



**A retrospective investigation of sudden unexpected death in the
young investigated at Salt River Mortuary, Cape Town**

by

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ABSTRACT

Sudden unexpected death in the young (SUDY) is the tragic fatality of seemingly healthy individuals aged between one and 40 years. Little is known about the demographics and risk factors of these cases at Salt River Mortuary (SRM), Cape Town. Therefore, this project aimed to retrospectively investigate the burden and profile of SUDY cases admitted to SRM, between 1 January 2016 and 31 December 2018. Of the total 11 588 cases admitted over this period, 833 (7.2 %) were SUDY cases, wherein males comprised the majority (64.3 %). Individuals were a median age of 31 ± 10.3 years at death, and the main location of death was 'residential' (43.5 %). There were also significantly more males than females in the age category of 31 - 40 years who were found outdoors compared to all other locations ($p < 0.001$). Risk factors included physical activity, substance abuse, and co-morbidities with concomitant use of chronic medication. More than a third of individuals experienced breathlessness prior to death (45.0 %). Of cases with a confirmed natural cause of death, the main organ systems involved were pulmonary, cardiovascular, central nervous system and gastrointestinal, which parallels international trends. Akin to local studies, in analogous amounts, TB and pneumonia were the leading causes of death. Additionally, 21.1 % of cases were identified as candidates for genetic testing which may resolve undetermined cases or elucidate underlying predisposing factors to sudden death. Fortunately, 81.8 % had biological samples available for these retrospective analyses. Cases often had missing documentation which advocates for training to ensure compliance to standardised procedures. This study shows that males aged 31 ± 10.3 years with pulmonary and cardiac-related co-morbidities are the most vulnerable for SUDY whilst sleeping. Awareness interventions targeted at this population are thus needed in an attempt to reduce these tragic fatalities.

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ABBREVIATIONS

AEDs	Anti-epileptic drugs
±	Approximately
BMI	Body Mass Index
CDC	Centers for Disease Control and Prevention
CDR	Child death review
CNS	Central nervous system
CVS	Cardiovascular system
DSI	Death Scene Investigation
FFPE	Formalin fixed paraffin embedded
FPS	Forensic Pathology Services
GIT	Gastrointestinal
>	Greater than
≥	Greater than and equal to
HIV	Human Immunodeficiency Virus
ID	Identity Document
<	Less than
≤	Less than and equal to
LODOX	Low dosage x-ray
N	Total number of cases in population
n	Sample size
%	Percentage
SAPS	South African Police Services
SCD	Sudden cardiac death

SDG	Sustainable development goal
SDY-CR	Sudden Death in the Young Case Registry
SRM	Salt River Mortuary
SUD	Sudden unexpected death
SUDA	Sudden unexpected death in adults
SUDC	Sudden unexpected death in children
SUDEP	Sudden unexpected death in epilepsy
SUDI	Sudden unexpected death in infants
SUDY	Sudden unexpected death in the young
TB	Tuberculosis
UK	United Kingdom
US	United States

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CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

1.1. Introduction

1.1.1. Background

Sudden unexpected death in the young (SUDY) is the unforeseen and distressing demise of ostensibly healthy individuals between the ages of one and 40 years (Dewar *et al.*, 2012). In 2016, there were 5.6 million deaths of individuals worldwide under the age of 5 years, with almost 15 000 deaths per day (World Health Organization, 2019a). Despite the decline to 5.3 million deaths in 2018 (World Health Organization, 2019b), these numbers are alarming, considering the global average life expectancy of the human population is 72 years of age (World Health Organization, 2019a). In 2019, a large proportion of deaths pertaining to low-income countries, such as the African region, were attributed to communicable disease, maternal, perinatal and nutritional deficiencies (World Health Organization, 2019c). The proportion of SUDY relating to these statistics, however, remains unknown due to minimal research pertaining to these deaths.

Numerous definitions have been provided for sudden unexpected death (SUD) wherein it is regarded as the demise of an individual occurring either instantaneously or between one and 24 hours since the onset of symptoms (Bowker *et al.*, 2003; Byard, 2010; World Health Organization, 2010). However, a definition which seems to be widely accepted, especially in the medico-legal field, has been provided by Mason (1995) whereby he defines SUD as “unexpected death following so rapidly from the onset of symptoms that the cause of death could not be certified with confidence by the medical practitioner familiar with the patient”.

To date, forensic studies pertaining to SUD in infants (SUDI), children (SUDC) and adults (SUDA) respectively have been performed across South Africa (Tiemensma, 2010; Tiemensma & Burger, 2012; Mathews *et al.*, 2016; van Deventer, Rossouw & du Toit-Prinsloo, 2016; Bennett, Martin & Heathfield, 2019). In the Western Cape and Salt River Mortuary (SRM) specifically, however, minimal research has been conducted on the SUDY group. Relevant information such as the number of SUDY cases, their demographic profile, extent of post-mortem examination conducted, cause of death, and social and clinical history pertaining to this group has not been well-documented. Obtaining this information on SUDY will aid in identifying risk

factors, thereby promoting targeted interventions and translatable research. Determining these factors may also aid in reducing the mortality rate by identifying living relatives who may be at risk of a similar death.

Although the United Nations millennium goals were somewhat met in terms of reducing child mortality and improving maternal health (Mathews *et al.*, 2016), these statistics can be further improved through understanding and addressing underlying causes and risk factors. For example, the implementation of a ‘molecular autopsy’ could ultimately aid in providing cause of death in undetermined SUDY cases, whereby findings can be communicated with, and screened for in the deceased’s families. This will ultimately provide closure and promote good maternal and child health, which is in line with Sustainable Development Goal (SDG) number three (publicly accessible: <https://apps.who.int/iris/bitstream/handle/10665/311696/WHO-DAD-2019.1-eng.pdf>; date accessed: 2019, November 4).

In light of the paucity of information on SUDY in South Africa, this literature review therefore aimed to document the relevant legislation and guidelines, establish the common causes of death and risk factors for SUDY in other ancestral groups. It also aimed to highlight the significance of molecular autopsies as a possible approach to addressing the third SDG.

1.1.2. Search strategy

Three databases, namely Scopus, Web of Science and PubMed, were searched for the years 2000-2020 using the keywords “sudden unexpected death in the young”, “risk factors”, “undetermined“, and “cause of death”, in three varying combinations (Table 1.1). This resulted in nine searches with a total of 959 resultant publications.

Table 1.1: The three search combinations used in the search strategy

Search 1	sudden unexpected death in young AND risk factors AND undetermined AND cause of death
Search 2	sudden unexpected death in young AND risk factors AND cause of death
Search 3	sudden unexpected death in young AND risk factors

Subsequent to (i) viewing the titles and abstracts, (ii) the exclusion of duplicates across the databases, and (iii) the application of the inclusion and exclusion criteria as depicted below (Table 1.2), a total of 64 peer-reviewed original articles resulted. Thirteen additional original peer-reviewed documents, including abstracts, were identified from Primo. Therefore, based on overall relevance, a total of 77 documents were selected for this review. The South African Child Death Review pilot (Mathews *et al.*, 2016), National Health Act (Act 61 of 2003), Inquest Act (No. 58 of 1959) and Centers for Disease Control and Prevention (CDC) guidelines (publicly accessible: https://www.cdc.gov/sids/pdf/508suidiguidelinesingles_tag508.pdf; date accessed: 2020, March 10) were also read in conjunction to the literature.

Table 1.2: Search strategy inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> • Ages: > 1 years and ≤ 40 years • Sudden unexpected death in epilepsy • Sudden cardiac death • Cause of death and/or risk factors • Undetermined causes 	<ul style="list-style-type: none"> • Non-human • Not available in English • Reviews, case reports and editorials • Infant only studies (≤ 1 year old) and > 40 years old only studies • Irrelevance (<i>i.e.</i> gene studies, purely clinical based, bereavement counselling)

1.2. Legislation and guidelines surrounding SUD

1.2.1. South African legislation

In accordance with the Regulations regarding the rendering of Forensic Pathology Services (FPS) (No. R. 359 of 2018) of the National Health Act (Act 61 of 2003) of South Africa, fatalities attributable to unnatural causes, such as those that are “sudden and unexpected, or unexplained, or where the cause of death is not apparent”, are required to undergo medical-legal investigation in terms of the Inquest Act (No. 58 of 1959) (National Health Act, No. 61 of 2003, 2003:s1; du Toit-Prinsloo *et al.*, 2013).

The Inquest Act (Act 58 of 1959) mandates that a post-mortem investigation is to be performed to aid in ascertaining cause of death in all cases suspected to be of unnatural cause (Inquest Act, No. 58 of 1959, 1959:s2). In conjunction with the definition for SUD provided by Mason (1995), it can be noted that it is a fundamental

task of a forensic pathologist to distinguish between natural and unnatural deaths through the performance of post-mortem investigations (Tiemensma & Burger, 2012).

The Regulations (No. R. 359 of 2018) have provided a basis for the investigation of all unnatural deaths in South Africa which is inclusive of (i) obtaining information relevant to the death scene from witnesses and family members, (ii) collecting any exhibits or specimens from the scene, (iii) obtaining medical records and information pertaining to clinical and social history of the deceased, as well as (iv) performing an autopsy which may involve both an internal and external examination of the deceased (National Health Act, No. 61 of 2003, 2003:s1). It is essential that these autopsies are conducted thoroughly to aid in determining the cause of death and to provide closure for grieving relatives of the deceased.

During the medico-legal or post-mortem investigation, biological samples may be retained for ancillary investigations which may ultimately aid in establishing cause of death. For example, blood and/or tissue may be retained for toxicology or histology testing, respectively. However, this is done at the discretion of the forensic pathologist performing the investigation, and the type of samples taken is not mandated by legislation. Shortcomings arise in SUDY cases deemed as 'natural' as no further investigations are warranted by law to identify the exact cause of death - resulting in these cases having unspecific 'natural causes'. In many resource-constrained mortuaries, including in South Africa, investigations for determining the cause of natural deaths is often based purely on clinical and social history, an external examination and an Xmplar-dr chest X-ray (Lodox Systems, Johannesburg) (Mathews *et al.*, 2016), thus overlooking sample retention for further analysis. This is an area of concern, especially in the epidemiology and public health sectors, as transmissible conditions may exist, but may go undetected.

1.2.2. International guidelines for death scene investigation

Death scene investigation (DSI) guidelines have been established internationally by both the United States (US) Department of Justice and US Department of Health and Human Services (Centers for Disease Control and Prevention, 1996; U.S. Department of Justice, 1999). Not only do these guidelines aid in establishing cause of death, thereby differentiating between unnatural and natural deaths and ensuring that justice

and closure is received, but they also provide a basis for the DSI which can be implemented in other countries.

Prior to the nineties, there was an absence of standardised procedures pertaining to the collection and assessment of information on SUDI cases, wherein procedures varied amongst the different states (Centers for Disease Control and Prevention, 2016). Considering the burden of SUDI cases in the US (Centers for Disease Control and Prevention, 2018), a national standardised protocol was established for the DSI of these tragic cases. Pivotal information was incorporated within this protocol to aid in identifying risk factors and establishing the cause of death, as well as acquiring information regarding the manner and circumstances surrounding death (Centers for Disease Control and Prevention, 1996).

The CDC thereafter implemented a Case Registry in 2009 to enhance understanding and establish the burden of SUDI cases within the population (Centers for Disease Control and Prevention, 2018). Due to a paucity in epidemiological studies on SUDC (Chugh *et al.*, 2008), this was expanded into a Sudden Death in the Young Case Registry (SDY-CR) in 2013. The SDY-CR was implemented in seven states in 2016, incorporating SUD up until the age of 20 years, including both children and adolescents (Centers for Disease Control and Prevention, 2018). Furthermore, the SDY-CR actively sought after two common causes of death amongst this age group, namely sudden cardiac death (SCD) and SUD in epilepsy (SUDEP) (Centers for Disease Control and Prevention, 2016). Although various DSI protocols has been established internationally, they have not been adopted globally (Bennett, Martin & Heathfield, 2019) and thus there is a paucity of DSI information relevant to SUD in general.

1.2.3. The Child Death Review

An additional global guideline of considerable value in understanding SUDY is the Child Death Review (CDR) wherein deaths of individuals under 18 years of age referred for medico-legal investigation are reviewed (Mathews *et al.*, 2016). CDR teams have been established globally in many high-income regions, such as the US, wherein data surrounding the circumstances of death pertaining to child deaths are reviewed by a multidisciplinary team (Shanley, Risch & Bonner, 2010). This was

established to minimise child mortality by highlighting preventable deaths through the capturing of this data and the subsequent implementation of targeted interventions and public awareness.

Prior to 2014, South Africa did not have a CDR team, hence this concept was piloted at SRM in the Western Cape and Phoenix Mortuary in KwaZulu-Natal (Mathews *et al.*, 2016). This pilot study was successful in providing a platform to further explore cause of death in natural cases, which would otherwise be disregarded due to the legislation. Furthermore, it aided in rapidly identifying cause of death and risk factors in these cases, expedited police and legal proceedings and linked social workers to at-risk households (Mathews *et al.*, 2016). Consequently, the CDR has been implemented across the Western Cape, and is considered the gold standard for child death investigations.

1.3. Cause of death and risk factors in SUDY

1.3.1. Overview

A plethora of articles have documented cause of death and risk factors, such as the circumstances surrounding death and demographic data, whereby associations between these variables and conditions were established. SUD is generally categorised into the various organ systems (Dempers & Van Vuuren, 2006), and in the majority of studies, the following systems have been involved: circulatory, central nervous, respiratory and gastrointestinal (GIT).

Based on the literature reviewed, within the SUDY age group (1-40 years old), a recurrent cause of death has been identified as either cardiac or epileptic in nature and thus termed SCD and SUDEP respectively (van Deventer, Rossouw & du Toit-Prinsloo, 2016; Haas, 2018). To support this, a summary of the literature identifying the main causes of death in various populations and age groups can be seen below (Table 1.3). Although the ages characterised in these articles extend beyond that mentioned in the inclusion criteria of this review, they do encompass the SUDY group of 1-40 years and have thus been incorporated.

SUD due to infections with risk factors such as co-sleeping and smoking has shown greater association with younger individuals and infant deaths (Mathews *et al.*, 2016). A study by Amital *et al.* (2004) had additionally attributed SUDY to meningitis and

respiratory conditions, such as asthma, pneumothorax, pneumonia, or pulmonary embolism. Hence, it is evident that different causes of death and risk factors tend to be associated with different ages at death.

Table 1.3: Main causes of death associated with SUD as identified in literature reviewed.

Leading cause of death	Region	Age group	Study size (n)	Reference
SUDEP	Denmark	1 month – 18 years	1 974	(Grønborg & Uldall, 2014)
	Sweden	16-74 years	255	(Sveinsson <i>et al.</i> , 2020)
	Iceland	11-63 years	3 514	(Einarsdottir, Sveinsson & Olafsson, 2019)
	San Diego	18-45 years	3 732	(Karlovich <i>et al.</i> , 2020)
	UK	≥ 20 years	83	(Kiani <i>et al.</i> , 2014)
	Sweden	≥ 11 years	660	(Sveinsson <i>et al.</i> , 2017)
	Finland	1 month – 16 years	245	(Sillanpää & Shinnar, 2013)
	North America	1-70 years	530	(Verducci <i>et al.</i> , 2019)
	Netherlands	4-69 years	179	(Vlooswijk <i>et al.</i> , 2007)
	West China	5-75 years	3 569	(Mu <i>et al.</i> , 2011)
	Kenya	0-50 + years	232 164	(Ngugi <i>et al.</i> , 2014)
	Cornwall, UK	2-82 years	93	(Shankar <i>et al.</i> , 2014)
	Korea	6-69 years old	35 638	(Ryu <i>et al.</i> , 2015)
	Toronto, Canada	19-65 years	24	(Pollanen & Kodikara, 2012)
	Victoria, Australia	11 month-70 years	357	(Opeskin <i>et al.</i> , 2000)
	Victoria, Australia	4-71 years	166	(Opeskin & Berkovic, 2003)
	Norway*	20-40 years	26	(Aurlien <i>et al.</i> , 2012)
	New Zealand	1.5-67 years	190	(Brennan, Scott & Bergin, 2020)
	Istanbul, Turkey	1-60 years	112	(Melez <i>et al.</i> , 2017)
	China	2-80 years	1562	(Ge <i>et al.</i> , 2017)
Denmark	1-35 years	33 022	(Holst <i>et al.</i> , 2013)	
Turkey	24-56 years	9	(Gungor <i>et al.</i> , 2016)	
Stroke	Japan	≥ 20 years	1 934	(Nagata <i>et al.</i> , 2013)
	Denmark	1-49 years	14 567	(Ågesen <i>et al.</i> , 2018)
SCD	UK	16-43 years	80	(Krexī & Sheppard, 2017)
	Brazil	10-80 years	899	(Braggion-Santos <i>et al.</i> , 2014)
	UK	< 35 years	1 033	(Finocchiaro <i>et al.</i> , 2018)
	Israel	18-39 years	151	(Amital <i>et al.</i> , 2004)
	Toronto	2-45 years	2 937	(Allan <i>et al.</i> , 2019)
	Germany	19-40 years	10	(Hellenthal <i>et al.</i> , 2017)

Table 1.4 continued: Main causes of death associated with SUD as identified in literature reviewed.

Leading cause of death	Region	Age group	Study size (n)	Reference
SCD	Minnesota, Tuscany & Genoa	7-78 years	744	(Maron <i>et al.</i> , 2000)
	Spain	14-50 years	52	(Campuzano <i>et al.</i> , 2017)
	North Carolina	18-64 years	190	(Lewis <i>et al.</i> , 2016)
	Denmark	1-49 years	1 066	(Risgaard, 2016)
	Denmark	1-35 years	625	(Winkel <i>et al.</i> , 2011)
	Bosnia & Herzegovina	15-80 years	421	(Omerkić <i>et al.</i> , 2009)
	Northwest China	< 75 years	1 244	(Zhang <i>et al.</i> , 2019)
	Ontarro, Canada	28 days - 18.8 years	80	(Sanatani <i>et al.</i> , 2006)
	India	18-35 years	64	(Chaturvedi <i>et al.</i> , 2011)
	Italy*	12-35 years	300	(Corrado <i>et al.</i> , 2003)
SCD/ Pneumonia	Cape Town, South Africa	≥ 18 years	816	(Tiemensma & Burger, 2012)
Pneumonia	Pretoria, South Africa	1-18 years	98	(van Deventer, Rossouw & du Toit-Prinsloo, 2016)
Pulmonary embolism	Spain	1-35 years	243	(Romero, Gálvez & Gonzalez, 2017)
Asthma	Denmark	1-35 years	49	(Gullach <i>et al.</i> , 2015)
*Note: studies marked with an asterisk denote a sub-group of the country's population was included in the study				

Out of the studies reviewed, almost half (49 %) had epilepsy-related causes of death, followed by cardiac-related (33 %), with the remaining causes of death comprising less than 5.0 % each.

1.3.2. SUDY in the South African population

Pneumonia, ischaemic heart disease, tuberculosis (TB) and thrombo-embolism seemed to be the common causes of death in the South African studies (Tiemensma & Burger, 2012; van Deventer, Rossouw & du Toit-Prinsloo, 2016), however, this was based on only two studies. Risk factors were identified for each of these causes and are presented below. Some associations made by Tiemensma & Burger (2012) were that pneumonia and ischaemic heart disease were the common causes of natural death in both females and males, whereas pulmonary TB was more associated with males and thrombo-embolism with females. In cases where cause of death was

ascertained following routine investigation, pneumonia was prominent in the age group of 1-5 years in the Pretoria, Gauteng study (van Deventer, Rossouw & du Toit-Prinsloo, 2016). This is in contrast to infectious diseases being associated with the age group of 18-29 years in the Eastern Metropole of the City of Cape Town, Western Cape SUDA study (Tiemensma & Burger, 2012).

Some of the risk factors associated with the SUDA cases (aged eighteen years and above) in the Western Cape were acute alcohol poisoning and substance use such as “antidepressants, anticholinergic medication, anticonvulsant medication, morphine and MDMA” (Tiemensma & Burger, 2012). Moreover, prior medical history demonstrated that hypertension and TB were reported in numerous cases. Whilst these studies have highlighted causes of death in the South African population, many still remain ‘undetermined’ or ‘unspecified’ thus signifying the value of post-mortem genetic testing in detecting underlying conditions which could be of cardiac origin (van Deventer, Rossouw & du Toit-Prinsloo, 2016). To date, these are the only studies encompassing the SUDY age group in South Africa. There is thus a need to collate data on SUDY cases, which encompass a wide array of ages, from other mortuaries in the Western Cape. SRM is one of the two busiest mortuaries in the Western Cape, serving the Western Metropole of the City of Cape Town. It is an academic mortuary that currently investigates approximately 4 000 deaths per year and should thus be evaluated for SUD.

1.3.3. Common causes of death and risk factors in international populations

1.3.3.1. Sudden cardiac death

Although Winkel *et al.* (2011) stated that SCD in children and adults had not been as thoroughly investigated as compared to infant studies, it is an area of research that has begun to gain substantial attention due to increasing prevalence of undetermined SUD cases. Studies on SCD generally encompass the ages of one to 35 years (Burns *et al.*, 2017). However, some studies have identified SCD to affect individuals up to 80 years of age wherein majority of deaths occur above 40 years of age (Braggion-Santos *et al.*, 2014). Nevertheless, these studies do provide insight into SCD predisposition.

According to Maron *et al.* (2014), cardiac conditions such as inherited cardiomyopathies, channelopathies and ischaemic heart disease are a well-known

cause of death in the young. However, this may differ in the South African population, but this is currently unknown. Recently, molecular studies have been performed, highlighting that fatal cardiac conditions are often due to inheritable genetic variants (Farwell & Gollob, 2007; Campuzano *et al.*, 2017; Hellenthal *et al.*, 2017). Studies have identified several risk factors for SCD which can be beneficial for at-risk relatives. To this end, future investigations should aim to identify high-risk individuals and promote genetic and/or clinical screening, with the intention of providing a medically actionable or preventative intervention to ultimately reduce the number of SUD cases (Burns *et al.*, 2017).

These risk factors, to varying extents, include physical endurance, hypertension, smoking, diabetes, and obesity (Amital *et al.*, 2004; Braggion-Santos *et al.*, 2014; Finocchiaro *et al.*, 2018; Allan *et al.*, 2019). Obesity, however, is not always a contributory factor to SCD. In the study by Finocchiaro *et al.* (2018) on individuals with SCD under 35 years of age, only 20 % of their study population was considered obese (BMI \geq 30). Nevertheless, it is a risk factor to be considered in understanding this condition. Furthermore, medicinal and illicit substance use (Braggion-Santos *et al.*, 2014; Allan *et al.*, 2019), familial history, asthma and hypercholesterolemia (Amital *et al.*, 2004) have also been implicated. In terms of demographics, men are often more affected than women (Skinner *et al.*, 2011; Braggion-Santos *et al.*, 2014; Allan *et al.*, 2019), however, this may fluctuate depending on the study population analysed.

Winkel *et al.* (2011) mentions that literature pertaining to population sub-groups is more prevalent than nationwide studies due to public awareness campaigns and media coverage of these deaths. Nevertheless, these studies do provide insight into locally relevant or population-specific risk factors and should thus not be overlooked. For example, a study by Amital *et al.* (2004) conducted on military personnel further supports that cardiac diseases are a well-known cause of SUD. In this study, ischaemic heart disease was predominantly in the age group of 30-39 years accounting for 84 % of deaths, as compared with 9.7 % in the age group of 18-29 years.

In terms of the young athlete sub-group, literature has also demonstrated that individuals with a family history of cardiac disease are also prone to SCD due to physical exertion which exacerbates fatal cardiac arrhythmias (Corrado *et al.*, 2003). Unlike the risk factors mentioned above, these deaths were inclusive of hyperthermia

with subsequent central nervous system (CNS) dysfunction due to heat stroke, CNS trauma, uncontrolled asthma and vessel rupture due to injury especially in the neck (Maron *et al.*, 1980).

Although the studies mentioned above exclusively pertain to SCD, other studies have demonstrated that cardiac conditions are often interlinked with SUDEP thus concomitantly leading to sudden death (Burns *et al.*, 2017; Melez *et al.*, 2017). Therefore, understanding SUDEP as a cause of death is also imperative.

1.3.3.2. Sudden unexpected death in epilepsy

Although SUDEP can be observed in all age groups, it is considered to be most prevalent in individuals aged 20-40 years (Holst *et al.*, 2013; Shankar *et al.*, 2013), thus comprising the upper end of the SUDY age group. Findings concerning SUDEP risk factors have been diverse, hence further research and analysis is required to exhibit potential SUDEP risk factors in a clear and concise manner.

While many studies have concluded well-defined risk factors for SUDEP as grand mal seizures, use and lack of use of antiepileptic drugs (AEDs) and polytherapy (Burns *et al.*, 2017; Melez *et al.*, 2017; Brennan, Scott & Bergin, 2020), many have noted mental disabilities (Hesdorffer *et al.*, 2011; Holst *et al.*, 2013) and the administration of anxiolytic drugs (Harden *et al.*, 2017) to be associated with these deaths. Examples of AEDs that had been administered included sodium valproate and carbamazepine (Aurlien *et al.*, 2012; Brennan, Scott & Bergin, 2020), which may have also been used to treat mood disorders. In a case-control study by Aurlien *et al.* (2012), the use of lamotrigine for both mental disability and seizure control had been highly associated with SUD in females. Other substances such as recreational drugs, alcohol, antidepressants and antipsychotic drugs had also been noted (Brennan, Scott & Bergin, 2020).

Hesdorffer *et al.* (2011) declared that male sex and early-onset epilepsy are also potential risk factors for SUDEP, which is supported by numerous studies (Holst *et al.*, 2013; Ge *et al.*, 2017; Melez *et al.*, 2017; Brennan, Scott & Bergin, 2020). The circumstances surrounding these deaths have also been documented in numerous studies (Melez *et al.*, 2017; Brennan, Scott & Bergin, 2020), however, individuals found alone are noteworthy as these individuals may have suffered a seizure which could

have been controlled had a witness been present. Although the position in which the deceased is found is often documented as being prone, this may not necessarily be a risk factor for SUDEP but rather a consequence thereof. Overall, it is evident that these risk factors demonstrate some overlap with those of SCD thereby substantiating that a more comprehensive investigation into these deaths is required.

1.3.3.3. Respiratory-related deaths

Mathews *et al.* (2016) conducted a study at SRM, wherein the child (1-14 years) mortality rate was established as 34 per 100 000 live births with 60.6 % of deaths attributed to natural causes and 4 % remaining undetermined. In addition, this study highlighted that deaths of children over the ages of 14 years tended to occur in public spaces as compared to younger children who died at home where the principal cause of death was pulmonary-related infections (Mathews *et al.*, 2016). However, this is one of the few studies which assessed pulmonary-related deaths in the young and thus the need for further investigation is highlighted.

In a study by Chaturvedi *et al.* (2011), whereby SUD accounted for less than 1 % of the population analysed, all cases of respiratory-related disease were female where causes of death were due to infection. Analogous to the study by Tiemensma & Burger (2012), these infections included pneumonia and TB. Although marginal, asthma and pulmonary embolism have also been observed as a cause of SUD (de la Grandmaison, 2004; Manu, Kane & Correll, 2011; Berg *et al.*, 2013; Braggion-Santos *et al.*, 2014).

A study was performed in Denmark on SUDY cases where individuals previously had uncontrolled asthma (Gullach *et al.*, 2015). Asthma is a common chronic condition amongst young individuals in Western regions and the presence of other health conditions and diseases, such as long-QT syndrome, may propagate sudden death. At autopsy, there may be histological signs of conduction system abnormalities (Gullach *et al.*, 2015). However, asthma may only be identified as a contributory factor, should there be a previous medical history of the condition, as signs of this condition are not exclusively present. Medical history may note that asthmatic individuals had symptoms such as chest pain, palpitations, fatigue and seizures prior to death, had

there been a witness in their presence (Gullach *et al.*, 2015). Nevertheless, asthma as a cause of SUDY is a perplexing matter.

A pulmonary embolism, conversely, is a pathological condition common to individuals aged 1-35 years (Romero, Gálvez & Gonzalez, 2017). It is a blood clot that often originates in the deep veins of the leg and subsequently travels to the lung, whereby it results in vasoconstriction, ultimately leading to death. More than 90 % of cases go undiagnosed and thereby do not receive the necessary treatment to prevent fatalities (Konstantinides *et al.*, 2014). Konstantinides *et al.* (2014) found that older individuals are more prone to the condition as compared to young. Risk factors such as prolonged immobilisation, a clinical and family history of the disease, use of oral contraceptives, age and pregnancy have all been associated with pulmonary embolisms (Romero, Gálvez & Gonzalez, 2017). Risk factors were inclusive of trauma, morbid obesity, kidney disease and a clinical history demonstrating inadequate treatment for symptoms such as limb pain and arrhythmias. The presence of recent ingestion of psychotropic drugs and alcohol was also identified, as well as cocaine metabolites. Although the number of SUDY cases due to a pulmonary embolism are few globally, it should be considered in cases of SUD, especially in patients with a history of surgery and trauma (Dempers & Van Vuuren, 2006).

Despite there being common risk factors amongst the literature reviewed, it is evident that some of these variables merely suggest potential inheritable conditions and do not stand as a confirmation of the inherited disease; unless supported by post-mortem genetic testing *i.e.* molecular autopsies.

1.3.4. Molecular autopsies

Upon routine investigation, the cause of death is often conclusive. However, in some cases, the cause of death may be inconclusive, unspecified (even if deemed as natural) or undetermined (Sanchez *et al.*, 2016). These cases therefore warrant further research and novel investigative techniques such as a molecular autopsy (Dewar *et al.*, 2015), a method using (often retrospectively collected) biological samples to establish genetic abnormalities resulting in these deaths. A molecular autopsy thus potentially aids in defining cause of death. This is supported by a study by Skinner *et al.* (2011) wherein cases between the ages 1-40 years that remained undetermined

following post-mortem investigation underwent genetic analysis and long QT syndrome was identified as the cause of death in 15 % of cases.

The neurological, cardiac, and pulmonary conditions mentioned above could potentially compromise the health of surviving relatives as several of these are inheritable. Therefore, the collection of biological samples is pivotal so that the necessary investigative techniques can be applied which may assist in reducing the SUD rates. Therapeutic interventions can also be implemented to both manage and prevent these potentially diagnosed genetic disorders (Semsarian & Hamilton, 2012). However, biological materials are often not retained for molecular autopsies to be performed, due to it being discretionary rather than mandatory by law, and thus these conditions may go undetected (Dewar *et al.*, 2012).

Not only has the documentation of these variables allowed for inheritable conditions amongst the young to be identified, but it has also emphasised the value of post-mortem molecular testing. Moreover, it has assisted researchers in identifying which genetic variants to screen for. Therefore, these studies have provided insight and motivation for similar studies to be performed in a local context.

1.4. Rationale

Studies pertaining to incidence and risk factors in SUDY have been conducted in many developed countries and although this aids in understanding possible risk factors concerning individuals in these geographical regions, it does not necessarily highlight the risk factors prevalent in the South African population which comprises primarily of individuals of African and Admixed ancestries. Nevertheless, these studies have underlined the importance of acquiring the relevant information in resolving cause of death of these tragic SUDY cases.

Whilst many of these studies have investigated risk factors in SUDC and SUDA, few have investigated SUDY specifically, and more so from a South African perspective. As highlighted by Tiemensma & Burger (2012), there is a need to explore SUD so as to better understand the risk factors contributing to and surrounding these deaths. It is inferred that by obtaining information surrounding the clinical and social history of the deceased, it could potentially identify risk factors that increase the risk for (or predispose) individuals to SUD.

With respect to SRM, there is a deficit of research on individuals classified under SUDY and as a consequence of this, an unknown incidence. Establishing the number of SUDY admissions pertaining to SRM will allow us to determine the burden that these cases place on this mortuary. Additionally, data pertaining to the demographics, social and clinical history, cause of death and extent of the post-mortem investigation conducted of these cases, have previously not been well-documented in the literature. Moreover, it is not evident as to how many of these cases remain 'undetermined' following post-mortem and could possibly benefit from the developing molecular autopsy; and of these, how many have stored biological material to aid in defining the cause of death.

SRM serves the Western Metropole of the City of Cape Town and specifically encompasses the catchment areas of 'Western, Southern, Klipfontein and Mitchells Plain districts' (Clark, Mole & Heyns, 2016). The percentage of these SUDY cases wherein cause of death still remains undetermined should be calculated for SRM, to allow for comparison with data obtained from other mortuaries within South Africa, such as Tygerberg (Tiemensma, 2010) and the Pretoria Medico-legal Laboratory (van Deventer, Rossouw & du Toit-Prinsloo, 2016). Furthermore, this data will add to the current body of literature.

The 'undetermined' cases that are identified in this project as having biological samples available, can be prioritised for future research and/or testing. This may include molecular autopsies, to aid in identifying genetic abnormalities, which may assist in resolving cause of death. Although this project will not incorporate molecular genetic testing, it will seek to identify individuals who may be candidates for additional genetic testing, whereby an undiagnosed genetic disease may have predisposed or contributed to death. If genetic abnormalities that are potentially contributory to the death of an individual are detected, this will eventually allow for these high-risk individuals to potentially receive screening for these abnormalities in future research (Vaartjes *et al.*, 2009).

Determining these genetic factors and statistics will not only allow one to gain knowledge of SUDY cases at SRM, but also contribute to the public health sector as individuals can receive education on the risk factors that could potentially lead to SUD. This will allow these individuals to make the necessary lifestyle changes, thereby improving their health and mitigating risk for these fatalities; which aligns to the third

SDG. Furthermore, should population sub-groups such as young athletes be identified as at-risk individuals, awareness campaigns at various athletic facilities could be established to promote awareness about SUDY risk factors.

In conclusion, this literature review has substantiated the need for South Africa to adopt similar protocols as those applied internationally in order for the number of undetermined SUDY cases to be reduced. Fundamentally, it has provided insight into more comprehensive post-mortem investigation process through the inclusion of molecular testing. Although cause of death has been primarily cardiac and neurological in nature according to literature, the South African population may not be alike. There may be varying risk factors within the SUDY age group (1-40 years) as demonstrated in previous publications and thus documenting the ages and sub-categorising this age group is necessary.

1.5. Aim and objectives

Therefore, motivated by the literature critically evaluated in this review, the aim of this research project was to retrospectively investigate the burden and profile of SUDY cases, admitted to SRM, Cape Town, between 1 January 2016 and 31 December 2018.

To this end, this research project sought to achieve the following objectives:

- Determine the number of SUDY admissions to SRM during the stipulated period
- Document the demographics, post-mortem details, and cause of death outcome in these cases
- Determine the number of cases which remained 'undetermined'
- For cases classified as natural, undetermined or under investigation, document the social and clinical history, and which have biological samples available

CHAPTER 2: METHODS

2.1. Study design

The study was a quantitative, retrospective, and cross-sectional investigation of medico-legal records concerning SUDY admitted to SRM for a three-year period from 1 January 2016 to 31 December 2018.

2.2. Characteristics of study population

Deaths which were “sudden, unexpected and unexplained” as per the Inquest Act (Act 58 of 1959) were considered in this study. This study focused on all SUDY admitted to SRM from the years 2016-2018 (inclusive) within the age group of 1-40 years.

2.3. Ethics

Ethical approval for this study was granted by the Human Research Ethics Committee of the University of Cape Town (HREC Ref: 171/2020) (Appendix A).

2.4. Data collection

Autopsy records for the stipulated time period were obtained from the Office Autopsy Database (HREC: R036/2014) with authorisation from the FPS Clinical Head at SRM (Appendix B). These records were filtered and reviewed to identify the SUDY cases after which medico-legal cases folders of these cases were retrieved from the archives.

The following documentation was consulted during data collection: Identification Documents (ID) or birth certificate, ‘Contemporaneous Note (Lab. 27): Salt River Forensic Pathology Laboratory’, FPS 006(a) FPS 006(b) questionnaire for SUD of adults and young children respectively, ‘South African Police Service sudden and unexpected death in adults’ form, ‘Road to Health Card’ and an ‘Affidavit in terms of Section 212(4), Act 51 of 1977’ generated by the forensic pathologist on the post-mortem conducted. The contents affiliated with each of these documents have been summarised (Appendix C).

The variables that were collected from these documents included demographics, post-mortem details, circumstances surrounding death, cause of death, as well as the social and clinical history relevant to these SUDY cases (For a full list: Appendix D). The data were captured on a single workbook using Microsoft Excel® 2016 in a macro-enabled file format, wherein certain variables only pertained to certain cases as depicted (Appendix D).

Regarding the post-mortem details, a full body low dosage x-ray (LODOX) Xmplar-DR (Lodox Systems, Johannesburg) is performed in all cases at SRM prior to further investigations. The 'external' post-mortem does not require incisions for biological sample retention as ancillary investigations are not usually performed, whereas the 'full' post-mortem comprises of a complete internal organ dissection with possible ancillary investigations. Furthermore, the 'partial' post-mortem comprises of dissection of a targeted organ; mainly the neurological region or chest cavity. Both 'full' and 'partial' may include ancillary investigations should the forensic pathologist deem it necessary.

Ancestry, as per the FPS 006(a) or (b) form, was only collected for undetermined cases that were positively identified and with biological samples available, as these cases would be candidates for a future a molecular autopsy. The variable of 'ancestry' would guide which mutations to screen for in future studies, given the population differences in allele frequencies (Nel, 2017). However, the results pertaining to ancestry will not be presented herein. Lastly, where discrepant information was noted between South African Police Services (SAPS) and FPS records, the information provided to FPS was used.

Double entry validation was performed on all data captured to minimise discrepancies. These cases were captured independently and thereafter compared against the original workbook to ensure accuracy and consistency. Prior to statistical analysis, the cases were recoded using a unique study number to ensure anonymity.

2.5. Data analysis

The percentage of SUDY admissions was calculated based on the number of SUDY cases admitted to SRM out of the total cases during that period, and the sub-group of 'undetermined' cases was tallied and noted. When analysing age data in a biomedical

setting, a standard sub-grouping divides ages into five-year categories, for example, 0-4 years, 5-9 years, *etc.* (Statistics Canada, 2017). However, due to scarce observations, multiple testing and the exclusion of infants (< 1 years old), age categories were formed in ten-year increments (*i.e.* 1-10 years, 11-20 years, 21-30 years, 31-40 years). Basis for these age categories was as a result of a previous publication in a forensic setting (Faduyile *et al.*, 2017), as well as recent COVID-19 statistics on infection rates by age across the South African population (Hartle, 2020; Spaul, 2020). This sub-grouping subsequently allowed for effective statistical procedures to be performed and the retention of meaningful information on which individuals were most at-risk.

In terms of social history, substances of abuse, and participation in physical activity were evaluated. However, in the age category of 1-10 years, additional aspects of social history were evaluated which included 'maternal level of education' and 'annual household income'.

In terms of clinical history, use of medicinal substances, symptoms that preceded or transpired at death, medical history and family history were evaluated. All aspects of social and clinical history have been graphically represented ranked from highest to lowest for each of the age categories. Furthermore, they have been divided per sex for each sub-category. Where clinical history variables contributed less than 6.0 % each, these were grouped together as 'other', but the detailed breakdown of all data can be found in Appendix E.

Statistical tests performed on the data to address the aims and objectives of this study included a test of proportions, Wilcoxon rank-sum (Mann-Whitney) test, Chi-squared and Fischer's Exact. A p-value of 0.05 was considered to be statistically significant and where multiple tests were performed, a post-hoc Bonferroni's correction factor was applied. Significant p-values have been denoted by an asterisk in figures and tables. To identify whether significant differences exist, variables were compared per sex for each age category.

The software used for analyses and for visualisation was Stata Version 15 and Microsoft Excel 2016. The data has been reported herein in a collective format using percentages, graphs, and tables to ensure anonymity. However, in many cases information was not available for every variable either due to lack of response, missing

documentation or it was not specified. This means that each variable has a different denominator which represents the number of cases for which this data was available. Therefore, the percentages portrayed have been calculated from the available data pertaining to that variable. For more information on these amounts of missing data, see Appendix E.

CHAPTER 3: RESULTS

3.1. Burden of SUDY at SRM

A total of 11 588 cases were received at SRM for the three-year period between 1 January 2016 and 31 December 2018 with an average of 3 863 cases annually. There was a considerable increase in the percentage of SUDY cases between 2016 (195/3 660; 5.3 %) and 2017 (315/3 885; 8.1 %), followed by a minor decline in 2018 (323/4 043; 8.0 %). Nevertheless, out of the total cases for the three-year period, 833/11 588 (7.2 %) were SUDY cases and thus included for further analysis (Figure 3.1). All cases which were under investigation, undetermined or had non-specific natural causes were identified as candidates for future molecular autopsies (176/833; 21.1 %). Fortunately, 144/176 (81.8 %) of candidate cases had biological samples available for these future investigations. Biological samples available for molecular autopsies were tallied, wherein 46 cases had blood, 12 cases had formalin fixed paraffin embedded (FFPE) tissue and 86 cases had both.

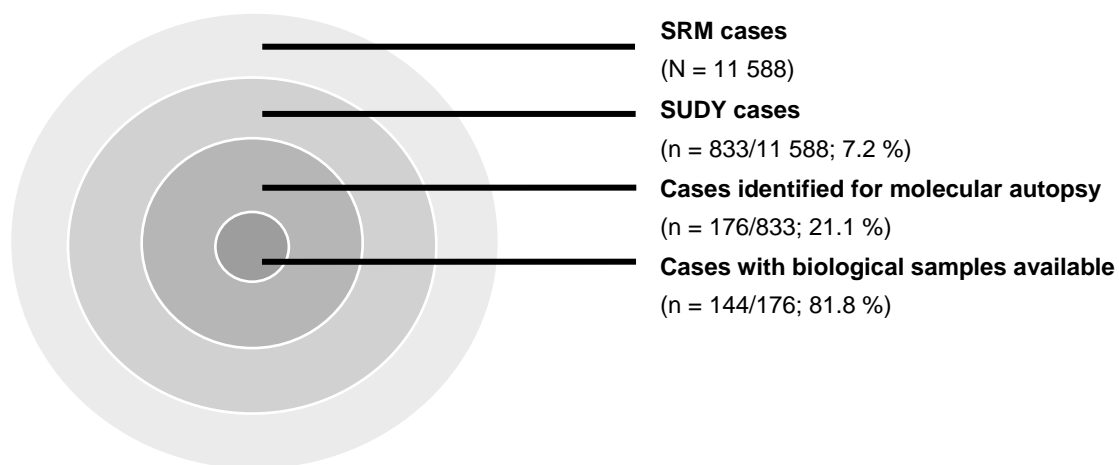


Figure 3.1: Onion chart describing the total number of cases admitted to SRM between 01 January 2016 and 31 December 2018, and the subsets of cases relevant to this study. SUDY cases comprised 7.2 % of the cases admitted to SRM.

SRM: Salt River Mortuary. SUDY: sudden unexpected death in the young.

3.2. Demographics of study population

Upon admission, the demographic details of the study population were documented. Males comprised the majority of cases (536/833; 64.3 %) and the median age of SUDY individuals was 31 ± 10.3 years. While perhaps not clinically relevant, the median age

for males (31 ± 10.2 years) was significantly different from that of females (29 ± 10.5 years) ($p = 0.01$) (Figure 3.2).

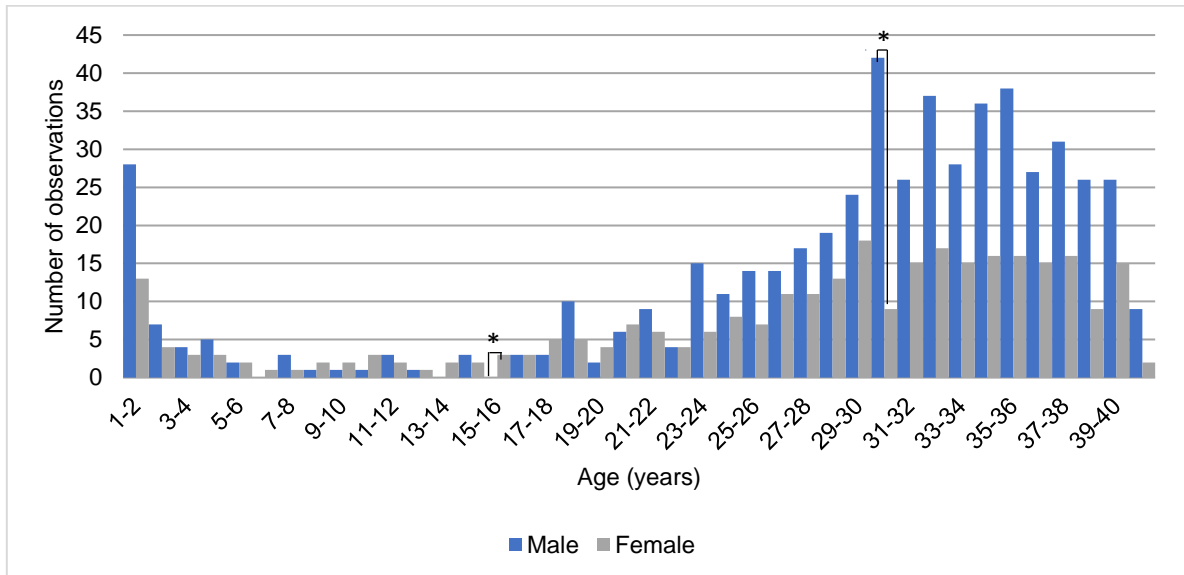


Figure 3.2: Age distribution between males and females in SUDY cases. Males comprised the majority of the study population (536/833; 64.3 %). The median age of the SUDY population was significantly different between males and females, specifically in the 15-16 year old and 30-31 year old age brackets (denoted by an asterisk).

3.3. Profile of SUDY cases

When considering the profile of these cases, factors such as geographical location, day of the week, month of year and circumstances surrounding death were reviewed. Identified geographical hotspots, wherein almost a quarter of SUDY cases had occurred (199/833; 23.9 %), were the neighbouring suburbs of Nyanga and Gugulethu (Figure 3.3).

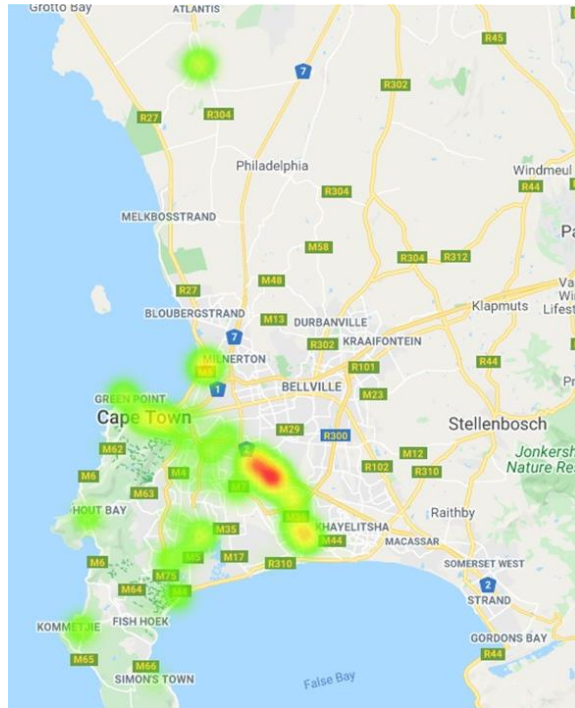


Figure 3.3: Heatmap of SUDY cases admitted to SRM. Red denotes the suburbs with hotspots, namely Nyanga and Gugulethu.

There was a relatively even distribution of SUDY cases over the week, with an increase in deaths over the weekend period for individuals aged 21-40 years. (Figure 3.4).

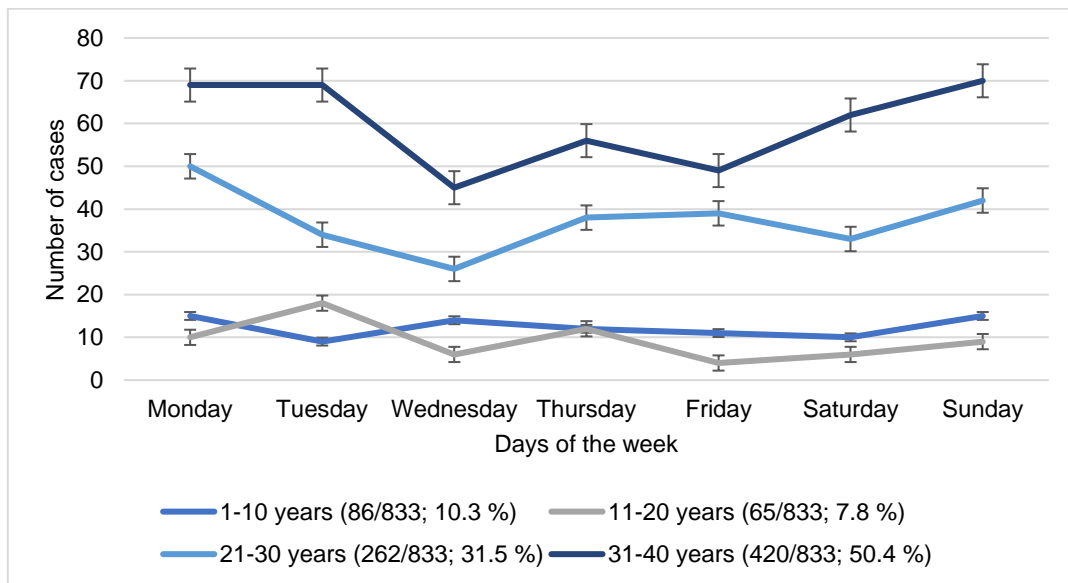


Figure 3.4: Days of the week portrayed for SUDY cases wherein cases were fairly even distributed throughout the week for individuals below 20 years with an escalation on weekends for individuals above 21 years.

Cases aged 1-20 years were fairly evenly distributed over the months. However, in the 21-30 year age group, there was a spike in June with a slight upward trend until December. In the 31-40 year age group, there was an upward trend throughout the year except for plummets in May and August. (Figure 3.5).

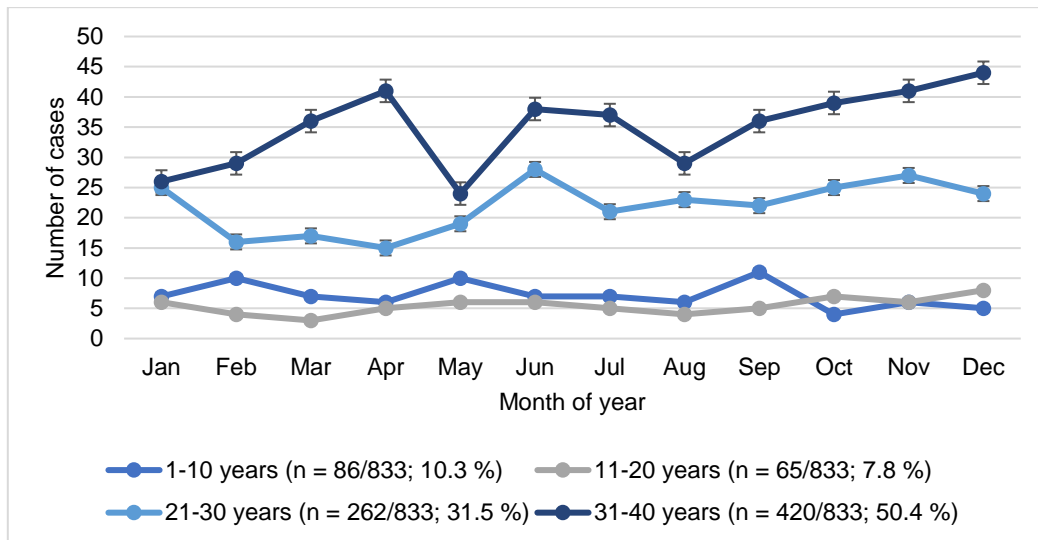


Figure 3.5: Median SUDY cases per month of year for the different age categories. December was the month with the most SUDY cases overall.

The circumstances surrounding death were reviewed which showed that in almost half of the cases, activity at death had not been specified during the interview with the family (372/833; 44.7 %) and in a further 18.4 % (153/833) of cases, it was unknown as a result of being unwitnessed. However, when it was specified, death occurred during sleep (176/308; 57.1 %), during rest (79/308; 25.6 %) or whilst walking (21/308; 6.8 %). The remainder of the activities did not have any major contribution (< 3.0 % each) (Figure 3.6). Furthermore, when comparing activity at death, no significance was identified between males and females per each age category.

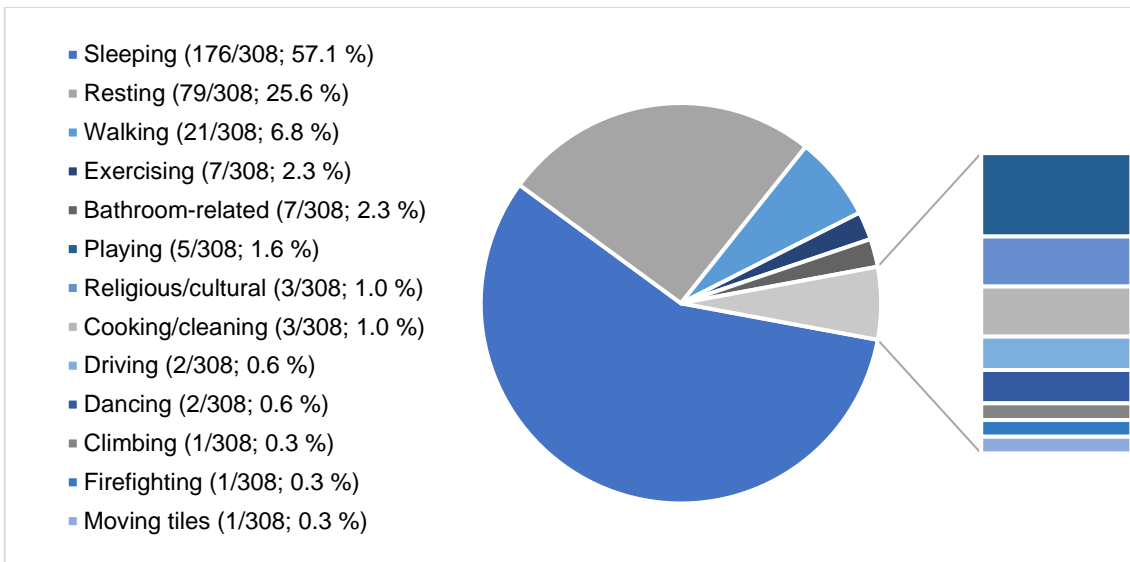


Figure 3.6: Varying activities at death. The leading activities at death were sleeping (176/308; 57.1 %), resting (79/308; 25.6 %) and walking (21/308; 6.8 %).

The main position of individuals was lying down (430/452; 95.1 %), most commonly in the supine position (Figure 3.7). However, in 45.7 % (381/833) of the cases, the position at death was not specified. The minority of cases were reported to be ‘sitting’ (14/452; 3.1 %). No significance was identified between males and females per each age category when comparing position at death.

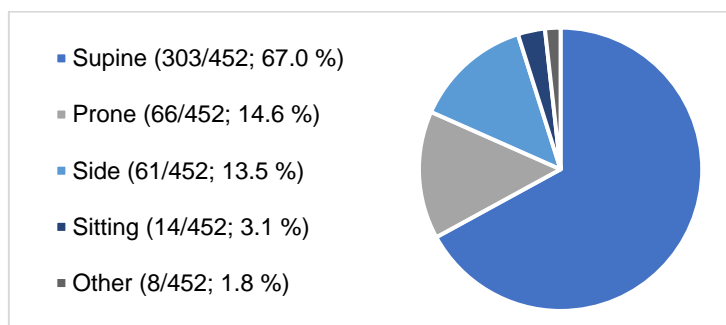


Figure 3.7: Varying positions of the deceased at death. The main position at death was supine (303/452; 67.0 %) followed by prone (66/452; 14.6 %).

The main location of death was residential (362/832; 43.5 %) followed by medical centre (292/832; 35.1 %) and outdoors (96/832; 11.5 %) (Figure 3.8). There were also significantly more males than females in the age category of 31-40 years who were found outdoors at death compared to all other locations ($p < 0.001$).

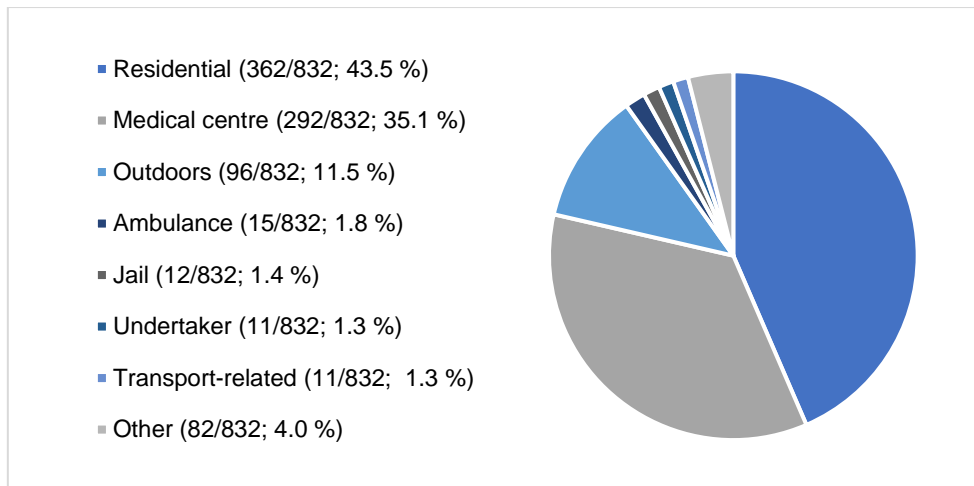


Figure 3.8: Counts and percentages of varying locations at death. Most SUDY cases occurred in residential locations (362/832; 43.5 %), medical centres (292/832; 35.1 %) and outdoors (96/832; 11.5 %).

3.4. Post-mortem details

The post-mortem examination was conducted by the forensic pathologist with the purpose of determining cause of death. The mean number of days between the date of death declaration and date of post-mortem was 4 ± 4.6 days and ranged between 0 and 97 days. Alleged cause of death was documented in 581/833 (69.7 %) of SUDY cases, whereas the remainder were still being investigated and thus a final post-mortem report had not yet been issued. Nevertheless, of the cases where a preliminary or final post-mortem report was available (704/833; 84.5 %), the majority of cases had a full post-mortem examination (385/704; 54.7 %), followed by external (266/704; 37.8 %) and partial (53/704; 7.5 %) respectively.

The main ancillary investigation performed in these SUDY cases was LODOX (673/704; 95.6 %), followed by toxicology (205/704; 29.1 %), histology (198/704; 28.1 %) and microbiology (41/704; 5.8 %). Furthermore, in 2.4 % (17/704) of the cases, alternate ancillary investigations, such as genetics, haematology, biochemistry, immunology, and neuropathology were performed. In numerous cases, more than one ancillary investigation was performed to aid in establishing cause of death, and in four cases all categories of ancillary investigations were performed (Figure 3.9).

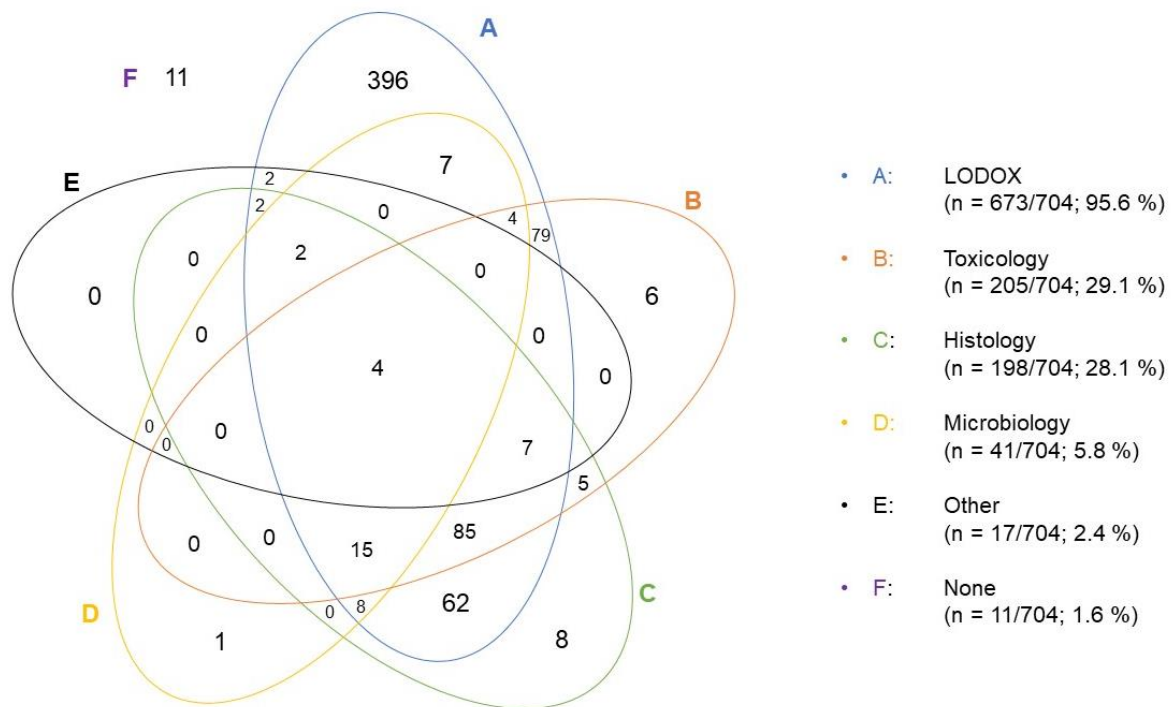


Figure 3.9: Venn diagram indicating counts of ancillary investigations performed. LODOX was the main ancillary investigation performed both solely (396/704; 56.3 %) and in conjunction with other ancillary investigations i.e. toxicology (79/704; 11.2 %).

LODOX: Low dosage X-ray

3.5. Cause of death outcome

The majority of SUDY cases were deemed to have demised from natural causes (515/833; 61.8 %), while 5.2 % (43/833) had unnatural causes following post-mortem examination. The minority of cases had undetermined causes of death (23/833; 2.8 %), while a further 123/833 (14.8 %) cases were still under investigation. Cases where post-mortem reports were unavailable or missing were marked as ‘unknown (missing)’ (129/833; 15.5 %) (Figure 3.10).

With respect to the unnatural cases, there was no need to further investigate these cases for risk factors or a genetic predisposition as the alleged cause of death was deemed to be from unnatural causes. Moreover, it is unknown whether the cases that were ‘unknown (missing)’ were either natural or unnatural and thus these were excluded from further analyses pertaining to risk factors to avoid assumptions.

Nevertheless, the unnatural deaths were mainly due to blunt trauma (13/43; 30.2 %), alcohol toxicity (6/43; 14.0 %), the ingestion of a noxious substance (6/43; 14.0 %), or the aspiration of gastric contents (6/43; 14.0 %) as depicted (Figure 3.10).

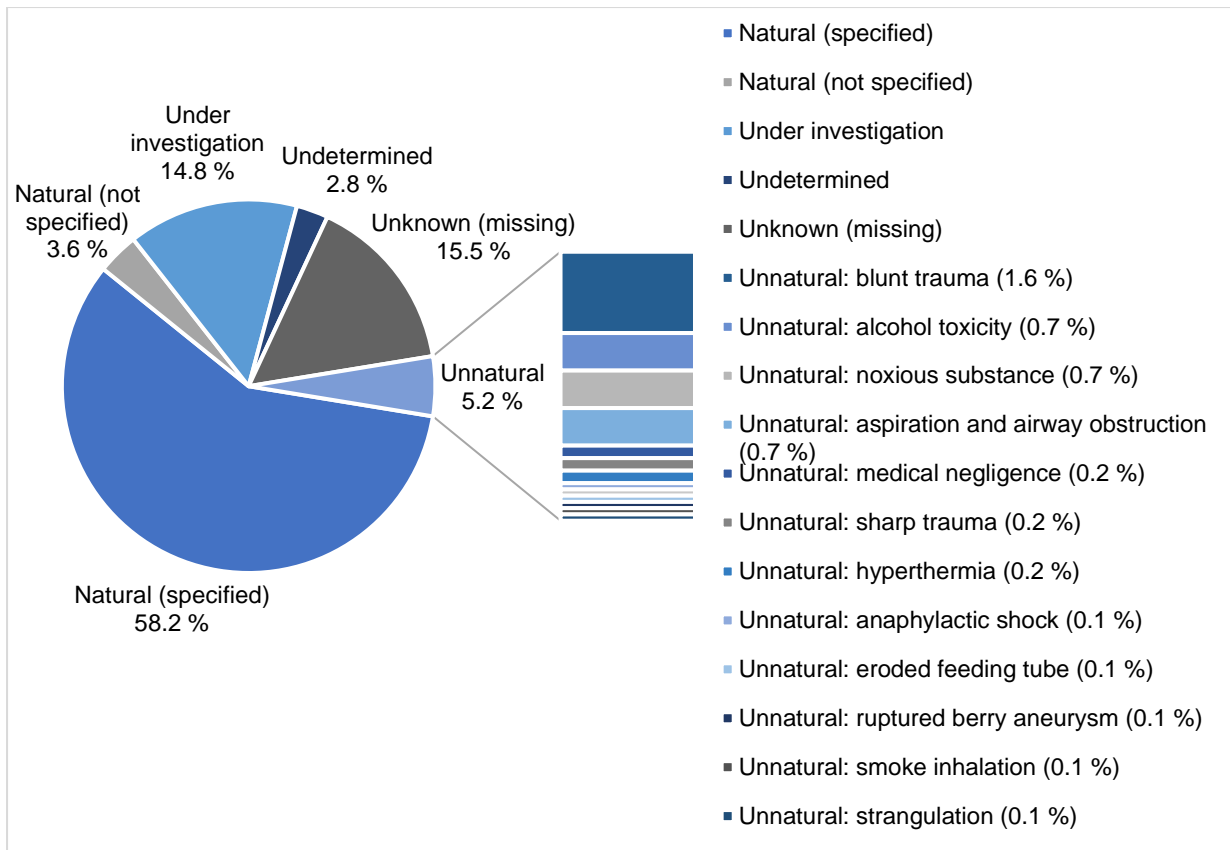


Figure 3.10: Alleged manner of death in all SUDY cases with specific cause of death for unnatural cases. Blunt trauma was the main unnatural cause of death to transpire (13/43; 30.2 %).

Of the natural cases, 485/515 (94.2 %) had specified natural causes which aligned to one or more organ system. The main organ systems involved in SUDY were pulmonary (235/485; 48.5 %), cardiovascular system (CVS) (153/485; 31.5 %), CNS (54/485; 11.1 %) and GIT (50/485; 10.3 %) (Appendix E). The ‘other’ organ system category included the lymphatic, integumentary, reproductive, endocrine, and multi-system (< 2.0 % each) (Figure 3.11). Moreover, infectious diseases accounted for 64.9 % (315/485) of specified natural cases overall.

There was an overlap between the pulmonary and CVS in 29/485 (6.0 %) cases, and there were significantly more males than females in the age category of 31-40 years whose cause of death pertained to the CVS compared to all other systems ($p = 0.02$).

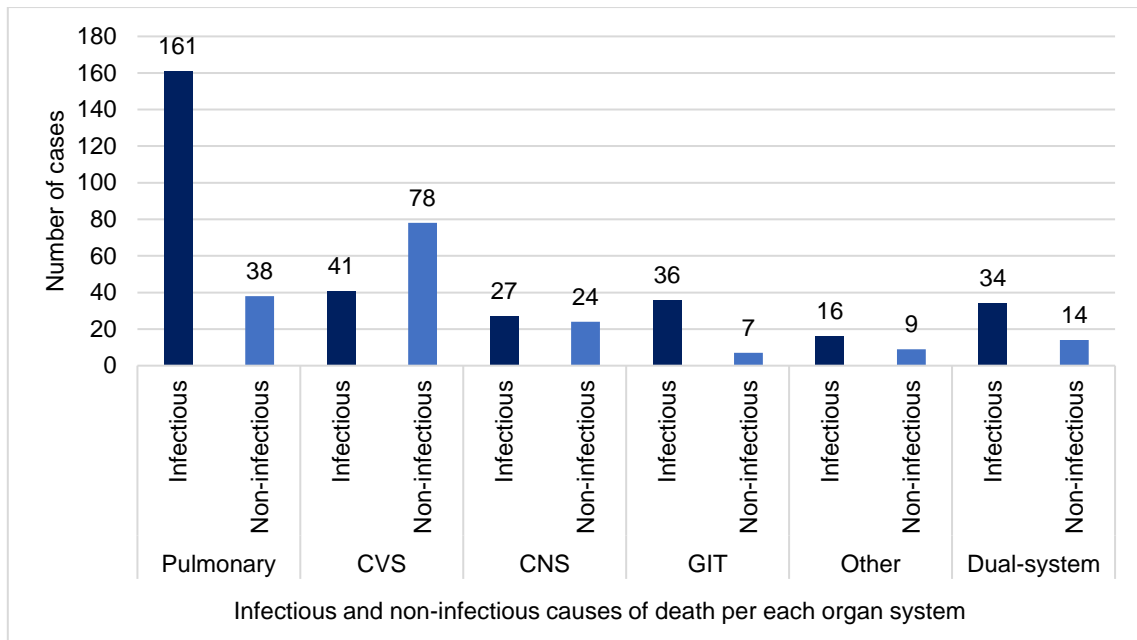


Figure 3.11: The main organ systems involved in natural deaths, wherein the causes of death in all organ systems except cardiovascular were predominately infectious in nature.

CVS: Cardiovascular; CNS: Central nervous system; GIT: Gastrointestinal

Cause of death was summarised for all specified natural cases, whereby the ‘other’ category accounts for causes of death with less than five cases per cause (Figure 3.12).

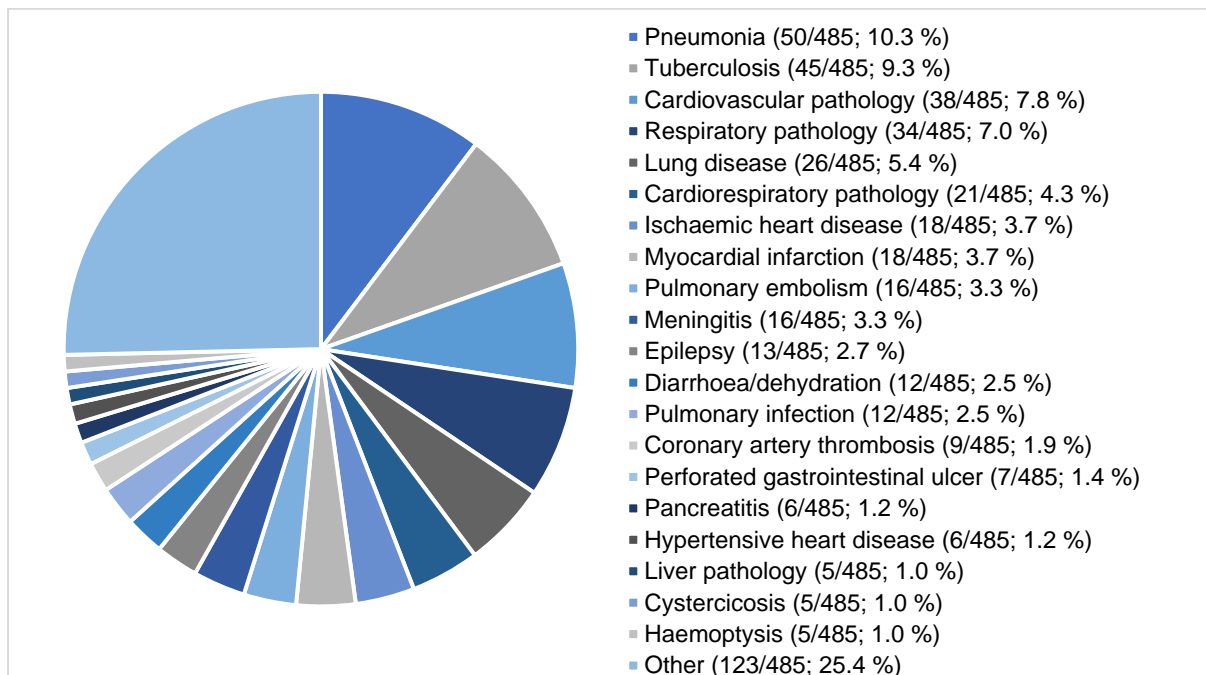


Figure 3.12: Summary chart of the specified causes of death involved in natural deaths. Pulmonary and cardiovascular-related causes of death were predominant.

There were more than 50 different causes of death, wherein the leading causes of death overall were pneumonia (50/485; 10.3 %) and TB (45/485; 9.3 %). Other pulmonary-related causes were non-specific respiratory pathologies (34/485; 7.0 %), lung disease (26/485; 5.4 %) and pulmonary embolism (16/485; 3.3 %).

Non-specific cardiovascular pathologies (21/485; 4.3 %), ischaemic heart disease (18/485; 3.7 %) and myocardial infarction (18/485; 3.7 %) were common causes pertaining to the CVS. Moreover, meningitis (16/485; 3.3 %) and epilepsy (13/485; 2.7 %) were the main causes pertaining to the CNS. Lastly, diarrhoea/dehydration (12/485; 2.5 %), perforated gastrointestinal ulcers (7/485 %) and liver pathology (5/485 %) were prominent in the GIT.

When analysing cause of death according to age categories, the major trend was that pneumonia was among the leading two causes of death per each age category (Appendix F). However, there were no significant differences between sex per age category for the varying causes of death.

3.6. Social and clinical history

The social and clinical history of the deceased was the final aspect reviewed which allowed for the identification of potential risk factors contributing to SUDY. These variables were collated for the SUDY cases which were natural, under investigation, and undetermined (*i.e.* those which were not unnatural).

3.6.1. Social history

Overall, more than half of SUDY cases (330/568; 58.1 %) engaged with one or more substance(s) of abuse. These substances were documented under three main categories: (i) alcohol (225/568; 39.6 %), whereby 75.1 % was beer (169/225), 26.2 % was brandy (59/225) and 22.6 % was wine (51/225); (ii) illicit drugs (133/568; 23.4 %), whereby Methamphetamine (72/133; 54.1 %), Cannabis (70/133; 52.6 %), and Mandrax (53/133; 39.8 %) were the main drugs used; (iii) tobacco products (181/568; 31.9 %), whereby 90.6 % were cigarettes (164/181). Engagement with alcohol and smoking occurred in 65/568 (11.4 %) cases and in 42 cases (7.4 %) all three substances were used (Figure 3.13).

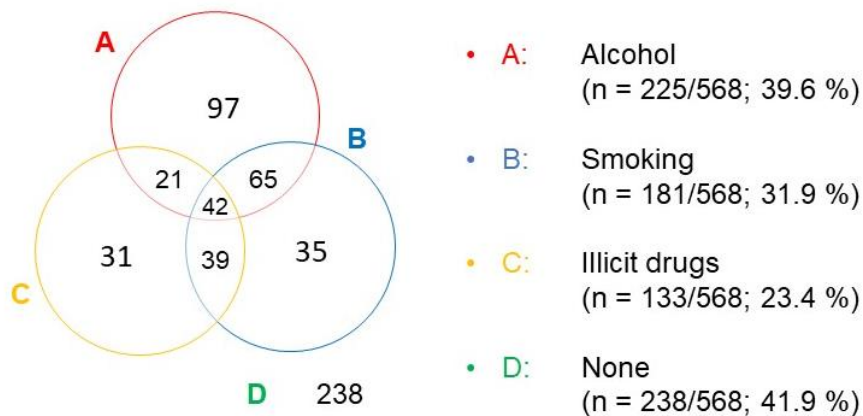


Figure 3.13: Venn diagram showing the number of cases where more than one substance of abuse was used. Numerous substances were used concomitantly and in 42 cases all substances were used. Alcohol was the main substance used both solely (97/568; 17.1 %) and in conjunction with another substance i.e. smoking (65/568; 11.4 %).

Although substances of abuse had not been used in the majority of cases in the age category of 1-10 year olds, engagement with smoking was noted in a single case (Figure 3.14). The specific substance, however, was not stipulated. The main substance of abuse used in the remaining three age categories was alcohol wherein more males had engaged with alcohol and smoking than females, but this was not of statistical significance. In the age category of 31-40 years, however, there were significantly more males than females who engaged with illicit drugs compared to all other substances of abuse ($p = 0.012$).

Of the 661 cases, 12 individuals were documented to have engaged with physical activity prior to death with a median age of 31 ± 10.3 years. Seven of these individuals (7/12, 58.3 %) were considered to have demised from cardiovascular causes and one from asthma (1/12; 8.3 %), while the remainder (4/12, 33.3 %) were still under investigation. A significant association was found between death during physical activity and individuals who had suffered demise due to a comprised CVS (7/8; 87.5 %) ($p = 0.011$), however, the sample size was very small.

Two additional aspects of social history were documented for the 1-10 year age category due to the vulnerability of these individuals. In 34/66 (51.5 %) cases, the maternal level of education was documented, wherein majority of these cases, the mother had a secondary (grade 8-12) education (31/34; 91.2 %) (Figure 3.14). Although household income was not documented in the majority of cases, when provided (10/66; 15.2 %), it had ranged from R 0 to R 120 000 per annum.

■ Yes ■ No

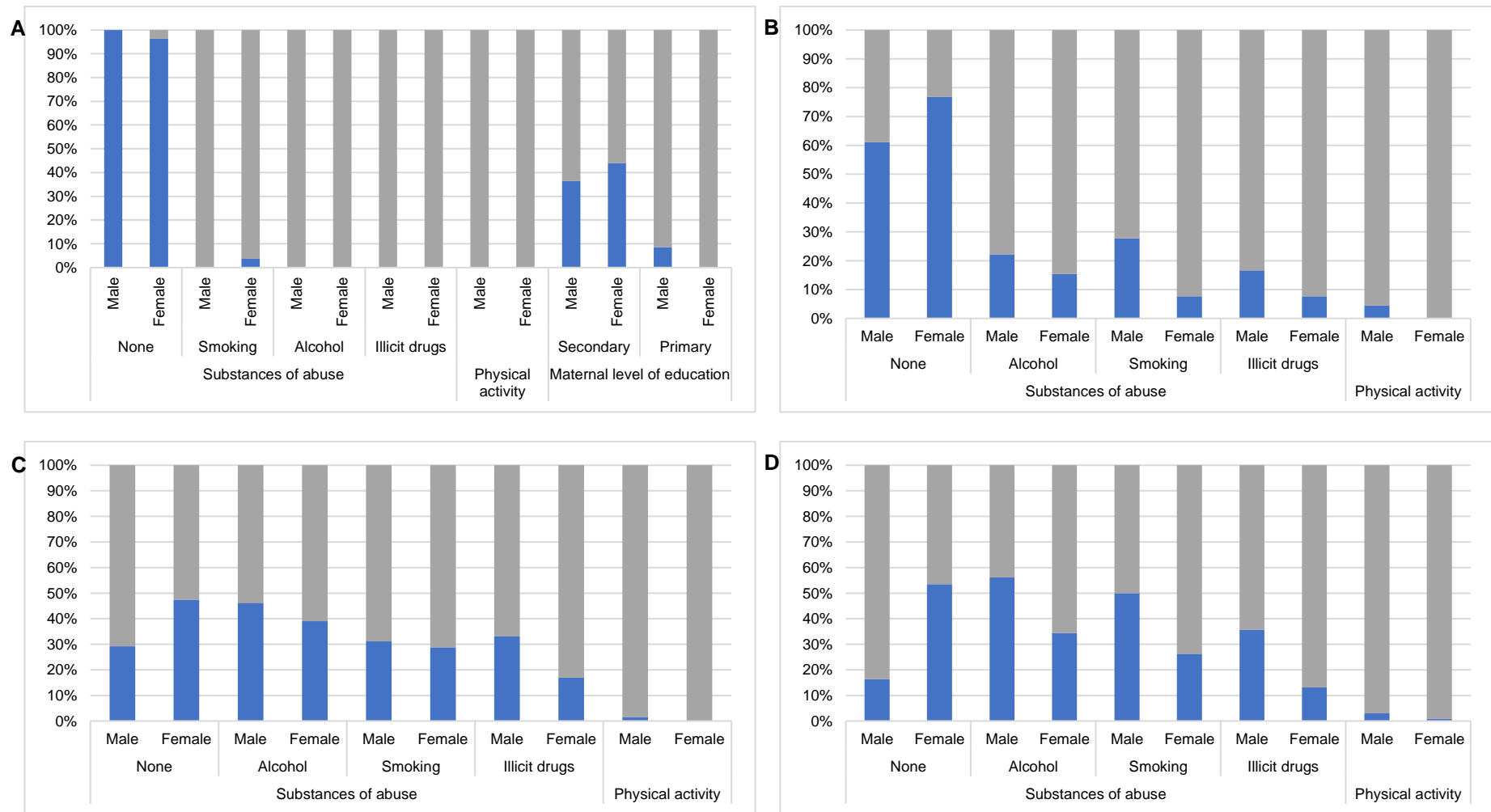


Figure 3.14: Social history percentage per sex in (A) 1-10 years (B) 11-20 years (C) 21-30 years and (D) 31-40 years. One female aged 1-10 years had engaged with smoking and majority of cases had a secondary maternal level of education. More males than females aged 11-20 years had engaged with each substance of abuse with smoking being the main. (More males aged 21-30 years and 31-40 years old had engaged with each substance of abuse with alcohol being the main.)

3.6.2. Clinical history

In more than half of the cases, no medicinal substance was used (315/553; 57.0 %). Nonetheless, within the pharmaceutical products category, chronic medication accounted for 42.3 % (234/553) and traditional medicine accounted for 1.5 % (8/553) (Figure 3.15). No significance was identified between the specific medicinal substance used and any of the causes of death nor medical history identified.

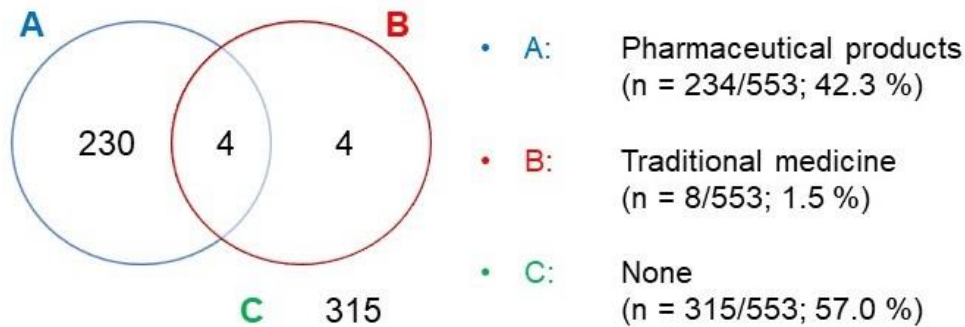


Figure 3.15: Venn diagram showing number of cases where medicinal substances were used. In more than half of the cases (315/553; 57.0 %), no medicinal substance was used.

Additional clinical risk factors have been graphically represented herein for each age category per sex. Symptoms that contributed more than 10 % have been depicted (Figure 3.16), whereas medical (Figure 3.17) and family history (Figure 3.18) that contributed more than 5 % has been portrayed. These risk factors have been ranked from highest to lowest for each age category. Medical history included both chronic and acute illnesses and/or infections. For further information on the remaining risk factors, see Appendix E.

In all age categories, there were no significant differences between males and females for any of the clinical aspects. Vomiting was identified as one of the leading symptoms in all age categories accounting for more than a quarter of cases (163/540; 30.2 %). In the age category of 1-10 years, fever (21/63; 33.3 %) and diarrhoea (19/63; 30.2 %) occurred in approximately a third of cases. Furthermore, breathlessness had occurred primarily in the three older age categories followed by chest pain in individuals 21-40 years old. (Figure 3.16).

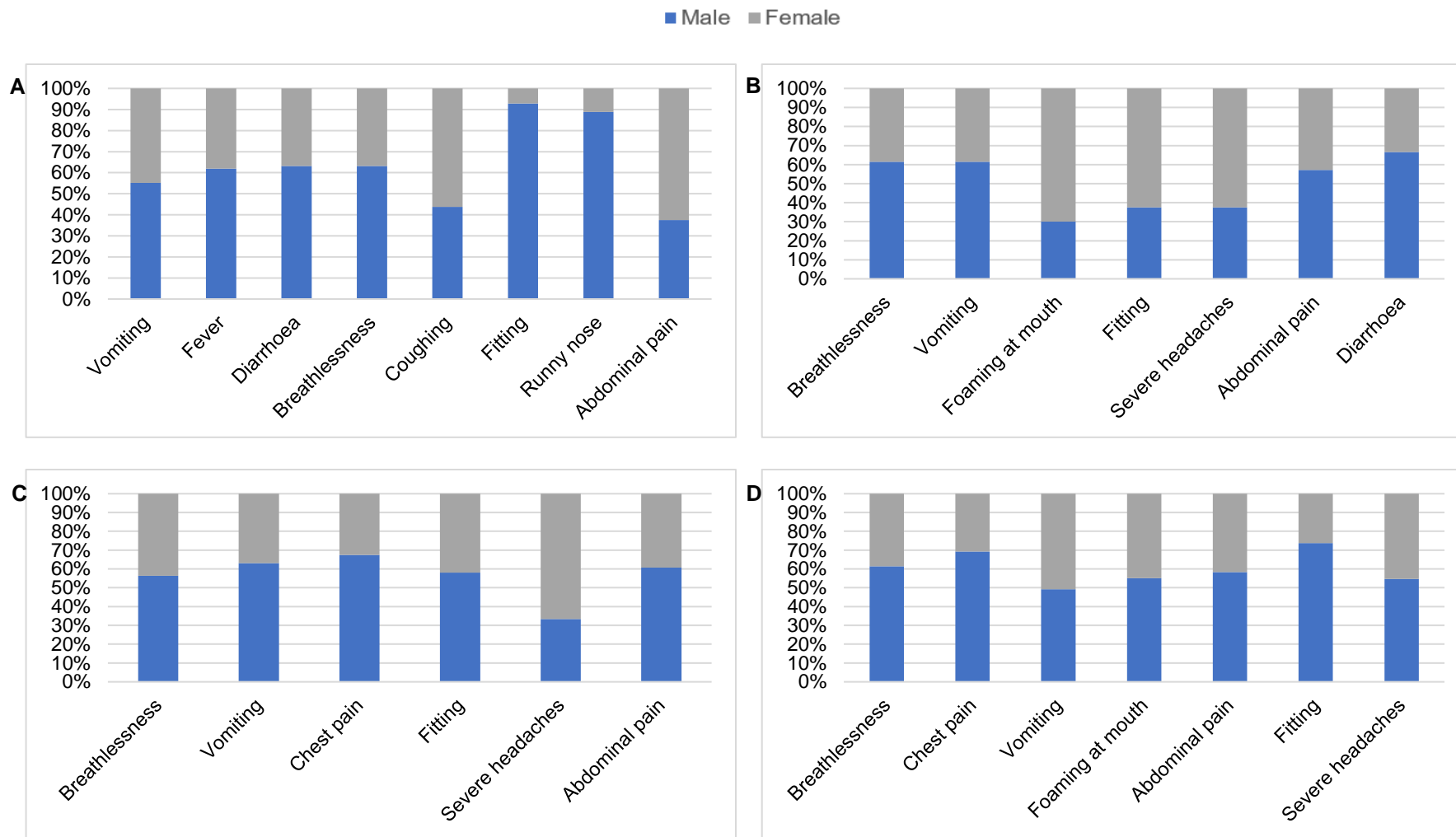


Figure 3.16: Percentage of symptoms that preceded and/or transpired at death per sex in (A) 1-10 years (B) 11-20 years (C) 21-30 years and (D) 31-40 years. Individuals aged 1-10 years experienced leading symptoms of vomiting, fever and diarrhoea, whereas breathlessness, vomiting and chest pain were among the leading symptoms experienced in the latter three age groups.

Majority of cases had no documented medical history in all age categories. Nonetheless, a history of TB exposure and HIV exposure was well-identified in individuals 1-10 years and 31-40 years compared to other conditions noted in those age categories. Furthermore, approximately 13 % of cases had a history of epilepsy in the age categories of 11-20 (6/44) and 21-30 (20/175) years. (Figure 3.17)

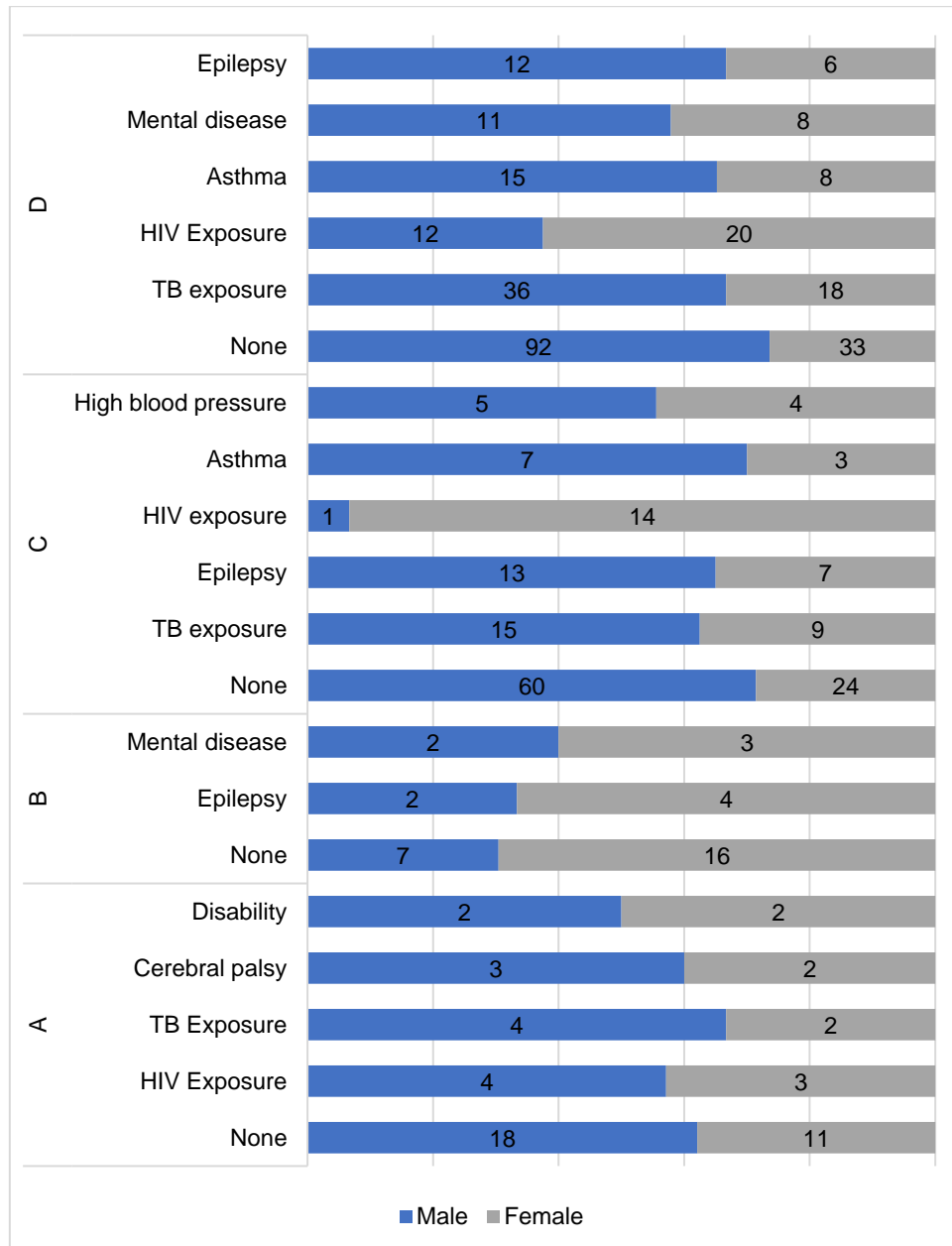


Figure 3.17: Medical history counts per sex in (A) 1-10 years (B) 11-20 years (C) 21-30 years and (D) 31-40 years. In individuals ≤ 10 years and ≥ 31 years, HIV and TB exposure were prominent. Moreover, numerous individuals experienced epilepsy in ages 11-30 years.

HIV: Human Immunodeficiency Virus; TB: Tuberculosis

Parallel to medical history, the majority of cases in all age categories did not have a family history of ailments. However, in the latter three age groups, asthma, previous sudden death, and heart disease were presented. In contrast, individuals aged 1-10 years showed a family history of HIV and high blood pressure (Figure 3.18).

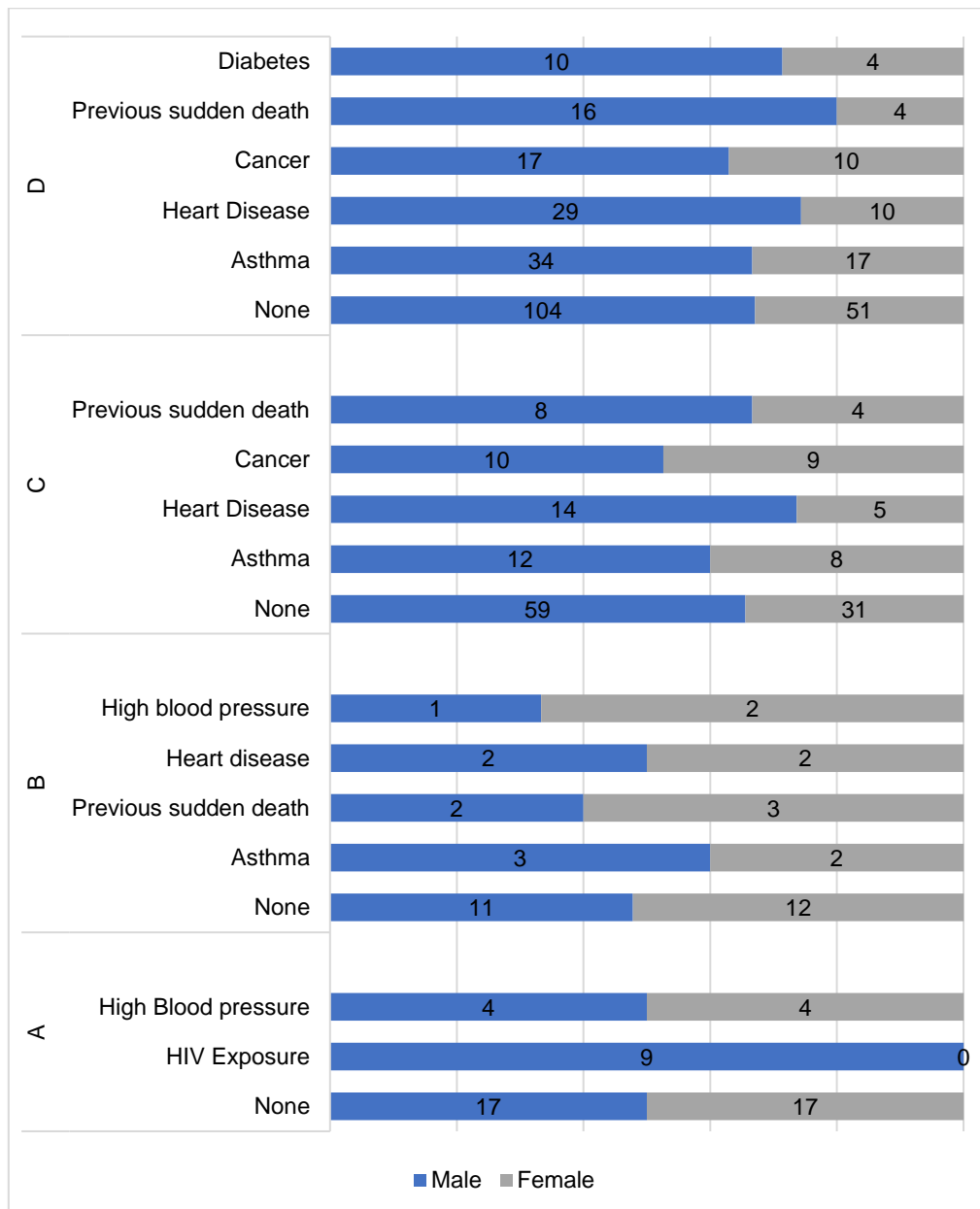


Figure 3.18: Family history counts per sex in (A) 1-10 years (B) 11-20 years (C) 21-30 years and (D) 31-40 years. In all age categories, majority of cases had no known family history. More males than females aged 1-10 had a family history of HIV exposure, however there was no significance when comparing this to all symptoms.

CHAPTER 4: DISCUSSION AND CONCLUSION

4.1. Introduction

This study sought to collate data pertaining to SUDY at one of the busiest mortuaries in the Western Cape, with the intention of describing the profile and risk factors of individuals who most vulnerable. SUDY has not been studied before at SRM and thus this dissertation documents the first empirical data pertaining to this important, yet under-studied, population group.

Although previous studies have been conducted internationally and at other forensic facilities within South Africa on SUDC and SUDA, which overlap with the SUDY age group (1-40 years), local publications on SUDY as a focus have also not been produced. Research conducted by Tiemensma (2010) at Tygerberg Mortuary between 2001 and 2005 established that there had been no previous studies performed on SUDA (>18 years) in South Africa and thus the need was highlighted to further investigate these cases to aid in establishing common causes of death within this population. It was stated that out of the approximate 2 700 cases received annually, 250-380 cases were rendered “sudden and unexpected” or “unknown” (Tiemensma, 2010). Additionally, van Deventer, Rossouw and du Toit-Prinsloo (2016) performed a study on SUDC (1-18 years) pertaining to the Pretoria Medico-legal Laboratory wherein less than one percent of deaths were considered to be SUD (van Deventer, Rossouw & du Toit-Prinsloo, 2016).

While the proportion of these deaths may be small, this may be overshadowed by the large burden of homicide investigations in South Africa (Mole, 2019). The absolute number of SUDY cases is nevertheless substantial, which is concerning considering the emotional distress that accompanies these cases. Thus, it is crucial to establish means to minimise these tragic fatalities and provide closure to grieving relatives. Therefore, the collation of data on the burden, profile and risk factors surrounding SUDY cases from other mortuaries in South Africa such as SRM is befitting. Investigating this wide-ranging age group is imperative as it encompasses both vulnerable individuals (children) and key determinants of our South African economy (young adults) (Statistics South Africa, 2020). Limitations, however, arise in that the findings presented herein cannot be fully compared within the local context due to the paucity of comparable literature. Nonetheless, this study has added to the current body

of literature by shedding light on SUD from the Western Metropole of the City of Cape Town perspective.

SRM is one of the busiest mortuaries in the country, having received an average of 3 863 forensic cases annually between the study period of 1 January 2016 and 31 December 2018. Out of the total forensic cases for the three-year period, SUDY accounted for 7.2 %. Of this 7.2 %, approximately 1.0 % were aged 1-18 years (Appendix E), which is similar to the aforementioned local SUDC study (van Deventer, Rossouw & du Toit-Prinsloo, 2016). Whereas the remaining 6.2 % pertained to 18-40 years which also parallels the local SUDA study (Tiemensma & Burger, 2012).

4.2. General profile and characteristics of SUDY

In South Africa, approximately 35.1 % of the total population comprise the youth (15-34 years) (Statistics South Africa, 2020). Within this study, the median age of individuals was 31 ± 10.3 years, with majority of cases occurring above eighteen years (Figure 3.2). In the majority of studies, mean age is provided rather than median thus comparison is hindered. However, in a SUDY study which focused on stroke as a cause of death, the median age was fairly similar - 33 years (Ågesen *et al.*, 2018). Males had comprised the majority of cases (64.3 %) overall and there were significantly more males in the 15-16 year and 30-31 year age brackets specifically ($p = 0.01$). The trend for more males parallels numerous international studies (Skinner *et al.*, 2011; Zhuo *et al.*, 2012; Berg *et al.*, 2013; Allan *et al.*, 2019).

In the majority of cases, individuals had demised whilst sleeping (57.1 %) which is in accordance with the main location of death being residential (43.5 %). This trend for residential locations is indeed consistent with literature (Nilsson *et al.*, 1997; Lear-Kaul, Coughlin & Dobersen, 2005). However, in contrast to other study settings wherein many deceased were found in a prone position (Kloster & Engelskjøn, 1999; Melez *et al.*, 2017), individuals had been found positioned supine herein. Though none of these circumstances surrounding death demonstrated significant differences between sex in any of the age categories, they do depict the unexpectedness of these cases. Thus, taking heed of the lifestyle choices and behavioural patterns of these young individuals to safeguard their well-being is an unquestionable obligation. With the South African youth being primarily responsible for financial security of numerous households and

the country as a whole (Brand South Africa, 2015), ensuring that they receive adequate education, access to resources and healthcare which will ultimately enhance longevity is sagacious.

4.3. The substance abuse crisis in South Africa

A distinct substance abuse crisis has emerged amongst the youth of our country with ramifications of violent behaviour (Auckloo & Davies, 2019), unsafe sexual practices, chronic morbidities and tragic fatalities (Ferrell, 2016). Engagement with substances of abuse (*i.e.* alcohol, tobacco products or illicit drugs) was identified as a potential risk factor for SUDY in our study which counterparts the local study on SUDA by Tiemensma & Burger (2012), as well as international literature (Braggion-Santos *et al.*, 2014; Allan *et al.*, 2019). It was determined that individuals had engaged with one or more substance of abuse in more than half of SUDY cases (330/568; 58.1 %) with alcohol being the primary substance consumed (Figure 3.12).

The Western Cape has numerous suburbs of low socio-economic status, wherein residents often have access to unlicensed taverns (*i.e.* shebeens) (Ferrell, 2016) and limited accessibility to medical services and resources (Taani & Muller, 2012). Within this study, the densely populated and low socio-economic status neighbouring suburbs of Nyanga and Gugulethu were identified as hotspots for SUDY (Figure 3.3), accounting for approximately a quarter of cases (199/833; 23.9 %). Most cases (494/833; 59.3 %) had occurred over the weekend period (Friday-Monday) (Figure 3.4), which is potentially a result of more individuals engaging with substances of abuse during this time (Parker & Williams, 2003; Van Wersch & Walker, 2009; Kuntsche & Labhart, 2012).

In the age category of 31-40 years specifically, there were significantly more males than females who had engaged with illicit drugs compared to all other substances of abuse ($p = 0.012$). Recent statistical reports on substance abuse in our youth have demonstrated that more males had engaged with Cannabis in its various forms compared to females, thus corroborating this finding (Statistics South Africa, 2020).

Interestingly, a single case within the 1-10 year age bracket had documented engagement with smoking (Figure 3.13), though the specific substance was not documented. This result was unsurprising given that 6.8 % of adolescents engage with

tobacco products prior to ten years old according to a South African based survey conducted in 2008 (Reddy *et al.*, 2010). The World Health Organisation has additionally indicated that learners often use substances as a coping mechanism for verbal or physical abuse, amongst others (World Health Organization, 2020). This case remains under investigation following a full post-mortem and thus further research should be conducted to understand whether physical or verbal abuse did in fact play a role in this case. Nonetheless, this finding does highlight that substance abuse is present in our communities and should physical and verbal abuse be identified, there may be a need for programmes to be implemented to counteract this.

Given that only 29.1 % of cases herein had toxicology performed (Figure 3.9), the true prevalence of substances in these SUDY cases may be under-reported. For instance, a prospective study was recently performed within the local setting, where toxicology was applied to a cohort of SUDI cases who would ordinarily not have been candidates for toxicology testing based on their clinical and social history. The results showed that 83.0 % of infants had at least one substance detected, and 11 % infants had Methamphetamine present in their bodies (Louw, 2020). These results demonstrated that the true presence of toxicological substances is likely to be greater than reported, and it motivates for routine toxicology to be performed in all cases of SUD.

Thus, raising awareness through public campaigns on the impact of substance abuse on lifestyle and implementing policies to curtail this risky behaviour would be prudent measures to reduce fatalities. Educational awareness has not necessarily been efficacious (Ferrell, 2016), however, the enhancement of our healthcare systems to identify individuals at-risk and the subsequent implementation of policies regarding substance use has. Thus, the latter may be an indispensable measure. Such interventions, which have demonstrated success, include increasing the age for alcohol consumption, restrictions on the amount of individuals allowed within an alcohol retailer, or reducing alcohol advertisements to name a few (Room, Babor & Rehm, 2005; Hope, 2006; Ferrell, 2016). Nonetheless, the findings reported on substance abuse herein highlight that similar interventions to reduce this addictive habit are urgently needed.

4.4. Infectious diseases

While many studies have concluded cause of death as being cardiovascular and neurological in nature in SUDY cases, only a few have investigated cause of death from a South African stance. Comparable to local studies (du Toit-Prinsloo *et al.*, 2011; Kruger, 2016; van Deventer, Rossouw & du Toit-Prinsloo, 2016), more than half of the cases had natural causes of death (Figure 3.10), out of which there was an overwhelming amount of infectious causes (64.9 %) (Figure 3.11). Pneumonia and TB were among the leading causes of death in all age categories (Appendix F), and the involvement of the pulmonary system in SUDY was comparable to both local (Tiemensma & Burger, 2012; van Deventer, Rossouw & du Toit-Prinsloo, 2016) and international studies (Amital *et al.*, 2004).

Infectious disease is a major cause for concern both locally and globally (Kruger, 2016; World Health Organization, 2019d). In 2017, pneumonia particularly was the prime cause of infectious death globally, accounting for 15 % of all deaths in children less than 5 years old (World Health Organization, 2019d). With pneumonia being a transmissible disease, research into the identification of pneumonic pathogens is vital to establish means to prevent and treat this condition. One such mean could be inoculation development, and in order for this to materialise, enhanced understanding of transmissible pathogens is necessary. Achieving this could potentially result from increasing ancillary testing to a full scope, which will contribute towards public health and ultimately reduce mortalities. However, given that numerous mortuaries in South Africa are resource-constrained (Mathews *et al.*, 2016), this may not be possible.

In the current study, post-mortem histology had only occurred in 28.1 % of cases and microbiology in 5.8 % (Figure 3.9). Hence, these findings highlight the limited testing conducted and advocate for increased microbiological and histological ancillary investigations. Additionally, it prompts for these tests to become mandatory in the investigative process of cases of an infectious nature. This would lead to the identification of causative pathogens which can then be prioritised for inoculation development. The ultimate reduction of such fatalities via increasing immunity in the background population, aligns to the third SDG. Not only does this pertain to SUDY solely, but to all cases of SUD both locally and internationally.

4.5. Ill-defined causes of death

Despite cause of death being defined in the majority of cases herein, the cause of death in many of the SUDY cases globally remains undetermined or ill-defined due to major inconsistencies in the DSI process and post-mortem examination of these deaths (Dewar *et al.*, 2012). This is often a consequence of disparities in national standardised guidelines and non-compliance to policies and procedures (du Toit-Prinsloo *et al.*, 2013) - the CDC guidelines are an exception. Vital registration data published by Statistics South Africa in 2012 stated that there had been a fluctuation over the years in the number of fatalities noted as having “ill-defined and unknown causes” (Statistics South Africa, 2012). However, the number of undetermined cases in relation to these fatalities is unknown due to insufficient data capturing and reporting.

Whilst a local study had contributed to this data from a Pretoria and Western Cape Eastern Metropole perspective (du Toit-Prinsloo *et al.*, 2011), data from SRM was unknown. In light of this, a total of 23/833 (2.8 %) cases were identified in this study as undetermined following a full post-mortem examination (Figure 3.10).

Molecular autopsies in a local setting are currently being developed to address and aid in defining cause of death, particularly in cases where the cause of death is undetermined. Resolving these cases will not only aid in providing closure, but the technique demonstrates potential in that results can also be used to screen and educate at-risk individuals who may be oblivious to their potentially fatal genetic predisposition (Burns *et al.*, 2017). This concept would also apply to some natural cases where cause of death is cardiac-related or even unspecified. Cause of death had been deemed as natural but not specified in 3.6 % of cases in this study. Although the proportion is relatively small, the non-specific natural cases will likely remain. This is due to legislation stating that it is only necessary for forensic pathologists to decipher natural from unnatural death (National Health Act, No. 61 of 2003, 2003:s1).

A molecular autopsy is a fairly novel subsidiary investigation that has shown value in cases with ill-defined causes of death, whereby the analysis of the DNA of the deceased individual has been able to pinpoint genetic variants which could explain the death (Farwell & Gollob, 2007; Campuzano *et al.*, 2017; Hellenthal *et al.*, 2017). The undetermined, under investigation, and non-specific natural cases herein were

henceforth identified as candidates for molecular autopsies in future investigations. Whilst biological sample retention is currently discretionary (National Health Act, No. 61 of 2003, 2003:s1), fortunately 81.8 % (144/176) of candidate cases identified herein had samples available for future investigations (Figure 3.1). These samples included blood and FFPE tissue, as alternate samples had either not been retained or were discarded following other ancillary investigations. Although the percentage of retained samples was favourable herein, this may not always be the case due to its discretionary nature - a shortcoming of current protocols.

To further emphasise the need for standardised procedures and subsequent compliance to procedures, the extent of post-mortem was also evaluated. In contrast to SUDC studies wherein a full post-mortem examination was performed in all cases (van Deventer, Rossouw & du Toit-Prinsloo, 2016), a full post-mortem examination was performed in only 54.7 % of cases herein. Due to Pretoria Medico-legal Laboratory not having a LODOX, it would have been necessary to draw conclusions on cause of death based on a full examination. However, the unique nature of each case suggests that it is not always necessary for further ancillary investigations to be conducted due to the discernible cause of death based on case history and radiology, hence the varying results. Although, even if cause of death is established, these tests would aid in gaining data to assist with the implementation of preventative measures and thereby contribute to enhanced public health.

Nevertheless, with just over a third of cases herein having identified cause of death and organ system based on external examination and radiology alone, it is an area of concern in that inheritable conditions pertaining to these deaths may be overlooked. Radiology, however, is often performed solely as result of SRM being a resource-constrained mortuary (Mathews *et al.*, 2016). With subsidiary investigations being subsequently averted due to their discretionary nature, fatalities which could have otherwise been prevented in surviving relatives result. With a total of 40/661 (6.1 %) cases having had a family history with previous sudden death (Appendix E), this finding provides justification for a potential genetic link. However, the mandatory nature of LODOX at SRM provides justification for why it was the main ancillary investigation performed (95.6 %) while the remaining 4.4 % did not have a full-body scan due to equipment malfunctioning or maintenance.

4.6. Inheritable conditions

All natural, undetermined and under investigation cases were assessed for risk factors to understand which organ systems were involved. One of the uses of this information is to identify molecular pathways to target in future molecular autopsies. With the majority of causes being transmissible or inheritable in nature, identifying these potential risks may assist in educating surviving relatives of a potential genetic predisposition, therapeutic measures to implement, and social and clinical aspects to be cautious of, thus possibly reducing mortality (Anastasakis *et al.*, 2018).

Overall, the main organ systems involved in these cases were the pulmonary, CVS, CNS and GIT which parallels international trends (Vennemann *et al.*, 2007; Grønberg & Uldall, 2014). Whilst these are the main organ systems necessary for survival, the leading exact causes of death (Figure 3.12) contrasted international studies. There were 29/485 (6.0 %) cases that had an overlap in systems, specifically the pulmonary and CVS. Vomiting was identified as one of the leading symptoms in all age categories accounting for more than a quarter of cases (163/540; 30.2 %). In the 1-10 year age category specifically, other leading symptoms to have transpired prior to/at death were fever (21/63; 33.3 %) and diarrhoea (19/63; 30.2 %) (Figure 3.18). Moreover, a medical history of TB and HIV exposure were also well-noted in this age group and 31-40 year olds. These symptoms and medical histories thus allude to the main organ systems involved in death and should stand as warning signs for caregivers and healthcare workers considering that majority of cases occurred in residential locations and medical centres (Figure 3.8).

Closer observation of CVS deaths showed that the majority of these cases had non-specific cardiovascular causes (Figure 3.12). However, when specified, myocardial infarction and ischaemic heart disease were the leading causes which is similar to previous studies of SCD (Maron *et al.*, 2014; Rao *et al.*, 2014). Additional cardiovascular causes were coronary artery thrombosis and hypertensive heart disease. These cardiac conditions are all well-known for having genetic associations (Maron *et al.*, 2000; Anastasakis *et al.*, 2018). There was no significant difference between males and females for each cause noted in any of the cardiac conditions nor the remaining identified causes of death. However, the following question arises: “why do these cardiovascular cases specifically get referred to us and others not?”. In order to provide explanations to this question, it is necessary to collate this data with other

vital statistics and mortality data from a non-forensic setting – an area of research to be fulfilled.

While only a small number demised due to physical exertion, when death ensued, there was a significant association to a comprised CVS (7/8; 87.5 %) ($p = 0.011$). Furthermore, there were significantly more males who had engaged in physical activity compared to females ($p < 0.001$). These individuals were aged between 17-39 years. This finding is of potential value for future research as a previous study by Amital *et al.* (2004) indicated that physical activity was a potential risk for SCD.

With the leading symptom in individuals > 11 years being breathlessness and chest pain (Figure 3.16), which parallels international trends (Gullach *et al.*, 2015), further allusion to organ systems and cardiovascular diseases specifically results. Statistically, significantly more males than females in the age group of 31-40 years were located outdoors at death ($p < 0.001$). Hence, perhaps males present at outdoor sporting facilities, who are genetically predisposed to cardiovascular conditions and demonstrate symptoms of breathlessness and chest pain, could potentially be targeted for screening. Screening and therapeutic interventions have shown positive outcomes for these individuals internationally (Semsarian & Hamilton, 2012; Anastasakis *et al.*, 2018) and could thus subsequently be implemented. However, further studies should be performed to elucidate this finding due to the marginal proportion of these cases.

The leading cause of death in South Africans after Human Immunodeficiency Virus (HIV) is cardiovascular disease which is responsible for every 1 in 6 deaths (Byrne, Eksteen & Crickmore, 2016). Hence gaining insight into the molecular pathways involved in cardiovascular deaths and screening individuals with a history of heart disease in either family or medical history would be of utmost importance (Anastasakis *et al.*, 2018). In our local context, these molecular findings would be considerable for public health as South Africa is home to individuals of African and Admixed ancestries (Daya *et al.*, 2013; Nel, 2017). Within the population groups, factors may differ genetically from the rest of the world and thus interventions should align (Daya *et al.*, 2013).

Although neurological conditions were identified herein to a lesser extent compared to literature, epilepsy and mental disease were prevalent in 11-20 year olds, whereas TB

exposure and epilepsy were prevalent in the 21-30 year category (Figure 3.17). Moreover, the overall low percentage of epilepsy cases (2.7 %) identified herein contradicts international findings wherein SUDEP was the common cause of death (Table 1.3).

In light of epilepsy being the common cause of SUD internationally, resources were directed at SUDEP. However, based on the genetically diverse population within South Africa (Daya *et al.*, 2013), the low percentage of SUDEP may be attributed to an overwhelming number of infectious causes. Furthermore, given that SUDEP is a multi-factorial disease, it is possible that environmental differences may play a role (The University of Chicago Medical Center, 2020). It is also possible that these neurological conditions are being overlooked due to the partial or external scope of autopsy, for example where compounding factors are identified via routine toxicology or where neuropathological lesions, contusions or malformations are presented via brain cutting (Thom & Allinson, 2019). Hence, a mandatory full post-mortem examination may be beneficial in SUDY cases. Taking these inheritable neurological conditions into account and reviewing neurotrophin signalling pathways (Ozdemir *et al.*, 2019) would add to global data on molecular autopsies from a South Africa stance. However, directing resources at infections, cardiovascular causes and the substance abuse crisis within South Africa may be of greater value.

4.5. Limitations and discrepancies

Engaging with secondary data has inherent errors which cannot necessarily be rectified. Due to the retrospective and cross-sectional nature of this study, cases had missing documentation or information. This sub-optimal completion of paperwork may be due to several factors including the vast caseload experienced at forensic mortuaries in South Africa, the length and sensitive nature of the family interviews as well as possible inadequate training of investigative officers due to resource constraints (Mathews *et al.*, 2016). These limitations advocate for training of Forensic Pathology Officers to ensure compliance to standardised procedures.

Although the study period was 2016-2018, only 581/833 (67.9 %) cases had documented alleged cause of death based on the availability of the final post-mortem reports. This is significant from an operational stance and warrants further

investigation to identify why these cases are not being resolved within a three-year period. It is especially important in SUDY cases as there may be a familial or inherited disease and the findings could be relevant for surviving relatives. In addition, since only 438/704 (62.2 %) cases had full and partial post-mortem examinations performed cumulatively, this depicts that exact diagnosis was not confirmed in almost 40 % of cases. Had there been greater performance of ancillary investigations, such as toxicology, histology and microbiology investigations, more exact causes of death would have been identified leaving less cases for molecular autopsies and thus this operational limitation could have potentially been addressed.

It was previously noted that language barriers have also hampered abilities to obtain sufficient details of cases during family interviews (Tiemensma & Burger, 2012), especially in multi-lingual countries such as South Africa. Although language barriers were not investigated herein, this may be a potential justification for lack of information obtained in numerous cases. Additionally, had more information been gathered on circumstances surrounding death in these cases, cases that were initially reported as SUD but later identified as unnatural death could have been correctly noted as such upon entry to the mortuary. This further highlights a potential oversight from an operational viewpoint.

In unidentified cases, contact had not been made with a next-of-kin and thus social and clinical history remained unknown. Furthermore, parallel to local survey results, personal factors such as income was not documented in a large proportion of cases (Reddy *et al.*, 2010). A total of 51/833 cases either had missing identity documents or the deceased was unknown, thus the assumed age was taken as per the Contemporaneous Notes: Lab 27. Additionally, in 15.5 % (129/833) of SUDY cases, post-mortem reports were unavailable due to ongoing and inconclusive cases.

Lastly, based on the choice of age categories, hindrances were experienced when comparing findings literature. Thus, re-grouping in five-year age intervals may be preferential for future research in order to aid international comparisons.

4.8. Conclusion

In essence, it is evident that individuals aged 31 ± 10.3 years with co-morbidities and who engaged with substances of abuse were the most vulnerable for SUDY. The

cause of death in these cases was most likely of an infectious nature. Given the imminent substance abuse crisis within our country, interventions targeted at the youth should be implemented in SUDY hotspots, in an attempt to reduce this risk factor.

While in all age categories, majority of cases had no known prior illnesses or family history (Figure 3.17-3.18), many individuals showed symptoms of vomiting and breathlessness prior to death (Figure 3.16). These results suggest public awareness aimed at the social arena, sporting centres, and amongst caregivers and healthcare workers needs to be raised to recognise early symptoms in our young. If observed, they should seek medical aid immediately.

This study has also highlighted the value of ancillary investigations performed in these SUDY cases, specifically toxicology, histology, microbiology, and molecular assays. Given the resource-constraints prevalent in South African mortuaries (Mathews *et al.*, 2016), perhaps molecular assays would be preferential due to the inheritable and transmissible nature of infectious diseases. The findings herein also provide basis to advocate for adaptations to be made to standard operating procedures - to ensure that these investigations become mandatory in the post-mortem examination process of SUD. Additionally, it has accentuated the need for biological sample retention to become incumbent on law so as to aid in defining cause of death in ill-defined and undetermined cases. With cases having missing information and documentation, advocacy for individuals to receive training to ensure compliance is warranted. Furthermore, operational aspects should be reviewed to address the operational limitations in terms of collecting information regarding the circumstances surrounding death.

With a SDY-CR having been implemented internationally and demonstrated effectiveness in monitoring SCD and SUDEP cases below the ages of 20 years (Centers for Disease Control and Prevention, 2016), perhaps a similar concept or registry should be established in our local context. This potential registry should be devised to include individuals aged 1-40 years and should be directed at infections, cardiovascular conditions, and the substance abuse crisis in South Africa in light of the findings presented herein. Moreover, while the CDR is the 'gold standard' in the Western Cape for cases aged < 18 years (Mathews *et al.*, 2016), a 'Young Death Review' team should be devised to aid in the further exploration of the cause of death

and risk factors pertaining to our young. A DSI protocol could subsequently be formulated to address these SUDY cases specifically since DSI protocols have not been well-established locally (Bennett, Martin & Heathfield, 2019).

In conclusion, this project has highlighted the burden and profile of SUDY cases admitted to SRM between 1 January 2016 and 31 December 2018 thereby achieving the aim of this research project and adding to a growing body of literature from a South African stance.

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APPENDIX A: ETHICS APPROVAL



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



Room G50 -G Floor
Old Main Building
Groote Schuur Hospital
Observatory 7925

Telephone [021] 650 1236

Email: hrec-enquiries@uct.ac.za

Website: www.health.uct.ac.za/fhs/research/humanethics/forms

16 April 2020

HREC REF: 171/2020

Dr Laura Heathfield

Division of Forensic Medicine and Toxicology
Entrance 3, Level 1
Falmouth Building – FHS
Anzio Road,
Observatory

Dear Dr Laura Heathfield

PROJECT TITLE: A RETROSPECTIVE INVESTIGATION OF SUDDEN UNEXPECTED DEATH IN THE YOUNG INVESTIGATED AT SALT RIVER MORTUARY, CAPE TOWN (SUB-STUDY – 211/2019) (MPHIL DEGREE – MS YUVIKA VANDAYAR)

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

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 30 April 2021.

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 note that for all studies approved by the HREC, the principal Investigator **must** obtain appropriate Institutional approval, where necessary, before the research may occur.

The HREC acknowledge that the student: Ms Yuvika Vandayar will also be involved in this study.

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

Please quote the HREC REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

HREC 171/2020 SC

APPENDIX B: OFFICE AUTOPSY DATABASE APPROVAL



Acting Head of Division: Division of Forensic Medicine and Toxicology

Dr Gavin Kirk

Falmouth Building
Level 1, Entrance 3
Anzio Road
Observatory
Tel: +27 (0) 21 406 6099 E-mail: Lornaj.martin@uct.ac.za
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To whom it may concern,

I, Dr Gavin Kirk, **do** hereby grant final permission for the following researchers to have access as specified for the research project as stipulated:

Principal Investigator: *Dr Laura Heathfield*
Staff number: *01426764*

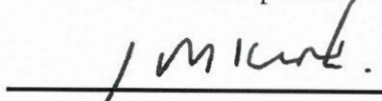
Researcher: *Ms Yvika Vandayar*
Student number: *VDYYUV001*

Project Title: *A retrospective investigation of sudden unexpected death in the young investigated at Salt River Mortuary, Cape Town*

Access to:

✓	<i>Please tick all that apply</i>
	The autopsy allocations
✓	The Office Autopsy Database and related records
	Forensic Pathology Services Laboratory, Salt River for observation and collection of data
	Forensic Pathology Services Laboratory, Salt River for the collection of tissue samples
	Forensic Pathology Services Laboratory, Salt River for conducting Interviews
	Forensic Pathology Services Laboratory, Salt River for obtaining informed consent

For the data collection period of 16/04/2020 to 31/12/2020



Dr Gavin Kirk (*Signature*)

05/06/2020

Date (*dd/mm/yyyy*)

APPENDIX C: DESCRIPTION OF DOCUMENTATION REVIEWED IN DATA COLLECTION PROCESS

DOCUMENTS	CONTENT
Identification Document (ID)/birth certificate	Unique identity number which includes date of birth, sex and country of birth.
FPS 002 Scene Script	Scene details including preliminary manner of death and SAPS station.
'Contemporaneous Note (Lab. 27): Salt River Forensic Pathology Laboratory'	Basic details surrounding death.
FPS 006(a) form	Clinical and clinical history for adults attained at family interview including substance use, type of housing, medical history and family history.
FPS 006(b) form	Clinical and clinical history for babies attained at family interview, including substance use, type of housing, medical history and family history, maternal level of education and annual household income.
'South African Police Service (SAPS) sudden and unexpected death in adults'	Clinical and clinical history for adults attained at family interview including type of housing.
Road to Health Card	Information regarding HIV exposure.
'Affidavit in terms of Section 212(4), Act 51 of 1977'	Post-mortem report generated by the Forensic Pathologist which summarises the main post-mortem findings including the extent of post-mortem and ancillary investigations conducted, as well as stipulated manner and alleged cause of death.

APPENDIX D: DATA COLLECTION VARIABLE TABLE

VARIABLE NUMBER	VARIABLE	VARIABLE TYPE	METHOD OF DATA CAPTURE
ALL CASES			
v1	Unique study number	Categorical nominal	xxxx/yyyy
v2	Date of death declaration	Categorical nominal	dd/mm/yyyy
PROFILE			
v3	SAPS Station	Categorical nominal	Free text
DEMOGRAPHICS			
v4	Age (years)	Numerical continuous	Range (1-40)
v5	Sex	Categorical binary	Drop-down - Male - Female
POST-MORTEM DETAILS			
v6	Date of post-mortem	Categorical nominal	dd/mm/yyyy
v7	Extent of post-mortem	Categorical nominal	Drop-down - External - Partial - Full - Unknown
v8	Ancillary Investigation	Categorical nominal	Tick-box - None - Toxicology - Histology - Microbiology - Other (Specify: _____)
v9	LODOX (yes/no/unknown)	Categorical nominal	Drop-down - No - Yes - Unknown
CIRCUMSTANCES SURROUNDING DEATH			
v10	Location of death	Categorical nominal	Drop-down - Residential - Outdoors - Medical centre - Workplace - Jail - Motor vehicle - Sports ground - Unknown - Farming centre - Educational facility - Other (Specify: _____)
v11	Position of deceased at death	Categorical nominal	Drop-down - Prone - Supine - Other (Specify: _____) - Not specified
v12	Activity at death	Categorical nominal	Drop-down - Sleeping - Resting - Driving - Walking - Exercising - Other (Specify: _____) - Unknown (not witnessed) - Not specified

VARIABLE NUMBER	VARIABLE	VARIABLE TYPE	METHOD OF DATA CAPTURE
ALL CASES			
CAUSE OF DEATH			
v13	Manner of death	Categorical nominal	Coding 0 - Unnatural 1 - Natural 2 - Undetermined 3 - Under investigation 4 – Unknown (missing) If 0 > v14 only If 1 > v14 If 2 or 3 > v16
v14	Exact cause of death	Categorical nominal	Free text - as reported by pathologist.
v15	Organ system	Categorical nominal	Drop-down - Cardiovascular - Central nervous system - Pulmonary - Gastrointestinal - Other (Specify: _____)
NATURAL, UNDETERMINED AND UNDER INVESTIGATION ONLY			
SOCIAL HISTORY			
v16	Highest level of education of mother	Categorical nominal	Drop-down - Primary - Secondary - Tertiary - Unknown
v17	Type of housing	Categorical nominal	Drop-down - Formal - Informal - Unknown
v18	Annual household income	Categorical nominal	Free text – as per FPS006a form.
v19	Did the deceased engage with any of the following substances?	Categorical nominal	Tick-box – Alcohol - Illicit drugs - Tobacco products - Pharmaceutical products - Traditional medicine - Unknown - None Specify: _____
v20	Did the deceased participate in physical activity (e.g. gym/competitive sport)?	Categorical binary	Drop-down - Yes - Unknown
CLINICAL HISTORY			
v21	Symptoms prior to death	Categorical nominal	Drop-down - None - Unknown (not witnessed) - Chest pain - Fitting - Holding head in pain - Abdominal pain - Severe headaches - Nose bleeds - Foaming at mouth - Breathlessness - Paralysis of limbs - Vomiting - Diarrhoea - Other (Specify: _____)

VARIABLE NUMBER	VARIABLE	VARIABLE TYPE	METHOD OF DATA CAPTURE
NATURAL, UNDETERMINED AND UNDER INVESTIGATION ONLY			
CLINICAL HISTORY CONTINUED			
v22	Chronic illness/acute illness/ infection during lifetime	Categorical nominal	Tick-box - Diabetes - Epilepsy - Asthma - Cancer - High blood pressure - Heart problems - Kidney problems - HIV exposure - TB exposure - Allergies - Mental disease - Malaria - Other (Specify: _____) - None
v23	Chronic medication	Categorical nominal	Drop-down - Unknown - No - Yes If yes, specify: _____
v24	Family history of illness	Categorical nominal	Tick-box - Heart disease - Asthma - Cancer - Epilepsy - Sudden death - Other (Specify: _____) - None - Unknown
NON-SPECIFIC NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES			
OTHER			
v25	Are biological samples available? (yes/no)	Categorical binary	Drop-down - No - Yes If yes, specify: _____
UNDETERMINED CASES ONLY			
v26	Was the body identified (yes/no)	Categorical binary	Drop-down - No - Yes If no, v24 receives option "unknown"
v27	Ancestry* (European/African/Asian/Mixed/Unknown)	Categorical nominal	Drop-down - European - African - Asian - Mixed - Unknown

APPENDIX E: FULL VARIABLE LIST

ALL CASES		
PROFILE		
Day of week	n	% of available data (n=833)
Monday	144	17.3
Tuesday	130	15.6
Wednesday	91	10.9
Thursday	118	14.2
Friday	103	12.4
Saturday	111	13.3
Sunday	136	16.3
Month of year	n	% of available data (n=833)
January	64	7.7
February	60	7.2
March	62	7.4
April	68	8.2
May	58	7.0
June	79	9.5
July	72	8.6
August	61	7.3
September	74	8.9
October	75	9.0
November	79	9.5
December	81	9.7

ALL CASES		
PROFILE CONTINUED		
SAPS station	n	% of available data (n=833)
Nyanga	121	14.5
Gugulethu	78	9.4
Milnerton	62	7.4
Mitchells Plain	61	7.3
Woodstock	45	5.4
Phillippi-East	44	5.3
Cape Town Central	34	4.1
Atlantis	33	4.0
Grassy Park	32	3.8
Lentegeur	26	3.1
Seapoint	25	3.0
Manenberg	23	2.8
Ocean View	21	2.5
Table View	21	2.5
Athlone	20	2.4
Wynberg	20	2.4
Muizenberg	19	2.3
Langa	18	2.2
Kirstenhof	17	2.0
Philippi	17	2.0
Hout Bay	16	1.9
Steenberg	12	1.4
Mowbray	10	1.2
Claremont	9	1.1
Diep River	9	1.1

ALL CASES		
PROFILE CONTINUED		
SAPS station continued	n	% of available data (n=833)
Lansdowne	9	1.1
Maitland	8	1.0
Simonstown	5	0.6
Fish Hoek	3	0.4
Kensington	3	0.4
Rondebosch	3	0.4
Camps Bay	2	0.2
Pinelands	2	0.2
Strandfontein	2	0.2
Harare	1	0.1
Melkbos	1	0.1
Table Bay Harbour	1	0.1
DEMOGRAPHICS		
Ages (years)	n	% of available data (n=833)
1	41	4.9
2	11	1.3
3	7	0.8
4	8	1.0
5	4	0.5
6	1	0.1
7	4	0.5
8	3	0.4
9	3	0.4
10	4	0.5
11	5	0.6

ALL CASES		
DEMOGRAPHICS CONTINUED		
Ages (years) continued	n	% of available data (n=833)
12	2	0.2
13	2	0.2
14	5	0.6
15	3	0.4
16	6	0.7
17	8	1.0
18	15	1.8
19	6	0.7
20	13	1.6
21	15	1.8
22	8	1.0
23	21	2.5
24	19	2.3
25	21	2.5
26	25	3.0
27	28	3.4
28	32	3.8
29	42	5.0
30	51	6.1
31	41	4.9
32	54	6.5
33	43	5.2
34	52	6.2
35	54	6.5
36	42	5.0

ALL CASES			
DEMOGRAPHICS CONTINUED			
Ages (years) continued	n	% of available data (n=833)	
37	47	5.6	
38	35	4.2	
39	41	4.9	
40	11	1.3	
Sex	n	% of available data (n=833)	
Males	536	64.3	
Females	297	35.6	
POST-MORTEM DETAILS			
Extent of post-mortem	n	% with missing data (n=833)	% of available data (n=704)
Full	385	46.2	54.7
External	266	31.9	37.8
Partial	53	6.4	7.5
Unknown	129	15.5	-
Ancillary investigations	n	% with missing data (n=833)	% of available data (n=704)
None	1	0.1	0.1
Toxicology	205	24.6	29.1
Histology	198	23.8	28.1
Microbiology	41	4.9	5.8
Biochemistry, Mast cell tryptase	1	0.1	0.1
Full blood count, Urea and electrolytes, Liver function test	1	0.1	0.1
Genetics	1	0.1	0.1
Mast cell tryptase	4	0.5	0.6
Mast cell tryptase, IgE level	1	0.1	0.1
Neuropathology	4	0.1	0.1

ALL CASES			
POST-MORTEM DETAILS CONTINUED			
Ancillary investigations	n	% with missing data (n=833)	% of available data (n=704)
Platelet count, Urea & creatinine level	1	0.1	0.1
Protein C & S testing	1	0.1	0.1
Urea & creatinine level	1	0.1	0.1
Full blood count, Urea & creatinine level	1	0.1	0.1
White cell count, Urea & creatinine level	1	0.1	0.10
Unknown	129	15.5	-
LODOX	n	% with missing data (n=833)	% of available data (n=704)
Yes	673	80.08	95.6
No	31	3.7	4.4
Unknown	129	15.5	-
CIRCUMSTANCES SURROUNDING DEATH			
Location at death	n	% with missing data (n=833)	% of available data (n=832)
Residential	362	43.5	43.5
Medical centre	292	35.1	35.1
Outdoors	96	11.5	11.5
Ambulance	15	1.8	1.8
Jail	12	1.4	1.4
Undertaker	11	1.3	1.3
Transport-related	11	1.3	1.3
Workplace	8	1.0	1.0
Fire station	6	0.7	0.7
Sports ground	3	0.4	0.4
Educational facility	3	0.4	0.4
Shop-related	3	0.4	0.4

ALL CASES			
CIRCUMSTANCES SURROUNDING DEATH CONTINUED			
Location at death continued	n	% with missing data (n=833)	% of available data (n=832)
Industrial facility	3	0.4	0.4
Convention centre	2	0.2	0.2
Lodging facility	2	0.2	0.2
Financial institution	1	0.1	0.1
Pub	1	0.1	0.1
Farming centre	1	0.1	0.1
Unknown	1	0.1	-
Position at death	n	% with missing data (n=833)	% of available data (n=452)
Not specified	381	-	84.3
Supine	303	45.7	67.0
Prone	66	36.4	14.6
Side	61	7.9	13.5
Sitting	14	7.3	3.1
Other	8	1.7	1.8
Activity at death	n	% with missing data (n=833)	% of available data (n=308)
Not specified	372	-	44.7
Sleeping	176	21.1	57.1
Resting	79	9.5	25.6
Walking	21	2.5	6.8
Exercising	7	0.8	2.3
Bathroom-related	7	0.8	2.3
Playing	5	0.6	1.6
Religious/cultural	3	0.4	1.0

ALL CASES			
CIRCUMSTANCES SURROUNDING DEATH CONTINUED			
Activity at death continued	n	% with missing data (n=833)	% of available data (n=308)
Cooking/cleaning	3	0.4	1.0
Driving	2	0.2	0.6
Dancing	2	0.2	0.6
Climbing	1	0.1	0.3
Firefighting	1	0.1	0.3
Moving tiles	1	0.1	0.3
Unknown	153	18.4	-
CAUSE OF DEATH			
Manner of death	n	% with missing data (n=833)	% of available data (n=704)
Unnatural	43	5.2	6.1
Natural	515	61.8	73.2
Under investigation	122	14.6	17.3
Undetermined	23	2.8	3.3
Unknown (missing)	128	15.4	-
Exact cause of death	n	% with missing data (n=833)	% of available data (n=704)
Unknown (missing)	129	15.5	18.3
Under investigation	123	14.8	17.5
Pneumonia	50	6.0	7.1
TB	45	5.4	6.4
Cardiovascular pathology	38	4.6	5.4
Respiratory Pathology	34	4.1	4.8
Natural (not specified)	30	3.6	4.3
Lung disease	26	3.1	3.7
Undetermined	23	2.8	3.3

ALL CASES			
CAUSE OF DEATH CONTINUED			
Exact cause of death continued	n	% with missing data (n=833)	% of available data (n=704)
Cardiorespiratory pathology	21	2.5	3.0
Ischaemic heart disease	18	2.2	2.6
Myocardial infarction	18	2.2	2.6
Meningitis	16	1.9	2.3
Pulmonary embolism	16	1.9	2.3
Blunt trauma	13	1.6	1.8
Epilepsy	13	1.6	1.8
Coronary artery thrombosis	12	1.4	1.7
Diarrhoea & Dehydration	12	1.4	1.7
Pulmonary infection	12	1.4	1.7
Aspiration of gastric contents/airway obstruction	9	1.1	1.3
Perforated gastrointestinal ulcer	7	0.8	1.0
Alcohol toxicity	6	0.7	0.9
Hypertensive heart disease	6	0.7	0.9
Noxious substance	6	0.7	0.9
Pancreatitis	6	0.7	0.9
Cysticercosis	5	0.6	0.7
Gastroenteritis	5	0.6	0.7
Haemoptysis	5	0.6	0.7
Liver pathology	5	0.6	0.7
Ruptured berry aneurysm	4	0.5	0.6
Asthma	3	0.4	0.4
Cardiac tamponade	3	0.4	0.4
Cardiomyopathy	3	0.4	0.4

ALL CASES			
CAUSE OF DEATH CONTINUED			
Exact cause of death continued	n	% with missing data (n=833)	% of available data (n=704)
Diabetes	3	0.4	0.4
Intestine disease	3	0.4	0.4
Sepsis	3	0.4	0.4
Cardiomegaly	2	0.2	0.3
HIV	2	0.2	0.3
Infection. HIV	2	0.2	0.3
Intracerebral haemorrhage	2	0.2	0.3
Medical negligence	2	0.2	0.3
Myocarditis	2	0.2	0.3
Perforated appendix	2	0.2	0.3
Peritonitis	2	0.2	0.3
Pneumothorax	2	0.2	0.3
Sharp trauma	2	0.2	0.3
Cardiovascular pathology. abdominal disease	1	0.1	0.1
Renal disease	1	0.1	0.1
Abdominal pathology. HIV	1	0.1	0.1
Anaemia	1	0.1	0.1
Anaphylactic shock	1	0.1	0.1
Aortic aneurysm	1	0.1	0.1
Arrhythmia	1	0.1	0.1
Bleeding diathesis with anaemia	1	0.1	0.1
Bowel torsion	1	0.1	0.1
Brain disease	1	0.1	0.1
Brain tumour	1	0.1	0.1

ALL CASES			
CAUSE OF DEATH CONTINUED			
Exact cause of death continued	n	% with missing data (n=833)	% of available data (n=704)
Brain tumour. abdominal abscess	1	0.1	0.1
Bronchiectasis	1	0.1	0.1
Cardiovascular pathology. Lung disease	1	0.1	0.1
Cerebellar abscess	1	0.1	0.1
Cerebral pathology	1	0.1	0.1
Cerebrovascular accident	1	0.1	0.1
Collapsed lung. diabetes	1	0.1	0.1
Complications of pregnancy. hypertension	1	0.1	0.1
Congenital heart disease	1	0.1	0.1
Congestive heart failure. Bronchiectasis	1	0.1	0.1
Coronary artery aneurysm	1	0.1	0.1
Coronary artery atherosclerosis	1	0.1	0.1
Coronary artery disease. Infection	1	0.1	0.1
Diabetes. Respiratory pathology	1	0.1	0.1
Drowning	1	0.1	0.1
Eroded feeding tube	1	0.1	0.1
Gastritis	1	0.1	0.1
Gastrointestinal haemorrhage	1	0.1	0.1
Gastrointestinal pathology	1	0.1	0.1
Gastro-intestinal sepsis and skin infection	1	0.1	0.1
Haemoptysis. Epilepsy	1	0.1	0.1
Haemorrhagic pneumonia	1	0.1	0.1
Haemorrhagic stroke	1	0.1	0.1
Haematological in nature	1	0.1	0.1

ALL CASES			
CAUSE OF DEATH CONTINUED			
Exact cause of death continued	n	% with missing data (n=833)	% of available data (n=704)
Heart failure	1	0.1	0.1
Heat stroke	1	0.1	0.1
Hypertension	1	0.1	0.1
Hyperthermia	1	0.1	0.1
Hypothermia. TB	1	0.1	0.1
Idiopathic hydrocephalus	1	0.1	0.1
Infarcted brain. Cardiovascular pathology	1	0.1	0.1
Infection (non-specific)	1	0.1	0.1
Intestinal bowel obstruction	1	0.1	0.1
Intestinal torsion	1	0.1	0.1
Intracranial haemorrhage	1	0.1	0.1
Ischaemic bowel disease	1	0.1	0.1
Ischaemic cerebral infarct. HIV	1	0.1	0.1
Left lung abscess	1	0.1	0.1
Meningo-encephalitis	1	0.1	0.1
Myocardial infarction. Pneumonia	1	0.1	0.1
Perforated spleen	1	0.1	0.1
Pericarditis	1	0.1	0.1
Pneumonia. Cardiomyopathy	1	0.1	0.1
Pneumonia. Dehydration	1	0.1	0.1
Pneumonia. diarrhoea	1	0.1	0.1
Pneumonia. Myocarditis	1	0.1	0.1
Polycystic renal disease	1	0.1	0.1
Post varicella zoster toxic shock syndrome	1	0.1	0.1

ALL CASES			
CAUSE OF DEATH CONTINUED			
Exact cause of death continued	n	% with missing data (n=833)	% of available data (n=704)
Post-partum haemorrhage	1	0.1	0.1
Renal disease	1	0.1	0.1
Rheumatic heart disease	1	0.1	0.1
Ruptured aneurysm of pulmonary trunk	1	0.1	0.1
Ruptured ectopic pregnancy	1	0.1	0.1
Saddle embolism	1	0.1	0.1
Sigmoid volvulus	1	0.1	0.1
Skin wounds	1	0.1	0.1
Smoke inhalation	1	0.1	0.1
Strangulation	1	0.1	0.1
Subarachnoid haemorrhage	1	0.1	0.1
Subclavian-aortic bypass graft	1	0.1	0.1
Subdural empyema	1	0.1	0.1
Syphilitic meso-aortitis	1	0.1	0.1
T-Cell lymphoma	1	0.1	0.1
Thymic tumour	1	0.1	0.1
Thyroid mass	1	0.1	0.1
Tonsillitis	1	0.1	0.1
Tonsillitis. Sepsis	1	0.1	0.1
Urinary tract infection	1	0.1	0.1
Viral infection (cardiovascular)	1	0.1	0.1
Viral myocarditis	1	0.1	0.1
Viral myocarditis. Pneumonia	1	0.1	0.1

ALL CASES			
CAUSE OF DEATH CONTINUED			
Infectious or non-infectious	n	% with missing data (n=833)	% of available data (n=704)
Infectious	315	37.8	44.7
Non-infectious	170	20.4	24.1
Not specified	30	3.6	4.3
Unknown	129	15.5	-
Organ system	n	% with missing data (n=833)	% of available data (n=704)
Pulmonary	235	28.2	34.9
Cardiovascular	153	18.4	22.7
Central nervous system	54	6.5	8.0
Gastrointestinal	50	6.0	7.4
Multiple	11	1.3	1.6
Urinary	9	1.1	1.3
Lymphatic	7	0.8	1.0
Endocrine	7	0.8	1.0
Reproductive	3	0.4	0.4
Integumentary	2	0.2	0.3
Unknown	129	15.5	-

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)						
AGE CATEGORY 1 – 10 YEARS						
SOCIAL HISTORY						
Maternal level of education	All			Males		Females
	n	% with missing data (n=66)	% of available data (n=34)	n	n	
Secondary (Grades 8-12)	31	47.0	91.2	20	11	
Primary (Grades 1-7)	3	4.5	8.8	3	0	

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 1 – 10 YEARS					
SOCIAL HISTORY CONTINUED					
Maternal level of education continued	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=34)	n	n
Unknown	32	48.5	-	16	16
Types of housing	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=44)	n	n
Formal	23	34.8	52.3	15	8
Informal	21	31.8	47.7	12	9
Unknown	22	33.3	-	12	10
Annual Household income	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=44)	n	n
South African Rands					
0	3	4.5	6.8	1	2
9 600	1	1.5	2.3	1	0
24 000	1	1.5	2.3	1	0
31 200	1	1.5	2.3	1	0
54 000	1	1.5	2.3	1	0
78 000	1	1.5	2.3	1	0
96 000	1	1.5	2.3	1	0
120 000	1	1.5	2.3	1	0
Not specified	23	34.8	-	15	8

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 1 – 10 YEARS					
SOCIAL HISTORY CONTINUED					
Substances of abuse	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=64)	n	n
None	63	95.5	98.4	37	26
Alcohol	0	0.0	0.0	0	0
Tobacco	1	1.5	1.6	0	1
Illicit drugs	0	0.0	0.0	0	0
Unknown	2	3.0	3.1	2	0
Specific substances	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=1)	n	n
Not specified	1	1.5	100.0	1	0
Physical activity	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=66)	n	n
Yes	0	0	0	0	0
Unknown	66	100	-	39	27
CLINICAL HISTORY					
Symptoms prior to death	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=63)	n	n
Vomiting	29	43.9	46.0	16	13
Fever	21	31.8	33.3	13	8

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 1 – 10 YEARS					
CLINICAL HISTORY CONTINUED					
Symptoms prior to death continued	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=63)	n	n
Diarrhoea	19	28.8	30.2	12	7
Breathlessness	16	24.2	25.4	7	9
Coughing	14	21.2	22.2	13	1
Fitting	12	18.2	19.0	8	4
Runny nose	9	13.6	14.3	8	1
Abdominal pain	8	12.1	12.7	3	5
Foaming at mouth	6	9.1	9.5	1	5
Severe headaches	6	9.1	9.5	2	4
Paralysis of limbs	4	6.1	6.3	2	2
Difficulty swallowing	4	6.1	6.3	2	2
None	3	4.5	4.8	3	0
Blood from mouth	3	4.5	4.8	2	1
Stiff neck	3	4.5	4.8	2	1
Chest pain	2	3.0	3.2	2	0
Nose bleeds	1	1.5	1.6	0	1
Abdominal distension	1	1.5	1.6	0	1
Dizzy	1	1.5	1.6	0	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 1 – 10 YEARS					
CLINICAL HISTORY CONTINUED					
Symptoms prior to death continued	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=63)	n	n
Mucus from nose	1	1.5	1.6	0	1
Swollen neck/face	1	1.5	1.6	1	0
Crying	1	1.5	1.6	0	1
Not specified	2	3.0	-	1	1
Unknown (not witnessed)	1	1.5	-	1	0
Chronic illness/acute illness/infection during lifetime	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=66)	n	n
None	29	43.9	43.9	18	11
HIV exposure	7	10.6	10.6	4	3
TB exposure	6	9.1	9.1	4	2
Cerebral palsy	5	7.6	7.6	3	2
Disability	4	6.1	6.1	2	2
Epilepsy	3	4.5	4.5	1	2
Sinus	3	4.5	4.5	3	0
Mental disease	2	3.0	3.0	2	0
Flu	2	3.0	3.0	1	1
Lung problems	2	3.0	3.0	2	0

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 1 – 10 YEARS					
CLINICAL HISTORY CONTINUED					
Chronic illness/acute illness/infection during lifetime continued	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=66)	n	n
Jaundice	2	3.0	3.0	1	1
Stomach bug	2	3.0	3.0	1	1
Asthma	1	1.5	1.5	1	0
Heart problems	1	1.5	1.5	0	1
Kidney problems	1	1.5	1.5	1	0
Septic wounds	1	1.5	1.5	1	0
Pneumonia	1	1.5	1.5	1	0
Malnutrition	1	1.5	1.5	1	0
Bronchitis	1	1.5	1.5	1	0
Abdominal pain	1	1.5	1.5	1	0
Chicken pox	1	1.5	1.5	0	1
Toothache	1	1.5	1.5	0	1
Sore throat	1	1.5	1.5	0	1
Down syndrome	1	1.5	1.5	0	1
Ear infection	1	1.5	1.5	1	0
Parotitis	1	1.5	1.5	0	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 1 – 10 YEARS					
CLINICAL HISTORY CONTINUED					
Chronic illness/acute illness/infection during lifetime continued	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=66)	n	n
Cytomegalovirus infection	1	1.5	1.5	0	1
Eczema	1	1.5	1.5	1	0
Growth problems	1	1.5	1.5	0	1
Hydrocephalus	1	1.5	1.5	0	1
High blood sugar	1	1.5	1.5	1	0
Virus	1	1.5	1.5	0	1
Meningitis	1	1.5	1.5	1	0
Prada Willi Syndrome	1	1.5	1.5	1	0
Pierre-Robinsons Syndrome	1	1.5	1.5	1	0
Central Hyper Thyroidism	1	1.5	1.5	1	0
Rubella	1	1.5	1.5	1	0
Medicinal substance use	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=65)	n	n
Pharmaceutical products	42	63.6	64.6	25	17
None	20	30.3	30.7	10	10
Traditional medicine	3	4.5	4.6	2	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 1 – 10 YEARS					
CLINICAL HISTORY CONTINUED					
Medicinal substance use continued	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=65)	n	n
Unknown	3	4.5	-	3	0
Chronic medication	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=63)	n	n
No	48	72.7	76.2	27	21
Yes	15	22.7	23.8	9	6
Unknown	3	4.5	-	3	0
Medicinal substances	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=66)	n	n
Paracetamol	20	30.3	30.3	10	10
Antibiotics	3	4.5	4.5	2	1
Antiretrovirals	3	4.5	4.5	3	0
Chlorpheniramine	3	4.5	4.5	1	2
Cotrimoxazole	3	4.5	4.5	3	0
Phenobarbital	3	4.5	4.5	3	0
Allergy medication	2	3.0	3.0	2	0
Pyrazinamide	2	3.0	3.0	2	0
Pyridoxine	2	3.0	3.0	2	0

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 1 – 10 YEARS					
CLINICAL HISTORY CONTINUED					
Medicinal substances continued	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=66)	n	n
Acetylsalicylic acid	1	1.5	1.5	1	0
Amoxicillin, Clavulanic acid	1	1.5	1.5	1	0
Cough medicine	1	1.5	1.5	1	0
Diarrhoea tablet	1	1.5	1.5	1	0
Diazepam	1	1.5	1.5	1	0
Glucose	1	1.5	1.5	1	0
Isotretinoin	1	1.5	1.5	1	0
Jamaica ginger	1	1.5	1.5	1	0
Lactobacillus acidoph-pectin	1	1.5	1.5	1	0
Metoclopramide	1	1.5	1.5	1	0
Multivitamin syrup	1	1.5	1.5	1	0
Muti	1	1.5	1.5	1	0
Nose drops	1	1.5	1.5	1	0
Omeprazole	1	1.5	1.5	1	0
Pramoxine	1	1.5	1.5	0	1
Prescription medication	1	1.5	1.5	0	1
Pyroxamine	1	1.5	1.5	1	0

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 1 – 10 YEARS					
CLINICAL HISTORY CONTINUED					
Medicinal substances continued	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=66)	n	n
Ritonavir	1	1.5	1.5	1	0
Salbutamol	1	1.5	1.5	1	0
Salt solution	1	1.5	1.5	1	0
TB medication	1	1.5	1.5	0	1
Teething syrup	1	1.5	1.5	1	0
Umhlonyane	1	1.5	1.5	0	1
Vitamin C	1	1.5	1.5	1	0
Zinc tablets	1	1.5	1.5	0	1
Not specified	2	3.0	-	0	2
Family history of illness	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=55)	n	n
Unknown	11	16.7	-	7	4
None	34	51.5	61.8	17	17
HIV	9	13.6	16.4	9	0
High blood pressure	8	12.1	14.5	4	4
Previous sudden death	3	4.5	5.5	2	1
Asthma	1	1.5	1.8	0	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 1 – 10 YEARS					
CLINICAL HISTORY CONTINUED					
Family history of illness continued	All			Males	Females
	n	% with missing data (n=66)	% of available data (n=55)	n	n
Cancer	1	1.5	1.8	0	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 11 – 20 YEARS					
SOCIAL HISTORY					
Types of housing	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=23)	n	n
Formal	12	23.5	52.2	7	5
Informal	11	21.6	47.8	5	6
Unknown	28	54.9	-	10	18
Substances of abuse	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=44)	n	n
None	31	60.8	70.5	11	20
Alcohol	9	17.6	20.5	5	4
Tobacco	6	11.8	13.6	4	2
Illicit drugs	5	9.8	11.4	3	2
Unknown	7	13.7	-	4	3
Specific substances	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=26)	n	n
Ciders	1	2.0	3.3	0	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 11 – 20 YEARS					
SOCIAL HISTORY CONTINUED					
Specific substances continued	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=26)	n	n
Spirits	1	2.0	3.3	0	1
Wine	1	2.0	3.3	0	1
Beer	5	9.8	16.7	2	3
Brandy	3	5.9	10.0	1	2
Methamphetamine	2	3.9	6.7	0	2
Cannabis	5	9.8	16.7	4	1
Ecstasy	1	2.0	3.3	1	0
Methaqualone	2	3.9	6.7	0	2
Glue	1	2.0	3.3	1	0
Cigarettes	4	7.8	13.3	3	1
Hubbly	1	2.0	3.3	1	0
Not specified	3	5.9	10.0	2	1
Physical activity	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=1)	n	n
Yes	1	2.0	2.3	1	0
Unknown	50	98.0	-	21	29
CLINICAL HISTORY					
Symptoms prior to death	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=39)	n	n
Breathlessness	13	25.5	33.3	8	5
Vomiting	13	25.5	33.3	8	5
Foaming at mouth	10	19.6	25.6	3	7

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 11 – 20 YEARS					
CLINICAL HISTORY CONTINUED					
Symptoms prior to death continued	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=39)	n	n
Fitting	8	15.7	20.5	3	5
Severe headaches	8	15.7	20.5	3	5
Abdominal pain	7	13.7	17.9	4	3
Diarrhoea	6	11.8	15.4	4	2
Fever	5	9.8	12.8	5	0
Nose bleeds	5	9.8	12.8	3	2
Chest pain	4	7.8	10.3	1	3
Paralysis of limbs	3	5.9	7.7	1	2
Blood from mouth	2	3.9	5.1	1	1
Abdominal distension	2	3.9	5.1	2	0
Urinated	2	3.9	5.1	1	1
Foaming at nose	2	3.9	5.1	0	2
Salivating	2	3.9	5.1	1	1
Coughing	1	2.0	2.6	1	0
Vomiting blood	1	2.0	2.6	0	1
Stiff neck	1	2.0	2.6	0	1
Runny nose	1	2.0	2.6	0	1
Nausea	1	2.0	2.6	1	0
Leg pain	1	2.0	2.6	1	0
Not specified	2	3.9	-	0	2
Unknown (not witnessed)	10	19.6	-	3	7

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 11 – 20 YEARS					
CLINICAL HISTORY CONTINUED					
Chronic illness/acute illness/infection during lifetime	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=45)	n	n
None	23	45.1	51.1	7	16
Epilepsy	6	11.8	13.3	2	4
Mental disease	5	9.8	11.1	2	3
TB exposure	2	3.9	4.4	0	2
Obesity	2	3.9	4.4	0	2
Flu	2	3.9	4.4	2	0
Allergies	2	3.9	4.4	1	1
Disability	2	3.9	4.4	1	1
Cerebral palsy	2	3.9	4.4	1	1
HIV exposure	1	2.0	2.2	0	1
Asthma	1	2.0	2.2	1	0
Diabetes	1	2.0	2.2	1	0
Kidney problems	1	2.0	2.2	0	1
Lung problems	1	2.0	2.2	0	1
Septic wounds	1	2.0	2.2	0	1
STD	1	2.0	2.2	1	0
Down syndrome	1	2.0	2.2	1	0
Tuberous sclerosis	1	2.0	2.2	0	1
Blood clot deficiency	1	2.0	2.2	0	1
Unknown	7	13.7	-	5	2

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 11 – 20 YEARS					
CLINICAL HISTORY CONTINUED					
Medicinal substance use	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=43)	n	n
None	27	52.9	62.8	10	17
Pharmaceutical products	16	31.4	37.2	7	9
Traditional medicine	0	0.0	0.0	0	0
Unknown	8	15.7	-	5	3
Chronic medication	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=43)	n	n
No	32	62.7	74.4	11	21
Yes	11	21.6	25.6	6	5
Unknown	8	15.7	-	5	3
Medicinal substances	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=29)	n	n
Contraceptive	4	7.8	13.8	0	4
Prescription medication	3	5.9	10.3	3	0
Paracetamol	2	3.9	6.9	1	1
Acetaminophen	1	2.0	3.4	1	0
Antibiotics	1	2.0	3.4	1	0
Carbamazepine	1	2.0	3.4	0	1
Ceftriaxone	1	2.0	3.4	1	0
Clobazam	1	2.0	3.4	0	1
Clonazepam	1	2.0	3.4	1	0
Constipation medication	1	2.0	3.4	1	0
Dexamethasone	1	2.0	3.4	1	0

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 11 – 20 YEARS					
CLINICAL HISTORY CONTINUED					
Medicinal substances continued	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=29)	n	n
Diazepam	1	2.0	3.4	0	1
Lorazepam	1	2.0	3.4	1	0
Mesalamine	1	2.0	3.4	0	1
Metoclopramide	1	2.0	3.4	1	0
Morphine	1	2.0	3.4	1	0
Pantoprazole	1	2.0	3.4	0	1
TB medication	1	2.0	3.4	0	1
Theophylline	1	2.0	3.4	1	0
Triamcinolone	1	2.0	3.4	1	0
Valproic acid	1	2.0	3.4	1	0
Vigabatrin	1	2.0	3.4	0	1
Vitamin C	1	2.0	3.4	1	0
Family history of illness	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=39)	n	n
None	23	45.1	59.0	11	12
Asthma	5	9.8	12.8	3	2
Previous sudden death	5	9.8	12.8	2	3

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 11 – 20 YEARS					
CLINICAL HISTORY CONTINUED					
Family history of illness continued	All			Males	Females
	n	% with missing data (n=51)	% of available data (n=39)		n
Heart disease	4	7.8	10.3	2	2
High blood pressure	3	5.9	7.7	1	2
Cancer	1	2.0	2.6	0	1
Diabetes	1	2.0	2.6	1	0
Blood clot deficiency	1	2.0	2.6	0	1
Unknown	12	23.5	-	5	7

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
SOCIAL HISTORY					
Types of housing	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=106)	n	n
Formal	54	27.1	50.9	38	16
Informal	52	26.1	49.1	34	18
Unknown	93	46.7	-	56	37
Substances of abuse	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=165)	n	n
None	59	35.8	35.8	31	28
Alcohol	72	43.6	43.6	49	23

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
SOCIAL HISTORY CONTINUED					
Substances of abuse continued	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=165)	n	n
Tobacco	50	30.3	30.3	33	17
Illicit drugs	45	27.3	27.3	35	10
Unknown	34	-	-	22	12
Specific substances	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=208)	n	n
Beer	52	26.1	25.0	38	14
Cigarettes	42	21.1	20.2	27	15
Cannabis	24	12.1	11.5	21	3
Methamphetamine	22	11.1	10.6	17	5
Brandy	19	9.5	9.1	15	4
Methaqualone	15	7.5	7.2	14	1
Wine	12	6.0	5.8	7	5
Spirits	4	2.0	1.9	4	0
Heroin	4	2.0	1.9	3	1
Whoonga	3	1.5	1.4	2	1
Hubbly	3	1.5	1.4	3	0
Ciders	2	1.0	1.0	0	2

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
SOCIAL HISTORY CONTINUED					
Specific substances continued	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=208)	n	n
Whiskey	2	1.0	1.0	1	1
Sniff	1	0.5	0.5	0	1
Cat	1	0.5	0.5	1	0
Cocaine	1	0.5	0.5	1	0
Buttons	1	0.5	0.5	1	0
Not specified	16	8.0	-	12	4
Physical activity	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=2)	n	n
Yes	2	1.0	100.0	2	0
Unknown	197	99.0	-	126	71
CLINICAL HISTORY					
Symptoms prior to death	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=156)	n	n
None	5	2.5	3.2	4	1
Breathlessness	55	27.6	35.3	31	24
Vomiting	46	23.1	29.5	29	17
Foaming at mouth	41	20.6	26.3	25	16

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
CLINICAL HISTORY CONTINUED					
Symptoms prior to death continued	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=156)	n	n
Chest pain	40	20.1	25.6	27	13
Fitting	31	15.6	19.9	18	13
Severe headaches	30	15.1	19.2	10	20
Abdominal pain	28	14.1	17.9	17	11
Vomiting blood	13	6.5	8.3	10	3
Blood from mouth	12	6.0	7.7	7	5
Fever	10	5.0	6.4	5	5
Nose bleeds	10	5.0	6.4	6	4
Diarrhoea	9	4.5	5.8	3	6
Paralysis of limbs	9	4.5	5.8	4	5
Coughing	7	3.5	4.5	2	5
Coughing up blood	7	3.5	4.5	7	0
Foaming at nose	6	3.0	3.8	4	2
Urinated	5	2.5	3.2	1	4
Abdominal distension	4	2.0	2.6	2	2
Dizzy	4	2.0	2.6	3	1
Swollen legs	3	1.5	1.9	1	2

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
CLINICAL HISTORY CONTINUED					
Symptoms prior to death continued	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=156)	n	n
Stiff neck	2	1.0	1.3	1	1
Salivating	2	1.0	1.3	1	1
Lethargy	2	1.0	1.3	2	0
Heart burn	2	1.0	1.3	2	1
Difficulty swallowing	1	0.5	0.6	0	1
Nausea	1	0.5	0.6	1	0
Arm blisters	1	0.5	0.6	1	0
Mucus from nose	1	0.5	0.6	0	0
Swollen neck/face	1	0.5	0.6	1	0
Allergic reaction	1	0.5	0.6	0	0
Back pain	1	0.5	0.6	1	0
Not specified	1	0.5	-	1	0
Unknown (not witnessed)	42	21.1	-	31	11
Chronic illness/acute illness/infection during lifetime	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=175)	n	n
None	84	48.0	48.0	60	24

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
CLINICAL HISTORY CONTINUED					
Chronic illness/acute illness/infection during lifetime continued	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=175)	n	n
TB exposure	24	13.7	13.7	15	9
Epilepsy	20	11.4	11.4	13	7
HIV exposure	15	8.6	8.6	1	14
Asthma	10	5.7	5.7	7	3
High blood pressure	9	5.1	5.1	5	4
Mental disease	8	4.6	4.6	6	2
Obesity	6	3.4	3.4	2	4
Heart problems	5	2.9	2.9	2	3
Flu	5	2.9	2.9	2	3
Allergies	5	2.9	2.9	4	1
Disability	3	1.7	1.7	3	0
Diabetes	2	1.1	1.1	1	1
Kidney problems	2	1.1	1.1	0	2
Cancer	2	1.1	1.1	1	1
Malnutrition	2	1.1	1.1	1	1
Lung problems	1	0.6	0.6	0	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
CLINICAL HISTORY CONTINUED					
Chronic illness/acute illness/infection during lifetime continued	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=175)	n	n
Septic wounds	1	0.6	0.6	1	0
Ulcers	1	0.6	0.6	0	1
Jaundice	1	0.6	0.6	0	1
Abdominal pain	1	0.6	0.6	1	0
Arthritis	1	0.6	0.6	0	1
Malaria	1	0.6	0.6	0	1
Fainting	1	0.6	0.6	0	1
Chicken pox	1	0.6	0.6	0	1
STD	1	0.6	0.6	1	0
Low blood pressure	1	0.6	0.6	0	1
Seizures	1	0.6	0.6	0	0
Acute limb ischaemia	1	0.6	0.6	1	0
Marfan syndrome	1	0.6	0.6	1	0
Sleep apnia	1	0.6	0.6	1	0
Norwegian scabies	1	0.6	0.6	0	1
Liver failure	1	0.6	0.6	0	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
CLINICAL HISTORY CONTINUED					
Chronic illness/acute illness/infection during lifetime continued	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=175)	n	n
Gangrene	1	0.6	0.6	0	1
Headaches	1	0.6	0.6	1	0
Meningitis	1	0.6	0.6	1	0
Mumps	1	0.6	0.6	0	1
Unknown	24	13.7	-	18	6
Medicinal substance use	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=158)	n	n
None	97	61.4	61.4	68	29
Pharmaceutical products	61	38.6	38.6	31	30
Traditional medicine	1	0.6	0.6	0	1
Unknown	41	25.9	-	29	12
Chronic medication	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=168)	n	N
No	122	72.6	72.6	80	42
Yes	46	27.4	27.4	26	20
Unknown	31	18.5	-	22	9

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
CLINICAL HISTORY CONTINUED					
Medicinal substances	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=96)	n	n
Contraceptive	9	4.5	9.4	0	9
Paracetamol	9	4.5	9.4	6	3
Prescription medication	9	4.5	9.4	7	2
Epilepsy medication	8	4.0	8.3	6	2
TB medication	8	4.0	8.3	4	4
Asthma medication	5	2.5	5.2	2	3
Antiretrovirals	4	2.0	4.2	0	4
Pain medicine	3	1.5	3.1	1	2
Tramadol	3	1.5	3.1	2	1
Blood pressure medication	2	1.0	2.1	2	0
Chlorpheniramine	2	1.0	2.1	1	1
Psychiatric medication	2	1.0	2.1	1	1
Risperidone	2	1.0	2.1	2	0
Valproic acid	2	1.0	2.1	2	0
Acamprosate calcium	1	0.5	1.0	1	0
Acetaminophen	1	0.5	1.0	1	0
Amoxicillin	1	0.5	1.0	1	0

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
CLINICAL HISTORY CONTINUED					
Medicinal substances continued	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=96)	n	n
Bisacodyl enema	1	0.5	1.0	0	1
Brown powder	1	0.5	1.0	0	1
Carbamazepine	1	0.5	1.0	1	0
Ciprofloxacin	1	0.5	1.0	0	1
Erythromycin	1	0.5	1.0	0	1
Flu pill	1	0.5	1.0	1	0
Fluoxetine	1	0.5	1.0	1	0
Flupentixol decanoate	1	0.5	1.0	1	0
Freshen	1	0.5	1.0	1	0
Furosemide	1	0.5	1.0	0	1
Ibuprofen	1	0.5	1.0	0	1
Lithium carbonate	1	0.5	1.0	1	0
Lorazepam	1	0.5	1.0	1	0
Metoclopramide	1	0.5	1.0	1	0
Orphenadrine	1	0.5	1.0	1	0
Pantoprazole	1	0.5	1.0	0	1
Phenytoin	1	0.5	1.0	0	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
CLINICAL HISTORY CONTINUED					
Medicinal substances continued	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=96)	n	n
Promethazine	1	0.5	1.0	1	0
Rizatriptan	1	0.5	1.0	0	1
Rufinamide	1	0.5	1.0	1	0
Scopolamine	1	0.5	1.0	1	0
Sulfamethoxazole	1	0.5	1.0	0	1
Ulcer medication	1	0.5	1.0	0	1
Warfarin	1	0.5	1.0	0	1
Water medication	1	0.5	1.0	1	0
Not specified	18	9.0	-	12	4
Family history of illness	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=145)	n	n
Unknown	55	37.9	-	34	21
None	90	62.1	62.1	59	31
Asthma	20	13.8	13.8	12	8
Heart disease	19	13.1	13.1	14	5
Cancer	19	13.1	13.1	10	9
Previous sudden death	12	6.0	8.3	8	4

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 21 – 30 YEARS					
CLINICAL HISTORY CONTINUED					
Family history of illness continued	All			Males	Females
	n	% with missing data (n=199)	% of available data (n=145)	n	n
Diabetes	7	3.5	4.8	4	3
High blood pressure	5	4.8	4.8	3	2
Stroke	1	0.7	0.7	1	0
TB	1	0.7	0.7	1	0
Renal failure	1	0.7	0.7	1	0

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
SOCIAL HISTORY					
Types of housing	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=183)	n	n
Formal	88	25.5	48.1	58	30
Informal	95	27.5	51.9	66	29
Unknown	162	47.0	-	109	53
Substances of abuse	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=295)	n	n
None	85	24.6	28.8	32	53

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
SOCIAL HISTORY					
Substances of abuse continued	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=295)		n
Alcohol	144	41.7	48.8	110	34
Tobacco	124	35.9	42.0	98	26
Illicit drugs	83	24.1	28.1	70	13
Unknown	50	14.5	16.9	37	13
Specific substances	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=486)	n	n
Cigarettes	118	34.2	24.3	94	24
Beer	112	32.5	23.0	89	23
Methamphetamine	49	14.2	10.1	39	10
Cannabis	41	11.9	8.4	39	2
Wine	37	10.7	7.6	23	14
Brandy	37	10.7	7.6	32	5
Methaqualone	36	10.4	7.4	31	5
Spirits	15	4.3	3.1	10	5
Heroin	15	4.3	3.1	13	2
Papsak	7	2.0	1.4	6	1
Whiskey	4	1.2	0.8	3	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
SOCIAL HISTORY					
Specific substances	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=486)	n	n
Ciders	4	1.2	0.8	0	4
Whoonga	3	0.9	0.6	3	0
Cocaine	2	0.6	0.4	1	1
Traditional beer	1	0.3	0.2	1	0
Sniff	1	0.3	0.2	0	1
Buttons	1	0.3	0.2	1	0
Glue	1	0.3	0.2	0	1
E-cigarettes	1	0.3	0.2	1	0
Speed	1	0.3	0.2	1	0
Not specified	25	7.2	-	21	4
Physical activity	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=8)	n	n
Yes	9	2.6	100.0	7	2
Unknown	337	97.7	-	226	111

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY					
Symptoms prior to death	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=269)	n	n
None	13	3.8	4.8	8	5
Breathlessness	96	27.8	35.7	59	37
Chest pain	75	21.7	27.9	52	23
Vomiting	67	19.4	24.9	33	34
Foaming at mouth	49	14.2	18.2	27	22
Abdominal pain	48	13.9	17.8	28	20
Fitting	42	12.2	15.6	31	11
Severe headaches	42	12.2	15.6	23	19
Nose bleeds	20	5.8	7.4	17	3
Diarrhoea	19	5.5	7.1	13	6
Vomiting blood	19	5.5	7.1	14	5
Coughing	18	5.2	6.7	13	5
Fever	15	4.3	5.6	7	8
Blood from mouth	14	4.1	5.2	12	2
Paralysis of limbs	14	4.1	5.2	7	7
Abdominal distension	12	3.5	4.5	7	5
Urinated	6	1.7	2.2	5	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY CONTINUED					
Symptoms prior to death continued	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=269)	n	n
Stiff neck	6	1.7	2.2	3	3
Difficulty swallowing	6	1.7	2.2	3	3
Coughing up blood	5	1.4	1.9	3	2
Dizzy	5	1.4	1.9	4	1
Nausea	5	1.4	1.9	3	2
Arm blisters	5	1.4	1.9	1	4
Salivating	4	1.2	1.5	3	1
Swollen legs	4	1.2	1.5	2	2
Leg pain	4	1.2	1.5	3	1
Lethargy	4	1.2	1.5	1	3
Heart burn	4	1.2	1.5	3	1
Foaming at nose	3	0.9	1.1	1	2
Mucus from nose	2	0.6	0.7	0	2
Allergic reaction	1	0.3	0.4	1	0
Vaginal discharge	1	0.3	0.4	0	1
Bleeding heavily	1	0.3	0.4	0	1
Anal bleeding	1	0.3	0.4	1	0

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY CONTINUED					
Symptoms prior to death continued	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=269)	n	n
Fluid from ear	1	0.3	0.4	1	0
Shoulder pain	1	0.3	0.4	1	0
Not specified	2	0.6	-	2	0
Unknown (not witnessed)	74	21.4	-	56	18
Chronic illness/acute illness/infection during lifetime	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=312)	n	n
None	125	36.2	40.1	92	33
TB exposure	54	15.7	17.3	36	18
High blood pressure	35	10.1	11.2	19	16
HIV exposure	32	9.3	10.3	12	20
Asthma	23	6.7	7.4	15	8
Mental disease	19	5.5	6.1	11	8
Epilepsy	18	5.2	5.8	12	6
Obesity	16	4.6	5.1	8	8
Diabetes	14	4.1	4.5	8	6
Heart problems	13	3.8	4.2	11	2

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY CONTINUED					
Chronic illness/acute illness/infection during lifetime continued	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=312)	n	n
Flu	11	3.2	3.5	6	5
Allergies	8	2.3	2.6	4	4
Kidney problems	7	2.0	2.2	4	3
Cancer	4	1.2	1.3	3	1
Lung problems	3	0.9	1.0	2	1
Pneumonia	3	0.9	1.0	3	0
Septic wounds	2	0.6	0.6	2	0
Sinus	2	0.6	0.6	2	0
Ulcers	2	0.6	0.6	2	0
Bronchitis	2	0.6	0.6	1	1
Arthritis	2	0.6	0.6	0	2
Hernia	2	0.6	0.6	1	1
Anaemic	2	0.6	0.6	0	2
Disability	1	0.3	0.3	0	1
Jaundice	1	0.3	0.3	1	0
Stomach bug	1	0.3	0.3	1	0

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY CONTINUED					
Chronic illness/acute illness/infection during lifetime continued	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=312)	n	n
Abdominal pain	1	0.3	0.3	0	1
Malaria	1	0.3	0.3	1	0
Fainting	1	0.3	0.3	1	0
Toothache	1	0.3	0.3	0	1
Sore throat	1	0.3	0.3	0	1
Low blood pressure	1	0.3	0.3	0	1
High cholesterol	1	0.3	0.3	1	0
Psoriasis	1	0.3	0.3	0	1
Urinary problems	1	0.3	0.3	0	1
Hidradenitis	1	0.3	0.3	0	1
Gastroesophageal disease	1	0.3	0.3	0	1
Appendicitis	1	0.3	0.3	0	1
Ataxia with non-obstructive jaundice	1	0.3	0.3	1	0
Broken leg	1	0.3	0.3	1	0
Stroke	1	0.3	0.3	1	0

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY CONTINUED					
Chronic illness/acute illness/infection during lifetime continued	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=312)	n	n
Sore feet and legs	1	0.3	0.3	1	0
Subcutaneous emphysema	1	0.3	0.3	1	0
Unknown	33	9.6	-	27	6
Medicinal substance use	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=289)	n	n
None	171	49.6	59.2	129	42
Pharmaceutical products	115	33.3	39.8	60	55
Traditional medicine	4	1.2	1.4	3	1
Unknown	56	16.2	-	41	15
Chronic medication	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=306)	n	n
No	212	61.4	69.3	150	62
Yes	94	27.2	30.7	52	42
Unknown	39	11.3	-	31	8

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY CONTINUED					
Specific substances	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=182)	n	n
Prescription medication	19	5.5	10.4	11	8
Antiretrovirals	14	4.1	7.7	4	10
Paracetamol	13	3.8	7.1	5	8
TB medication	11	3.2	6.0	8	3
Contraceptive	10	2.9	5.5	0	10
Asthma medication	7	2.0	3.8	4	3
Blood pressure medication	7	2.0	3.8	4	3
Epilepsy medication	7	2.0	3.8	6	1
Acetylsalicylic acid	5	1.4	2.7	3	2
Depression medication	5	1.4	2.7	3	2
Amitriptyline hydrochloride	4	1.2	2.2	1	3
Enalapril maleate	3	0.9	1.6	1	2
Hydrochlorothiazide	3	0.9	1.6	0	3
Tramadol	3	0.9	1.6	1	2
Amlodipine	2	0.6	1.1	1	1
Antacid	2	0.6	1.1	1	1
Carvedilol	2	0.6	1.1	2	0

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY CONTINUED					
Specific substances continued	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=182)	n	n
Flu medication	2	0.6	1.1	1	1
Ibuprofen	2	0.6	1.1	1	1
Insulin	2	0.6	1.1	1	1
Magnesium	2	0.6	1.1	0	2
Muti	2	0.6	1.1	1	1
Repaglinide	2	0.6	1.1	1	1
Simvastatin	2	0.6	1.1	2	0
Aluminium-magnesium hydroxide	1	0.3	0.5	1	0
Amoxicillin	1	0.3	0.5	0	1
Analgesics	1	0.3	0.5	0	1
Antibiotics	1	0.3	0.5	0	1
Antirejection medication	1	0.3	0.5	1	0
Atenolol	1	0.3	0.5	1	0
Atorvastatin calcium	1	0.3	0.5	1	0
Bipolar medication	1	0.3	0.5	0	1
Camphor	1	0.3	0.5	0	1
Cancer medication	1	0.3	0.5	1	0

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY CONTINUED					
Specific substances continued	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=182)	n	n
Carbamazepine	1	0.3	0.5	0	1
Cimetidine	1	0.3	0.5	1	0
Ciprofloxacin	1	0.3	0.5	0	1
Clopidogrel	1	0.3	0.5	1	0
Codeine	1	0.3	0.5	0	1
Corenza C	1	0.3	0.5	1	0
Dextromethorphan	1	0.3	0.5	0	1
Diabetes medication	1	0.3	0.5	0	1
Diclofenac sodium	1	0.3	0.5	1	0
Ferritin	1	0.3	0.5	0	1
Fluoxetine	1	0.3	0.5	0	1
Furosemide	1	0.3	0.5	1	0
Green fluid	1	0.3	0.5	0	1
Green tablets	1	0.3	0.5	1	0
Hydrocortisone	1	0.3	0.5	0	1
Isosorbide dinitrate	1	0.3	0.5	1	0
Kidney medication	1	0.3	0.5	0	1

NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY CONTINUED					
Specific substances continued	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=182)	n	n
Lorazepam	1	0.3	0.5	0	1
Meperidine	1	0.3	0.5	0	1
Morphine	1	0.3	0.5	1	0
Ondansetron hydrochloride	1	0.3	0.5	1	0
Orphenadrine	1	0.3	0.5	1	0
Orange powder	1	0.3	0.5	1	0
Pain medication	1	0.3	0.5	1	0
Phenobarbital	1	0.3	0.5	0	1
Phentermine	1	0.3	0.5	1	0
Pneumonia medication	1	0.3	0.5	1	0
Prednisone	1	0.3	0.5	1	0
Propranolol	1	0.3	0.5	0	1
Pyridoxine	1	0.3	0.5	1	0
Rehydrat	1	0.3	0.5	1	0
Salt solution	1	0.3	0.5	1	0
Sandoz	1	0.3	0.5	1	0
Sleeping medication	1	0.3	0.5	0	1

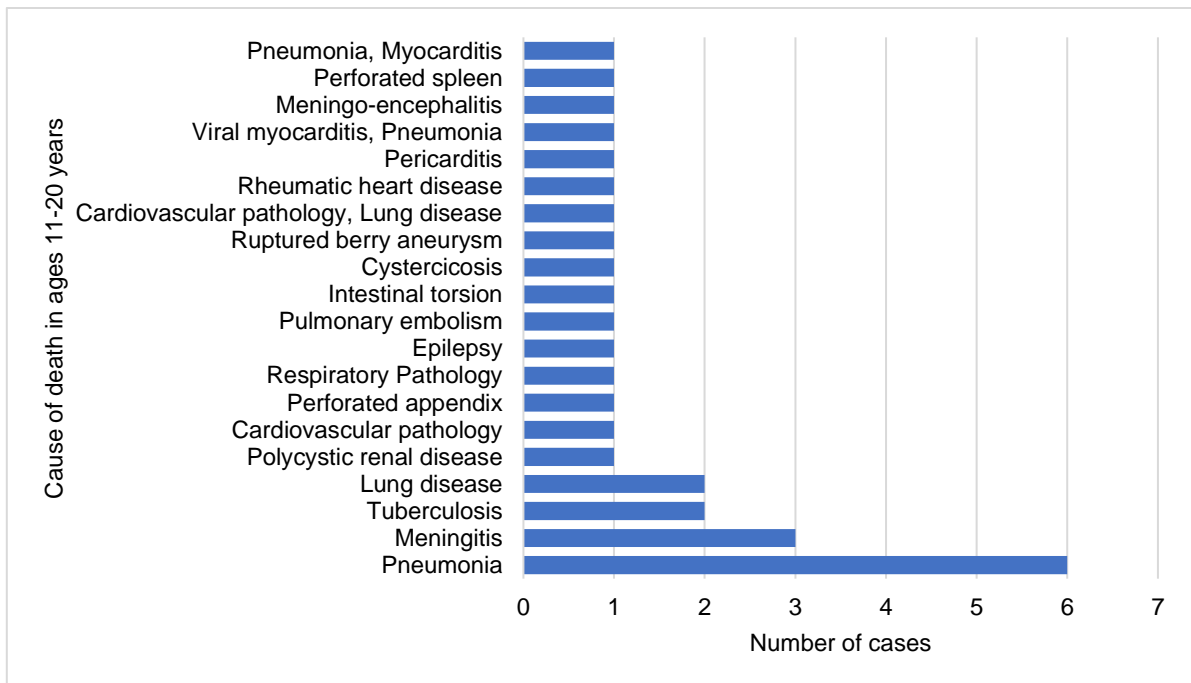
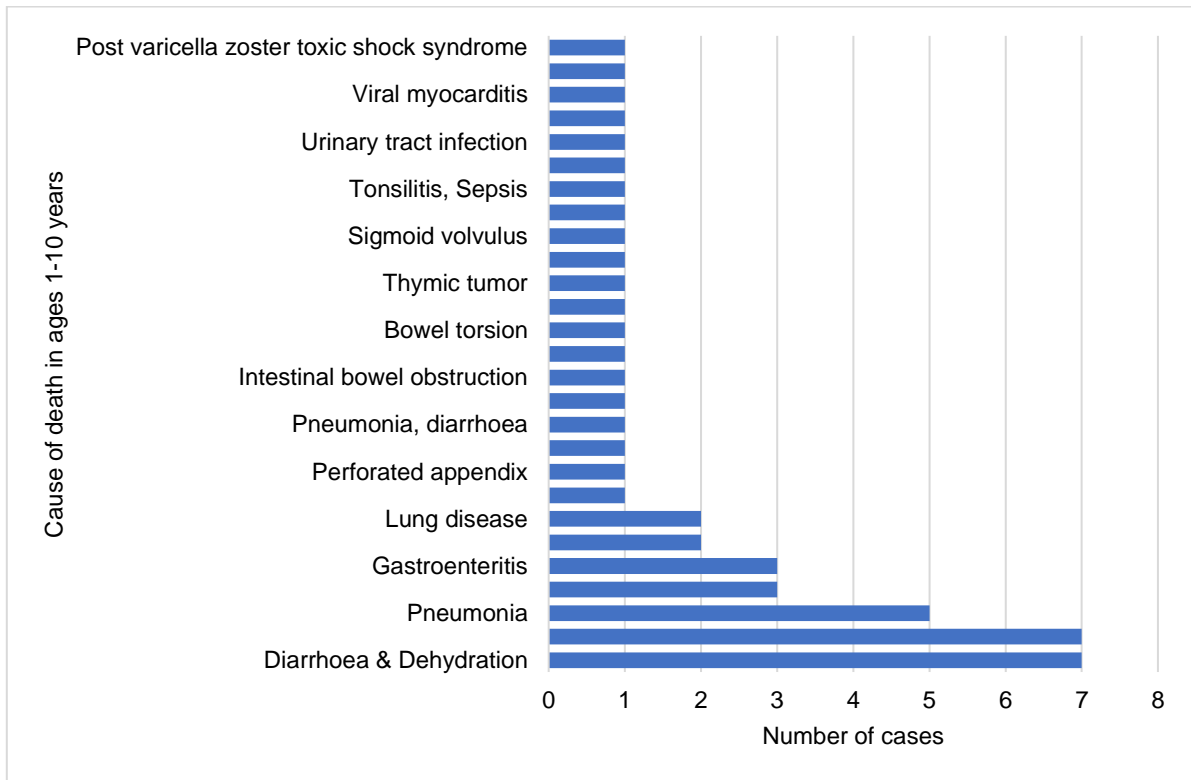
NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY CONTINUED					
Specific substances continued	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=182)	n	n
Sodium bicarbonate	1	0.3	0.5	1	0
Sulfamethoxazole-trimethoprim	1	0.3	0.5	1	0
Triamcinolone	1	0.3	0.5	1	0
Vitamin C	1	0.3	0.5	0	1
Vulform	1	0.3	0.5	0	1
Water medication	1	0.3	0.5	1	0
Zolpidem	1	0.3	0.5	0	1
Not specified	7	2.0	-	5	2
Family history of illness	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=272)	n	n
None	155	44.9	57.0	104	51
Asthma	51	14.8	18.8	34	17
Heart disease	39	11.3	14.3	29	10
Cancer	27	7.8	9.9	17	10
Previous sudden death	20	5.8	7.4	16	4
Diabetes	14	4.1	5.1	10	4
High blood pressure	11	3.2	4.0	6	5

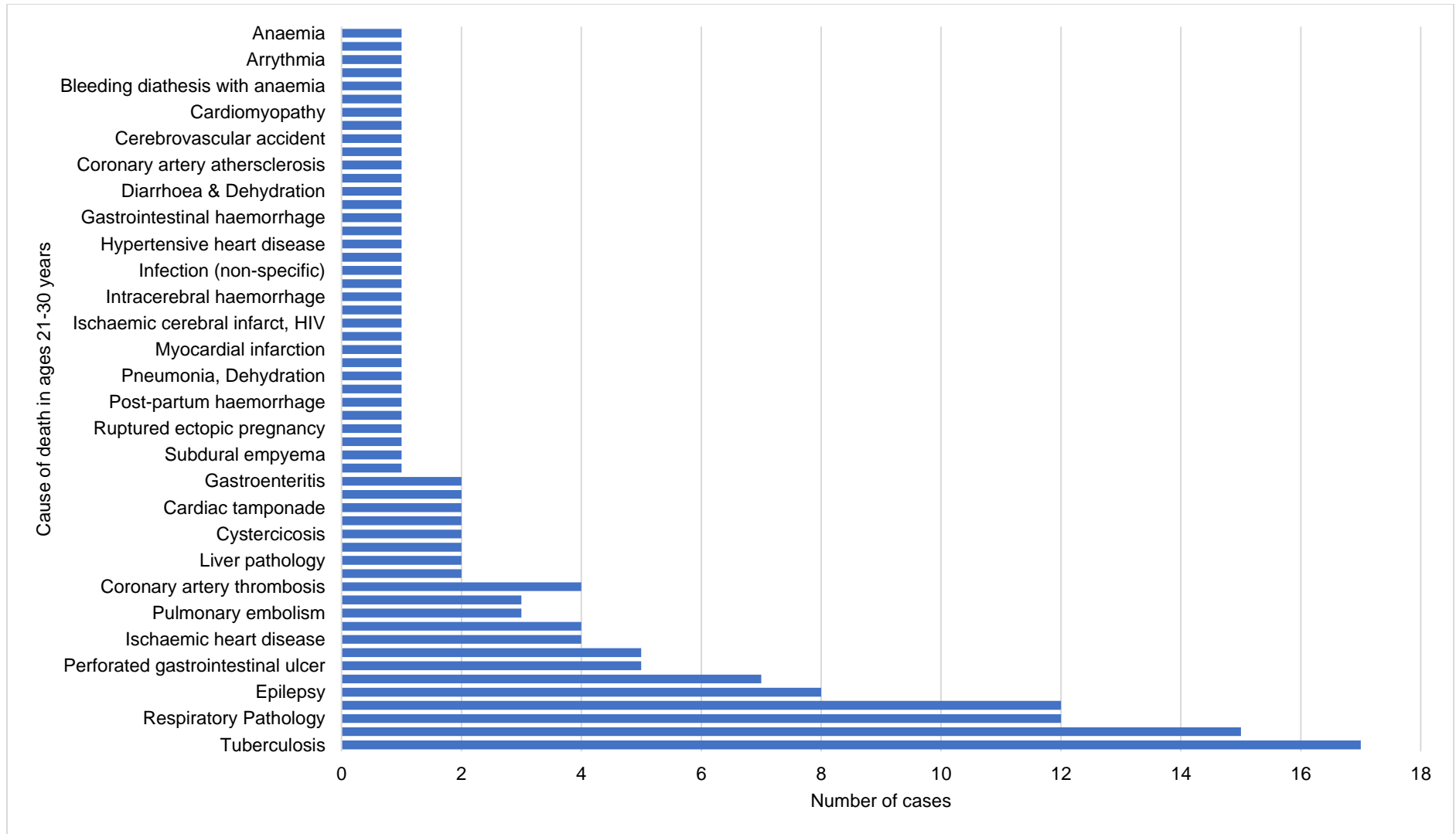
NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES ONLY (n=661)					
AGE CATEGORY 31 – 40 YEARS					
CLINICAL HISTORY CONTINUED					
Family history of illness continued	All			Males	Females
	n	% with missing data (n=345)	% of available data (n=272)	n	n
Stroke	1	0.3	0.4	0	1
Epilepsy	1	0.3	0.4	1	0
Arthritis	1	0.3	0.4	0	1
Low blood pressure	1	0.3	0.4	1	0
Unknown	73	21.2	-	49	24

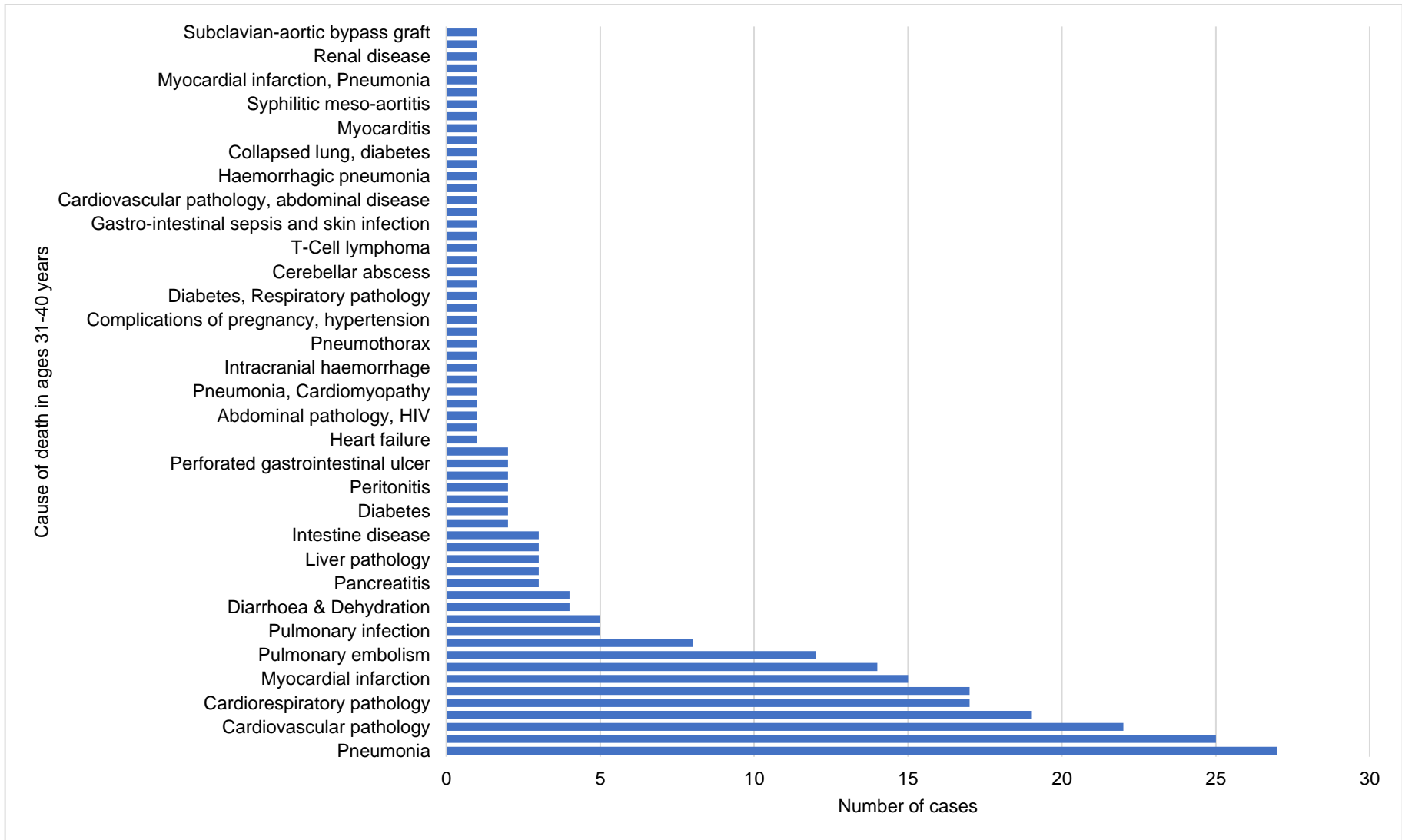
NON-SPECIFIC NATURAL, UNDETERMINED AND UNDER INVESTIGATION CASES (n=176)		
Biological sample availability	n	% of available data (n=176)
Yes	144	81.8
No	32	18.2
Specific sample	n	% of available data (n=144)
Blood only	46	31.9
Tissue only	86	59.7
Blood and tissue	12	8.3

UNDETERMINED CASES ONLY (n=23)		
Was the body identified?	n	% of available data (n=23)
No	7	30.4
Yes	16	69.6

APPENDIX F: CAUSES OF DEATH PER AGE CATEGORY







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