervisors: Laura Heathfield, Prof. Lorna Martin and Dr. Sairita Maistry

Division of Forensic Medicine and Toxicology, Department of Pathology

DECLARATION

I, Maria Magdalena Kruger, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.
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ABSTRACT

Infection related death is of major concern world-wide. This is especially true in developing countries where there is a high burden of disease. In some cases infections may present atypically and death occurs without a diagnosis in life. Many countries, including South Africa, classify these deaths as sudden unexpected or unexplained, which, under the Inquests Acts, necessitates a medico-legal autopsy. In order to understand the mechanisms underlying such deaths, a systematic review of the literature was undertaken on sudden death due to infection. Data from published research and reports identified many pathogens associated with sudden or unexplained death in infants and older individuals. However it remains important to understand locally relevant pathogens. In addition, many risk factors have been identified in different age groups but it is not known what risk factors are prevalent in a local setting and if these correspond to international trends.

In order to contribute to local data a case file review was undertaken of infection related deaths at Salt River Mortuary between 1 January 2013 and 31 December 2014 (n=809). Deaths due to respiratory infections were the leading cause of death across all ages and in both sexes. It is not known to what degree this is a true reflection of the cause of death as the extent of autopsy, ancillary investigations and availability of ante-mortem clinical information varied widely. There has been a call for standardised protocols for the post-mortem investigation of these deaths and the data analysed reiterated this need. Many of the modifiable risk factors for infant death identified in the literature review were also identified in the Western Cape Metropole area, with the exception of sleeping position: side sleeping, as opposed to prone sleeping, was identified as the distinctive risk factor. In older individuals tuberculosis was identified as either the cause of death or a major contributor to co-morbid conditions, which highlights the importance of further surveillance of vulnerable individuals. These data have provided insight into the extent of infection related death and associated risk factors in a local context. A standardised protocol for the investigation of these deaths across mortuaries would enable more accurate data to be collected which in turn could be fed back into the healthcare system.

ACKNOWLEDGEMENTS

This dissertation would not have been possible without the wonderful support I have received from many people over the past year. To the following people I wish to offer my most heartfelt thanks.

To my supervisor, Laura Heathfield. Thank you for your dedication, guidance and support. The wisdom with which you approach research is an example to all. Everything you have done for me will be remembered with the greatest appreciation.

To my co-supervisors, Prof. Lorna Martin and Dr. Sairita Maistry. The insight and knowledge you provided laid the foundation for this dissertation and is invaluable. I would like to acknowledge that I feel extremely fortunate to have been a student of yours.

To the pathologists in the division. Your dedication allowed this project to become a possibility. Your tireless work is the root of my project and has instilled in me an immense appreciation for what you do, not only professionally but in our community.

To all the staff and students in the division. Throughout the year every one of us face challenges and the support I have received from staff and students will never be forgotten. It is a privilege to be part of an environment where people care for the well-being of others.

To my parents, siblings and family. You have always understood my thirst for knowledge and encouraged me to keep studying. Without your support, my move to Cape Town, and this degree would not have been possible. Thank you for providing me with such love over the years.

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ABBREVIATIONS

%	Percent
~	Approximation
≤	Less than or equal to
AIDS	acquired immune deficiency syndrome
CDR	Child Death Review
COD	Cause of death
CSF	Cerebrospinal fluid
EE	External examination
FA	Full autopsy
FPS	Forensic Pathology Service
GBA	Group A Streptococcus
GBS	Group B Streptococcus
GIT	Gastrointestinal tract
HIV	Human Immunodeficiency Virus
HREC	Human research ethics committee
IL-10	Interleukin 10
IL-1β	Interleukin 1β
IL-6	Interleukin 6
Incl.	Including
LRTI	Lower respiratory tract infection
MDG	Millennium Development Goal
MeSH	Medical Subject Headings
n	Number of individuals
OAD	Office Autopsy Database

OTC	Over the counter
PA	Partial autopsy
PID	Primary immunodeficiency disorders
PMI	Post-mortem interval
p-value	The probability of the occurrence of an event
SAPS	South African Police Service
SES	socioeconomic status
SIDS	Sudden infant death syndrome
SUDA	Sudden unexpected death of an adult
SUDI	Sudden unexpected death of an infant
TB	Tuberculosis
TNF-α	Tumour necrosis factor α
WHO	World Health Organisation
χ2 test	Chi-square test

Chapter 1

A systematic review exploring the relationship between infection and sudden unexpected death between 2000 and 2016: a forensic perspective

Summary

Death due to infectious diseases is a major health concern worldwide. This is of particular concern in developing countries where poor-socio economic status and a lack of healthcare resources contribute to the high burden of disease. In some cases death due to infection can be acute and aggressive, and death may occur without a diagnosis whilst the person is still alive. These deaths may ultimately lead to a medico-legal autopsy being performed.

There are various mechanisms by which sudden death due to infection may occur. In addition, there are many risk factors associated with sudden death due to infection, which differ between infants and older individuals. However, it is unclear which pathogens and risk factors are most frequently associated with sudden death due to infection. Therefore a systematic review of articles and case reports published between 1 January 2000 and 30 June 2016 was undertaken in order to (1) explore the relationship between pathogens and their causative role and (2) identify the relationship between predisposing and/or risk factors associated with sudden death due to infection. Major databases were searched and after critical appraisal 143 articles were identified. It was found that respiratory infections and deaths involving bacterial pathogens were most commonly associated with these deaths. In addition the most common risk factors in infants were exposure to tobacco smoke and co-sleeping. In adults the most common risk factors were co-morbid conditions and illnesses. This information could be used to compare with South African trends which would aid in a better understanding of these deaths.

1.1 Introduction

Each year the vast majority of deaths worldwide are attributed to natural causes. According to the World Health Organisation (WHO) the top seven leading causes of death worldwide are due to a natural disease, process or event, with lower respiratory tract infections being fourth on the list [1].

The WHO estimates that death due to communicable diseases is approximately 611.6 per 100 000 people in South Africa [2]. Some of these deaths occur suddenly and unexpectedly or the cause of death is not immediately apparent. Sudden, unexpected or unexplained deaths are defined as unnatural deaths in the Regulations (No. 636 of 2007) of the National Health Act (Act 61 of 2003) [3]. Therefore they require a medico-legal autopsy to be performed as per the Inquests Act 58 of 1959 [4].

Sudden and unexpected deaths in adults (SUDA) are often due to cardiac related events [5]. However many sudden unexpected deaths in infants (SUDI) are due to infections, notably in developing countries [6,7]. Sudden unexpected death in infants is defined as death of an infant occurring under one year of age [8]. Sudden and unexpected death due to infection occurs when the infection presents acutely and aggressively, and death occurs without a prior clinical diagnosis [9].

Infant mortality due to natural causes is of concern, particularly in developing countries such as South Africa. However in some cases the exact cause of death remains unclear [10]. The common bacterial toxin hypothesis for sudden infant death syndrome (SIDS) aims to explain the complex interplay between viral infection, bacterial toxin accumulation, the immune response and environmental risk factors such as prone sleeping and exposure to cigarette smoke [11]. Since this hypothesis was first presented, much research has sought to explicate this interplay. More recently the body of evidence increased to support that an infectious aetiology could be present in many SIDS cases [12].

In contrast, not many studies have been conducted on infection related sudden death in individuals older that one year, although many single case reports have been published. In addition, there are some case reports in the literature that disentangle suspected foul play by elucidating an underlying infection as cause of death [13–16]. This is an important aspect to consider in the forensic pathology setting.

The WHO established Millennium Development Goals (MDGs) in 2000. MDG number 4 was to reduce child mortality and number 6 was to combat HIV/AIDS, malaria and other diseases (including tuberculosis) [17]. As infection is one of the leading causes of child mortality [18], it is important to understand which pathogens and risk factors are associated with these deaths, when death occurs suddenly and unexpectedly.

The identification of these pathogens and risk factors in a global context is important in order to establish comparative data with which locally sourced information can be compared and contrasted. By adopting this approach a more comprehensive body of evidence can be presented to the healthcare system which may aid prevention campaigns and strategies which include the updating of vaccination schedules and creating awareness surrounding modifiable risk factors. To this end, a systematic approach was adopted to review the literature on infection related sudden and unexpected or unexplained deaths between 2000 and 2016.

1.2 Objectives

The first objective was to explore the relationship between pathogens and their causative role in the sudden unexpected deaths of (i) infants and (ii) older individuals.

The second objective was to explore the relationship between predisposing and/or risk factors associated with sudden death due to infection in (i) infants and (ii) older individuals.

1.3 Search Strategy

The search strategy applied for this review included searching the databases PubMed and Scopus and the meta-database, Web of Science™. "Hand-searching" was done by evaluating every reference in the reference list of a journal article. The meta-database www.crossref.org was used to find publications referenced in journal articles recalled during a database search. Crossref is a reference linking service which allows for citations to be linked via their Digital Object Identifiers (DOI). This meta-database does not contain full text articles but rather serves to efficiently link scholarly literature [19].

A "hand-search" of PubMed and Web of Science™ yielded additional articles. A "hand-search" of articles selected from Scopus revealed only unsuitable and redundant articles. Additionally, five discipline specific journals were chosen to ensure that relevant articles were not overlooked during database searching. A summary of articles returned (the results that the database or journal displays) and retrieved (articles chosen according to inclusion and exclusion criteria), with the results of "hand-searching" is represented in Table 1 (section 3.3.5). As a result of the systematic approach adopted redundant articles were immediately identified in the search and not included in the body of literature used in the analysis of this review. Review articles were included in the article count; however they were only used as sources to "hand-search" for original research papers and case reports.

1.3.1 Inclusion and exclusion criteria

The inclusion and exclusion criteria were applied by reading the abstract and/or scanning the article. Only English articles adhering to the concepts as set out in Table 1.1 were included.

Articles published before the year 2000 were excluded. Limiting the publication years in this way ensured that the most up-to-date information was reviewed.

The only exception to this was an article by J.A. Morris in 1999, as it is deemed seminal work related to the common bacterial toxin hypothesis in SUDI cases [11].

Table 1.1 Inclusion and exclusion criteria applied to articles during the search of the literature

Inclusion criteria	Exclusion criteria
• Infection related to sudden death. • The diagnosis of infection at autopsy or necroscopy. • Trends in sudden death. • Complicating factors related to infection and sudden death. • Inflammation or inflammatory responses and sudden death. • Sudden unexpected death in an infant (SUDI) or sudden infant death syndrome (SIDS). • Sudden unexpected death in an adult (SUDA). • Sudden death related to any virus, bacteria, fungus or other pathogen.	• Iatrogenic deaths. • Animal model studies. • Traumatic or procedure related deaths. • Cardiac related deaths that did not have an infectious cause. • Sudden deaths attributed to a neurological incident that did not have an infectious cause.

1.3.2 Systematic search of literature

1.3.2.1 PubMed search terms

The Medical Subject Headings (MeSH) database was used to create the search in PubMed. MeSH was used to index articles in PubMed via a controlled vocabulary thesaurus. The following is the search output generated from the MeSH terms:

((("Infection/microbiology"[Mesh] OR "Infection/immunology"[Mesh]) OR "Infection/physiopathology"[Mesh]) OR "Infection/virology"[Mesh]) AND "Death, Sudden"[Mesh].

1.3.2.2 Web of Science™ search terms

Web of Science™ was used to incorporate additional databases in the search for appropriate literature. Searching within this website allows for the search to be done within the following databases:

Web of Science™ Core Collection; Biological Abstracts®; KCI-Korean Journal Database; MEDLINE®; Russian Science Citation Index; SciELO Citation Index; Zoological Record®. The following keywords were used: Sudden death AND acute death AND infection.

1.3.2.3 Journal specific search terms

Due to the nature of this review searches were conducted within five subject specific journals. The keywords used were sudden AND unexpected AND death AND infection.

1.3.2.4 Scopus search terms

A search within the database Scopus was conducted. For the full text search parameters, refer to the supplementary material.

1.3.2.5 Summary of articles retrieved for the search strategy

Through the systematic search of the literature and after applying the inclusion and exclusion criteria a total of 213 articles were identified as presented in Table 1.3 (section 1.3.3).

1.3.3 Quality criteria

The search strategy outlined above returned 213 articles; including case reports, retrospective studies and original research. Case reports generally represent exceptions rather than the rule; however, given the rarity and complicated nature of sudden deaths due to infection, case reports when collated may represent valuable information and data. Certain criteria were applied to these articles to assess the quality of the data and information contained therein. Quality criteria (Table 1.2) stem from the objectives of this review and allowed for appropriate analysis of the available literature. If 'no' was answered to any of the core criteria the article was excluded which resulted in a total of 143 articles used in the analysis of the literature. Additional literature was used to contextualise concepts and arguments.

Table 1.2 Quality criteria applied to the 213 identified articles

Case Reports	Retrospective studies and original research
• Does the information contained within the case report fall within the scope of this review? *(Core criteria)* • Does the case report contain adequate information in order to appraise the outcome of the report? *(Core criteria)* • Were the same results discussed in different journal articles?*(Core criteria)* • Did the author(s) cite appropriate literature? • How recent is the report? • Is it a 'novel' report, i.e. would this be the first time it is reported in the literature (according to the author)?	• Does the information relate to either objective 1 or 2 of this review? *(Core criteria)* • Was the information reported in the study outlined in a way that is easy to follow or understand? • Did the authors report any novel findings? • Did the authors corroborate or 'disprove' previous findings or reports? • How recently was the study conducted? • Over how many years was the review conducted? • Did the authors use appropriate statistical tests to validate their findings? • What are the strengths and limitations of the study? • Were the same results discussed in different journal articles? *(Core criteria)*

Through the systematic search of the literature and applying inclusion and exclusion criteria a total of 213 articles were returned of which 143 were used in the analysis of the literature following assessment according to the quality criteria. In this review the most common pathogens were determined based on the actual number of medico-legal cases and not the number of articles associated with the pathogen.

Table 1.3 Summary of the articles returned during the search strategy and total number used in the analysis of the literature

Source	Date accessed	Articles returned	Articles retrieved (section 3.1 and 3.2)	Articles found via "hand-searching"	Total number of articles
PubMed	01/04/2016	96	25	81	106
Web of Science™	12/04/2016	276	29	48	77
Forensic Science International	21/04/2016	117	9	0	9
Journal of Forensic Sciences	21/04/2016	64	8	0	8
International Journal of Legal Medicine	21/04/2016	41	5	0	5
Legal Medicine	21/04/2016	42	4	0	4
Journal of Forensic and Legal Medicine	21/04/2016	43	10	0	10
Scopus	23/04/2016	166	12	0	12
				Total	231
Total number of articles used in literature analysis following the application of the quality criteria = 143					

1.4 Interpretation and analysis of the literature

1.4.1 The relationship between infection and sudden unexpected death with particular attention to the identification and/or causative role of the pathogen

A systematic appraisal of the literature on SUDI and sudden death in older individuals was conducted to identify cases and research studies where infection and causative pathogens were reported. Articles on SUDI amounted to nineteen research studies and ten case reports. A summary of the case reports can be found in Appendix A, Table A.1.1. A total of eight research articles and 51 case reports were analysed to identify pathogens and associated infections in the sudden death of a person older than one year. The literature on this topic tended to be in the form of single case reports, which was in contrast to the literature on SUDI.

1.4.1.1 Pathogens associated with the cause of death in SUDI

The most commonly reported pathogens in research papers associated with SUDI are *Staphylococcus aureus* [20–24] and cytomegalovirus (CMV) [25–29] followed by the fungal pathogen *Pneumocystis jirovecii,* formerly known as *Pneumocystis carinii* [30–32] (Fig. 1.1).

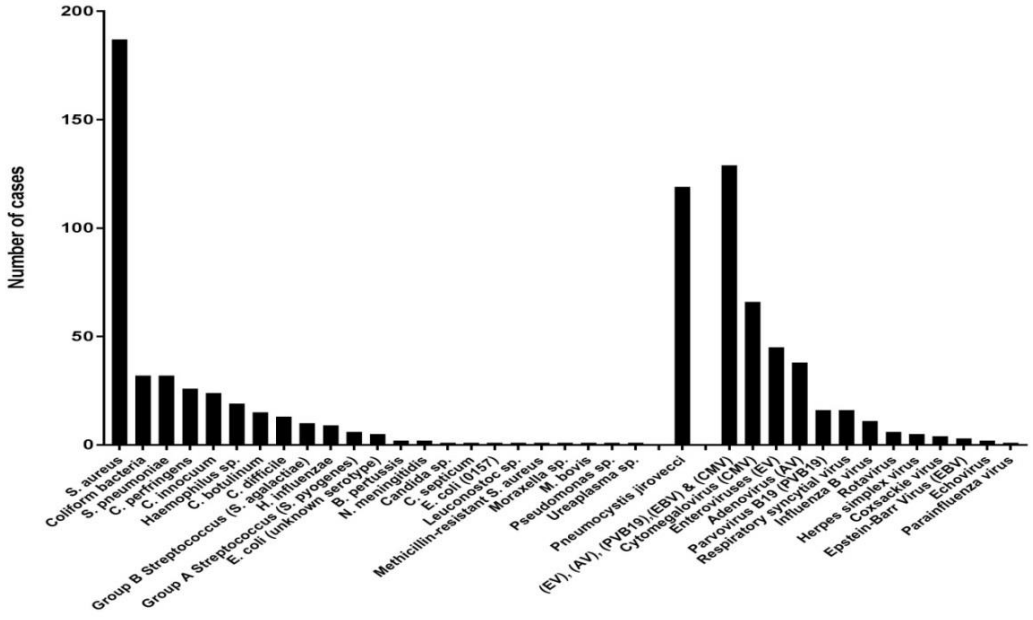

Figure 1.1 Graphical representation of the pathogens (n=852) associated with sudden death in infancy**.** [20–22,24–32,158,200,202–206]

Bacteria

A retrospective case review at a specialist centre over a ten year period was excluded from the quantitative analysis in this review due to nature in which the results were reported. However the authors' findings contribute significantly toward understanding infection related SUDI and are therefore discussed here: Cultures (n=1628) from infant deaths due to infection showed significantly more growth of *S. aureus* (p=005) and *Escherichia coli* (p=003) than cultures from infants that died from a non-infective cause [8].

SUDI death attributed to sepsis where there was no obvious focus of infection was also researched in the article mentioned above [8]. The most significant organisms associated with sepsis in SUDI were; *S. aureus*, *E. coli*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus pneumoniae* and *Neisseria meningitidis*. There was a significant difference ($p<0.0001$) between cultures from sepsis related SUDI (N=322) and cultures from infants with a non-infective cause of death (n=243) [8].

The role of *S. pneumoniae* in sepsis associated SUDI was highlighted in a case where a ten week old infant displayed bone and soft tissue injuries (eventually declared accidental). Following a full autopsy with extensive microbiological testing it was found that a retropharyngeal abscess had formed which led to eventual septicaemia and death [33]. Another case report of a nine month old infant highlighted the role of a full autopsy when the death appeared suspicious. Microbiological analysis of the cerebrospinal fluid, blood and lung swabs grew pure Clostridium perfringens cultures and the death was deemed natural [34].

Neonatal sepsis and meningitis due to Group B Streptococcal (GBS) infections is a major health concern in South Africa [6]. In the forensic post-mortem setting it is often difficult in obtaining ante-mortem information from parents and caretakers of SUDI cases, not just in South Africa but globally. In Japan a GBS infection is

routinely screened for in pregnant women before giving birth. An atypical case of late-onset disease (LOD) GBS infection was presented when a pregnant woman was not screened for a GBS infection and, although the infants' Apgar score was 10, the infant died four days after birth. Pathologists suspected vertical transmission from mother to child [35]. Recently it has been suggested that South Africa screen for a GBS infection in all pregnant women and administer intravenous antibiotics a minimum of four hours before birth [7]. The limitation in most low to middle income countries is the high cost associated with antibiotic therapy. However a recent vaccine which can potentially prevent up to 80% of invasive GBS infections has passed the phase-II evaluation in clinical trials. This vaccine could present a more cost-effective strategy to combat neonatal sepsis and meningitis in South Africa [7].

Conflicting results exist with regards to the pathogenic role of *Heliobacter pylori* as a causative pathogen in the sudden death of infants. In 2000, Kerr et al. reported a highly significant association between *H. pylori* and cases of SIDS [36]. However much concern was raised regarding this association by others in the field at the time. Concerns ranged from researchers critiquing the (then) new technology of PCR to possible post-mortem sample contamination [37]. In 2005 another research group concluded that there was no association between the detection of *H. pylori* and sudden death in infants [38]. The research on this pathogen did not move forward until 2008 when Stray-Pederson et al. concluded that the detection of *H. pylori* antigen in the stool of SIDS cases may explain the cause of death as this pathogen may be the initial event that triggers sudden death in infants, specifically those less than five months of age [39]. There are thus many caveats present with regards to the understanding of the role that this pathogen plays in the sudden death of infants.

Viruses

Viral infections has been recognised as an important co-factor which may trigger the events leading to SUDI but may be rare as the direct causal infection [40]. However certain enteroviral and CMV infections may cause acute myocarditis in infants leading to sudden death [41–44]. With application of molecular techniques on heart tissue the Coxsackie B3 virus (N=4) and a CMV (N=3) infection was identified in

unexplained infant deaths which indicated acute myocarditis. These may otherwise have been diagnosed as SIDS which highlights the importance of continual application of new techniques in SUDI investigations [42,43]. This was also demonstrated in a local context where a research at a large medico-legal mortuary indicated the great disparity between standard shell vial cultures and molecular techniques in detecting viral pathogens such as CMV, RSV and adenoviruses [28].

Other viral infections associated with SUDI include the influenza virus A, Epstein-Barr virus and human herpes simplex virus 6 [44]. A recent report indicated that the relatively benign Coxsackie Virus A16 may also be a contributing factor in SUDI [45].

Chicken pox is caused by the varicella zoster virus and usually affects young children as opposed to infants. The German Standing Committee recommends vaccination against chicken pox for all children over the age of eleven months [46] however vaccination for varicella zoster is not part of the required immunisation schedule in South Africa [47]. A report in 2013 found that the co-infection of CMV and varicella zoster lead to the sudden death of a two month old infant [48]. A vaccine against CMV has been a top priority for the past four decades but until recently, the development of a safe and protective vaccine has been limited. Phase-II clinical trials for a CMV vaccine showed promising results in 2014 which encouraged further research [49]. Factors such as these contribute to the development of immunisation schedules around the world, which is a critical part of the healthcare system.

Cardioviruses are viruses that occur in rodents and lead to myocarditis and encephalomyelitits. Human cardioviruses (hCV) have been detected in clinical samples from children who suffered from diarrhoea and respiratory infections [50]. In 2011 hCV was detected in the CSF of an infant where the cause of death was initially classified as SIDS. This is the first reported case where hCV was detected in a body compartment (i.e. the central nervous system) other than the respiratory or gastro-intestinal organ systems [51].

Fungi

A molecular typing technique was developed in 2004 for the typing of Pneumocystis species in formalin fixed paraffin embedded tissue. A case series involving three infants under the age of three months whose cause of death was initially SIDS was investigated. After applying the molecular typing technique the researchers identified *Pneumocystis jirovecii* in the lung tissue of the infants, thus altering the cause of death from SIDS to *P. jirovecii* pneumonia [31]. Their findings supported the hypothesis set forth by Morgan et al. in 2001 that humans can act as a reservoir for this fungus and that it plays a causative role in respiratory infections leading to sudden death in infants [30].

1.4.1.2 Pathogens associated with the cause of death in sudden unexpected deaths in children and adults

Case report analysis of the literature in this review found *Mycobacterium tuberculosis, E. coli, S. pyogenes and S. agalactiae* were the most commonly reported bacterial pathogens associated with sudden infectious deaths [13–15,52–57] (Fig. 1.2). The tapeworm Echinococcus granulosus was also reported a number of times where the affected individual died as a result of a ruptured hydatid cyst leading to septicaemia and toxic shock [58–61].

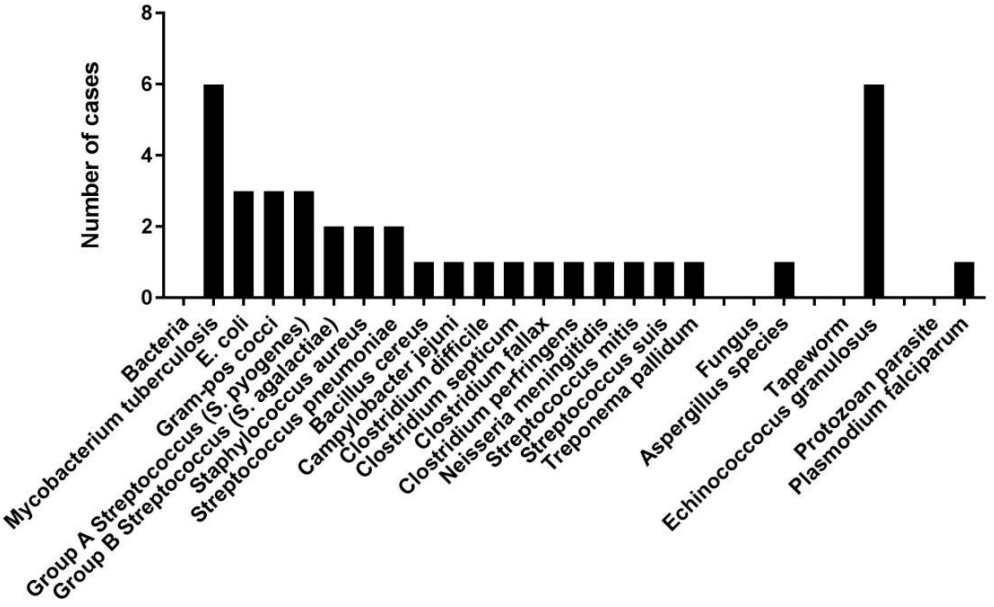

Figure 1.2 Case report analysis of the pathogenic bacteria, fungi and parasites reported to be associated with sudden infectious death [13–16,52–61,81,83,87,88,90–93,95,97–105]

Bacteria

Septicaemia is a life-threating response to infection when the infection damages the tissue and organs of the individual. The course of these infections can be lethal causing death as a result of sepsis [62]. However, as mentioned before, ante-mortem clinical information may be difficult to obtain in the forensic setting and may be the reason behind the medico-legal autopsy of an individual. Sudden or unexplained death due to sepsis have been associated with the following bacteria; *Acinetobacter baumanii, E. coli*, *Enterococcus species*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Proteus mirabilis*, *S. aureus*, *Enterobacteria species*, *S. pneumoniae* and the yeast like fungus *Candida albicans* [63]. Although post-mortem microbiology can be difficult to interpret [64] it is beneficial with regards to determining the point of origin in suspected sepsis cases, providing insight into emergent species and can aid in profiling drug resistance [63].

A fulminant bacterial infection which leads to sudden death might indicate a chronic underlying disease [65]. A mechanism of action was proposed whereby bacteria which enter the bloodstream and are resistant to phagocytosis will invade the blood via the intestinal tract, after which the pathogens migrate to the liver through the portal vein. Once the bacteria are in the liver proliferation and migration to the bloodstream occurs, leading to bacteraemia and sudden death, especially in individuals with chronic underlying conditions such as liver cirrhosis and splenic dysfunction [66].

Viruses

The most commonly reported viruses from case reports were Parvovirus B19, Adenovirus, Epstein-Barr virus and Influenza A virus [44,67–77] (Fig.1.3).

A parvovirus B-19 infection may cause acute fatal myocarditis [26,67,69], especially in the young, although it has been detected in individuals who died of non-invective causes. Thus a parvovirus B-19 infection may present as a long-term infection and it is uncertain to what degree it contributes to the inflammation of the myocardium [78].

A CMV infection [26] and infection from the Coxsackie virus B3 [9,79] have also been associated with acute fatal myocarditis.

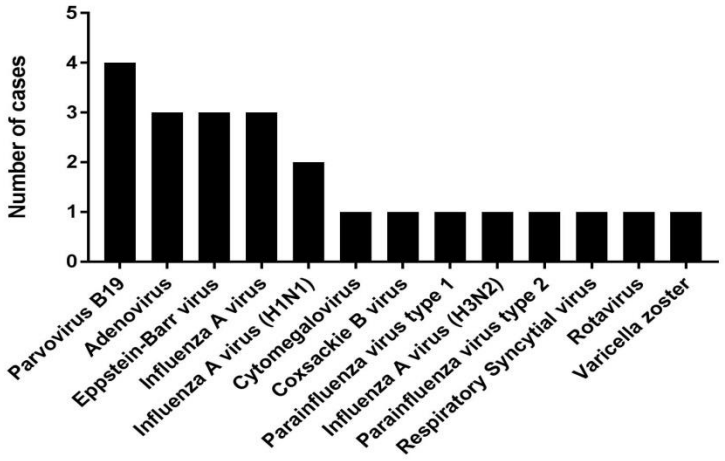

Figure 1.3 Pathogenic viruses reported to be associated with sudden infectious death in individuals older than one year [16,44,67,69–77,84,89,94,96,106,222,223]

Parasites

Hydatid disease, also known as human echinococcosis is a zoonotic infection caused by the tapeworm, *Echinococcus granulosus*. In most cases these cysts are found in the liver and occur mostly in young adults. A traumatic event may cause the cyst to rupture and death is due to anaphylactic shock. If the traumatic event precipitates a medico-legal autopsy and a ruptured cyst is found it may aid to distinguish whether the manner of death was homicidal or accidental [80].

Discussion

Case report analysis of infection related sudden death in children and adults non-infants revealed that the highest number of case reports originated from Germany (21%) and America (14%), followed by Australia, India and Japan (9% each) (Appendix A, Fig. A.11). Resources, as allocated through legislation, in developed countries lend themselves towards aiding the investigation of sudden unexpected deaths and as a result many case reports are published. The lack of resources in many developing countries may hinder these investigations and thus the publication

of case reports. Locally there are medico-legal mortuaries that are classified as M6 academic facilities which allow research to be conducted and published on topics such as sudden death and case reports. One such case report revealed the sudden death of an apparently healthy adult male was due to myocardial TB [81]. Adding to local research would better our understanding of the temporal differences in infection related sudden death.

Respiratory infections were the leading cause of death and had the highest number of associated pathogens from the collated case reports between 2000 and 2016. Sepsis and myocarditis were also highly cited as causes of sudden death with multiple associated pathogens (Table 1.4).

Respiratory infections include deaths due to pulmonary tuberculosis (TB) although *M. tuberculosis* may disseminate in the body and be associated with infections such as pericarditis and [54]. The WHO estimates that the incidence of active TB in South Africa was 450,000 cases in 2013. Of the 52 districts in South Africa there are only ten in which TB is not the leading cause of death [82]. However there is a lack of uniform information regarding the prevalence of TB in the South African medico-legal mortuary setting.

Table 1.4 A summary of the organ system, type of infection and associated pathogen compiled from case reports [13–16,18,52–61,67,69–77,81,83–106]

Organ System affected	Type of infection	Associated Pathogens
Multi-organ involvement	Acute rheumatic fever	*group A streptococcus*
	Bilateral tonsillar enlargement & narrowing of upper airway	*Epstein-Barr virus*
	Necrotizing fasciitis	*group A streptococcus*
	Septicaemia	*Clostridium fallax* *Clostridium perfringens* *Escherichia coli* *Staphylococcus aureus*
	Toxic Shock Syndrome	*group A streptococcus* *Streptococcus suis*
Cardiovascular system	Acute coronary thrombosis	*Coxsackie virus B2*
	Endocarditis	*Gram-positive cocci* *Staphylococcus aureus* *Streptococcus mitis*
	Infectious aortitis	*Clostridium septicum*
	Myocarditis	*Campylobacter jejuni* *Epstein-Barr virus* *Influenza A (H3N2) virus* *Parvovirus B19*
	Pericarditis	*Mycobacterium tuberculosis*
	Cardiac hydatid cyst	*Echinococcus granulosus*
	Syphilitic aortitis	*Treponema pallidum*
	Viral myocarditis	*Adenovirus serotype 3*
Nervous system	Cerebral malaria	*Plasmodium falciparum*
	Encephalopathy	*Rotavirus*
	Influenza encephalopathy	*Influenza A virus*
	Meningitis	*Streptococcus pneumoniae*
	Meningococcemia	*Neisseria meningitides*
	Meningoencephalitis	*group B streptococcus*
	Viral meningitis	*Adenovirus* *Influenza A virus*
Respiratory System	Laryngotracheitis	*Human parainfluenza virus–1*
	Pneumonia	*group B streptococcus*
	Respiratory infection	*Adenovirus* *Aspergillus species* *Influenza A/H1N1* *Mycobacterium tuberculosis* *Parainfluenza virus type 2 (PIV2)* *Respiratory syncytial virus* *Streptococcus pneumoniae* *Varicella zoster*
GIT System	Gastrointestinal Infection	*Bacillus cereus* *Clostridium difficile*

1.4.2 The risk or predisposing factors that are related to sudden unexpected death due to infection.

There are vast amounts of literature available for risk factors associated with sudden infant death. In this review, research conducted on SUDI, with particular attention to an infectious aetiology (24 articles), was appraised. In addition, the risk factors for non-infants were compiled through assessment of case reports and case series descriptive studies (31 articles).

1.4.2.1 Risk factors associated with sudden infant death due to infection

The broad categories for risk factors were: developmental, maternal, environmental, genetic, health-status related, illness and other/modifiable factors such as prone sleeping position (Table 1.5).

Table 1.5 Risk factors associated with infection as a cause of sudden infant death

Type of Risk Factor	Specific Risk Factor	Reference(s)
Developmental	2-4 months of age	[83]
Maternal Risk Factors	Alcohol use during pregnancy	[84]
	Illicit drug use during pregnancy	[84]
	Pre-natal smoking	[84–86]
Environmental	Air pollution	[83,87]
	Co-sleeping	[84,85,87,88]
	Contaminated food	[89]
	Overheating	[83]
	Quality of mattress	[83,84,87,90]
	Second hand smoke exposure	[83,84,91–94]
	Poor socio-economic conditions	[83,84]
Genetic	Ethnicity	[83]
	Male sex	[83,95,96]
	IL-6 polymorphisms	[83,97,98]
	IL-10 polymorphisms	[83,99–101]
	IL-1β polymorphisms	[83,102]
	TNF-α polymorphisms	[103]
Health status related	No or late vaccinations	[83,104]
	Lack of maternal vaccination against GBS	[7]
Illness	Mild respiratory infections	[83,84,93]
Other/ modifiable	Physical Injury	[33]
	Lack of breast-feeding	[83]
	Mode of delivery	[87]
	Prone sleeping position	[83,84,88,93]

The most common risk factor for SUDI identified in this review (6 research articles) was exposure to second hand smoke [83,84,91–94]. Second hand smoke inhalation implies that there is less exposure to the harmful constituents of smoke; however, some research indicated that there were detectable levels of nicotine (in hair) and cotinine (in pericardial fluid and CSF) in infants who succumbed to sudden death [105–108]. Recent local research has also shown that detectable levels of cotinine can be found in infant urine, indicating the need for urgent intervention in local communities [109]. Cotinine is a metabolite of nicotine and has shown to increase the production of pro-inflammatory mediators. In an experimental model it was shown that buccal epithelial cells treated with cigarette smoke increased the binding of staphylococci bacteria [110]. A comparison can thus be drawn between second hand smoke inhalation as a risk factor and the prevalence of *S. aureus* as the causative pathogen in many infection related sudden death cases of infants. In addition, recent research has indicated that when exposure to second hand smoke is combined with co-sleeping, the risk of sudden death in an infant increased significantly [85].

The common bacterial toxin hypothesis for SIDS includes risk factors such as prone sleeping and exposure to second hand smoke [11]. Many studies have aimed to elucidate the mechanism of death in SIDS cases and there is a recent trend towards exploring an infectious aetiology for these deaths [84]. There are well recognised risk factors for SIDS and these parallel those for infection.

The toxins produced by bacteria such as *S. aureus* and *E. coli* are absorbed in mucosal membranes. This creates "channels" in the membranes which disrupt the transport of smooth ions. This in turn affects the function of the cardiovascular and respiratory systems [84]. Due to the immature immune system of an infant a mild viral infection can be a risk factor for colonisation and toxin production by bacteria which can lead to sudden death [28,40]. These observations add to the body of evidence for the common bacterial toxin hypothesis as a possible mechanism in some SIDS cases.

Prone sleeping position and co-sleeping were the second most common risk factor [83–85,87,88,93]. The underlying reason for prone sleeping as a risk factor was described as the pooling of secretions into the upper airways of the infant in this position. This caused an increased risk of bacterial growth and thus bacterial toxin production [11,111].

Polymorphisms in genes *IL-1β* (NG_008851.1), *IL-10 (NG_012088.1)*, *IL-6* (NG_011640.1) and *TNF-α* (NG_007462.1) have been associated with an increased risk for sudden infant death [83,97–103]. Disturbances in inflammatory responses contribute significantly to tissue damage as a result of the response to infections [112]. Powerful pro-inflammatory responses and suppression of anti-inflammatory responses such as IL-10 lead to sudden death in infants with infections. These responses are dictated by the genetic make-up of the infant but are mediated or exacerbated by environmental factors such as cigarette smoke [83].

Primary immunodeficiency disorders (PID) are a rare group of inherited immune system defects [113]. PID predisposes an individual to a wide range of infections which may present atypically and is dependent on the underlying variation. There exist almost 250 different PIDs grouped into nine categories to which new sub-types are continually being added [114]. These disorders are diagnosed in infants and young children [113] and could be one mechanism underlying the infectious cause of sudden unexpected deaths in infants.

A higher proportion of male SUDI deaths have been described in the literature. However the exact reason for this difference is not well understood. One hypothesis is that an increase in testosterone levels in male infants might affect the dysregulation of inflammatory responses to ‘mild’ infections [95]. In turn these ‘mild’ infections are an additional risk factor for sudden infant death under the common bacterial toxin hypothesis [11,84].

1.4.2.2 Risk factors for sudden death in children and adults

Health status related risk factors was the category most commonly associated with an increased risk for sudden death due to infection (Table 1.6). The possible biological mechanism is intuitive as many of the conditions and diseases lead to a compromised immune system, leaving the individual vulnerable to infection.

Illicit drug use, particularly methamphetamine abuse, was the most commonly associated specific risk factor [115–117]. Opiates, marijuana and cocaine all modify the immune system and immune response to infection in a variety of ways leading to increased susceptibility and severity of infection. Alcohol, a commonly abused substance, inhibits the production of cytokines such as TNF-α, which play an important role in antimicrobial immunity [118].

Illicit drug injection was a major risk factor for infective endocarditis (IE). There was a variety of mechanisms by which intravenous drug abuse can cause IE. Some of these include; (1) particulates in the drugs that damage cardiac valves (2) poor hygiene associated with illicit drug injection (3) injecting contaminated drug solutions with a high microbial load [119]. In one case study the mechanism of death was a fatal pulmonary embolism caused by the detachment of a large vegetation at the tricuspid valve. This vegetation was as a result of IE precipitated by long-term injection of illicit drugs [120].

Male gender was also a reported risk factor for non-infants. It was proposed that there may be an underlying genetic cause for the male excess seen in these deaths [96] since the X chromosome contains the largest amount of immune system related genes in the genome [121]. Therefore the loss of heterozygosity in the male genome could explain the increased susceptibility of males to infection throughout their lifetime [96].

Table 1.6 Risk factors associated with sudden death due to infection in individuals older than one year

Type of Risk Factor	Specific Risk Factor	Reference(s)
Drugs of abuse	Alcohol	[53,118]
	Illicit drug injection	[119]
	Illicit drug use	[16,118,120,122,123]
	Methamphetamine abuse	[115–117]
	Nicotine	[118]
Environmental	Contaminated food	[59,124,125]
Genetic	Male sex	[96,126]
	IL-1β polymorphisms	[127]
Health status related	Atherosclerosis	[128,129]
	Body mass index	[53,126]
	Cholesterol (HDL & Total)	[126]
	HIV status	[116]
	Hypertension	[126]
	Lack of immunisation	[130,131]
	Active smoking	[126]
	Diabetes mellitus	[53,126]
	Kidney disease	[16]
	Liver cirrhosis	[132]
	Tuberculosis	[133]
	Varicella	[15,134]
Pre-existing conditions	Congenital ventricular septal defect	[16]
	Hematologic disorder	[132]
	Reye's syndrome	[74]
	Sjögren syndrome	[135]
Therapy/Treatment/Medication	Delayed anti-biotic treatment	[136]
	Long term steroid therapy	[135]
	Methadone	[9]
Other	Exercise	[54,137,138]
	Age	[126]
	Burns/wounds	[134]

Many of the risk factors associated with sudden death are related to the optimal functioning of the individual's immune system. However some risk factors leading to a compromised immune system are modifiable (e.g. drug use, exposure to cigarette smoke, lack of immunisation). Additional research into the prevalence of locally relevant risk factors would help to identify vulnerable communities.

1.5 Conclusion

Many pathogens have been associated with an increased risk for SUDI. However regional data reflects the environmental, social and epidemiological factors and it is important to understand not only globally recognised pathogens but also locally relevant infections triggering SUDI. This is especially critical in low and middle income countries where the burden of disease is higher than in the developed world.

Globally, well-recognised risk factors for SUDI, including second hand smoke exposure and sleeping position, have been studied extensively over the course of many years. However, the prevalence of modifiable risk factors known to decrease the likelihood of SUDI has not been extensively investigated in developing countries such as South Africa. There may also be risk factors unique to local communities which need to be assessed.

Pathogens identified to cause sudden death in children and adults are often associated with nosocomial infections affecting immunocompromised individuals. In addition, *M. tuberculosis* was highly reported in the literature which indicates the particular attention paid to this pathogen not just in South Africa but abroad. As South Africa has a high incidence of TB it is relevant to understand the prevalence of TB in the context of local forensic autopsies. Thus the health status of an individual plays a crucial role in their susceptibility to infection and consequential sudden death. Monitoring community specific risk factors would be beneficial in understanding locally relevant infections seen at medico-legal mortuaries.

The information compiled in this review allows for an understanding of the role of infection as a cause of sudden and unexpected death. There are certain pathogens that are globally recognised to be more prevalent in different age groups which may direct assessment of local data. It would be beneficial to add to the existing information from local medico-legal mortuaries in South Africa in order to better the understanding of locally relevant pathogens and risk factors.

Chapter 2

Investigating the Prevalence of Infection Related Death at Salt River Mortuary for the years 2013-2014

Summary

In many developing countries there is a high burden of communicable diseases and risk factors for infections are widespread due to poor socio-economic status and a lack of resources within the healthcare system. Some infections present atypically and death may occur without diagnosis whilst the person is alive. In these cases a medico-legal autopsy may be performed in order to establish the cause of death.

Since a standardised protocol is not yet available in South Africa, it is unknown what variations in autopsy approach exist, in how many cases microbiological tests are conducted and what are the associated pathogens. Furthermore the risk factors for these deaths have not been critically analysed in a local context. In addition, analysis of the demographics of these individuals would aid in identifying at-risk groups. In order to address these gaps a retrospective review of case of files was undertaken at Salt River Mortuary which services the Western Cape Metropole area. In total there were 809 cases identified in this study, with almost half (n=392) consisting of infants. Respiratory infections were the most common cause of death at all ages. However, ancillary investigations were only conducted in 18,5% (n=150) of cases and in only 54.7% (n=82) of those was a pathogen identified. In infants, co-sleeping and the side sleeping position were significantly associated ($p<0.0001$). In addition, the month of death and sex of the infant were significantly associated ($p=0.013$) with more than twice the percentage of male (10.97%) compared to female (4.85%) deaths in June. In children and adults the most common co-morbid condition was tuberculosis and most of the identified pathogens were opportunistic, usually affecting immunocompromised individuals.

A standardised protocol would aid to better direct autopsy investigations and resources in the local setting. In addition this would allow for information to be uniformly shared in South Africa and could be used in the healthcare system to promote awareness and identify vulnerable individuals.

2.1 Introduction

2.1.1 Background

In the year 2012 the World Health Organisation (WHO) estimated that deaths due to communicable diseases in South Africa were 611.6 per 100 000 people [2]. In addition, the leading cause of mortality in Africa for children under five was infectious diseases [139]. Most of these deaths occur after diagnosis, either from intervention occurring too late or as a result of a drug resistant pathogen or various other factors (ref). However, there are some cases in which infections are not diagnosed before death and the cause of death remains unexplained until the deceased undergoes a medico-legal autopsy.

In South African law, the Inquests Act (Act 58 of 1959), mandates that all unnatural deaths undergo a medico-legal autopsy [4]. An unnatural death, as defined in the Regulations (No. 636 of 2007) of the National Health Act (Act 61 of 2003), can be as a result of force (physical, chemical or other), an act of commission or omission, as a result of a medical procedure or a death that is unexpected or unexplained [3].

In some cases the course of an infection can present atypically, acutely and/or aggressively and death subsequently occurs without a diagnosis whilst the individual is alive [9] making them sudden, unexpected and unexplained. The World Health Organisation (WHO) defines sudden unexpected death as death within 24 hours from the onset of symptoms [140]. In South Africa, these deaths are referred to a Forensic Pathology Service (FPS) mortuary where an autopsy is performed in order to establish the cause of death. These deaths often occur in infants and the young and it is important to understand the underlying cause of death [10] as this has social consequences as well as implications within healthcare systems [9]. At the M6 Academic Salt River Mortuary, at least 3000 cases are admitted per annum. Of these, nearly one third are admitted as sudden and unexpected/unexplained. Furthermore, many of these have an apparent underlying infectious cause.

2.1.2 Rationale

Although sudden and unexpected or unexplained deaths can occur at any age, these deaths are unevenly distributed across ages from infants to adults. Children under the age of five remain the most vulnerable and these deaths often have an underlying infectious aetiology [8,141–145]. Typically, in older individuals sudden deaths are associated with cardiovascular causes and this has been studied extensively [146–148]. In addition, sudden cardiac deaths in young adults have been studied [149], with special attention on athletes [150]. However, there is a lack of information on the role of infection in [151] sudden or unexplained deaths in young adults and older individuals [152].

It has been regularly reported that the majority of deaths that occur suddenly as a result of infection have an underlying respiratory cause [141,153–155]. This has been shown to be particularly true in sudden infant deaths [40,91,156,157].

A diagnosis of infection as a cause of death ideally relies on the successful isolation and identification of a pathogen from a post-mortem sample, coinciding with other post-mortem findings and/or clinical history [64]. This type of investigation thus requires a full autopsy to be performed, within the scope of an appropriate standardised protocol [28,158,159], such as that proposed by Dempers et al. (2016) [160].

There is a lack of standardised protocols in the investigation of sudden or unexplained deaths in South Africa [28,148,159], with mortuaries often functioning according to internal standard practises[160]. This leads to a lack of uniform data across the country which would be useful for feedback into the healthcare system [157]. There has been a call for the standardisation of protocols for the investigation of sudden infant deaths in South Africa [28,159]. Recently one such protocol was implemented in a feasibility study at Tygerberg mortuary in Cape Town. This protocol was shown to be effective and could be used as a guide for other mortuaries in South Africa [160].

An extension of such a protocol for children and adult sudden deaths would be beneficial as some of these deaths might be attributed to an incidental infection whilst overlooking various other causes [161].

Therefore, the aim of this study was to identify the types of infections at Salt River Mortuary (Cape Town, South Africa) that contribute to the sudden unexpected death of an individual with the following specific objectives: (i) analysis of variables surrounding the circumstances of death; (ii) evaluation of identified risk factors in each age group; and (iii) assessment regarding the outcome and extent of the post-mortem investigation.

2.2 Materials and Methods

2.2.1 Study design

A retrospective study design was adopted for the time period 1 January 2013 to 31 December 2014. The two years were chosen to review case files as these cases would have been resolved by the time the study commenced. The study was conducted using the Office Autopsy Database (OAD) and case files from Salt River Mortuary (Cape Town, South Africa).

This study received approval by the University of Cape Town, Human Research Ethics Committee (HREC REF: 102/2016).

2.2.2 Data collection

Relevant cases were identified by filtering the OAD (HREC REF: R036/2014) for all cases linked to an infectious cause. . The generated dataset was used to identify the relevant hard-copy case files from which further information, not contained in the OAD, was extracted. Individuals of all ages and both sexes were included in the study.

All autopsies conducted at Salt River Mortuary contain a “Contemporaneous Note (Lab. 27): Salt River Forensic Pathology Laboratory” form, where basic information surrounding the death is recorded. The case file also contains an ‘Affidavit in terms of Section 212(4), Act 51 of 1977’, which serves as the report generated by the forensic pathologist on the major findings during post-mortem examination. In cases of sudden unexpected death in an adult, an FPS006(a) form is completed to record additional information on the clinical and social history of the deceased. In cases of sudden or unexplained death in an infant, an FPS006(b) form is completed to record additional medical, social and maternal information. Due to the nature of a retrospective case file study, one limitation was that some documentation or information was missing from the case file. This contributed to some variables being unknown for certain cases. In cases of deceased infants, information regarding vaccination status and exposure to human immunodeficiency virus (HIV) was obtained from the “Road to Health Card”, if attached to the case file.

2.2.3 Data management and statistical analysis

Data was recorded in a Microsoft Excel® spreadsheet which was kept on the premises of the Department of Pathology, University of Cape Town, Faculty of Health Science Campus. Data validation steps were performed within the created database to remove the possibility of erroneous data. An independent researcher randomly selected 30 case files from each year to verify data accuracy, completeness and consistency.

Age was used to classify cases into the following six groups:

Group A: Less than one year; Group B: 1 to 5 years; Group C: 6 to 17 years; Group D: 18 to 40 years; Group E: 41 to 60 years ; Group F: 61 years and older.

The main variables collected were: age, sex, month of death, cause of death, extent of autopsy and outcome of ancillary investigations. In addition, age specific variables were recorded. For a description of variables see Appendix B, section B1.1.

Statistical programs: STATA version 14 (StataCorp., 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP) and Microsoft Excel® (Microsoft Office Professional 2010, version 14.0.7172.5000) were used for statistical analyses. Numerical variables were tested for normality using the Shapiro-Wilk test. Hypothesis testing for categorical variables was done using the χ^2 test. A p-value of less than 0.05 was considered to be statistically significant. Data visualisation was done using STATA version 14 and GraphPad Prism version 7.00 for Windows (GraphPad Software, La Jolla California USA, www.graphpad.com).

2.3. Results

2.3.1 General description of the cohort

At Salt River Mortuary, from 1 January 2013 to 31 December 2014 there were a total of 2312 deaths that were initially classified as sudden and unexpected. Of these, 809 (35%) deaths were attributed to infection following a post-mortem investigation. The prevalence of sudden unexpected death due to infection was therefore estimated to be 6.54 per 100 000 in the Western Cape Province. Group A (infants) represented the highest number of deaths in the case series (48.5%, n=392).

Group A and B:

The majority (n=211, 53.8%) of infant (Group A) deaths occurred below the age of three months (Fig. 2.1).

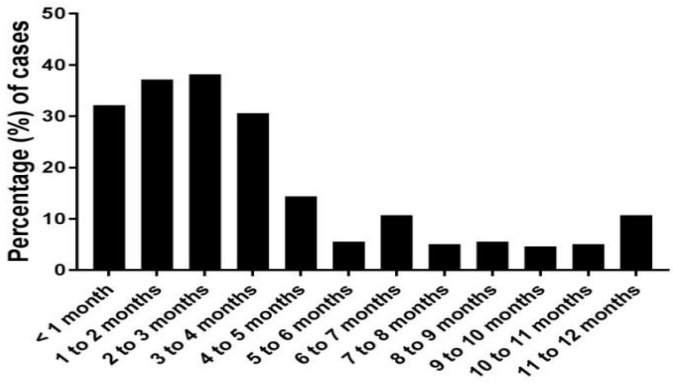

Figure 2.4 Group A: Percentage (%) of infant deaths by age range. The majority of infant deaths under 3 months of age were n=211 (53.8%), there was a plateau seen between 7 and 11 months of age with between 10 (2.6%) and 11 (2.8%) cases per age range. Between 11 and 12 months there was an increase in deaths with 21 (5.6%) cases.

In group B (one to five years) the highest number of cases occurred between the age of one and two (n=24, 64.87%) (Fig. 2.2)

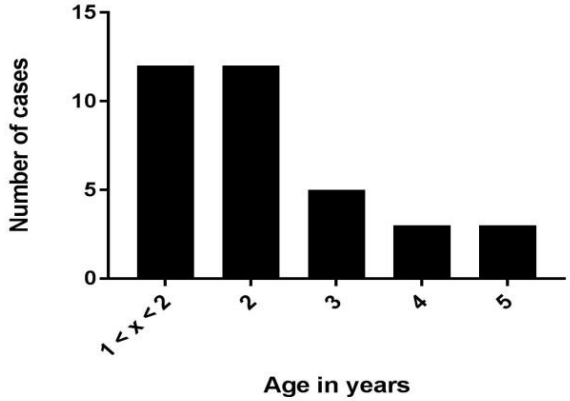

Figure 2.5 Group B: Number of cases as per age for children between one and five. The majority of cases occurred below the age of 2 years (n=24, 64.87%). At 3 years of age there were 8 (21.62%) cases, at 4 years there were 3 (8.1%) cases and at 5 years there were 2 cases (5.4%).

Groups A to F: There was a male preponderance in the majority of age groups with the exception of Group B (ages between one and five) which had 45.95% (n=17) males (Fig. 2.3). In total there were 501 male deaths (61.93%) and 308 female deaths (38.07%).

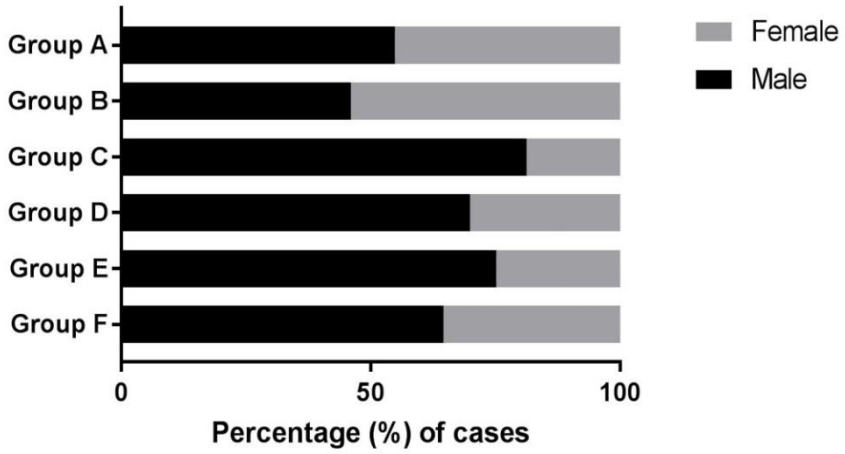

Figure 2.6 Percentage (%) of males and females for all ages (Group A to F). Male deaths accounted for the following number of cases; Group A: n=214 (52.04%); Group B: n=17 (45.95%); Group C: n=13 (81.25%); Group D: n=100 (69.93%): Group E: n=106 (75.18%); Group F: n=51 (64.56%).

Group C to F: Age was normally distributed for five and above with a median of 46 ($x = 46.42, sd = 17.47, \min(6); \max(94)$). Females had a median age of 47 ($x = 49.1, sd = 19.59, \min(8)\,; \max(94)$ and males had a median age of 46 ($x = 45.36, sd = 16.48, \min(6)\,; \max(92)$ (Fig. 2.4).

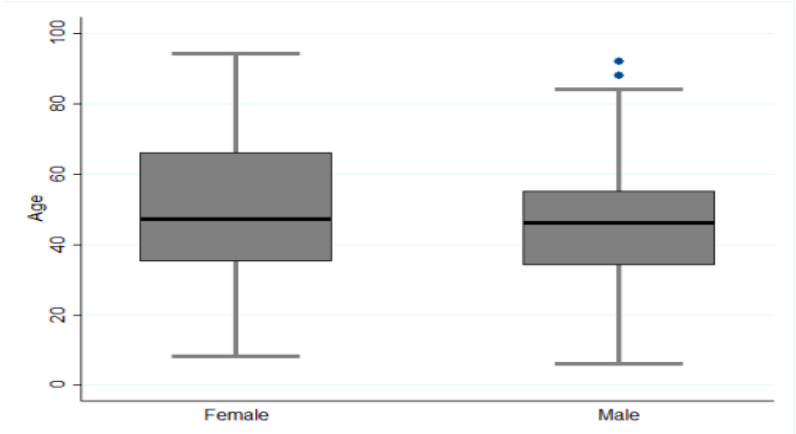

Figure 2.7 Age distribution according to sex for ages five and above (Groups C to F).

2.3.2 Cause of death and extent of autopsy

Respiratory infections were the leading cause of death in 2013 and 2014 (Tables 2.1 and 2.2). Respiratory infections were defined as: pneumonia, bronchopneumonia, lower respiratory tract infections (LRTI), pulmonary tuberculosis and bronchiolitis.

Table 2.7 Cause of death for all age groups in 2013

Age	Group A	Group B	Group C	Group D	Group E	Group F
	Infants	1 to 5 yr	6 to 17 yr	18 to 40 yr	41 to 60 yr	61+ yr
Cause of death	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Respiratory infection	163(86.53)	12(63.16)	6 (60.0)	47(70.15)	74(85.06)	36(73.47)
Gastroenteritis	15(7.77)	3(15.79)	1 (10.0)	3(4.48)	4(4.60)	2(4.08)
Both of the above	7(3.63)	1(5.26)		1(1.49)		
Meningitis	3(1.55)	1(5.26)	1(10.0)	7(10.45)	3(3.45)	1(2.04)
Sepsis	1(0.52)	1(5.26)	1(10.0)	5(7.46)	2(2.30)	9(18.37)
Other						
Acute myocarditis			1(10.0))			
Food poisoning					1(1.15)	
Gangrenous cholecystitis					2(2.30)	
Hydatid cyst				1(1.49)		
Meningitis & pneumonia		1(5.26)				
Necrotising fasciitis					1(1.15)	
Neurocysticercosis				2(2.99)		
Phlegmonous colitis						1(2.04)
Ruptured colonic diverticular abscess				1(1.49)		

Table 2.8 Cause of death for all age groups in 2014

	Group A	Group B	Group C	Group D	Group E	Group F
	Infants	1 to 5 yr	6 to 17 yr	18 to 40 yr	41 to 60 yr	61+ yr
Cause of death	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Respiratory infection	160(80.40)	11(61.11)	2(33.33)	52(68.42)	45(83.33)	26(86.67)
Gastroenteritis	17(8.54)	5(27.78)	1(16.67)		1(1.85)	
Both of the above	7(3.52)					
Meningitis	3(1.51)	1(5.56)		8(10.53)	2(3.70)	
Sepsis	10(5.03)		3(50.0)	8(10.53)	3(5.56)	3(10.00)
Other						
Bullous impetigo	1(0.50)					
Disseminated herpes						1(3.33)
Disseminated TB		1(5.56)		5(6.58)	3(5.56)	
Myocarditis				1(1.32)		
Pericarditis				2(2.63)		

An external examination (EE) included the use of the Lodox® (Xmplar-dr) X-ray imaging system. In the majority of cases an EE was performed, with the exception of Group C (n=16), where 43.8% (n=7) received an EE and 56.2% (n=9) a full autopsy (FA). A partial autopsy (PA) was performed in a limited number of cases (Fig. 2.5).

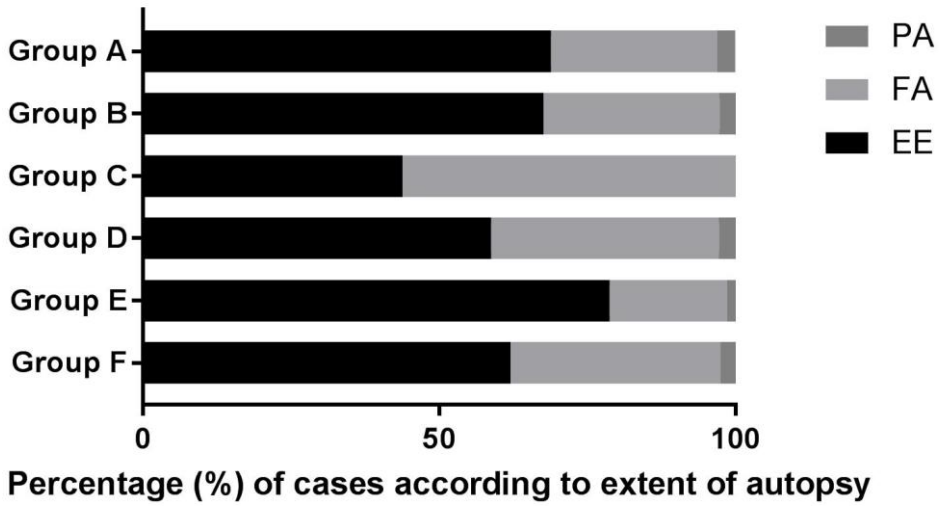

Figure 2.8 Percentage (%) of cases in each age group receiving either an external examination (EE), full autopsy (FA) or partial autopsy (PA). Group A: EE=68.8%; FA=28.1%; PA=3.1%. Group B: EE=67.6%; FA=29.7%; PA=2.7%. Group C: EE=43.8%; FA=56.2%. Group D: EE=58.7%; FA=38.5%; PA=2.8%. Group E: EE=78.7%; FA=19.9%; PA=1.4%. Group F: EE=62.0%; FA=35.4%; PA=2.6%.

Ancillary investigations were performed on 42 (21.1%) of the deceased infants (Group A) in 2014, and 38 (19.7%) in 2013. In 2014, 20 cases (10.1%) yielded a resultant pathogen and in 2013, 21 (10.9%) cases yielded a pathogen. In Group B (one to five years) microbiological analysis was requested once in 2014 and twice in 2013, all yielded pathogens (section 2.3.4).

Ancillary investigations were performed in 38 (17.8%) cases in 2013 and in 29 (17.5%) cases in 2014 in Groups C to F (individuals older than six years). For each year, 19 (8.9% in 2014; 11.4% in 2014) cases yielded a pathogen (section 2.3.4). The pathogens identified coincided with the major post-mortem findings and could be considered the causative pathogenic agent.

2.3.3 Risk factors and circumstances of death

Group A and B

Risk factors for deaths in infants and young children (one to five) differed from those recorded for individuals older than five years (Appendix C, supplementary material). The major risk factors identified for Group A and B were: sleeping position, co-sleeping, prematurity, second-hand smoke exposure and a history of a previous infant that died suddenly and unexpectedly (Table 2.3). Over the two year period, 51% (n=200) of infants were routinely put to bed on their side and 32.4% (n=127) in

the prone sleeping position. In addition, 44.9% (n=176) of infants co-slept with more than one person.

Table 2.9 Risk factors identified for infants ≤1 year (Group A) and young children between one and five years (Group B)

	2013		2014	
	Group A	Group B	Group A	Group B
Risk factor	N (%)	N (%)	N (%)	N (%)
Sleeping position				
Side*	100(51.8)	10(52.6)	100(50.3)	9(50.0)
Supine	14(7.3)	4(21.1)	27(13.6)	4(22.2)
Prone	65(33.7)	1(5.3)	62(31.2)	2(11.1)
Unknown	14(7.3)	4(21.1)	10(5.0)	3(16.7)
Co-sleeping				
No	11(5.7)	2(10.5)	6(3.0)	2(11.1)
Yes (1 other person)	99(51.3)	5(26.3)	80(40.2)	9(50.0)
More than one person	71(36.8)	9(47.4)	105(52.8)	5(27.8)
Unknown	12(6.2)	3(15.8)	8(4.0)	2(11.1)
Prematurity				
Yes	60(31.1)	1(5.3)	71(35.7)	2(11.1)
No	117(60.6)	14(73.7)	114(57.3)	13(72.2)
Unknown	16(8.3)	4(21.1)	14(7.0)	3(16.7)
Second-hand smoke exposure				
Yes	65(33.7)	3(15.8)	57(28.6)	1(5.6)
No	68(35.2)	8(42.1)	116(58.3)	15(83.3)
Unknown	60(31.1)	8(42.1)	26(13.1)	2(11.1)
Previous SUDI				
Yes	19(9.8)	4(21.1)	39(19.6)	8(44.4)
No	163(84.5)	11(57.9)	135(67.8)	9(50.0)
Unknown	11(5.7)	4(21.1)	25(12.6)	1(5.6)
***p<0.0001**				

There was a significant association between sleeping position and the number of people in the bed (p<0.0001), with 49.2% (n=193) of infants side sleeping with at least one other individual in the bed.

Infant deaths peaked during the winter months of June to August, with approximately equal percentages during the change of season during spring and autumn (Fig. 2.6).

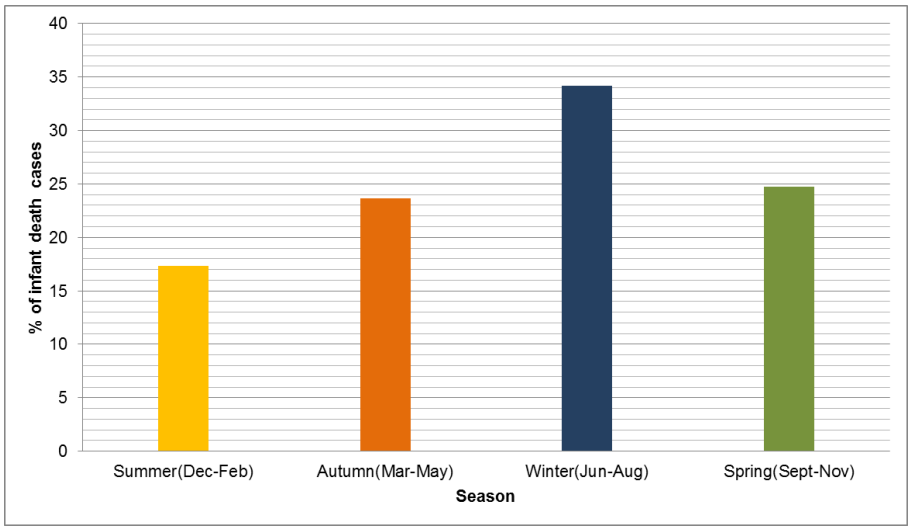

Figure 2.9 Infant deaths for December 2013 to November 2014 (n=190) according to season. Summer: 17.4%. Autumn: 23.7%. Winter: 34.2%. Spring: 24.7%.

There was a significant association between the month in which the infant died and the sex of the infant (p=0.013). Where 10.97% (n=43) of males demised in June and only 4.85% (n=19) of females in the same month. A similar trend could be seen in December where there were 6.12% (n=24) male deaths and 1.79% (n=7) female deaths (Fig. 2.7).

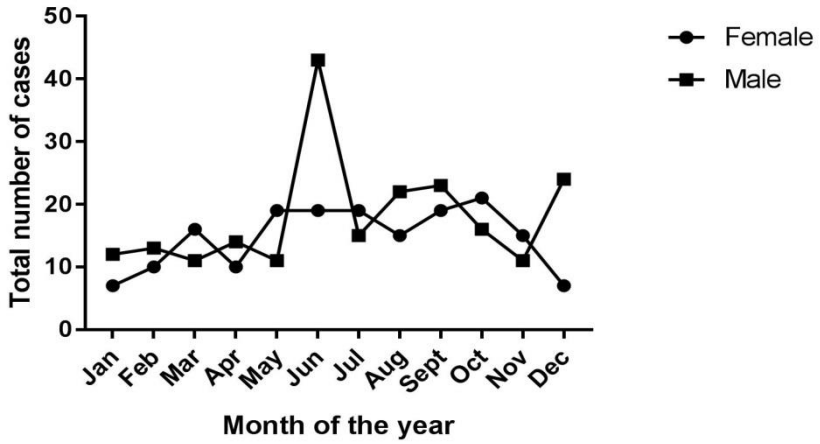

Figure 2.10 Total number of infant death cases by sex (Group A) per month of the year (p=0.013).

Group C to F

The main risk factors identified for individuals above the age of six were a history of co-morbid conditions and substance abuse. Over the two year period, a total of 49.1% (n=186) of individuals older than six years had a history of co-morbid conditions that could predispose to infectious diseases. These conditions included hypertension, diabetes, tuberculosis, asthma and HIV. Of those that reportedly had a

co-morbid condition, a total of 41.2% (n=95) had tuberculosis. A total of 20.1% (n=66) of individuals reportedly abused alcohol. In addition, some of these individuals abused other drugs, although in many cases the specific drug was not mentioned. In 7.4% (n=28) the specific illicit substance was reported (Table 2.6).

Table 2.10 Group C to F (older than six years): Clinical information, circumstances of death and reported substance abuse

	2014 N (%)	2013 N (%)
Co-morbid condition		
Yes	84(51.5)	102(47.9)
No	41(25.1)	62(29.1)
Unknown	38(23.3)	49(23.0)
TB	*53(41.2)*	*42(41.2)*
Medication		
None	39(23.9)	51(23.9)
Over the counter	5(3.1)	9(4.2)
Prescription	27(16.6)	29(13.6)
Chronic	38(23.3)	37(17.4)
Traditional	1(0.6)	3(1.4)
Unknown	53(32.5)	84(39.4)
Circumstances of death		
Sleeping/At rest	44(27.0)	53(24.9)
Daily activities	66(40.5)	92(43.2)
Hospital	21(12.9)	15(7.0)
Exercise/Physical altercation	2(1.2)	3(1.4)
Other	8(4.9)	10(4.7)
Unknown	22(13.5)	14(18.8)
Reported substance abuse		
Alcohol[a]	32(19.6)	44(20.7)
Other drugs (incl. Tik, Mandrax, Marijuana, Unga and Heroin)	15(9.2)	13(6.1)
None	53(32.5)	50(23.5)
Unknown	65(39.9)	105(49.3)

[a] The results for alcohol abuse include individuals reported to have abused other drugs

A total of 39.3% (n=149) of individuals took some form of medication in the peri-mortem period and a total of 19.8% (n=75) were taking chronic medication. In 41.7% (n=158) of cases the individual was performing a daily activity before death and in 25.6% (n=97) of cases the individual was discovered to have passed away during their sleep or whilst being at rest (Table 2.4).

2.3.4 Case series description - pathogens and associated risk factors

As reported in section 2.3.2 there were cases in each age group where a specific pathogen was identified. Of the 809 cases in the study, there were positive microbiological tests in 82 (10.14%). The demographic details of the case, pathogens and associated risk factors are set out in Appendix B (Tables B2.11-B2.15).

In total there were 94 pathogens identified. In eight cases more than one pathogen was detected. Bacterial pathogens (n=75, 79.8%) were detected in the majority of cases, followed by viral (n=5, 5.4%) and fungal pathogens (n=5, 5.4%). In two cases (2.1%) the tape worm, *Taenia solium* was identified. In all cases where a pathogen was detected the individual displayed one or more risk factors associated with that age group (Appendix B, Tables B2.11-B2.15).

2.4 Discussion

The aim of this study was to assess variables associated with death due to infection. From which, identified risk factors in conjunction with the extent of the autopsy and ancillary investigations, were analysed. Many of the variables collected had an "unknown" option which indicated that the information was not contained in the case file. This is a limiting factor with regards to data analysis, and unfortunately, a general characteristic of retrospective studies. However, there were a total of 82 (10.14%) cases over the two year period in which a pathogen was identified, which coincided with the major post-mortem findings. In these cases risk factors were identified and described.

2.4.1 Age and sex distribution

For infants (Group A) the highest number of deaths occurred from zero to three months (Fig 2.1). This is in contrast to literature from developed countries which suggest less frequent sudden death rates during the first month of life and a peak between two to four months [162]. In Group B (one to five years) the highest number of cases over both years occurred from one to two years of age. In Groups C to F (older than six years), the median age for males remained 46 years in both years whilst the median age for females declined from 52 years in 2013 to 38 years in 2014 (section 2.3.1).

Male sex has been identified as a risk factor for sudden infant death in several studies [84,86,163,164]. In this cohort, there was a 10% difference between male (55%) versus female (45%) infant deaths (Fig. 2.3 and 2.4). This coincides with the difference seen between male and female infants at five large medico-legal mortuaries in South Africa [159]. It has been suggested that an increase in testosterone levels during the first months of life is associated with lower levels of pro-inflammatory cytokines. Production of these cytokines is also reduced in the presence of tobacco smoke [95,111].

There was a marked increase in the percentage of males (64.5%-81.3%) in the older age categories (Groups C to F) compared to females. These figures correspond to a

similar study carried out at a medico-legal mortuary in South Africa where sudden death in adults over a five year period was investigated [148]. However, the underlying vulnerability of male sex in adults towards infection has only been discussed in literature under hypotheses. This includes the hypothesis that hemizygous males lack the protective measure of a second X-chromosome [96] which contains the majority of immune system related genes [121].

2.4.2 Identified risk factors

The sudden unexpected death of an infant (SUDI) rate in some areas of Cape Town has been estimated to be amongst the highest in the world [28]. Reasons behind this high rate of infant mortality need to be assessed, specifically with regards to risk factors in vulnerable populations. In this study, an average of 51% of infants were put to bed on their side and 32.5% on their stomach (Table 2.3). The prone sleeping position is a well-known risk factor for SUDI with an associated infectious aetiology [83]. Many infant death (or “cot death”) prevention campaigns world-wide have seen a decrease in infant deaths, following the recommendation that infants be put to sleep on their back [165].

In South Africa there are many informal settlements with associated low socioeconomic status (SES) and crowded living environments. An average of 56.21% (n=241) of infants and children, between one and five years, reportedly lived in informal housing (Appendix B, Fig. B2.11). It has been shown that low SES not only serves as a mediator, but can be an independent risk factor for SUDI. This may be due to low SES being a proxy for limited access to healthcare and inadequate protection from natural elements [166]. Some of the areas that Salt River Mortuary services include large informal settlements, where co-sleeping with more than one person remains a common phenomenon. There was a significant association between co-sleeping and sleeping position ($p<0.0001$), with 49.2% (n=192) of infants put to bed on their side whilst co-sleeping (Table 2.3). This leads to the deduction that the side sleeping position of the infant is perhaps due to lack of space in the sleeping environment. In this sleeping position, the face of the infant would still be in

contact with a mattress, cushion or person. Thus side sleeping could belong to the continuum that reflects the hypothesis behind the risk factor of prone sleeping.

In addition, established risk factors such as prematurity (33.4%) and exposure to tobacco smoke (31.2%) were also identified (Table 2.3). Maternal smoking in the prenatal, perinatal and postnatal periods have been associated with an increased risk for SUDI [86]. It has also been shown that this risk increases significantly when co-sleeping occurs in conjunction with exposure to tobacco smoke [85]. These risk factors were present in very high proportions in this cohort and indicate the need for educational campaigns regarding risk factors associated with infant mortality. Of much concern is the increased history of previous SUDI (Table 2.3) from 2013 (9.8%) to 2014 (19.8%). As the total amount of cases in this age category is similar in both years (n=193 in 2013 and n=199 in 2014) it would be beneficial to continue monitoring these rates in order to determine if there is indeed an upward trend.

A significant association was found (p=0.013) between sex and month of the year for infant deaths (Group A). During the month of June there was approximately twice the percentage of male (10.97%) deaths compared to female (4.85%) deaths (Fig. 2.10). It can be hypothesised that the risk factors of seasonality [10,145,167] (winter and summer) and the sub-optimal immune system of male infants (in particular those under 3 months of age) intersect to significantly increase the risk of infection and sudden death in these infants.

Co-morbid conditions were reported for 49.1% (n=186) of individuals in Groups C to F (older than six years). Of these, TB was reported in 41.2% (n=95) of cases (Table 2.4). In the year 2013 and 2014, the incidence of TB was estimated to be 292 (260-325) and 281 (250-313), respectively, per 100 000 population in Africa [168]. Although the largest number of new cases occurred in South-East Asia, Africa carried the highest burden of disease in 2014. TB remains a major health concern in the developing world with South Africa having the third highest incidence rate (802.2 per 100 000 population) after India and China [82]. In this cohort a total of 34.04% (n=129) individuals above the age of six were reported to either have pulmonary or disseminated TB precipitating or causing the death of the individual. Recently, the

sudden death of an apparently healthy 35-year old male due to a TB infection of the myocardium presented at a medico-legal mortuary in South Africa [81]. This case highlights the variety of ways in which death due to TB can manifest and the importance of this infection in the forensic setting.

Genetic variations have been studied in immune system related genes in infants [97,110,169]. However, there may be variants which could predispose to infection an individual throughout their lifetime. One such group of inherited disorders is Primary Immunodeficiency Disorders (PID). There are approximately 250 different types of PIDs, of which over 100 have been characterised at the genetic level [113]. Recently, concern has been raised regarding the under-reporting of PIDs in South Africa in disadvantaged areas. Clinical warning signs include severe and recurrent infections and in the case of infants, a mother who had a previous infant SUDI as a result of infection [114].

Molecular autopsies can be defined as post-mortem genetic testing in order to establish a cause of death in the case of negative autopsy findings. Molecular autopsies investigating the genetic variations associated with the risk for sudden cardiac death in young have been explored extensively in the literature [170–172]. Apart from variations in immune system related genes in infants [98,102,173–175], the role of genetic variants predisposing an individual to infection and subsequent sudden death have not yet been studied.

2.4.3 Ancillary investigations and post-mortem microbiology

Post-mortem microbiological analysis has been a contentious subject for many years [176,177]. As discussed in a review article by Tsokos et al. (2001) there is wide-spread belief that the large amount of positive cultures found in post-mortem cases is associated with bacterial invasion following death and some suggest inadequate sampling and handling procedures [178]. Although there is debate regarding interpretation of post-mortem microbiology, it has been shown that as few as 10% of positive cultures may be due to post-mortem bacterial translocation [64]. With the

use of molecular techniques it was shown that the liver and pericardial fluid remain the most sterile sites for sampling (up to 5 days post-mortem) and these techniques (such as RT-qPCR) may be used to detect normally uncultivable infectious pathogens [179]. Interpretation of microbiological results should however be conducted holistically in order to correctly identify possible pathogens in infectious deaths. Nevertheless, there is value in performing post-mortem microbiological testing in a forensic setting, where often ante-mortem clinical information is unavailable [64,180,181]. At Salt River Mortuary and at local South African Police Service (SAPS) stations there are questionnaires that are completed in the case of a sudden unexpected or unexplained death (Appendix C). In the absence of a clinical history the information obtained from these may be used to direct investigations and support the causative role of a pathogen. In addition, these questionnaires could form part of, or be used as the basis of a standardised protocol at medico-legal mortuaries.

However, in the majority of the cases included in this study ancillary investigations were not performed (section 2.3.2). A South African forensic pathologist is not mandated by law to investigate a death deemed natural [4]. Thus, the value of performing additional investigations needs to be critically assessed, particularly with regards to scarcity of resources. With this in mind, a standardised protocol might aid in uniformly directing the death investigation to not only establish cause of death but allow for the optimal allocation of resources.

The alarming number of infant death cases that are due to infections should be investigated further in a local context. Post-mortem bacteriology and virology is a valuable tool in elucidating SUDI [158] [10] and provides a mechanism by which SIDS cases can be differentiated [10]. Although the interpretation of positive microbiological cultures in infant death cases remain difficult, it has been shown that there is no association between a post-mortem interval (PMI) of several days and the translocation of micro-organisms [182]. In this cohort it is thus possible that the pathogens cultured from normally sterile sites can be seen as causative in the majority of cases.

In South Africa, up to 50% of deaths in children (between one and five) are due to natural causes [139]. One of the reasons behind the establishment of the Child Death Review (CDR) in 2014 was to address the gaps that are identified when an infant dies of a natural cause. One discussion point is whether an individual or system might still be at fault [183]. Can these deaths be classified as unnatural due to omission/co-mission of administering proper care? And if so would ancillary investigations, such as microbiology, virology, histology and pharmacology, add value to social or possible judicial intervention? [156]. Thus the CDR is a valuable tool in the forensic setting, of the local community, and represents a platform from which protocols can be derived.

A large multi-centre study regarding SUDI investigation protocols in South Africa highlighted the high degree of variation that exists within and between medico-legal facilities [184]. Medico-legal mortuaries attached to an academic institution may have the capacity to implement standardised protocols, and baseline data for five such South African mortuaries already exist [159].

2.4.4 Types of infection and related pathogens

Streptococcus pneumoniae was isolated in 12 cases where death was due to pneumonia or meningitis. Of the cases where a pathogen was identified for meningitis, *Neisseria meningitidis* was only isolated once, with the rest (n=7) associated with *S. pneumoniae.* Bacterial meningitis has been shown to be widely caused by *N. meningitidis* and *S. pneumoniae* [185].

Staphylococcus aureus was the second most prevalent pathogen identified (n=11). These bacteria have long been associated with infant death due to infectious diseases [11,22,94]. The oldest individual in this cohort where *S. aureus* was isolated was ten years old with the cause of death recorded as sepsis.

Staphylococci can be classified into two main groups, coagulase positive and coagulase negative. The most prevalent pathogenic coagulase negative

staphylococcus bacterium is *Staphylococcus epidermidis* which is the most commonly associated pathogen for nosocomial infections in the developed world. Therefore immunocompromised individuals are susceptible to this pathogen. This pathogen also has the potential for biofilm formation and can colonise a variety of surfaces [186]. In 2013 and 2014, this pathogen was only associated with respiratory infections in infants (Appendix B, Tables B.2.11 and B.2.12), with one case of brain pathology resulting in hydrocephalus (2014) in a 16 year old male (Table B.2.15) and with meningitis in a two year old female (2013) (Table B.2.13). In all infants where this pathogen was identified the infant was routinely put to sleep in the prone position (Tables B.2.11 and B.2.12) which may suggest colonisation occurs subsequent to contact with bedding potentially acting as a reservoir.

The tape worm, *T. solium* was identified in two cases in this cohort and cause of death was given as neurocystericercosis (Table B.2.4). Neurocysticercosis is the leading cause of parasitic central nervous system infection in the world and is one of the leading zoonotic diseases in developing countries [187]. It is also the leading cause of acquired epilepsy and is emerging as a serious health concern in developing countries including, Tanzania, Zambia and Mozambique [188–190].

Many of the pathogens identified in this cohort colonise, and may become lethal in immunocompromised individuals. As the majority of these deaths occurred out of hospital, and the infection is not nosocomial in nature, the immune status of the vulnerable population needs to be assessed. HIV infection in South Africa is still a major concern [191] and leads to the affected individual becoming immunocompromised. It has been shown that innate immune system development of HIV exposed infants is compromised during the early stages of life [192]. This increases the infant's risk for death due to infectious diseases [193]. In addition, it was shown that there is a high prevalence of HIV infection (43%) in sudden unexpected deaths of adults at a South African medico-legal mortuary [194]. HIV infection in these cases was 17% higher (p=0045) than the general population of the mortuary [194]. Thus the prevalence of HIV exposure in infants and the HIV status in older individuals in the mortuary setting could explain why opportunistic pathogens lead to sudden or unexplained death. However, in this cohort the role of HIV infection

cannot be assessed as it is not routinely screened for in cases at Salt River Mortuary.

Risk factors were identified in all cases of infant death where a pathogen was found. One such risk factor is the vaccination status of the infant. Whether an infant is 'up-to-date' with their vaccine schedule could possibly pose a means for the infant to become immunocompromised. Out of the 44 infant and children (under five) cases in which a pathogen was identified, seven (15.9%) where not 'up-to-date' with their vaccine schedule as per the "Road to Health Card". However, in 15 (34.1%) cases it was unknown whether the infant had received their most recent vaccine or not. Although, of those seven cases in which the deceased was not 'up-to-date', other recognised risk factors were identified and the contribution of the vaccination status should not be assessed in isolation.

2.4.5 Cause of death and extent of autopsy

The leading causes of death (i.e. sudden and unexpected death resulting in a medico-legal autopsy) in all age categories, for both years, were respiratory infections (Tables 2.1 and 2.2). This corresponds with both local [28,148,156], African [153] and international studies [9]. In addition, respiratory infections, including pneumonia, in infants and young children have been shown to be highly prevalent in the Western Cape [157,195]. This was followed by gastroenteritis, meningitis and sepsis.

Despite the high prevalence of respiratory infections in the Western Cape, only 10.5% (n=41) of all infant death cases in this cohort had a pathogen identified. This percentage is mainly attributed to many cases only receiving an external examination (including X-ray imaging) (Fig. 2.5 and Tables 2.1 and 2.2). Information on specific pathogens identified would be useful in order to monitor antibiotic resistance, emerging and re-emerging pathogens, vaccination schedules and the identification of 'at-risk' communities.

In the older age groups (age six and above) deaths were also mainly attributed to respiratory infections. The majority of these (74.93%, n=284) occurred from the ages 18 to 60 (Group D and E) which has mostly been associated with sudden cardiac, as opposed to infection related death in the literature [147,196–198]. Sudden cardiac deaths usually occur secondary to cardiac channelopathies with an underlying genetic predisposition [170,199]. Thereby, reiterating the need for and value of a standardised protocol in South Africa. This may eventually lead to the inclusion of a molecular autopsy in the case of negative autopsy findings.

There exists the possibility that respiratory infections are incidental findings in the death of an individual. In this cohort, many of the deaths of individuals older than six did not receive a full autopsy and thus it is uncertain whether the respiratory infection as seen on X-ray was the primary cause of death. Much literature exists which stresses the importance of microbiological analysis before concluding infection as a cause of death [53,63,133,185,200,201]. Therefore, the possibility exists that the percentage of deaths due to respiratory infections is lower than reported here.

2.5 Conclusion

There was a significant association ($p=0.013$) between sex and the month in which an infant dies, with approximately twice the number of male deaths as compared to female deaths during June and a similar trend in December. In addition, a male excess was seen in all age groups in this study, particularly in Groups C to F (older than six years). This supports the hypothesis that being male is a risk factor for infection and/or sudden unexpected death throughout life.

The side sleeping position of infants (Group A) was significantly associated ($p<0.0001$) with co-sleeping. This emphasises the need for local research to identify relevant risk factors and indicates the value of ongoing educational campaigns directed towards infant caregivers on the risks posed by the sleeping environment of the infant.

The presence of risk factors such as co-sleeping, exposure to tobacco smoke and the side or prone sleeping position might distinguish the self-limiting respiratory infections from fatal infectious events in infants. Therefore, when a caregiver presents an infant with a mild respiratory infection to a healthcare facility it is important to establish the presence of these risk factors within the household environment.

Tuberculosis remains a major health concern and it would be beneficial to further study the immune status of individuals receiving a medico-legal autopsy and whose cause of death is associated with tuberculosis. This will further the understanding of how immunocompromised individuals are vulnerable to acute and/or aggressive infections leading to sudden death.

The influence of genetic variants which could predispose an individual toward infections would further the understanding of this subject. This is in line with recent international trends towards molecular autopsies. These variations have been

studied in immune system related genes in infants; however there may be variants which could predispose an individual throughout their lifetime. In addition, molecular autopsies could delineate whether the sudden death of an individual was due to a genetic cardiac related event or other extraneous factors such as infection.

In the majority of cases the cause of death was a respiratory infection. This might be a true reflection with regards to infant deaths and an over-estimation in older age groups. A standardised protocol into the investigation of these deaths would allow information to be shared between mortuaries and can further be directed into the healthcare system. An accurate reflection of not only cause of death, but also the prevalence of pathogens at medico-legal mortuaries would be beneficial for communities in South Africa.

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Appendix A

Table A.1.1 Summary of ten SUDI case reports

Type of infection	Specific Pathogen	Type of Pathogen	#of cases	Age (s)	Country	Author	Journal
Cerebral infection	Coxsackievirus A16	Virus	1	3.5 months	Denmark	Astrup, Johnsen & Engsbro, 2016	Forensic Science International
Pulmonary extensive necrotizing inflammation	Cytomegalovirus and	Virus	1	2 months	France	Desmons et al., 2013	Journal of Clinical Virology
	Varicella zoster virus	Virus					
Septicaemia	Streptococcus pneumoniae	Bacteria	1	10 weeks	Australia	Byramji, Gilbert & Byard, 2009	Forensic Science, Medicine, and Pathology
Suspected nervous system infection	Human cardiovirus genotype 2	Virus	1	<1 year	Germany	Drexler et al., 2011	Emerging Infectious Diseases
Septicaemia (GBS)	Streptococcus agalactiae	Bacteria	1	10 days	Japan	Kawaguchi et al., 2013	Legal Medicine
Respiratory infection (SIDS)	Pneumocystis carinii (jirovecii)	Fungus	3	<3 months	Chile	Chabe et al., 2004	Microbiology
Myocarditis	Coxsackie-virus B3	Virus	4	<10 months	Germany	Dettmeyer et al., 2002	Pathology: Research and Practice
Myocarditis (2) and/or pneumonia (1)	Cytomegalovirus	Virus	3	<5 months	Germany	Dettmeyer et al., 2008	Forensic Science International
Undetermined, possible nervous system involvement	Human herpes simplex virus type 6	Virus	1	3 months	Spain	Fernández-Rodríguez et al., 2006	Forensic Science International
Respiratory Infection	Cytomegalovirus	Virus	1	3 months			
Pneumonia as a complication of EBV mononucleosis infection	Epstein-Barr Virus	Virus	1	1 year			
Respiratory infection	Cytomegalovirus	Virus	1	4 months			
Undetermined	Influenza A	Virus	1	Neonate			
Acute necrotizing tonsillitis	Clostridium perfringens	Bacteria	1	9 months	America	Gerber, 2001	The American Journal of Forensic Medicine and Pathology
Viral myocarditis	Enterovirus	Virus	1	7 months	Germany	Dettmeyer et al., 2001	Forensic Science International

Figure A.11 Published case reports on sudden death due to infection in individuals older than 1 year by country in this review

Table A.1.2 Scopus search terms

Terms used in the meta-search of the Scopus Database
(((((((TITLE-ABS-KEY ("sudden death") AND TITLE-ABS-KEY (infection) OR TITLE-ABS-KEY ("sudden unexpected death")) AND PUBYEAR > 1999) AND ((TITLE-ABS-KEY ("sudden death") AND TITLE-ABS-KEY (infection) OR TITLE-ABS-KEY (virus) OR TITLE-ABS-KEY (bacteria) OR TITLE-ABS-KEY (pathogen) OR TITLE-ABS-KEY (zoonotic)) AND PUBYEAR > 1999) AND ((TITLE-ABS-KEY ("sudden death") AND NOT TITLE-ABS-KEY (cardiac) AND NOT TITLE-ABS-KEY (iatrogenic) AND NOT TITLE-ABS-KEY (chronic) AND NOT TITLE-ABS-KEY (hospital) AND NOT TITLE-ABS-KEY (diagnosis) AND NOT TITLE-ABS-KEY (prognosis) AND NOT TITLE-ABS-KEY (mouse) AND NOT TITLE-ABS-KEY (dog)) AND PUBYEAR > 1999) AND (((TITLE-ABS-KEY ("sudden death") AND TITLE-ABS-KEY (infection) OR TITLE-ABS-KEY ("sudden unexpected death")) AND PUBYEAR > 1999) AND ((TITLE-ABS-KEY ("sudden death") AND TITLE-ABS-KEY (infection) OR TITLE-ABS-KEY (virus) OR TITLE-ABS-KEY (bacteria) OR TITLE-ABS-KEY (pathogen) OR TITLE-ABS-KEY (zoonotic)) AND PUBYEAR > 1999) AND ((TITLE-ABS-KEY ("sudden death") AND NOT TITLE-ABS-KEY (cardiac) AND NOT TITLE-ABS-KEY (iatrogenic) AND NOT TITLE-ABS-KEY (chronic) AND NOT TITLE-ABS-KEY (hospital) AND NOT TITLE-ABS-KEY (diagnosis) AND NOT TITLE-ABS-KEY (prognosis) AND NOT TITLE-ABS-KEY (mouse) AND NOT TITLE-ABS-KEY (dog)) AND PUBYEAR > 1999)) AND ((TITLE-ABS-KEY ("sudden death") AND NOT TITLE-ABS-KEY (idiopathic)) AND PUBYEAR > 1999) AND ((TITLE-ABS-KEY ("sudden death") OR TITLE-ABS-KEY (forensic) OR TITLE-ABS-KEY (medico-legal) OR TITLE-ABS-KEY (autopsy)) AND PUBYEAR > 1999)) AND ((TITLE-ABS-KEY ("sudden death") AND NOT TITLE-ABS-KEY (pigs) AND NOT TITLE-ABS-KEY (porcine) AND NOT TITLE-ABS-KEY (treatment)) AND PUBYEAR > 1999)) AND ((TITLE-ABS-KEY ("sudden death") AND NOT TITLE-ABS-KEY (plant) AND NOT TITLE-ABS-KEY (neuropathy)) AND PUBYEAR > 1999)) AND ((TITLE-ABS-KEY ("sudden death") AND NOT TITLE-ABS-KEY (sickle cell) AND NOT TITLE-ABS-KEY (cancer) AND NOT TITLE-ABS-KEY (carcinoma) AND NOT TITLE-ABS-KEY (complic*)) AND PUBYEAR > 1999)) AND ((TITLE-ABS-KEY ("sudden death") AND NOT TITLE-ABS-KEY (epilepsy) AND NOT TITLE-ABS-KEY (sudep) AND NOT TITLE-ABS-KEY (congenital)) AND PUBYEAR > 1999)) AND ((TITLE-ABS-KEY ("sudden death") AND NOT TITLE-ABS-KEY (cattle)) AND PUBYEAR > 1999) AND (LIMIT-TO (SUBJAREA , "MEDI") OR LIMIT-TO (SUBJAREA , "IMMU") OR LIMIT-TO (SUBJAREA , "BIOC") OR LIMIT-TO (SUBJAREA , "PHAR") OR LIMIT-TO (SUBJAREA , "SOCI") OR LIMIT-TO (SUBJAREA , "NEUR") OR LIMIT-TO (SUBJAREA , "NURS")) AND (LIMIT-TO (LANGUAGE , "English"))

Appendix B

Section B.1.1 Variable definitions

Housing: Informal, Formal, Other, None, Unknown.

Housing was recorded as it was reported within the case file. If the type of housing was not recorded in the case file but an address or GPS coordinates for the area of death was provided this was used to look up the type of housing. Informal housing was defined as a 'makeshift dwelling not constructed from typical building materials and/or which has no indoor plumbing and/or no electricity supply'. Formal housing was defined as a building or structure that has been constructed from approved building materials. 'Other' housing was defined as housing which, although not formal in nature still provide a form of shelter from the elements and which may or may not have plumbing or electricity, e.g. a 'Wendy House' attached to a formal dwelling. The 'None' category was assigned if the person was a recorded as a known vagrant. If there was no information on housing in any of the documents provided in the case file it was assigned to 'unknown' category.

Extent of autopsy: External examination, partial autopsy, full autopsy.

An external examination involved the use of the Lodox® (Xmplar-dr) X-ray imaging system. This type of examination did not include the internal examination of organs and thus no histology or microbiological analyses were performed. A full autopsy was defined as the internal examination of organs and tissues in a defined and systematic manner. This type of autopsy allows for tissue and other samples to be taken at the discretion of the forensic pathologist. A partial autopsy was defined as the internal examination of only a certain body compartment or organ at the discretion of the forensic pathologist.

Medication: None, Chronic, Over the Counter, Prescription, Traditional, Unknown.

Information regarding the type of medication the individual received was retrieved either from the information supplied by a family member (recorded in the case file) or from clinical documents attached to the case file (e.g. doctors notes). If it was stated that no medication was taken by the deceased this was recorded as none. If the information was not recorded (i.e. *missing* information) this was recorded as unknown. Chronic medication included prescription medication taken over a period of time for a chronic disease, disorder or condition (e.g. hypertension, diabetes, anti-retrovirals). Over the counter medication was defined as medication that the deceased purchased at a pharmacy or convenience store which require no doctor's prescription (e.g. Aspirin, Paracetamol). Prescription medication was defined as that which the deceased received as a result of a doctor's visit and which could not otherwise have been obtained (e.g. anti-biotics). Traditional medication was noted if the family member explicitly stated that the deceased had taken such medication.

Circumstances of death: Daily activity, Sleeping, At rest, Exercise, Physical altercation, Other, Unknown, Hospital.

A daily activity was defined as the deceased being ambulatory with cognitive function (as witnessed by another) moments before death (e.g. walking to the bathroom). Sleeping was defined as the deceased being discovered in a normal sleeping environment for that individual. At rest was defined as the individual being discovered in a resting position, such as on a couch. Exercise was defined as the deceased being involved in strenuous activity moments before death. Physical altercation was recorded if witnessed as such by another. Other circumstances included an activity which did not adhere to the any of the other circumstances. Unknown circumstances were recorded if no information on this variable could be derived from the case file. Hospital deaths were recorded separately in order to distinguish these from individuals demising at rest or sleeping out of hospital.

All other variables were part of and defined in the standard questionnaires attached to the case

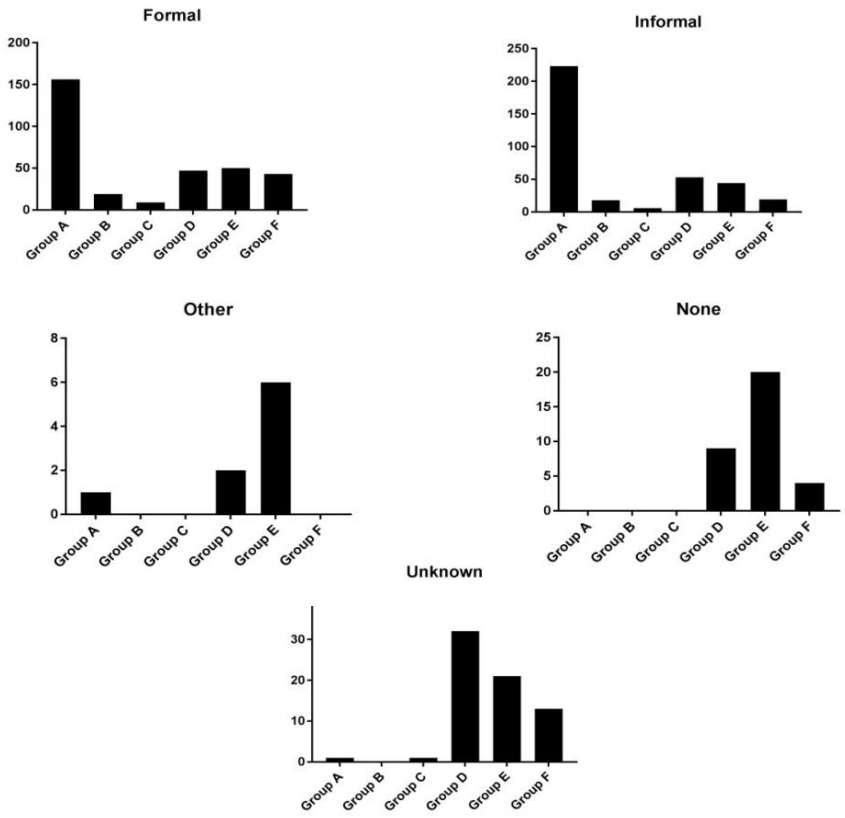


Figure B2.12 Housing according to age group

Table B.2.11 List of infants (2013) ≤1 year (Group A) where a pathogenic agent was identified with associated risk factors

Age (Months)/Sex	Cause of death	Bacteria	Virus	Fungus	HIV Exposed	Sleeping position	Co-sleeping [a]	Prematurity	Exposure to TS	Vaccines up to date
0/F	Respiratory infection	Staphylococcus aureus			x	side	√(3)	√	√	x
0/M	Bronchopneumonia	Escherichia coli Streptococcus pneumoniae			√	side	√(1)	x	x	√
0/M	Respiratory infection	Staphylococcus aureus			x	prone	√(1)	x	√	√
1/F	LRTI	Staphylococcus haemolyticus			x	prone	√(1)	x	√	√
1/M	Respiratory infection	Staphylococcus aureus			u	unknown	u	u	u	u
1/F	LRTI	Moraxella sp. (Moraxella catarrhalis*)			x	prone	√(1)	x	√	√
1/M	LRTI	Group B Streptococcus Klebsiella pneumoniae Haemophilus influenza			u	side	√(1)	x	u	u
2/M	URTI & LRTI	Proteus mirabilis			u	supine	√(4)	u	u	u
2/F	Bronchopneumonia	Klebsiella pneumoniae			x	side	√(1)	x	√	u
2/F	Pneumonia		Respiratory syncytial virus		x	prone	x	x	x	√
2/M	LRTI		Enterovirus		x	prone	√(3)	x	√	√
3/F	LRTI	Raoultella planticola			u	prone	√(1)	x	u	u
3/M	Respiratory infection	Escherichia coli			x	side	√(1)	x	x	√
3/M	Meningitis	Staphylococcus haemolyticus			x	side	√(2)	x	x	u
3/F	Respiratory infection	Coagulase negative staphylococcus Klebsiella pneumoniae	Respiratory syncytial virus		x	prone	√(2)	x	x	√
3/M	Pneumonia	Streptococcus pneumoniae			u	side	√(3)	x	u	u
3/M	Pneumonia			Fungal elements in lung tissue	u	unknown	u	u	u	u
4/M	Pneumonia	Coagulase negative staphylococcus			x	prone	√(2)	√	√	√
4/M**	Respiratory infection	Escherichia coli			x	prone	√(2)	√	u	u
4/M**	Respiratory infection	Escherichia coli			x	prone	√(2)	√	u	u
6/M	Gastroenteritis	Enterobacter aerogenes			x	side	√(1)	x	x	√

Key: M=Male; F=Female; u=unknown; x=no; √=yes; TS= Tobacco smoke a – Number in () brackets indicate the number of people in the bed other than the infant
***Usually resides in respiratory tract, but can gain access to the lower respiratory tract in patients with chronic chest disease or compromised host defences. **Twins**

Table B.2.12 List of infants (2014) ≤1 year (Group A) where a pathogenic agent was identified with associated risk factors

Age (Months)/Sex	Cause of death	Bacteria	Virus	Fungus	HIV Exposed	Sleeping position	Co-sleeping [a]	Prematurity	Exposure to smoke	Vaccines up to date
0/F	Sepsis	Streptococcus salivarius			x	prone	x	x	x	x
0/M	Pneumonia	Pseudomonas putida			√	side	√(2)	u	x	√
0/M	Pneumonia	Gram-negative bacilli Gram-positive cocci			√	prone	√(1)	x	x	√
1/F	URTI	Raoultella planticola			u	side	√(5)	u	u	u
1/M	Respiratory infection	Coagulase negative staphylococcus			x	side	√(3)	x	√	√
1/F	Sepsis	Gram-negative bacilli Gram-positive cocci			x	side	√(1)	√	√	√
1/M	Gastroenteritis	Klebsiella pneumoniae			x	side	√(3)	√	√	x
1/M	Respiratory infection	Coagulase negative staphylococcus			x	prone	√(4)	x	√	√
2/M	LRTI	Staphylococcus aureus			u	supine	√(2)	u	u	u
2/M	LRTI	Acinobacter baumanii			√	side	√(2)	x	√	u
2/M	Bronchopneumonia	Staphylococcus aureus			x	side	√(2)	x	√	√
2/M	Respiratory infection	Staphylococcus aureus			x	side	√(1)	x	x	x
2/M	Viral Pneumonitis		Respiratory syncytial virus		x	side	√(2)	x	x	x
3/F	Respiratory infection	Klebsiella pneumoniae			x	prone	√(1)	x	√	√
3/F	Pneumonia	Streptococcus pneumoniae			x	prone	√(2)	x	√	√
4/M	Respiratory infection	Streptococcus pneumoniae Staphylococcus aureus			x	prone	√(2)	x	x	√
5/M	LRTI	Staphylococcus aureus			x	side	√(1)	x	x	√
5/M	LRTI	Staphylococcus aureus			x	side	√(3)	x	√	√
6/F	Respiratory infection	Coagulase negative staphylococcus			√	prone	√(2)	x	x	√
7/M	Gastroenteritis	Group B Streptococcus			x	prone	√ (1)	x	x	x
8/M	Sepsis	Gram-negative bacilli		Candida albicans	x	side	√(1)	x	√	√
9/F	Meningitis	Streptococcus pneumoniae			u	side	√(1)	√	u	u

Key: M=Male; F=Female; u=unknown; x=no; √=yes
a – Number in () brackets indicate the number of people in the bed other than the infant

Table B.2.13 List of children between one and five years (Group B) where a pathogenic agent was identified with associated risk factors

Age (Months or Years)/Sex	Year	Cause of death	Bacteria	Virus	HIV Exposed	Sleeping position	Co-sleeping [a]	Prematurity	Exposure to smoke	Vaccines up to date
14(M)/F	2013	Respiratory infection	Escherichia coli Corynebacterium sp.	Metapneumovirus	u	unknown	u	x	x	x
2(Y)/F	2013	Meningitis and pneumonia	Coagulase negative staphylococcus		u	side	√(1)	x	u	u
16(M)/M*	2014	Respiratory infection	Haemophilus influenzae		x	side	x	√	x	√

Key: M=Male; F=Female; u=unknown; x=no; √=yes
***Trisomy 21 child**
a – Number in () brackets indicate the number of people in the bed other than the child

Table B.2.14 List of cases in Group C to F (2013) where a pathogen was identified with associated risk factors

Age (Years)	Sex	Cause of death	Bacteria	Fungus	Other	Medication	Co-morbid condition	Drug abuse	Circumstances of death
7	M	Acute myocarditis	Gram positive cocci			OTC	x	x	DA
8	M	Sepsis	Streptococcus pyogenes			P	x	x	DA
8	F	Meningitis	Neisseria meningitidis			T	Mental disability	x	DA
22	M	Neurocysticercosis			Taenia solium*	OTC	x	x	S
26	F	Meningitis	Gram-positive cocci; Gram-negative bacilli			u	HIV	Heroin	DA
27	F	Lung pathology	Gram negative bacilli			u	x	x	O
28	M	Cryptococcus infection		Cryptococcus sp.		T	x	x	DA
30	M	Pneumonia		Pneumocystis jirovecii		u	TB	x	DA
31	F	Neurocysticercosis			Taenia solium*	x	x	x	DA
33	M	Meningitis	Streptococcus pneumoniae			x	x	Alcohol	u
34	M	Respiratory infection	Corynebacterium sp.	Candida albicans		P	x	Alcohol	PA
39	M	Respiratory infection	Escherichia coli			P	TB	x	U
47	M	Pneumonia		Pneumocystis jirovecii		C	HIV	x	S
51	M	Pneumonia	Gram-positive cocci			x	HIV	Alcohol & other unspecified drugs	S
59	F	Meningitis	Streptococcus pneumoniae			u	u	x	u
60	F	Food poisoning	Clostridium perfringens			P	Asthma	x	H
66	F	Sepsis	Gram positive & negative bacilli; Gram-positive cocci			C	Cancer	x	H
66	M	Sepsis	Gram negative bacilli			C	Cancer, arthritis	x	DA
76	F	Meningitis	Streptococcus pneumoniae			P	Diabetes, Hypertension	x	H

Key: M=Male; F=Female; OTC= Over the counter medication; P=Prescription medication; T=Traditional medication; C=Chronic medication; u=unknown; DA=Daily activity; S=Sleeping; PA= Physical altercation; H=Hospital; O=Other; TB=Tuberculosis; x=no; u=unknown

Table B.2.15 List of cases in Group C to F (2014) where a pathogen was identified with associated risk factors

Age(Years)	Sex	Cause of death	Bacteria	Medication	Co-morbid condition	Drug abuse	Circumstances of death
10	M	Sepsis	Staphylococcus aureus	x	x	x	S
16	M	Brain pathology - hydrocephalus	Coagulase negative staphylococcus	OTC	x	x	S
22	M	Pulmonary tuberculosis and Bronchopneumonia	Mycobacterium tuberculosis	C	TB & Cancer	u	S
23	F	Tuberculosis of heart muscles	Mycobacterium tuberculosis	x	TB endometritis	x	DA
28	M	Pneumonia	Streptococcus agalactiae	OTC	x	x	E
34	F	Sepsis	Treponema pallidum	C	TB, HIV, Syphilis, Renal failure	u	H
35	M	Meningitis	Streptococcus pneumoniae	u	u	u	H
35	F	Disseminated tuberculosis	Citrobacter youngae; Escherichia coli; Mycobacterium tuberculosis	u	u	x	DA
36	F	Bacterial meningitis	Streptococcus pneumoniae	P	Diabetes	x	H
37	F	Tuberculosis of abdomino-pelvic lymph nodes	Mycobacterium tuberculosis	C	Kidney infection	x	DA
38	M	Meningitis	Streptococcus pneumoniae	x	TB	Alcohol	H
39	F	Meningitis	Streptococcus pneumoniae	P	x	Alcohol	H
40	F	Neurological pathology	Staphylococcus aureus	u	x	Alcohol	DA
41	M	Pulmonary tuberculosis	Mycobacterium tuberculosis	x	TB, HIV	x	DA
42	F	Meningitis	Gram negative & positive bacilli; Gram positive cocci	u	u	u	O
50	F	Pulmonary tuberculosis	Acid-fast bacilli	x	TB	u	DA
50	F	Disseminated tuberculosis	Acid-fast bacilli	u	u	u	S
59	F	Pulmonary tuberculosis	Acid-fast bacilli	C	Hypertension	x	DA
74	M	Sepsis	Gram-positive cocci; Gram-negative bacilli	C	Asthma, hypertension, paraplegic	x	S

Key: M=Male; F=Female; OTC= Over the counter medication; P=Prescription medication; C=Chronic medication; u=unknown; DA=Daily activity; S=Sleeping; E= Exercise; H=Hospital; O=Other; TB=Tuberculosis; x=no; u=unknown

Appendix C

- Ethics approval
- Contemporaneous Note (Lab. 27): Salt River Forensic Pathology Laboratory" blank form
- FPS006(b) blank form
- FPS006(a) blank form
- Supplementary material – Group A and B variables
- Supplementary material – Group C to F variables

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
Email: sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

25 February 2016

HREC REF: 102/2016

Miss L Heathfield
Division of Forensic Medicine & Toxicology
Level 5, Entrance 2
Falmouth Building-FHS

Dear Miss Heathfield

PROJECT TITLE: THE PREVALENCE OF INFECTION RELATED DEATHS AT SALT RIVER MORTUARY IN THE WESTERN CAPE FROM 2010 TO 2014 (Mphil candidate- Maria Kruger)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 28 February 2017.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

We acknowledge that the student, Maria Kruger will also be involved in this study.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Yours sincerely

Signed

pp

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH

2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI),and Declaration of Helsinki (2013) guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

CONTEMPORANEOUS NOTE (LAB. 27) : SALT RIVER FORENSIC PATHOLOGY LABORATORY

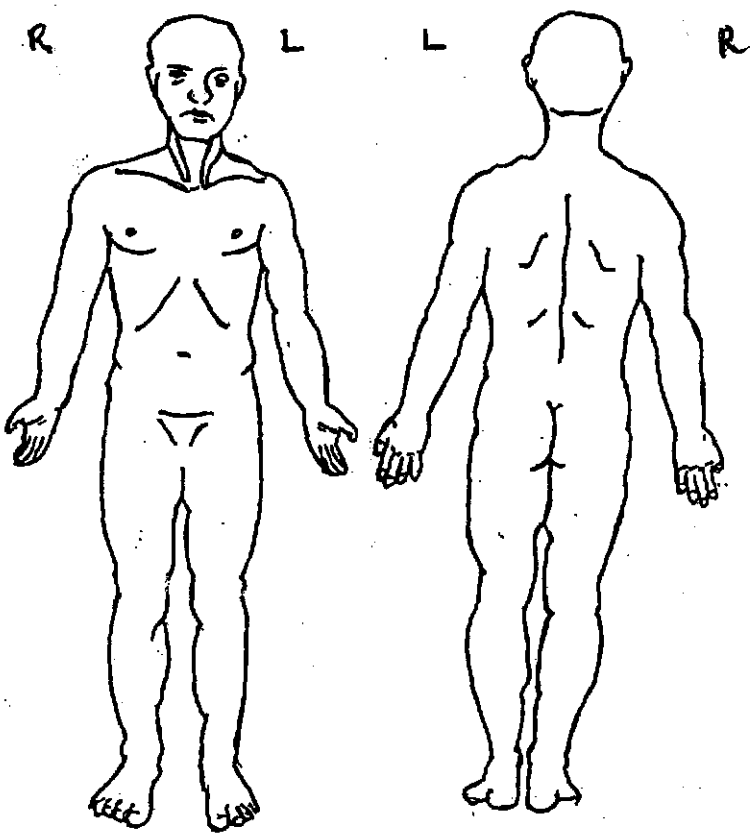
WC/11/_____ PATHOLOGIST _____ BODY BAG SEAL NO _____

ASSISTANT _____ DATE OF PM _____ TIME OF PM _____

1. RACE: White | Coloured | African | Asiatic
2. GENDER: Male | Female 3. AGE: _____
4. NAME OF DECEASED: _____
5. AREA OF DEATH: _____ 6. **SAPS STATION:** _____
7. DATE OF DEATH: _____ 8. TIME OF DEATH: _____
9. DIED IN:

House	Shack	Road	Dam	River
Swimming pool	Bucket / Bin	Shebeen	Sea	Lake
Hospital	Railway track	Open land	Toilet	Other

HISTORY _____



EXTERNAL FEATURES _____

CHIEF POST-MORTEM FINDINGS

1.
2.
3.
4.
5.

CAUSE OF DEATH _____

ALCOHOL SEAL NUMBERS Received by:	Inner	Outer
Exhibits received by:		
Photographer:		

Signature: _____

WC/11/.....

1. HEIGHT WEIGHT PHYSIQUE NUTRITION
2. IDENTIFYING FEATURES

TEETH																	
	R	M	M	M	PM	PM	C	I	I	I	I	C	PM	PM	M	M	M
	L																
	R	M	M	M	PM	PM	C	I	I	I	I	C	PM	PM	M	M	M
	L																

3. PM Changes: Rigor Mortis: Arms/Legs/Mandible Lividity
   Temperature
4. External Appearance
5. Skull
6. Brain Brain Mass:
7. Eyes: Ears: Nose:
8. Mouth, tongue and pharynx
9. Neck
10. Thoracic cage
11. Mediastinum
12. Airways
13. Lungs Mass: R
    Mass: L
14. Heart Mass:
15. Large blood vessels
16. Peritoneal cavity
17. Stomach Contents
18. Intestines
19. Liver Mass:
20. Pancreas Mass:
21. Spleen Mass:
22. Adrenals Mass: R
    Mass: L
23. Kidneys Mass: R
    Mass: L
24. Bladder Urine: Clear/turbulent/blood-stained
25. Pelvic Walls
26. Genitalia: MALE: EXTERNAL PENIS: Circ/uncirc. SCROTUM INTERNAL: Testes Prostate
    FEMALE: External Internal Uterus/Ovaries
27. Spinal Column
28. Spinal Cord

SPECIMENS RETAINED

1. Blood/Eye Fluid for alcohol Outer seal: Inner seal:
2. Toxicology Outer seal: Inner seal:
3. Histology

ADDITIONAL SPECIMENS:

1.
2.
3.
4.

DEPARTMENT of HEALTH
Provincial Government of the Western Cape

FPS006(b)

FORENSIC PATHOLOGY SERVICE

SUDI (Complete If A Baby Should Suddenly And Unexpectedly Die)

FPS laboratory_____ WC _____

Name of baby _____

Part 1: Scene Questionnaire and Observations

Date: ***Time:*** ***Name of Forensic officer:***

Section A. **Who gives the history/ information in this case e.g. mother/father/granny/grandpa/other relative(give details)**	
Name:	Relationship:
Address:	Contact telephone number:
ID Number:	
Infants full name:	
Home Address:	
Age of Baby	Date of birth:
Race:	Sex:

Section B **Person(s) at/called to the scene and relationship**		
Name/relationship	Date	Time
Name/relationship	Date	Time
Name/relationship	Date	Time
Police response/name	Date	Time
Paramedic response/name	Date	Time
When was the death certified/by whom	Date	Time
If the baby was taken to hospital		
Name of hospital		

WC_____

Date of arrival:	Time of arrival:
Name of doctor seen / declared death:	
Comment: Get copies of doctors notes	
Was resuscitation done on the baby by the paramedic or the doctors at the hospital?	

Section C
Household environment:

Place where baby lives: house shack other –		
Number of bedrooms Is the room in which the baby is found well ventilated?		
Odour(s) present in the room the baby slept in?	Yes	No
Peeling paint in the room the baby slept in?	Yes	No
Fungal growth (mould) in the room the baby slept in?	Yes	No
Did people smoke cigarettes in the room the baby slept?	Yes	No
Are there pets in the house? If yes – type and number:	Yes	No
Did caregiver use alcohol or drugs on the night baby died?	Yes	No
Was there a heater or open fire or galley blik or other heating device in room where baby slept?	Yes	No
In what position was the baby found lying? Has the baby been moved? Were there any covers/ clothing etc over the baby's head? Was the baby squashed/wedged between anything (object)?	Yes	No
Was there overlaying (someone lay on top of the baby)?	Yes	No
Comments from forensic officer who attended the scene:		

WC_____

Part 2: Facility Questionnaire

Date: ***Time:*** ***Name of Forensic officer:***

Section D
Circumstances of death / details about events before death

1. When was the baby last seen alive				Date	Time
2. Who last saw the baby alive					
3. When was the baby found dead				Date	Time
4. Who found the baby dead at the scene					
5. Was the baby ill?				Yes	No
a) If yes – What was wrong and for how long?					
b) Was the baby taken to the doctor or pharmacy or clinic or traditional healer for the illness? When (date and time)?				Yes	No
c) If not, why not:					
d) Was the baby admitted to a hospital or clinic for the illness: When (date and time)?				Yes	No
e) If not, do you know why not?					
f) What medication was given (names please					
6. Where was the baby found dead	Bed	Couch	Cot	Floor	Other
Other:					
7. Did the baby sustain any injuries – eg by falling or being hit: If yes:				Yes	No
a) When did it happen?					
b) How did it happen?					
c) Where did it happen?					
d) What did the caretaker do about it?					

WC_____

8. a) On what was the baby placed to sleep	Bed with a pillow	Bed without a pillow	Couch with a pillow	Couch without pillow	Cot with pillow
	Cot without pillow	Floor with pillow	Floor without pillow	Other	
b) If placed on a bed/cot, what was the mattress type			Foam rubber	Inner spring	Other
c) Was the mattress covered with a blanket or sheet				Yes	No
d) What position was the baby placed when put to sleep?		Back	Stomach	Side	Other
Other -					
e) what was used to cover the baby: List items					
e) What position was the baby found dead?		Back	Stomach	Side	Other
Other –					
f) Has the baby been moved?				Yes	No
g) Face position when the baby was found dead			To the left	To the right	Face down
			Face up	Unknown	
h) Face and or chest squashed / wedged between any object(s) when the baby was found dead?			Yes	No	Unknown
If yes – details please –					
i) Was the nose and mouth of the baby covered by anything – eg blankets or anything else			Yes	No	Unknown
j) Were there other items in contact with the baby – eg pillow			Yes	No	Unknown
k) Did the baby use a Dummy (pacifier)?				Yes	No
l) Did the baby sleep in the same bed as the mother?				Yes	No
m) Did the baby sleep in her arms?				Yes	No
n) Did the baby sleep on her chest?				Yes	No
o) Did the baby sleep with the mother on a couch?				Yes	No
p) How many other people slept on the same bed as the baby at the time the baby died?					
q) Was anyone found on top of the baby while in the bed (Overlaying)?				Yes	No
r) Was the window where the baby slept on the day /night the baby died				Open	Closed
s) Did the mother or anyone in the house smoke while the baby slept on the night/day of death?					
t) When was the baby last fed?				Date	Time

WC_____

u) Did the mother/caregiver use alcohol before going to bed with the baby on the night/day the baby was found dead? If yes, how much?			Yes	No
v) Did the mother/caregiver use drugs before going to bed with the baby on the night/day the baby was found dead? If yes, what drugs?			Yes	No
w) Did the mother/caregiver give the baby medication on the night/day of death? If yes, name of medication:			Yes	No
Section E **About the baby**				
1. Where was the baby born?	Hospital	Clinic	Home	Other
Name of hospital/clinic/other				
2. How was the baby born?			Normal vaginal delivery	Caesarian section
3. How much did the baby weigh at birth?				
4. Was the baby		Premature	Full term	Post dates (Overdue)
5. If the baby was premature, how premature was it?				
6. Did the baby receive Kangaroo care (KMC)			Yes	No
7. Did the mother carry the baby on her back?			Yes	No
8. Was the baby		Breast fed	Bottle/formula fed	Both breast and bottle fed
If formula, name of the milk –				
9. Was boiling water used to make the bottle?			Yes	No
10. What other food was use to feed the baby?				
11. Does the mother have the clinic card?			Yes	No
If yes – keep the card for the pathologist. If no – ask the mother to bring it to the facility				
12. Was the baby sick before it died?			Yes	No
If yes	<24h	>24h	> 2 weeks	Never
a) Did the baby have a cold/ runny nose?				
b) was the baby coughing?				
c) did the baby have diarrhea (runny tummy)?				

WC_____

d) Was the baby unusually restless / irritable?				
e) Was the baby crying more than usual?				
f) Was there a difference /change in the appetite / feeding?				
g) Was the baby vomiting?				
h) Any fits / seizures?				
i) did the baby have a fever / showed increased sweating?				
j) Was the baby listless? (floppy)				
k) did the baby turn blue?				
13. Was the now deceased baby taken to	Hospital	clinic	doctor	Pharmacy
	Traditional healer	Other		
14. Did the baby come in contact with someone who is sick in the past two weeks?			Yes	No
If yes – who?				
15. Did the baby ever suddenly stopped breathing?		Yes	No	Unknown
16. When was the baby's last vaccination?				
18. Is the baby known to be allergic to anything?		Yes	No	Unknown
If yes, what?				
19. Did the family visit another country prior to the death of the baby?			Yes	No
If yes, give details				
20. Was the baby admitted to hospital in the past week before the death?			Yes	No
a) If yes, for how long and where:				
b) Why?				
c) Discharge date?				
d) Condition of baby after discharge:				
e) Medication after discharge from the hospital (names please)				
21. Was the baby taken to a traditional healer?			Yes	No
a)If yes, date when the baby was taken to the healer:				

b) What was given?
c) Ask for the medication to be given to the pathologist.
d) Condition of the baby after going to the healer?
21. What did the baby wear when it died? (list clothing)

Section F
About the mother

1. Is the mother	Married	Single
2. Is the mother employed?	Yes	No
3. Age of the mother?		
4. What standard of schooling did she achieve?		
5. Was she on contraception before she fell pregnant?	Yes	No
6. Did she take iron and vitamin tablets during her pregnancy?	Yes	No
7. Did she receive antenatal care?	Yes	No
8. Did the mother have diabetes in pregnancy?	Yes	No
9. Did the mother have high blood pressure in pregnancy?	Yes	No
10. Did the mother gain weight adequately in pregnancy?	Yes	No
11. Was she diagnosed with any illness during the pregnancy eg. HIV?	Yes	No
12. Was the mother on any medication during the pregnancy?	Yes	No
If yes, what medication:		
13. Were there any difficulties during the delivery?	Yes	No
If yes, what?		
14. Were there any problems with the baby after the delivery?	Yes	No
If yes, what?		

WC_____

15. Was any specific instruction given about specific health care for the baby?				Yes	No
If yes, what?					
16. Was she depressed after the pregnancy?				Yes	No
17. Did she get any treatment?				Yes	No
18. How many babyren does she have?					
19. How old are they?					
20. Are they healthy?				Yes	No
21. Do any of the babyren have learning disability?				Yes	No
22. Do the living babyren have the same father as the deceased baby?				Yes	No
23. Does she look after the baby?				Yes	No
24. If not, who looks after the baby?					
25. Why is the mother unable to look after the baby?					
26. Did the mother smoke during the pregnancy?				Yes	No
If yes, how many per day?					
27. Did the mother drink during the pregnancy?				Yes	No
a) What did she drink?	Beer	Wine		Spirits	Other
b) how much did she drink?		Every day		Now and again	Weekends
1 glass		Every day		Now and again	Weekends
> 1 glass		Every day		Now and again	Weekends
A bottle of alcohol		Every day		Now and again	Weekends
> 1 bottle		Every day		Now and again	Weekends
28. Does she use drugs?				Yes	No
a) If yes, what drugs does she use?	Tik	Cocaine	Heroin	Mandrax	Other
b) How often does she use drugs?		Every day		Now and again	Weekends
29. Does the mother smoke after the pregnancy?				Yes	No
30. Does the mother know that smoking harms the unborn baby?				Yes	No
31. Does the husband/partner drinks?				Yes	No

WC_____

32. Does the mother drink after the pregnancy?	Yes	No
33. Do the parents of the mother drink?	Yes	No
34. Does the mother know that alcohol harms the unborn baby?	Yes	No
35. Did the mother have a previous baby that died suddenly?	Yes	No
a) If yes, how many died?		
b) At what age?		
c) Was a PM done?	Yes	No
If yes, where was it done?		
36. Did the mother have a previous stillbirth?	Yes	No

Section G
Household environment

1. Place where the baby lives	House		Shack	Other
2. Number of bedrooms?				
3. Is the room in which the baby was found well ventilated?			Yes	No
4. Odour(s) present in the room the baby slept in?			Yes	No
5. Peeling paint in the room the baby slept in?			Yes	No
6. Fungal growth (mould) in the room the baby slept in?			Yes	No
7. Are there pets in the house?			Yes	No
If yes, type and number:				
8. Was the following in the room where the baby slept to heat the room?	Electric heater	"Galley"	Fire	Other
Describe other –				
9. Number of adults in the dwelling?				
10. Number of babyren in the dwelling?				
11. Total number of people in the dwelling?				
12. Estimated monthly income?				
13. Number of smokers in the dwelling?				
14. Are there mentally retarded/ challenged people in the dwelling?			Yes	No

WC_____

COMMENTS TO PATHOLOGIST FROM THE FORENSIC OFFICER WHO ATTENDED THE SCENE AND INTERVIEWED DURING ID PROCESS:

ITEMS RETAINED AT THE SCENE OR FROM THE MOTHER DURING INTERVIEW

Date:

Signature / Thumbprint of deponent

I certify that the above statement was taken down by myself and that the deponent has acknowledged that he / she knows and understands the contents hereof.

Date _____ Time: _____

Place: _____

_____

Department of Health
Forensic Pathology Laboratory

FPS 006(a)

FORENSIC PATHOLOGY SERVICE

SUD [Complete If a person older than one year of age Should Suddenly And Unexpectedly Die]

FPS laboratory_____ WC _____

Full Name of deceased _____ Scene Address

Part 1: Scene Questionnaire and Observations

Date: ***Time:*** ***Name of Forensic officer:***

Section A. **Who gives the history/ information in this case e.g. husband/wife/partner/son/daughter/mother/father/brother/sister/other relative(give details)**	
Name:	Relationship:
Address:	Contact telephone number:
ID Number:	
Home Address of Deceased:	
Age of Deceased	Date of birth:
Race:	Sex:

Section B
Person(s) at/called to the scene and relationship

Name/relationship	Date	Time
Name/relationship	Date	Time
Name/relationship	Date	Time
Police response/name	Date	Time
Paramedic response/name	Date	Time
If the deceased was taken to hospital	Yes	No
Name of hospital		

Date of arrival:	Time of arrival:		
Name of attending doctor	Contact Number:		
When was the death certified and by whom		Date	Time
Was resuscitation done? Who by; Where:			
Comment: Get copies of doctors notes			
Section C **Household environment:**			
Place where deceased lived at time of death:	Formal	Informal	Other
Did the deceased live alone?		Yes	No
Did anyone witness the death?		Yes	No
Number of bedrooms in dwelling:			
Is the room in which the deceased adult is found well ventilated?		Yes	No
Was the room locked from the inside?		Yes	No
Odour(s) present in the room the deceased adult slept in?		Yes	No
Peeling paint in the room the deceased adult slept in?		Yes	No
Medication present on the scene; if so record.		Yes	No
Alcohol present on the scene?		Yes	No
Was the medication retained by FPS?		Yes	No
Illegal substances present on the scene; if so describe.		Yes	No
Did the deceased call a friend/someone prior to death?		Yes	No
Are there pets in the house? If yes – type and number?		Yes	No
Was there a heater or open fire/gas heater/ galley blik or other heating device in room where deceased adult slept?		Yes	No

In what position was the deceased found lying?			
Has the body of the deceased been moved?		Yes	No
Were there any covers/ clothing etc over the deceased adult's head?		Yes	No
Was the deceased adult squashed/wedged between anything /(object- was the person lying under any heavy material eg bricks/rubble? If so, describe.		Yes	No
Comments from forensic officer who attended the scene:			

SECTION D – Did the deceased suffer from any of the following symptoms prior to death?

Swelling of ankles	Yes	No
Weight loss	Yes	No
Fever	Yes	No
Coughing up blood	Yes	No
Fits	Yes	No
Breathlessness	Yes	No
Foaming at the mouth	Yes	No
Chest pain	Yes	No
Other symptoms prior to death- If yes, please describe	Yes	No

Part 2: Facility Questionnaire

Date: ***Time:*** ***Name of FPS Official:***

Section E
Circumstances of death / details about events before death

1. When was the deceased last seen alive?	Date	Time
2. Who last saw the deceasedalive?		
3. When was the deceased found dead?	Date	Time
4. Who found the deceased's body on the scene?		

Relationship of finder		
Age of finder		
5. Did anyone witness the death?	Yes	No
If yes, what did the deceased **do** prior to death? Was he/she		
Fitting	Yes	No
Holding head in pain	Yes	No
Breathlessness	Yes	No
Foaming at the mouth	Yes	No
Grabbing of chest	Yes	No
Other- Describe		
6. Did the deceased sustain any injuries at the time of death?	Yes	No
If YES: Describe how it happened		
7. Was the deceased ill prior to death?	Yes	No
a) If yes – What was wrong?		
b) For how long was the illness present as described above? (PLEASE CIRCLE AND ELABORATE) <24hrs 1day-2weeks >2weeks		
8. **a)** Did the deceased suffer from a **chronic** illness/infection? If so; what?		
Diabetes	Yes	No
Epilepsy	Yes	No
Asthma	Yes	No
Cancer and site of cancer	Yes	No

High blood pressure	Yes	No
Heart problems	Yes	No
Kidney problems	Yes	No
HIV	Yes	No
TB	Yes	No
Allergies	Yes	No
Other	Yes	No
Mental disease	Yes	No
Malaria	Yes	No
b) Was the deceased adult taken/go to a doctor or pharmacy or clinic or traditional healer for the illness?	Yes	No
When (date and time)	Date	Time
Did the deceased use the medication as prescribed?	Yes	No
Contact details of the attending doctor:		
9. Was the deceased recently adult admitted to a hospital or clinic for the illness?	Yes	No
When (date and time)?	Yes	No
Contact details of the attending doctor		
Retain hospital records if the admission was recent	Yes	No
10. Was the deceased on any medication including chronic medication?	Yes	No
If yes, What medication (names please of medication)		

11. Did the deceased vomit? **(**If the answer is **NO** please proceed to question **15)**	Yes	No	Don't know
12. For how long did the deceased vomit?	Days	Weeks	Months
13. Did the vomit look like a coffee coloured fluid or bright red like blood or some other?	Coffee	Blood	Other Describe

14. When the vomiting was most severe, how many times, did the deceased vomit per day?			
15. Did the deceased have abdominal pain? **(**If the answer is **NO** please proceed to question **21)**	Yes	No	Don't know
16. For how long did the deceased have abdominal pain?	Days	Weeks	Months
17. Did the deceased have abdominal distension/swelling?	Yes	No	Don't Know
18. For how long did the deceased have abdominal distension/swelling?	Days	Weeks	Months
19. Was there a period of a day or longer during which the deceased could not pass stool?	Yes	No	Don't know
20. Did the deceased have difficulty or pain when swallowing?	Yes	No	Don't know
21. Did the deceased have a headache? **(**If the answer is **NO** please proceed to question **25)**	Yes	No	Don't know
22. For how long did the deceased have a headache?	Days	Months	Years
23. Was the headache severe?	Yes	No	Don't know
24. Did the headache improve upon lying down?	Yes	No	Don't know
25. Did the deceased have a stiff or painful neck? **(**If the answer is **NO** please proceed to question **29)**	Yes	No	Don't know
26. Did the deceased have mental confusion?	Yes	No	Don't know
27. For how long did the deceased have mental confusion?	Days	Months	Years
28. Did the mental confusion start suddenly within a single day or slowly over many days?	Single day	Many days	
29. Did the deceased become unconscious? **(**If the answer is **NO** please proceed to question **32)**	Yes	No	Don't know
30. For how long was the deceased unconscious?	Min	Hours	Days
31. Did the unconsciousness start suddenly within a single day or slowly over many days?	Single day	Many days	
32. Did the deceased have convulsions/fits? **(**If the answer is **NO** please proceed to question **36)**	Yes	No	Don't know
33. For how long did the deceased have convulsions?	Days	Months	Years
34. How many times did the deceased have convulsions during the 72hours prior to death?			
35. Did the deceased have stiffness of the whole body?	Yes	No	Don't know
36. Did the deceased have weakness or paralysis of the body?	Yes	No	Don't

(If the answer is **NO** please proceed to question **43)**			know
37. Did the deceased have weakness or paralysis of one side of the body?	Yes	No	Don't know
38. For how long did the deceased have paralysis of one side of the body?	Days	Months	Years
39. Did the paralysis of one side of the body start suddenly within a single day or slowly over many days?	Single day	Many days	
40. Did the deceased have paralysis of the lower limbs?	Yes	No	Don't know
41. For how long did the deceased have paralysis of the lower limbs?	Days	Months	Years
42. Did the paralysis of the lower limbs start suddenly within a single day or slowly over many days?	Single day	Many days	
43. Did the deceased receive any treatment for the illness that led to death?	Yes	No	Don't know
SURGICAL HISTORY Did the deceased have an operation/s?	Yes	No	Don't know
If yes, when?	Date:		
Name of Hospital/Clinic			
Nature of operation-Describe			
TRAVEL HISTORY Did the deceased travel outside the Province / Country?	Yes	No	Don't know
If yes, where and when?			
FAMILY HISTORY OF ANY ILLNESS Heart disease	Yes	No	
Which family member had heart disease			
Asthma	Yes	No	
Cancer	Yes	No	
Sudden death	Yes	No	
At what age did they pass away			

TRAUMA HISTORY Was the deceased injured in an assault or in any accident?					Yes	No	Don't know
If yes, when did it occur?							
What specifically was injured?							
Did the person need admission to hospital after the injury?					Yes	No	Don't know
How was the person after the incident?					Well	OK	Unwell
If unwell, describe							
For how long did the illness last?					Days	Weeks	Months
SOCIAL HISTORY Did the deceased regularly use alcohol?					Yes	No	Don't Know
If yes, what?	Beer	Wine	Brandy		Papsak	Other	
If yes, how much?							
Did the deceased use alcohol on the day/night of death?					Yes	No	Don't Know
Did the deceased regularly use drugs?					Yes	No	Don't know
If yes, what drugs were used?		TIK	Mandrax		Dagga	Other	
Describe Other:							
is she pregnant					Yes	No	Don't know
If **YES** ask about antenatal clinic attendance What clinic							
If the deceased is female, was she on contraception	Name, if yes				Yes	No	Don't know
If **YES** name of contraceptive:							
f) Did the deceased smoke? If so what: cigarettes /pipe / other?					Yes	No	Don't know
How often/ many per day?							
EMPLOYMENT HISTORY Was the person employed					Yes	No	
If yes, what did he/she do?							
Was the person exposed to any hazardous substances prior to death, if so, what.							

Did the person ever work in a mine?	Yes	No	Don't know
History of an animal/insect/snake bite If yes what creature?	Yes	No	Don't know
History of Bee sting	Yes	No	Don't know

COMMENTS TO PATHOLOGIST FROM THE FORENSIC PATHOLOGY OFFICER WHO INTERVIEWED:

ITEMS RETAINED AT THE SCENE OR DURING INTERVIEW

Date:

Signature / Thumbprint of deponent

I certify that the above statement was taken down by myself and that the deponent has acknowledged that he / she knows and understands the contents hereof.

Date _____ Time: _____ Place: _____

_____

Name of Forensic Pathology Official: _____
Department of Health, Forensic Pathology Laboratory

	Age Group				
	Group A (Infant)	Group B (One to five)	Group A (Infant)	Group B (One to five)	
Variable	Year - 2013	Year - 2013	Year - 2014	Year - 2014	
Day of death	(n)	(n)	(n)	(n)	Total
Monday	28	2	30	3	63
Tuesday	24	3	21	0	48
Wednesday	27	3	32	1	63
Thursday	19	1	24	2	46
Friday	25	3	26	4	58
Saturday	27	4	30	7	68
Sunday	43	3	36	1	83
Month					
January	11	1	8	0	20
February	9	2	14	2	27
March	14	2	13	2	31
April	11	0	13	3	27
May	11	2	19	1	33
June	37	4	25	3	69
July	16	1	18	0	35
August	15	2	22	4	43
September	29	1	13	1	44
October	14	1	23	0	38
November	15	0	11	0	26
December	11	3	20	2	36
Housing					
Formal	75	10	81	9	175
Informal	116	9	107	9	241
Other	1	0	0	0	1
Unknown	1	0	11	0	12
Race					
African	116	15	117	15	263
Coloured	75	4	81	1	161
White	2	0	1	1	4
Asian	0	0		1	1
Sex					
Male	111	7	104	10	232
Female	82	12	95	8	197
Age					
0 to 1	33		30		63
1 to 2	30		43		73
2 to 3	33		42		75
3 to 4	31		29		60

4 to 5	20		8		28
5 to 6	4		7		11
6 to 7	10		11		21
7 to 8	5		5		10
8 to 9	5		6		11
9 to 10	5		4		9
10 to 11	6		4		10
11 to 12	11		10		21
13 M		1		2	3
14 M		2		2	4
15 M		0		1	1
16 M		0		1	1
18 M		1		1	2
19 M		0		1	1
2 Y		8		4	12
3 Y		3		5	8
4 Y		3		0	3
5 Y		1		1	2
Extent of Autopsy					
External examination	138	12	132	13	295
Full autopsy	52	6	58	5	121
Partial autopsy	3	1	9	0	13
Lodox					
Yes	189	19	193	18	419
No	4	0	6	0	10
Histo					
Yes	38	4	42	3	87
No	155	15	157	15	342
Micro					
Yes	33	5	40	3	81
No	160	14	159	15	348
Micro Result					
None	9	1	9	2	21
Missing document	5	2	11	0	18
Yes	21	2	20	1	44
RTHC Attached					
Yes	107	9	157	14	287
No	86	10	42	4	142
Vaccine up to date					
Yes	81	4	115	10	210
No	31	5	46	5	87

Unknown	81	10	38	3	132
Medicine					
None	130	10	135	8	283
OTC	21	3	19	2	45
Prescription	19	3	27	7	56
Chronic	7	0	6	1	14
Traditional	4	1	2	0	7
Unknown	12	2	10	0	24
Mattress Type					
Foam Rubber	56	4	45	6	111
Inner Spring	107	10	123	5	245
Other	18	1	18	1	38
Unknown	12	4	13	6	35
Sleeping position					
Side	100	10	100	9	219
Back	14	4	27	4	49
Stomach	65	1	62	2	130
Unknown	14	4	10	3	31
Co-Sleeping					
Yes	170	14	189	14	387
No	11	2	6	2	21
Unknown	12	3	4	2	21
People in Bed					
None	11	2	6	2	21
One	99	5	80	9	193
More than one	71	9	105	5	190
Unknown	12	3	8	2	25
Premature					
Yes	60	1	71	2	134
No	117	14	114	13	258
Unknown	16	4	14	3	37
Feeding					
Breast	87		107		194
Bottle	49		52		101
Both breast and bottle	43		37		80
Unknown	14		3		17
Symptoms					
Yes	84	16	92	14	206
No	103	2	107	4	216
Unknown	6	1	0	0	7
Mother marital status					
Single	136	10	153	10	309

Married	45	6	45	7	103
Unknown	12	3	1	1	17
Mother employed?					
Yes	28	0	32	6	66
No	107	11	144	10	272
Unknown	58	8	23	2	91
Antenatal care					
Yes	98	8	120	15	241
No	37	3	54	1	95
Unknown	58	8	25	2	93
Smoke prenatal					
Yes	48	3	57	1	109
No	83	8	116	15	222
Unknown	62	8	26	2	98
2nd Hand Smoke					
Yes	65	3	75	2	145
No	68	8	91	14	181
Unknown	60	8	33	2	103
Drink during preg.					
Yes	31	2	38	2	73
No	99	9	135	14	257
Unknown	63	8	26	2	99
Drugs during preg.					
Yes	15	1	12	1	29
No	116	10	161	15	302
Unknown	62	8	26	2	98
Specific drug					
Tik	12	0	8	1	21
Dagga	4	0	2	0	6
Mandrax	2	0	1	0	3
Heroin	0	1	2	0	3
Previous SUDI?					
Yes	19	4	28	3	54
No	163	11	170	14	358
Unknown	11	4	1	1	17
Exposure to HIV					
Yes	24	1	39	8	72
No	109	9	135	9	262
Unknown	60	9	25	1	95

	Age Group								
	2013				2014				
	Group C	Group D	Group E	Group F	Group C	Group D	Group E	Group F	
Variable	(6 to 17)	(18 to 40)	(41 to 60)	(61 +)	(6 to 17)	(18 to 40)	(41 to 60)	(61 +)	
Day of death	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	Total
Monday	1	10	13	5	1	8	13	1	52
Tuesday	0	8	12	12	1	9	10	5	57
Wednesday	2	9	14	4	2	10	6	7	54
Thursday	4	9	9	9	0	12	6	3	52
Friday	2	12	13	6	2	14	5	8	62
Saturday	0	7	11	5	0	10	7	0	40
Sunday	1	12	15	8	0	13	7	6	62
Month									
January	0	0	8	1	0	7	4	1	21
February	1	4	5	1	0	2	9	2	24
March	0	4	4	9	0	5	7	3	32
April	0	6	7	4	1	10	3	1	32
May	0	7	3	5	1	5	8	5	34
June	2	9	11	2	0	10	5	6	45
July	1	8	11	6	2	7	3	4	42
August	1	7	9	9	0	3	4	5	38
September	1	5	10	4	1	6	4	1	32
October	1	7	6	5	0	8	4	0	31
November	0	4	5	2	1	8	2	2	24
December	3	6	8	1	0	5	1	0	24
Housing									
Formal	5	22	31	28	4	24	17	15	146
Informal	4	26	31	13	2	27	13	6	122
None	0	4	9	2	0	5	11	2	33
Unknown	1	13	8	6	0	19	13	7	67
Other	0	1	6	0	0	1	0	0	8
Hospital	0	1	2	0	0	0	0	0	3
Age									

Min	7	18	41	61	6	19	41	61	
Median	8	34	49	70	9	33	52	69.5	
Mean		32	50	71		32	51	71	
Max	17	40	60	94	16	40	60	92	
Race									
African	6	43	36	11	3	44	21	5	169
Coloured	3	20	42	26	3	28	30	17	169
White	1	3	8	12	0	4	3	8	39
Asian	0	1	1	0	0	0	0	0	2
Sex									
Male	9	53	66	29	4	47	40	22	270
Female	1	14	21	20	2	29	14	8	109
Co-morbid conditions									
Yes	4	27	43	28	3	42	25	20	192
No	5	26	18	13	3	18	9	7	99
Unknown	1	14	26	8	0	16	20	3	88
TB	1	18	17	6	0	29	13	11	95
Symptoms									
Yes	6	45	51	31	6	52	24	19	234
No	4	10	16	8	0	9	10	4	61
Unknown	0	12	20	10	0	15	20	7	84
Medication									
None	4	19	19	9	1	11	17	9	89
Chronic	1	7	11	18	1	19	10	10	77
Over the counter	1	3	3	2	1	5	0	0	15
Prescription	2	11	12	4	2	12	7	5	55
Traditional	1	1	1	0	0	2	0	0	5
Unknown	1	26	41	16	1	27	20	6	138
Circumstances of death									
Daily activity	7	26	44	15	3	33	21	10	159
Sleeping	3	14	22	11	3	17	15	8	93
At rest	0	0	2	1	0	3	0	0	6
Exercise	0	0	1	2	0	1	0	0	4

Physical altercation	0	0	0	0	0	1	0	0	1
Other	0	4	3	3	0	2	3	2	17
Unknown	0	18	13	9	0	10	9	4	63
Hospital	0	5	2	8	0	9	6	6	36
Extent of autopsy									
Full autopsy	5	27	19	19	4	28	9	9	120
External examination	5	36	67	29	2	48	44	20	251
Partial autopsy	0	4	1	1	0	0	1	1	8
Lodox									
Yes	10	63	80	40	4	66	50	25	338
No	0	4	7	9	2	10	4	5	41
Histo									
Yes	5	14	13	6	4	14	7	4	67
No	5	53	74	43	2	62	47	26	312
Tox									
Yes	1	4	6	4	0	8	3	1	27
No	9	63	81	45	6	68	51	29	352
Micro									
Yes	4	4	4	3	2	10	1	1	29
No	6	63	83	46	4	66	53	29	350
Micro result									
Yes	3	4	2	3	2	7	1	1	23
Missing	1	0	2	0	0	3	0	0	6
No	0	0	0	0	0	0	0	0	0
Smoker									
Yes	0	10	16	8	0	18	18	9	79
No	9	8	16	16	5	18	9	8	89
Unknown	1	49	55	25	1	40	27	13	211
Substance abuse									
Yes	0	17	29	12	0	27	16	3	104
No	10	9	16	15	6	21	14	14	105
Unknown	0	41	42	22	0	28	24	13	170
Specific									

Alcohol	0	11	23	10	0	16	13	3	76
Dagga	0	2	5	1	0	8	7	0	23
Tik	0	2	0	0	0	6	0	0	8
Mandrax	0	1	1	1	0	4	1	0	8
Pregnant									
Yes	0	0	0	0	0	1	0	0	1
No	10	67	87	49	6	75	54	30	378
Vagrant									
Yes	0	11	17	8	0	14	14	3	67
No	10	56	70	41	6	62	40	27	312
Prisoner									
Yes	0	1	0	0	0	1	0	0	2
No	10	66	87	49	6	75	54	30	377
HIV									
Yes	0	12	8	0	0	7	5	0	32
No	8	27	27	31	2	32	25	10	162
Unknown	2	28	52	18	4	37	24	20	185