

**Investigating pesticide-related deaths admitted to Salt  
River Mortuary in Cape Town, South Africa: a  
retrospective, descriptive analysis**

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## **Abstract**

Pesticide-related poisonings place a burden on the public health system in low- and middle-income countries. Notification of pesticide poisonings and deaths is a legal requirement in South Africa, however, our understanding of the prevalence and type of pesticides involved in poisoning cases remains limited. This is further complicated by the emergence of ‘street pesticides’, which are unlabelled and illegally sold toxic pesticides. It is important to understand the role of these and other pesticides in local poisonings, and mortuary data provides an important resource to be able to investigate pesticide-related mortality specifically. This study aimed to build on previous research conducted at the Salt River mortuary (SRM) by expanding and updating our understanding of pesticide-related fatalities within the West Metropole of Cape Town.

A retrospective, cross-sectional review of all unnatural death cases admitted to the SRM between January 2016 and December 2019 (inclusive) was conducted so as to identify pesticide-related deaths for further investigation. A total of 15 761 cases were admitted to SRM over the 4-year study period (mean: 3941 cases per annum). From this total, 92 cases (0.58%) were identified as pesticide related. Most decedents were male (59.8%), with the cohort’s mean age being 26.2 years (range: 2 months to 66 years). The majority of cases were suicides (60.8%), and terbufos (an organophosphate) was detected in 50 cases (54.3%). Pesticide-related fatalities were found to predominately occur in lower socio-economic areas. According to the data adults and adolescents are most at risk of being exposed to the harmful effects of these harmful compounds.

Using a holistic approach to investigating pesticide-related fatalities could provide important clues that assist in gaining a better understanding of the factors that influence pesticide-related incidents. Combined efforts from healthcare practitioners and forensic investigators could help inform policy-makers on ways to minimise the use or distribution of pesticide compounds.

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To my *Source, Anchor, Sustainer and Keeper, YAHWEH, ELOHIM, ABBA FATHER, YASHUAH HAMASCHIACH* none of this would have been possible without *YOUR VERY HAND* orchestrating all things and breathing life into all that I do and strengthening me to make it through, even in the most difficult of circumstances. Thank *YOU* for keeping me grounded and focused. May *YOU* be honoured in all that I do.

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## List of abbreviations

AChE	acetylcholinesterase
BHC	benzene hexachloride
CEOHR	Division of Environmental Health and Centre for Environmental and Occupational Health Research
CN	cyano
CNS	central nervous system
CS-syndrome	choreoathetosis and salivation syndrome
DAFF	Department of Agriculture, Forestry and Fisheries
p,p'-DDE	dichlorodiphenyldichloroethylene
DDT	dichlorodiphenyltrichloroethane
DEA	Department of Environmental Affairs
DoH	Department of Health
DoL	Department of Labour
FCL	National Forensic Chemistry Laboratories
FPS	Forensic Pathology Services
GC-MS	gas chromatography coupled to mass spectrometry
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
HREC	Human Research Ethics Committee
LC <sub>50</sub>	median lethal concentration
LC-MS	liquid chromatography coupled to mass spectrometry LD <sub>50</sub> median lethal dose
NIOSH	National Institute for Occupational Safety and Health
NH <sub>2</sub> COOH	carbamic acid
NMC	notification of medical condition
OAD	office autopsy database
OC	organochlorine
OHSA	Occupational Health and Safety Act
OP	organophosphate
PChE	pseudocholinesterase

POPs	persistent organic pollutants
RCWMCH	Red Cross War Memorial Children's Hospital
RSA	Republic of South Africa
SA	South Africa
SRM	Salt River mortuary
T-syndrome	tremor syndrome
UCT	University of Cape Town
USA	United States of America
WC	Western Cape
WHO	World Health Organisation

# **Chapter 1: Introduction and literature review**

## **1.1 Background**

Pesticides, as defined by the National Institute of Environmental Health Sciences (NIEHS) refer to a wide range of chemical compounds used to kill or control pests (NIEHS, 2020). Pests are animals or plants whose effect is harmful to human health and quality of human life. Pesticides range from insecticides, fungicides, herbicides, and rodenticides (which kill insects, fungi, weeds, and rodents respectively) to molluscicides, nematocides and plant growth regulators (Aktar *et al.*, 2009). These chemical substances are generally used to eliminate agricultural pests, which, through crop and livestock damage, negatively affect crop productivity (Aktar *et al.*, 2009). In addition, pesticides are used within the public health sector to prevent disease or infection by controlling disease-causing insect vectors that transmit infectious pathogens or parasites from one living organism into another (Rivero *et al.*, 2010; Wilson *et al.* 2017). Generally, pesticides are classified according to their physicochemical properties and toxicity profiles (Yadav and Devi, 2017).

## **1.2 Pesticide classification**

Pesticides may be synthetic or naturally occurring, with synthetic pesticides usually being more hazardous (Yadav and Devi, 2017). Generally, pesticides are classified according to characteristics such as their mode of entry, mechanism of action, formulation and chemical composition, function, potency, the selected target organism and according to their toxicity (Büchel, 1983). Of these, classification based on chemical composition, mode of entry and toxicity provide the basis for pesticide use in industry. These classification methods also provide information on the expected outcomes of pesticide exposure on humans, animals, and the environment. A summary of common pesticide classifications is provided below.

### **1.2.1 Classification based on toxicity**

The classification of pesticides according to their toxicity (adverse effects on a target organism) was described by the World Health Organisation (WHO, 2009). The WHO uses the

Globally Harmonized System of Classification and Labelling of Chemicals (GHS) to classify pesticides based on toxicity (WHO, 2009) (Table 1). This toxicity is measured according to the pesticide's median lethal dose (LD<sub>50</sub>). The LD<sub>50</sub> is a measurement of the amount of pesticide per unit weight required to kill 50% of all experimental organisms exposed to the pesticide. These values are typically obtained in experiments conducted on rats where the rodents were exposed to oral and dermal doses of pesticides (Yadav and Devi, 2017). Other methods of pesticide testing involve exposing test animals to various concentrations of the active ingredient to determine the lethal concentration required to kill 50% of all test animals (LC<sub>50</sub>). Test animals often include dogs, pigs, rabbits, monkeys, and pigeons (Akhila *et al.*, 2007). Pesticides are grouped according to these five categories based on impact of oral or dermal exposure on living organisms. Categories 1 to 3 describe more hazardous chemical compounds that, as outlined in the hazard statement, result in the development of fatal neurological, carcinogenic, muscarinic, respiratory, reproductive, and corrosive effects. Categories 4 to 5 describe less hazardous compounds that produce mild irritant effects. The effects of exposure are based on the principle that a dose-response relationship exists between the amount of pesticide encountered during exposure and the response induced within the exposed body or organism (Alewu and Nosiri, 2010).

**Table 1.** Globally Harmonized System (GHS) pesticide classification based on toxicity (WHO, 2009)

Classification	Hazard Statement	LD <sub>50</sub> (mg/kg body weight)	
		Oral	Dermal
Category 1	Fatal if swallowed or in contact with skin	< 5	< 50
Category 2	Fatal if swallowed or in contact with skin	5 - 50	50 - 200
Category 3	Toxic if swallowed or in contact with skin	50 - 300	200 - 1000
Category 4	Harmful if swallowed or in contact with skin	300 - 2000	1000 - 2000
Category 5	May be harmful if swallowed or in contact with skin	2000 - 5000	2000 - 5000

### 1.2.2 Mode of entry

Classification according to mode of entry deals with how the pesticide enters the target organism to exert its effect (Alewu and Nosiri, 2010). There are two categories within this classification method, namely systemic and non-systemic (contact) pesticides. Systemic pesticides are pesticides which, through absorption at application site and translocation to other sites, effectively penetrate target organisms to bring about their desired effects (Soycheva, 2011). Examples include glyphosate, 2,4-dichlorophenoxyacetic acid (2,4-D) and stomach

poisons which exert their effects after consumption (Yadav and Devi, 2017). Contact pesticides only bring about the desired effect when they come into direct physical body surface contact with the target organism. Unlike systemic pesticides they cannot be translocated to other regions within the body but elicit localised effects within the region of physical contact (Nansen and Thomas, 2013). Examples include paraquat and diquat dibromide.

### **1.2.3 Chemical composition**

Pesticides are also classified according to their chemical composition. Classifying pesticides based on the chemical structure and physicochemical properties (solubility, partition coefficient, molecular hydrophobicity, volatility, bioavailability and reactivity) of the active ingredients enables pesticide characteristic determination such as its efficacy (Yadav and Devi, 2017). These properties also allow for development of optimal application procedures required for successful pest control ( Nicolopoulou-Stamati *et al.*, 2016; Quinn *et al.*, 2011 ). There are two categories of chemical classification: synthetic and naturally occurring (plant-based or mineral oil derivatives). The synthetic chemicals are further divided into four sub-categories, organochlorines, organophosphates, carbamates and pyrethroids (Büchel, 1983).

#### **1.2.3.1 Organochlorines (OCs)**

Organochlorines (OCs) are also known as chlorinated hydrocarbons. This pesticide class is described as organic compounds attached to five or more chlorine atoms (Yadav and Devi, 2017). OCs are used to eliminate insects and/or arthropods in the agricultural and healthcare industry for vector control, particularly in malaria-prone countries (Nicolopoulou-Stamati *et al.*, 2016). Included in this pesticide class is the infamous insecticide dichlorodiphenyltrichloroethane (DDT). DDT is a halobenzene derivative previously used to eliminate pests and control malaria, typhus and the bubonic plague (Alewu and Nosiri, 2010). Its mode of action involves altering nerve functioning and disrupting nerve impulses. Despite DDT's efficiency, the insecticide was found to have many toxic and hazardous effects derived from its metabolite, p,p'-dichlorodiphenyldichloroethylene (p,p'-DDE) (Ross, 2005). These harmful effects include endocrine disruption, carcinogenic action, and neurodevelopmental defects (Nicolopoulou-Stamati *et al.*, 2016). Due to DDT's environmental, human and wildlife toxicity, the use of this pesticide has been banned in multiple countries such as the United

States of America (USA), Canada, Argentina, Japan, and Ethiopia (Nicolopoulou-Stamati *et al.*, 2016).

Generally, OCs are associated with disrupted embryonic development, altered endocrine function, irregular lipid metabolism, altered neural functioning, and haematological alterations (Nicolopoulou-Stamati *et al.*, 2016). Other examples in this pesticide class include benzene hexachloride (BHC), chlordane, methoxychlor and lindane (Aktar *et al.*, 2009)

#### 1.2.3.2 Organophosphates (OPs)

Often described as multi-functional, organophosphates (OPs) can eliminate a wide range of insect pests and are thus typically used in homes and gardens. OPs are phosphate esters produced as a result of the esterification of phosphoric acid and alcohol (Adeyinka and Pierre, 2020). OPs act on the neuromuscular enzyme acetylcholinesterase (AChE) through irreversible inhibition. By covalently inhibiting AChE through irreversible phosphorylation, OPs disrupt neuromuscular function and alter neurotransmitter release and uptake, subsequently resulting in various levels of toxicity (Jaga and Dharmani, 2003).

This insecticide class was initially developed as a biodegradable alternative to OCs owing to the reduced ecological danger associated with OP use (Jaga and Dharmani, 2003). However, Karami and Abdollahi (2010) highlighted that despite improved biodegradability, OPs have been associated with disrupted cellular functioning, altered protein metabolism and oxidative stress-related genotoxic effects in exposed individuals, consequently making OPs potentially hazardous for humans and animals. Furthermore, a population-based study conducted by Hung *et al.* (2015) revealed that exposure to OPs may result in the development of cardiovascular diseases, diabetes and dementia whilst negatively impacting the reproductive system. Some of the commonly used OPs include chlorpyrifos, methamidophos, diazinon, glyphosate, malathion, and parathion (Yadav and Devi, 2017).

In the South African (SA) context, although there are over 500 pesticides currently registered for use within the agricultural industry (Pesticide Action Network (PAN), 2010), there is no formalised list of the commonly used OPs in SA, however, Quinn *et al.* (2011) have formalised a list of the most used pesticides within the agricultural industry. This list contains 230 commonly used pesticides, their chemical classification, application use, and the crops on

which they're used, as defined by the South African Department of Health (DOH) (South African Department of Health (DOH), 2005; PAN, 2010)). Included in this list are OPs such as fenthion, malathion, chlorpyrifos, parathion, phorate, methamidophos, diazinon and terbufos to name a few.

Typically, OP poisoning toxidrome clinically manifests as receptor-specific effects that target the muscuranic, nicotinic and central nervous systems (CNS) (Peter *et al.*, 2014). The muscuranic effects have been given the mnemonic DUMBELS which represent the defecation, urination, miosis, bronchorrhea, emesis, lacrimation, and salivation often observed in OP poisonings (Robb and Baker, 2021). Nicotinic effects include mydriasis, bradycardia, muscle weakness, hypertension, and muscle fasciculations (Robb and Baker, 2021) whilst hallucinations, lethargy, and changes in the individual's mental state form part of the effects associated with the CNS (Peter *et al.*, 2014). These clinical manifestations can occur within minutes or hours after exposure (Peter *et al.*, 2014).

#### 1.2.3.3 Carbamates

Carbamates are insecticides that resemble OP insecticides both mechanistically and structurally (Yadav and Devi, 2017). Commonly known as N-methyl carbamates, these compounds are carbamic acid ( $\text{NH}_2\text{COOH}$ ) derivatives produced through the esterification of N-methyl carbamic acid (Silberman and Taylor, 2020). Mechanistically, carbamates interrupt neuronal function through AChE carbamylation at both the neuronal synapses and neuromuscular junctions. The carbamylation of AChE results in AChE inhibition as the process prevents AChE from hydrolysing acetylcholine to acetic acid and choline. This inhibitory effect results in elevated AChE levels at the synapses and neuromuscular junctions which prevents the cessation of neurotransmitter signalling. The increased neurotransmitter signalling caused by raised acetylcholine levels leads to delirium, tremors, seizures, tachycardia or even death by poisoning (Silberman and Taylor, 2020; Yadav and Devi, 2017).

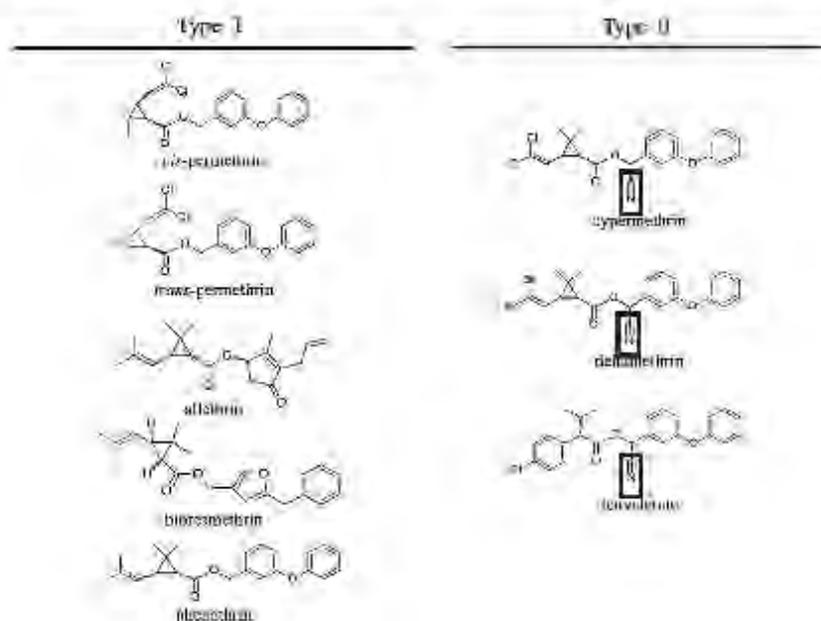
Although carbamate exposure presents a similar toxicological profile to OPs; carbamates bind reversibly to AChE (Ecobichon, 1996) with symptoms typically lasting for less than 24 hours (in less severe cases) (Vale and Lotti, 2015). These compounds are often used as fumigants, contact pesticides or stomach poisons (pesticides that are toxic when consumed orally). Carbamates are usually biodegradable with minimal ecological danger. Despite the eco-

friendly characteristics, carbamates such as carbaryl, have been shown to negatively impact reproductive ability in exposed humans and animals (Denison *et al.*, 1998). Furthermore, an *in-vitro* study conducted by Soloneski *et al.* (2015) demonstrated that carbamate-induced genotoxicity and cytotoxicity may facilitate human immune cell apoptosis (Nicolopoulou-Stamati *et al.*, 2016). Examples of commonly used carbamates include aldicarb, carbofuran, carbaryl, propuxur and trimethacarb (Silberman and Taylor, 2020).

#### 1.2.3.4 Pyrethroids

Pyrethroids mimic the structure of natural pyrethrins, which are derived from the flowers of *Chrysanthemum cinerariaefolium* (Chrustek *et al.*, 2018). The pyrethrum extracts may be used to produce stable, highly toxic, fast-acting insecticides. Pyrethroids are grouped into Type I and Type II pyrethroids based on chemical and toxicological characteristics.

Type I pyrethroids are pyrethrin derivatives that lack a cyano (CN) group whilst Type II pyrethroids contain a CN group, which increases their potency (Chrustek *et al.*, 2018). This structural difference results in two types of toxidromes: tremor (T)-syndrome (type I pyrethroids) and choreoathetosis and salivation (CS)-syndrome (type II pyrethroids). T-syndrome is characterised by ataxia, tremors, and hypersensitivity to sensory stimuli whilst CS-syndrome is characterised by hypersalivation, paralysis and sensitivity to external stimuli (Ramchandra *et al.*, 2019). Given below is a figure illustrating the structural differences between Type I pyrethroids and Type II pyrethroids, the blue outline highlights the CN group not found in Type I pyrethroids.



**Figure 1.** Structure of Type I and Type II pyrethroids as adapted from Fujino *et al.* (2019, p.2).

Pyrethroids are generally used as mosquito repellents, pet sprays, and pet shampoos. In terms of toxicity, pyrethroids exhibit high toxicity towards insects and fish in pyrethroid-treated water, whilst exhibiting low toxicity towards mammals and birds when administered in trace concentrations estimated to be 5000 mg/m<sup>3</sup> according to the National Institute for Occupational Safety and Health (NIOSH), (NIOSH, 1997). According to Ray and Forshaw (2000), at an LD<sub>50</sub> range of 0.5mg/kg to 250 mg/kg, pyrethroids are lethally toxic and may pyrethroids may lead to respiratory failure, pulmonary oedema, fasciculations and coma and death (WHO, 2005). Most synthetic pyrethroids undergo light-facilitated breakdown (unless trapped in sediment), making them biodegradable (Thatheyus and Gnana-Selvam, 2013).

This insecticide class is considered to be the safest, most ecologically friendly pesticide class currently available on the market (Ray and Fry, 2006). There is, however, evidence that pyrethroids may alter reproductive ability and disrupt endocrine function (Garey and Wolff, 1998; Mnif *et al.*, 2010). Examples include permethrin, cypermethrin, fenvalerate and sumithrin. Little research has been done on the effects of short-term pyrethroid exposure to mammals. A large majority of research has focused on long term exposure to pyrethroids, however, the National Research Council of America (1994) found that short-term dermal exposure to permethrins led to skin sensations, numbness, itching and paraesthesia. Animal studies conducted on rats by (National Research Council, 1994) found that short-term exposure to permethrins (a synthetic pyrethroid) led to the development of increased respiratory rates,

hyperexcitability, ataxia, convulsions, and paralysis. Long-term exposure results in morphological changes in the liver, increased hepatic enzyme changes and increased neurological activity that can lead to death. In addition, studies have shown that acute pyrethroid exposure can have genetic damage by inducing DNA damage in spermatozoa (Zhang *et al.*, 2021)

### **1.3 Pesticide uses, applications and benefits**

#### **1.3.1 Agricultural use**

The primary goal of the agricultural industry is to provide crops and livestock for human consumption. To achieve this, pesticides are used to create optimal conditions for successful plant growth and animal grazing. These agrochemicals (chemicals used in agriculture) assist in agricultural crop protection by reducing or eliminating any factors that threaten plant growth or development (Aktar *et al.*, 2009). These factors include pest infestations, invasive weeds, rodents, and various plant diseases (Quinn *et al.*, 2011). Popp *et al.* (2012) suggests that pesticides enhance overall crop quality, promote plant longevity (the time crops may be consumed without any risk of imminent danger) and improve crop yield. This translates to improved food productivity (Aktar *et al.*, 2009). Pesticide usage may also reduce labour costs for farmers as workers are not required to physically remove weeds or pests, again highlighting the economic benefit pesticides bring to the agricultural sector. By protecting crops from pests and associated dangers, ever-increasing population-based food supply needs can be met.

#### **1.3.2 Healthcare**

Nicolopoulou-Stamati *et al.* (2016) describes pesticide usage within the public health sector to protect humans from vector-borne diseases that pose a threat to human health. These include diseases such as Malaria, Typhus, Zika virus and Dengue fever. Furthermore, pesticide products prove key in eliminating potential human and animal health risks associated with biological agents as seen in the bactericidal treatment of anthrax. Additionally, pesticides like triclosan, are largely used as antimicrobials in antibacterial soaps for their antiseptic and disinfectant properties. According to Gildea *et al.* (2020), healthcare facilities, such as clinics and hospitals, may use pesticides as sterilants to prevent the spread of infectious diseases within these facilities. Recent work by Lafon *et al.* (2018) has shown that pesticides may play a role

in prion aggregation, potentially making them a possible treatment option for mitigating neurodegenerative diseases.

### **1.3.3 Domestic use**

Generally, the average individual uses pesticides to maintain clean living conditions (Nalwanga and Ssempebwa, 2011). Consumers use pesticides to keep their homes free from disease-carrying insects and rodents. This protects individuals from insect bites and protects personal property from insect or termite damage (Nalwanga and Ssempebwa, 2011). In some instances, household pesticides are used as cockroach repellents to prevent allergies and asthma development. Similarly, pesticides may be used in gardening to promote plant growth by either deterring weed growth or hindering the presence of unwanted pests. In urban settings, pesticides are used to maintain sports facilities, nurture lawns, golf courses, gardens, and roadsides whilst some lesser-known pesticide applications include their inclusion in pet shampoos and building materials (Hoffman *et al.*, 2000; Nicolopoulou-Stamati *et al.*, 2016).

## **1.4 Drawbacks associated with pesticide use**

Despite the agricultural, domestic and occasionally health benefits of pesticides, many of these chemicals have been shown to negatively impact human health and the environment. This is because of their high levels of biological activity, toxicity and ability to affect non-targeted organisms (Alewu and Nosiri, 2010). This has led to the banning of certain pesticides with legislation restricting the licensing of pesticides found to be harmful to humans, animals, and the environment (Alewu and Nosiri, 2010). Simultaneously, calls for the introduction and development of eco-friendly alternatives of pest control have been raised (Nicolopoulou-Stamati *et al.*, 2016).

### **1.4.1 Impact on the environment, flora, and fauna**

The application and incorrect disposal of pesticides negatively impacts the environment and associated ecosystem. Pesticides may contaminate water sources, soil and air whilst simultaneously harming non-targeted plants, birds, and insects. Run-off and leaching from pesticide-treated plants contaminate water sources, consequently impacting aquatic life whilst placing the general population's water supply in danger. In soil, hydrophobic bio-accumulative pesticides such as DDT strongly interact with soil particles, meaning that pesticide metabolites

may be found in soil long after plant pesticide treatment (Harrison, 2008). This contaminates the soil and results in reduced soil fertility. Santos and Flores (1995) found that heavily treated soil suppresses the growth and activity of nitrogen-fixing bacteria needed for successful plant symbiotic relationships. Additionally, pesticide sprays often volatilise into the air during application, subsequently contaminating the surrounding air and depleting vegetation by diminishing seed quality (Larson *et al.*, 2019). Non-targeted action against pollinators, like bees and fruit flies, affects crops and creates an imbalance in the ecosystem that may perpetuate pest numbers. Combining this, with reduced soil quality and water source contamination, highlights the ecological impact of pesticides on the environment.

#### **1.4.2 Impact on human health**

Human pesticide exposure can occur in different ways, namely, through direct skin contact and absorption, inhaling polluted air or ingesting contaminated food or water, or the pesticides themselves (Alewu and Nosiri, 2010; Sacramento, 2008). Some commercially available foods and beverages such as wine, fruit juices and fruits and vegetables, may contain pesticide residues if not properly decontaminated. Pesticide residue is described as any leftover pesticide chemical found remaining in food after its application during crop production. Following exposure, the pesticide may be absorbed, metabolised, and excreted or stored within the body where it bioaccumulates in the adipose tissue of an animal or human. Upon their entry within the body, these chemicals induce a response in the form of tissue damage or altered metabolic functioning (Nicolopoulou-Stamati *et al.*, 2016). The effects of exposure depend on many contributory factors, including the frequency and duration of exposure, dosage, type of pesticide and route of exposure (Sabino *et al.*, 2011). Generally, these effects include damage to the gastrointestinal, reproductive, and respiratory organs as well as carcinogenic, neurological, and endocrine effects. Toxicity, expressed as LD<sub>50</sub>, can either be acute or chronic as described below.

##### **1.4.2.1 Acute toxicity**

Acute toxicity is described as a chemical's ability to result in the rapid development of adverse health effects following exposure, with most of these effects occurring within minutes or hours following chemical exposure (Yadav and Devi, 2017). The adverse health effects that occur following a single exposure to a pesticide are termed acute effects and may include symptoms like nausea, dizziness, impaired vision, salivation, diarrhoea, cramps, panic attacks, headaches,

and muscle aches (Hu *et al.*, 2015). The severity of these effects vary based on the pesticide type, duration of exposure, pesticide dose and the route of exposure.

#### 1.4.2.2 Chronic toxicity

Chronic toxicity refers to adverse health effects that develop after prolonged exposure to a chemical or toxin. It follows then, that chronic effects are described as the harmful effects that occur because of prolonged exposure to a pesticide (usually in small doses) (Yadav and Devi, 2017). Clinically it is often difficult to distinguish between chronic or acute toxicity as repeated exposure to small doses of certain pesticides may cause chronic illnesses in humans, with symptoms only appearing at a later stage (Hu *et al.*, 2015). Symptoms include birth defects, genetic changes, haematopoietic changes, nerve disorders, endocrine disruption, and an altered reproductive system.

### 1.5 Pesticide poisonings

#### 1.5.1 International data

In 1990, the WHO published initial estimates concerning the extent of pesticide poisoning incidence globally (WHO, 1990). By using extrapolated data, the WHO estimated that three million pesticide poisonings occurred annually throughout the globe (WHO, 1990). Of these pesticide poisonings, an estimated 220,000 cases were fatal, a mortality rate of 7.3% (Jeyaratnam, 1990; World health statistics quarterly, 1990). Upon investigation, it was also found that most of these poisonings were intentional. Pesticide-facilitated suicides account for a third of the total number of suicides worldwide (Gunnell *et al.*, 2007). This coincides with data from Asia, which showed that pesticide-related poisoning was the most predominant suicide method, accounting for 60% of all suicidal deaths (Gunnell and Eddleston, 2003; Wang *et al.*, 2019). Gunnell and Eddleston (2003) estimate that approximately 300,000 cases of pesticide-related suicides occur annually for developing countries like China and South-East Asia. This is based on the fact that in 2001, the WHO reported that an estimated 517,000 suicides had occurred in these regions, of which 60% were pesticide-related (Gunnell and Eddleston, 2003; WHO, 2002).

A retrospective review conducted by Kamaruzaman *et al.* (2020), of poisoning cases referred to the Malaysia National Poison Centre (NPC), from 1 January 2006 to 31 December 2015 revealed that of the 39,088 cases reported, 28.4% (n=11,087) pertained to pesticides, making

up the second largest poisoning category. OPs were found to make up 40% of all pesticide-related poisonings with higher frequencies of pesticide poisonings in men (57.2%, n=6342) than women (42.8%; n=4, 745). The increased OP frequency in pesticide poisonings is also supported by Damalas and Eleftherohorinos (2011) and Sarkar *et al.* (2013) who reported that OPs are the primary cause of pesticide poisonings in Asian countries. Furthermore, intentional pesticide poisonings made up 60.1%, (n=6, 669) of total pesticide poisonings observed in Kamurazan *et al.*'s decade-long study with suicides dominating at 93.6% (n=6,328).

Increased frequencies of intentional poisonings and male predominance in this study's cohort were also corroborated by a separate pesticide study conducted by Cha *et al.* (2014) which reviewed mortality data for South Korea between 2006 and 2010 for seven metropolitan cities in South Korea. This study found that pesticide poisoning accounted for 66.9% (n=16, 161) of total poisoning deaths (N=24,157) identified over the study period. Intentional poisonings accounted for 85.9% (n=13,890) of all pesticide poisonings, with suicide by pesticide ingestion being the leading cause. Furthermore, similar numbers of pesticide poisoning deaths were seen in males (66.8%) and females (67.0%). However, Cha *et al.* (2014) noted that although the distribution according to sex was similar, the proportion of incidence in pesticide poisonings was higher in men than women (8.3% and 6.5% respectively) thus favouring male predominance.

Although international trends seem to point at higher male frequencies in pesticide poisonings, a retrospective study conducted by Soycheva (2011) reported higher frequencies of pesticide-related suicide attempts in females, with OPs, carbamates and organochlorines being the pesticides most used. Thus, it is important to note that there may be differences in the male-to-female ratios for different population groups.

Recent work has focused on determining the prevalence of pesticide-related poisonings in children. Fernando and Fernando (1997) conducted a retrospective hospital-based study specifically looking at hospital admissions for poisoning in 1986 within three districts of Sri-Lanka housing approximately 25% of the population. Data sourced from the 27 hospitals included in this study indicated that of the 4,556 patients admitted for poisoning, 540 were below the age of 15 years. These childhood poisonings (as defined by the researchers) made up 11.4% of the total number of hospital admissions for poisoning in these districts. Of these 540 childhood poisonings, 28% (n = 77) related to pesticides with 57% (n = 44) of these pesticide-related poisonings occurring in children under the age of 5 years old.

Similarly, Mutlu *et al.* (2009) retrospectively analysed paediatric poisoning admissions at hospital in Turkey, from January 2002 to December 2006, where the cohort ranged from patients under a year to patients aged 17. In this 4-year retrospective study, a total of 386 poisoning cases were admitted with 11.4% (n = 46) of these poisoning cases being attributed to rodenticides, pesticides and insecticides, with 84,7 % (n = 39) of these pesticide-related poisonings occurring in children under the age of 5 years old. Lastly, Kohli *et al.* (2008) reviewed paediatric poisonings from July 2004 to July 2006 by looking at the hospital records of patients aged 12 years and under from a paediatric emergency room of a tertiary care centre in New Delhi, India. Of the 111 patients admitted to the emergency room, 18.9 % (n = 21) were attributed to pesticides and insecticides.

Overall, these paediatric studies have shown that paediatric pesticide poisoning accounts for 12 to 19 % of all total poisoning cases admitted to hospitals (Fernando and Fernando, 1997; Kohli *et al.*, 2008 and Mutlu *et al.*, 2009). In addition, the prevalence of accidental poisonings in children is suggested to be a result of the negligent use of household pesticides (London *et al.*, 2005).

### **1.5.2 South African data**

Reliable and up-to-date data of pesticide morbidity and mortality in SA is limited. A cross-sectional retrospective study has been conducted by Razwiedani and Rautenbach (2017), which looked at data surrounding the notification of OP-related poisonings in a clinical patient population, as reported by medical practitioners for the Tshwane District from January 2012 to December 2014. The data was sourced from hospitals and medical centres within this district and referred to patients who survived the poisoning. The study also found that a majority of pesticide-related poisonings relate to OPs. Moreover, intentional pesticide poisonings were found to constitute over 50% of total poisoning cases in contrast to 21.7% accidental poisoning incidents (Razwiedani and Rautenbach, 2017). Of these intentional poisonings, 50.2% were suicides and 2.4% were homicides (Razwiedani and Rautenbach, 2017). In addition, the OP poisoning surveillance data showed that in this cohort, 58.9% of pesticide-related fatalities occur in men as opposed to only 50.2% in women, which is contrasting to the trend seen internationally.

These findings are consistent with reports by London and Baile (2001), which estimated that 67% pesticide-related fatalities occur in men, based on data sourced from a previous surveillance study (London *et al.*, 1996). This surveillance study was a retrospective review of all pesticide poisonings notified to the Western Cape's regional office of the Department of National Health and Population Development (DNHPD) between the years 1987 to 1991. General information on the demographics of the individuals, circumstances surrounding the poisoning and pesticides involved in the pesticide poisonings as well as whether or not the outcome was fatal were recorded (London *et al.*, 1996). Again, this study was a hospital-based review of clinical and fatal cases notified to the DNHPD. This review found that 34% were suicide-related, 42% accidental exposure-related and only 7% of the reported pesticide poisonings were because of occupational exposure. This could be because of over 61% of the study population being farmworkers, farmers, or their relatives (Engelbrecht, 2017; London *et al.*, 1996; Marks and Van Hoving, 2016; Van Hoving *et al.*, 2018 and Veale *et al.* 2013).

Regarding paediatric data surrounding pesticide poisonings in SA, data collated from health centres and facilities in the Tshwane District, Gauteng province, from January 2012 until December 2014 indicate that 23.2 % of all pesticide-related cases pertain to children under 10 years of age (Razwiedani and Rautenbach, 2017). In addition, a paediatric study conducted over a six-year period at the Red Cross War Memorial Children's Hospital (RCWMCH) reported that only 11% of all child-related fatalities identified throughout the six-year period were attributed to pesticide exposures and poisonings (Balme *et al.*, 2010).

## **1.6 Forensic aspects of pesticide-related deaths**

### **1.6.1 Medico legal investigation and forensic toxicology**

In SA, legislature makes provision for the investigation of all unnatural deaths by the Forensic Pathology Services (FPS). Thus, in line with the National Health Act (Act No. 61 of 2003) and the Inquests Act (Act No. 58 of 1959), FPS investigates all cases of suspected unnatural death. Unnatural deaths in this instance are defined as deaths that occur because of a physical or chemical influence, sudden unexpected deaths, procedural-related deaths or deaths that occur due to the act of omission or commission. The investigation takes the form of a multi-staged process which includes death scene investigation, a review of available information and a medico-legal autopsy. During autopsy, the deceased's body may undergo external and internal

examination with specimen collection and ancillary testing for toxicological or histological analysis (Inquests Act, Act No. 58 of 1959). This process aims to retrieve relevant evidence to determine the cause of death.

The investigation of a fatal pesticide poisoning case typically includes a review of death scene or hospital scene information (in addition to any history of pesticide ingestion), a medico-legal autopsy, and ancillary testing including toxicology and histology. Death scene findings are important when investigating pesticide-related fatalities as a thorough scene investigation can provide vital information for identifying the specific pesticide(s) involved (Sabino *et al.*, 2011). However, if, in a case of suspected fatal pesticide poisoning, no death or hospital scene information is available, autopsy findings and toxicology results assist in determining the cause of death (Sabino *et al.*, 2011).

Frequently encountered autopsy findings in pesticide deaths include pulmonary oedema, bluish discolouration of lips and limbs, foaming at the mouth or nose, vomit, the presence of granules or odours in gastric contents, and multiorgan congestion (Mlayeh *et al.*, 2020). According to Nigam *et al.* (2013) who conducted a cross-sectional hospital-based study, which assessed the histopathological changes caused by pesticide poisoning in deceased individuals, histopathological microscopic signs that are identified in pesticide poisoning include congestion, haemorrhaging, tubular degeneration, patchy necrosis, and pulmonary oedema. These results were obtained from the histopathological analysis of the liver, lung and heart of the deceased individuals that died from pesticide poisoning. These findings were also corroborated by Swapan *et al.* (2021) and Balasubramanian and Gokulakrishnan (2016) who each found that congestion, patchy haemorrhaging, necrosis, and sinusoidal dilation characterise some of the histopathological findings of pesticide poisoning on the liver.

These findings require toxicological confirmation (analytical identification of pesticides or metabolites) as some of these signs are non-specific and may be found in natural deaths (Mlayeh *et al.*, 2020). Toxicological analysis involves testing biological specimen and/or exhibits that may contain pesticides collected from the scene. Biological specimens used for post-mortem toxicological analyses include whole blood (usually sourced from the femoral vein), stomach contents, urine, and tissue samples (Dinis-Oliveira *et al.*, 2016). However, non-conventional alternative sample matrices such as vitreous humour and hair, are also considered (Soares *et al.*, 2019). The analysis of pesticides and their metabolites in biological specimens typically involves the use of analytical techniques such as gas chromatography coupled to mass

spectrometry (GC-MS or GC-MS/MS) and liquid chromatography coupled to mass spectrometry (LC-MS or LC-MS/MS). Quantitative analysis may be performed to determine the specific concentration of the pesticide compound found in the body fluid(s) in order to assist with interpreting exposure levels and determining possible cause of death (Sabino *et al.*, 2011).

Post-mortem toxicological analyses in SA were historically conducted by the National Forensic Chemistry Laboratories (FCL), which falls under the National Department of Health (DoH). The presence of pesticides was more frequently reported in gastric contents as compared to blood in a series of post-mortem cases (Patience, 2018). A possible explanation for this is the use of unsuitable specimen containers, resulting in the chemical instability of pesticides in post-mortem blood samples that contain sodium fluoride preservative (Park *et al.*, 2009). Moriya *et al.* (1999) suggested that the preservative facilitated chemical-induced pesticide degradation. Although organophosphates are more stable in biological specimens than aqueous solutions (Moriya *et al.*, 1999), blood samples containing sodium fluoride may accelerate organophosphate degradation.

Additionally, post-mortem chemical redistribution (PMR), post-mortem interval (PMI) and delays in analytical testing may also result in further sample or analyte degradation rendering potentially unreliable results. Regarding post-mortem redistribution, post-mortem chemical analyte concentrations don't necessarily reflect analyte concentrations at the time of death, as analyte levels may vary due to differences in the sampling site or the interval between specimen collection and time of death (Ferner, 2008). This is due to PMR, which is the process by which chemical poisons or toxins move between tissues and body fluids after death (Yonemitsu, 1993). This may lead to variations in chemical concentrations of chemical toxins and any particular analytes as analytes diffuse from cells to blood thereby changing ante-mortem versus post-mortem concentrations (Cook *et al.*, 2000). Similarly, the PMI, which is defined as the time between an individual's physiological death and discovery and death declaration (Gelderman *et al.*, 2018), is crucial to obtaining reliable post-mortem results. The longer the PMI, the greater the chance for changes in analyte concentrations in specimens to occur owing to PMR, cellular autolytic processes and putrefactive factors tissue pH decreases (Akcan *et al.*, 2009; Byard and Butzbach, 2012). Sampling time is therefore a key factor in minimising inaccuracies when it comes to post-mortem results.

Delays in analytical results can further impact analyte stability. The longer it takes for chemical analysis to occur, the longer the specimens are exposed to storage conditions and the greater the likelihood that chemical analyte instability or degradation can occur (Ferner, 2008). Chemical analyte instability or degradation may impact the detection and subsequent interpretation of results. This was one of the biggest challenges in toxicology results produced by the National FCL laboratories, as due to backlogs, toxicology results would only be provided months or years after the death of the individual.

Alternatively, pseudocholinesterase (PChE) levels may be assessed as an indicator of OP poisoning, specifically in cases where the decedent was hospitalised. Reduced serum PChE levels are predictive of pesticide poisoning owing to OPs inhibitory action on AChE activity (Chaudhary *et al.*, 2013). Estimating cholinesterase levels is not always routinely available in labs and can prove costly for under-resourced labs (Bhuthada *et al.*, 2020). Putrefaction and haemolytic activity in whole blood post-mortem, especially during prolonged PMI intervals, may affect blood cholinesterase activity prior to death. Delayed specimen collection and unrefrigerated transfer to testing facility, (Klette *et al.*, 1993) as well as the age, genetics, liver pathology and PMI, may also affect whole blood cholinesterase activity (Pathomrattanasiri *et al.*, 2021).

Mortuary data suggests that most pesticide-related fatalities relate to either suicides, homicides, or accidental ingestion (Sabino *et al.*, 2011). Overall, OPs and carbamate insecticides are the most prominent pesticides associated with pesticide fatalities (WHO, 2002). In a study conducted by Mlayeh *et al.* (2020), the total number of suicidal pesticide-related deaths was 41.9% with only 6.1 % being accidental. Similarly, a retrospective autopsy case study conducted by Idiz *et al.* (2012) in Turkey, reviewing pesticide poisonings between 2006 and 2009, reported that suicides accounted for 43.8% of all pesticide-related cases followed by accidental poisonings at 8% (Idiz *et al.*, 2012; Mlayeh *et al.*, 2020). According to work done by Sabino *et al.* (2011) pesticide-related homicides and suicides often take the form of contaminated food ingestion, where pesticide granules or liquids are mixed into the food for consumption. A thorough evaluation of the death scene is thus of great importance. Unfortunately, forensic and/or investigating officers are often not trained in pesticide identification at the scene and crucial evidence may be missed.

In SA, a recent post-mortem study revealed an increase in terbufos-related deaths (Patience (2018)). This study reviewed suspected pesticide-related cases in the West Metropole of Cape

Town between the years 2011 and 2015. Results from this study revealed that of the 16,453 suspected unnatural death cases were admitted to the mortuary, of which 104 related to pesticide-toxicity within the five-year period. Of the 104 pesticide-related cases, 60% related to suicide, 6% were accidental poisonings and 3% were homicides with equal numbers of pesticide poisonings in both males and females. Lastly, terbufos was identified as the most frequently detected pesticide, accounting for 61% of all suspected pesticide fatalities. Terbufos, is an organophosphate used as an insecticide on crops such as maize, banana, citrus, and potatoes to name a few (Quinn *et al.*, 2011). The WHO classifies terbufos as a Class Ia pesticide, indicating that it is an extremely hazardous compound (Liang *et al.*, 2017). Its increased detection in post-mortem casework may be allude to its role as a street pesticide in SA.

### **1.6.2 Street pesticides**

Peri-urban informal, township areas in SA are characterised by lack of service delivery (household water drainage and refuse disposal), poor water and sanitation, along with lack of adequate shelter and overcrowding (Nalwanga and Ssempebwa, 2011). The lack of good quality service delivery places these areas at risk of pest or vector-related health hazards that can contribute to mortality and morbidity. Poor environmental conditions in conjunction with inadequate housing may further give rise to problems associated with poor hygiene. For example, uncollected refuse can act as a breeding ground for disease-causing vectors such as mosquitoes, flies, and rats. Street pesticides are thus often used as a method of pest control to help maintain clean living conditions considering ever-increasing population numbers (Balme *et al.*, 2010). Street pesticides are highly hazardous decanted pesticide formulations often illegally sold in unlabelled, clear packaging as granules, powders, pellets, or liquid formulations (Balme *et al.*, 2010; Rother, 2012). These pesticides are sold by street vendors either door-to-door, at informal markets, taxi ranks, or train stations. Street pesticides are popular as these chemical substances are cheap, fast-acting, easily accessible, and efficient. Analysis of collected samples revealed that street pesticides may contain acutely toxic OP and carbamate groups as constituent active ingredients, however, because street pesticides are often unknown mixtures or formulations of different pesticide compounds, it is challenging for health practitioners to accurately diagnose poisoning due to street pesticides (Rother, 2012). Furthermore, users often do not follow the appropriate safety protocols when handling, storing,

and disposing of pesticide chemicals nor are they always informed of the dangers associated with pesticide use (Rother, 2010). This may lead to unintentional hazardous exposure associated with negligent pesticide use. Children are often prone to unintentional street pesticide poisoning events within the household. A study conducted by Swartz *et al.* (2018) reported that children often confuse unlabelled pesticides that are mixed with food or decanted into water bottles, with food believed to be safe for consumption. Furthermore, Rother (2010) concluded that as a result of their involvement in the selling, distribution, transportation and storage of street pesticides, the youth are a high-risk group for exposure. Communities may use street pesticides rather than commercial products as they are effective and hazardous to pests and may be cheaper and more accessible. Nalwanga and Ssempebwa (2011) report that individuals are also embarrassed about the presence of pests within their homes as this is associated with poor hygiene.

## **1.7 Pesticide legislation and poisoning notification system in South Africa**

### **1.7.1 Legislation**

Pesticide-related legislature in SA is governed by multiple statutory bodies namely, the Department of Agriculture, Forestry and Fisheries (DAFF), the Department of Health (DoH), the Department of Environmental Affairs (DEA) and the Department of Labour (DoL). Pesticide use, distribution and exposure is largely regulated through collaborative efforts by each department to ensure optimal pesticide use for enhanced pest control at reduced risk levels for humans, animals, and the environment (Naidoo *et al.*, 2010). The Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act, 1947 (Act No.36 of 1947) is responsible for setting parameters around the sale, use, distribution and banning of pesticides in SA (Wiese and Bot, 1971).

The DAFF has released a list of all the insecticides currently in use in SA. This list contains information on the active ingredient, formulation, the hazard class, the product names as well as the company from which the insecticide can be sourced (DAFF, 2010). The DAFF also has a list of all registered herbicides used in SA. This list is separate from that of the insecticides and contains information on the crops on which the herbicide is used as well as the herbicide's trade name and registration number (DAFF, 2007). The DoH also has a comprehensive list containing 230 commonly used pesticides containing similar information as the lists released by the DAFF (South African Department of Health (DOH), 2005; Quinn *et al.*, 2011).

The agricultural sector and food production industry are typically the main consumers of pesticides (particularly the most hazardous) with workers often being at high risk of exposure. To protect worker's rights and promote a safe working environment for workers, the DAFF also coordinates worker exposure to these harmful chemicals and training programs on the use and handling of pesticides in accordance with the Occupational Health and Safety Act (OHSA), 1993 (Act No. 85 of 1993). To address inappropriate pesticide and/ or other hazardous substance disposal, the Hazardous Substance Act, 1973 (Act No. 15 of 1973) was drafted (Naidoo *et al.*, 2010). This act seeks to prevent environmental damage and harm to human health stemming from reckless toxic waste disposal (Wiese and Bot, 1971).

Lastly, SA must maintain international obligations and agreements concerning pesticide banning. An example of this is compliance with the Stockholm Convention on Persistent Organic Pollutants (POPs). The convention, which was established in 2001, aims to reduce any danger associated with the use of POPs by promoting the deregistration and banning of any pollutant listed under this convention (Wiese and Bot, 1971). Currently SA has successfully banned the use of most POPs listed under the convention except for DDT. The DAFF is also expected to comply with the Vienna Convention on the Protection of the Ozone Layer (1985) in conjunction with the Montreal Protocol on Substances That Deplete the Ozone Layer (1992). These respective conventions were established to help mitigate the use of ozone-damaging chemicals such as methyl bromide (Wiese and Bot, 1971).

### **1.7.2 Notification**

Any pesticide poisoning related to a pesticide class registered under The Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act, 1947 (Act No.36 of 1947), is classified as a medically notifiable disease in SA (Rother, 2012). Healthcare practitioners are required by law, to report any acute pesticide poisonings associated with agricultural or stock remedies to the DoH by completing the Notification of Medical Condition (NMC) form. This is in accordance with the National Health Act (Act 61 of 2003) (Balme *et al.*, 2010). Despite this requirement, London and Baile (2001) report that only 10 to 20 % of all hospitalised pesticide-related cases are reported, compared to just a mere 5% for mortuary death cases. Hospitalised cases are those where an individual was admitted to hospital for pesticide poisoning or exposure and survived. Notification rates are poor and may not be a true reflection of pesticide poisoning incidence. This can be attributed to the non- or misdiagnosis of pesticide-related

cases (Rother and London, 2009). Rother (2012) suggests that misdiagnosis is due to the lack of adequate training or knowledge on diagnosing OP and non-OP-related exposures. These limitations impede patient treatment and impact notification rates. The notification system requires the collation of inter-departmental records for accurate pesticide-related data capturing (London and Baile, 2001).

Unfortunately, there is often a disconnect between the surveillance data systems for the DoH and DoL and Department of Home Affairs (DHA) as there are often discrepancies in the notification of pesticide-related fatalities between these different departments as well as information contained within these records. London And Baile (2001) note that the DoL may have work-related morbidity data on pesticides not contained in the DoH's database whilst the DHA may have different cause of death information derived from the death certificate and not necessarily that which has been determined by post-mortem examination and toxicological analysis. These discrepancies in information make it hard to determine the prevalence or incidence of pesticide-related fatalities. Furthermore, inconsistencies in the information recorded make it difficult to collate data which impacts surveillance data.

To tackle this, Rother (2012) and colleagues established a Pesticide Policy Reference Group with the purpose of developing policies with a multi-faceted approach for investigating pesticide-related poisonings, placing a particular focus on street pesticides. However, more research is required to determine the effectiveness of this group. Additionally, efforts have been made to improve notification efficiency through the development of a mobile health application (app) (Kabanda and Rother, 2019). Kabanda and Rother (2019) report that a pesticide notification guideline was recently established by the University of Cape Town (UCT)'s Division of Environmental Health and Centre for Environmental and Occupational Health Research (CEOHR) in partnership with various stakeholders. This pesticide notification guideline was embedded into a mobile app to assist healthcare professionals with diagnosing and reporting pesticide poisonings. Mobile health apps are computing technologies used by healthcare practitioners (HCPs) in clinical practice globally as a way of providing a platform to assist HCPs in effectively improving healthcare service delivery, especially in resource-poor countries (Free *et al.*, 2013). These medical health apps also help keep HCPs abreast with current advances in the medical field (Free *et al.*, 2013). Within the context of Kabanda and Rother's (2019) study the mobile app was designed to assist HCPs report acute pesticide poisonings specifically. The study found that although 87% of the surveyed healthcare professionals in the study reported regularly using medical mobile apps, only 33% were aware

of the mobile app with only 17% having made use of it (Kabanda and Rother, 2019). Despite these results, the recent introduction and rollout of this mobile app in the healthcare industry indicates that more time is required to familiarise healthcare workers with the app before assessing its effectiveness in improving notification rates.

## **1.8 Underreporting of pesticide exposures**

In clinical settings in SA, a medical professional will fill out an NMC (GW17/5) form to report a pesticide poisoning, especially if symptoms or clinical presentation are consistent with pesticide toxicity. This form is then submitted to the district health services and entered into a database by the DoH as part of surveillance data. In forensic or post-mortem settings, a forensic pathologist will complete a death notification form following their autopsy that outlines the preliminary cause of death. In pesticide-related poisonings often, some doctors may wait for toxicology results before completing an NMC form to notify the DoH. Considering the delays and a pre-existing backlog in FCL testing, pathologists often wait years to receive toxicology results. This means, notification rates from mortuaries would historically be much lower than those from clinical settings (Kabanda and Rother, 2019; Rother, 2012). Recently, there has been a drive to improve this by recommending pathologists complete NMC forms in any case where pesticides are suspected to be involved in death, even prior to receiving the toxicological results.

According to Razwiedani and Rautenbach (2017) only 10 to 20% of all hospitalised pesticide poisonings are reported by medical health professionals, indicating that many cases go unreported, especially in instances where individuals were not hospitalised and may be treated supportively at home. This translates to underestimations in pesticide-related poisoning numbers. An example of this is seen when comparing pesticide poisoning statistics from the RCWMCH with those of the DoH. According to the DoH, approximately 341 pesticide poisonings were reported for the WC in adults and children alike (Department of Health (DoH), 2009), whilst 211 cases were reported for children alone by the RCWMCH for the same time period (Balme *et al.*, 2010). This may be indicative of possible inaccuracies in calculating the true incidence of exposure. Underestimations in the number pesticide-related poisonings and fatalities are attributed to limitations in the notification system, missing or incomplete information within the database, limited expertise on the precise medical diagnosis, and poor collaborations between police services, FPS, hospitals as well as public health departments (Balme *et al.*, 2010; Razwiedani and Rautenbach, 2017).

Efforts to establish the degree of underreporting in SA prove difficult. Comparative studies are not able to provide accurate figures of pesticide poisoning prevalence. This is due to the differences in the amount of data available between regions, variations in accessibility to healthcare facilities, and the pesticide class recognised by HCPs when dealing with a pesticide poisoning (Rother, 2012; Wang *et al.*, 2019). HCPs report only OP-related pesticide poisonings and often miss pesticide poisonings related to carbamates, pyrethroids or even organochlorines which impedes accurate data collation (Rother, 2012). Most pesticide poisoning studies are retrospective and thus rely on secondary data or knowledge on previous pesticide exposure history. The danger in this is that it creates room for possible recall and diagnostic bias where certain cases go unreported, based on the lack of available information (Hu *et al.*, 2015). Lastly, the impact of street pesticides on pesticide-related fatality statistics remains unknown, further adding unto inaccuracies in existing figures (Rother, 2012). Overall, the limitations of an unregulated information transfer system from hospital to national toxicovigilance centres negatively impact statistical data relating to pesticide-related poisonings.

## **Conclusion**

South Africa has seen a gradual shift in hazardous pesticide use from mainly the agricultural industry to becoming directed towards the domestic use of toxic pesticides in informal settings (Rother, 2010). The danger in this is that these domestic pesticides are often mixtures of unknown hazardous pesticide formulations manufactured at varying levels of toxicity. These street pesticides, when used negligently, place individuals at risk of being exposed to the acute toxic effects of these compounds (Rother and London, 2009). Improved surveillance data is therefore crucial in ascertaining the role street pesticides play in pesticide-related poisonings (fatal and non-fatal).

Further research into the prevalence of pesticide-related fatalities can provide valuable insight into the trends and characteristics associated with pesticide-related deaths. This information may streamline efforts to improve legislation surrounding notification protocols whilst strengthening the implementation of stricter law enforcement on pesticide use and distribution. Lastly, improved knowledge on pesticide-related mortality prevalence can provide insight into which intervention strategies may be implemented as a way of reducing exposure and potential fatalities going forward.

## **References**

- Adeyinka, A. and Pierre, L. (2020). *Organophosphates*. Treasure Island (FL): StatPearls Publishing. PMID:29763035.
- Akcan, R., Hilal, A., Daglioglu, N., Cekin, N. and Gulmen, M. (2009). Determination of pesticides in postmortem blood and bone marrow of pesticide treated rabbits. *Forensic Science International*. 189(1-3):82-87. DOI: 10.1016/j.forsciint.2009.04.017.
- Akhila, J. (2007). Acute toxicity studies and determination of median lethal dose. *Current Science*. 93(7):917-920.
- Aktar, W., Sengupta, D. and Chowdhury, A. (2009). Impact of pesticides use in agriculture: their benefits and hazards. *Interdisciplinary Toxicology*. 2(1):1-12. DOI: 10.2478/v10102-009-0001-7.
- Alewu, B. and Nosiri, C. (2010). Pesticides and Human Health. *Pesticides in the Modern World: Effects of Pesticide Exposure*. 1(12): 231-250. DOI:10.5772/18734.
- Balasubramanian, S. and Gokulakrishnan, A. (2016). Study of incidence of histopathological changes in liver due to agricultural poisons – a prospective study conducted at Govt. Stanley Medical College, Chennai. *Indian Journal of Forensic and Community Medicine*. 3(4):263-266. DOI: 10.18231/2394-6776.2016.0008.
- Balme, K., Roberts, J., Glasstone, M., Curling, L., Rother, H., London, L., Zar, H. and Mann, M. (2010). Pesticide poisonings at a tertiary children's hospital in South Africa: an increasing problem. *Clinical Toxicology*. 48(9):928-934. DOI: 10.3109/15563650.2010.534482.
- Bhutada, T., Ray, A., Dash, B. and Panigrahi, A. (2020). Serum cholinesterase level in postmortem cases of pesticide poisoning: Devising a protocol for identifying exposure to organophosphate and carbamate compounds. *Journal of the Indian Academy of Forensic Sciences*. 42:282-287. DOI: 10.5958/0974-0848.2020.00074.3.
- Büchel, K. (1983). *Chemistry of pesticides*. New York: Wiley. ISBN-13: 978-0471056829.
- Byard, R. and Butzbach, D. (2012). Issues in the interpretation of postmortem toxicology. *Forensic Science, Medicine and Pathology*. 8(3): 205–207. DOI: 10.1007/s12024-011-9278-x

Cha, E., Khang, Y. and Lee, W. (2014). Mortality from and incidence of pesticide poisoning in South Korea: findings from national death and health utilization data between 2006 and 2010. *PLoS One*. 9(4):e95299. DOI: 10.1371/journal.pone.0095299.

Chaudhary, S., Jain, N., Atam, V., Agarwal, A., Singh, K., Sawlani, K., Vaish, A. and Patel, M. (2013). Prognostic significance of estimation of pseudocholinesterase activity and role of pralidoxime therapy in organophosphorous poisoning. *Toxicology International*. 20(3):214. DOI: 10.4103/0971-6580.121669.

Chrustek, A., Hołyńska-Iwan, I., Dziembowska, I., Bogusiewicz, J., Wróblewski, M., Cwynar, A. and Olszewska-Słonina, D. (2018). Current Research on the Safety of Pyrethroids Used as Insecticides. *Medicina*. 54(4):61. DOI: 10.3390/medicina54040061.

Cook, D., Braithwaite, R. and Hale, K. (2000). Estimating antemortem drug concentrations from postmortem blood samples: the influence of postmortem redistribution. *Journal of Clinical Pathology*. 53(4): 282–285. DOI: 10.1136/jcp.53.4.282

Damalas, C. and Eleftherohorinos, I. (2011). Pesticide exposure, safety issues, and risk assessment indicators. *International Journal of Environmental Research and Public Health*. 8(5):1402-1419. DOI: 10.3390/ijerph8051402.

Denison, M., Phelan, D., Winter, G. and Ziccardi, M. (1998). Carbaryl, a Carbamate Insecticide, Is a Ligand for the Hepatic Ah (Dioxin) Receptor. *Toxicology and Applied Pharmacology*. 152(2):406-414. DOI: 10.1006/taap.1998.9999.

Department of Agriculture, Forestry and Fisheries. (2007). Herbicide guide for 2007. List of marketed herbicides sorted alphabetically according to active ingredients, formulation, trade names, company name, registration number and claim or uses. Available at: [https://www.nda.agric.za/daaDev/sideMenu/ActNo36\\_1947/AR/Herbicides.htm](https://www.nda.agric.za/daaDev/sideMenu/ActNo36_1947/AR/Herbicides.htm) [Accessed September 29, 2021].

Department of Agriculture, Forestry and Fisheries. (2010). *Insecticides*. Available at: [https://www.nda.agric.za/daaDev/sideMenu/ActNo36\\_1947/AR/Insecticides.htm](https://www.nda.agric.za/daaDev/sideMenu/ActNo36_1947/AR/Insecticides.htm) [Accessed September 29, 2021].

Dinis-Oliveira, R., Vieira, D. and Magalhães, T. (2016). Guidelines for Collection of Biological Samples for Clinical and Forensic Toxicological Analysis. *Forensic Sciences Research*. 1(1):42-51. DOI: 10.1080/20961790.2016.1271098.

Ecobichon, D. (1996). Toxic effects of pesticides. *Casarett and Doull's Toxicology: The Basic Science of Poisons*. 5<sup>th</sup> ed (Klaassen, C. D., ed.). New York: McGraw-Hill, 643-689.

Engelbrecht, C., Blumenthal, R., Morris, N. and Saayman, G., (2017). Suicide in Pretoria: A retrospective review, 2007-2010. *South African Medical Journal*. 107(8):715-718. DOI: 10.7196/SAMJ.2017.v107i812034.

Fernando, R. and Fernando, D. (1997). Childhood poisoning in Sri Lanka. *The Indian Journal of Pediatrics*. 64(4):457-460. DOI: 10.1007/bf02737748.

Ferner, R. (2008). Post-mortem clinical pharmacology. *British Journal of Clinical Pharmacology*. 66(4):430-443. DOI: 10.1111/j.1365-2125.2008.03231.x

Free, C., Phillips, G., Watson, L., Galli, L., Felix, L., Edwards, P., Patel, V. and Haines, A. (2013). The Effectiveness of Mobile-Health Technologies to Improve Health Care Service Delivery Processes: A Systematic Review and Meta-Analysis. *PLoS Medicine*. 10(1):e1001363. DOI: 10.1371/journal.pmed.1001363.

Fujino, C., Watanabe, Y., Sanoh, S., Nakajima, H., Uramaru, N., Kojima, H., Yoshinari, K., Ohta, S. and Kitamura, S. (2019). Activation of PXR, CAR and PPAR $\alpha$  by pyrethroid pesticides and the effect of metabolism by rat liver microsomes. *Heliyon*. 5(9):e02466. DOI:10.1016/j.heliyon.2019.e02466

Garey, J. and Wolff, M. (1998). Estrogenic and Antiprogestagenic Activities of Pyrethroid Insecticides. *Biochemical and Biophysical Research Communications*. 251(3):855-859. DOI: 10.1006/bbrc.1998.9569.

Gelderman, H., Boer, L., Naujocks, T., IJzermans, A. and Duijst, W. (2018). The development of a post-mortem interval estimation for human remains found on land in the Netherlands. *International Journal of Legal Medicine*. 132 : 863–873. DOI: 10.1007/s00414-017-1700-9

Gilden, R., Huffling, K. and Sattler, B. (2010). Pesticides and Health Risks. *Journal of Obstetric, Gynaecologic and Neonatal Nursing*. 39 (1): 103 - 110. DOI: 10.1111/j.1552-6909.2009.01092.x.

Harrison, J. (2008). Lessons learned from pesticide drift: a call to bring production agriculture, farm labor, and social justice back into agrifood research and activism. *Agriculture and Human Values*. 25(2):163-167. DOI: 10.1007/s10460-008-9121-5.

- Hoffman, R., Capel, P. and Larson, S. (2000). Comparison of pesticides in eight U.S. urban streams. *Environmental Toxicology and Chemistry*. 19(9):2249-2258. DOI: 10.1002/etc.5620190915.
- Hu, R., Huang, X., Huang, J., Li, Y., Zhang, C., Yin, Y., Chen, Z. and Jin, Y. et al. (2015). Long- and Short-Term Health Effects of Pesticide Exposure: A Cohort Study from China. *PLOS ONE*. 10(6):e0128766. DOI: 10.1371/journal.pone.0128766.
- Hung, D., Yang, H., Li, Y., Lin, C., Chang, S., Sung, F. and Tai, S. (2015). The Long-Term Effects of Organophosphates Poisoning as a Risk Factor of CVDs: A Nationwide Population-Based Cohort Study. *PLoS ONE*. 10(9): e0137632. DOI: 10.1371/journal.pone.0137632.
- İdiz, N., Karakus, A. & Dalgıç, M. (2012). The Forensic Deaths Caused by Pesticide Poisoning Between the Years 2006 and 2009 in Izmir, Turkey\*. *Journal of Forensic Sciences*. 57(4):1014-1016. DOI: 10.1111/j.1556-4029.2012.02085.x.
- Inquest Act. (1959). *Inquest Act No. 58 of 1959*. Pretoria, South Africa: Union Gazette Extraordinary.
- Jaga, K. and Dharmani, C. (2003). Sources of exposure to and public health implications of organophosphate pesticides. *Revista Panamericana de Salud Pública*. 14(3):171-185. DOI: 10.1590/s1020-49892003000800004.
- Jeyaratnam, J. (1990). Acute pesticide poisoning: a major global health problem / J. Jeyaratnam. *World health statistics quarterly 1990*. 43(3):139-144
- Kabanda, S. and Rother, H. (2019). Evaluating a South African mobile application for healthcare professionals to improve diagnosis and notification of pesticide poisonings. *BMC Medical Informatics and Decision Making*. 19(1). DOI: 10.1186/s12911-019-0791-2.
- Kamaruzaman, Y., Leong, Y., Jaafar, N., Khan, H., Rani, N., Razali, M. and Majid, M. (2020). Epidemiology and risk factors of pesticide poisoning in Malaysia: a retrospective analysis by the National Poison Centre (NPC) from 2006 to 2015. *BMJ Open*. 10(1). DOI: 10.1136/bmjopen-2019-036048.
- Karami-Mohajeri, S. and Abdollahi, M. (2010). Toxic influence of organophosphate, carbamate, and organochlorine pesticides on cellular metabolism of lipids, proteins, and carbohydrates. *Human & Experimental Toxicology*. 30(9):1119-1140. DOI: 10.1177/0960327110388959.

- Karami-Mohajeri, S. and Abdollahi, M. (2010). Toxic influence of organophosphate, carbamate, and organochlorine pesticides on cellular metabolism of lipids, proteins, and carbohydrates. *Human & Experimental Toxicology*. 30(9):1119-1140. DOI: 10.1177/0960327110388959.
- Klette, K. , Levine, B., Dreka, C., Smith, M. and Goldberger, B. (1993). Cholinesterase activity in postmortem blood as a screening test for organophosphate/chemical weapon exposure. *Journal of Forensic Sciences*. 38(4):950–955. PMID: 8355009.
- Kohli, U., Kuttia, V., Lodha, R. and Kabra, S. (2008). Profile of childhood poisoning at a tertiary care centre in North India. *The Indian Journal of Pediatrics*. 75(8):791-794. DOI: 10.1007/s12098-008-0105-7.
- Konradsen, F., van der Hoek, W., Gunnell, D. and Eddleston, M. (2005). Missing deaths from pesticide self-poisoning at the IFCS Forum IV. *Bulletin World Health Organisation*. 83 (2): 157 - 158. PMID:15744410
- Lafon, P., Imberdis, T., Wang, Y., Torrent, J., Robitzer, M., Huetter, E., Alvarez-Martinez, M. and Chevallier, N. *et al.* (2018). Low doses of bioherbicide favour prion aggregation and propagation in vivo. *Scientific Reports*. 8(1). DOI: 10.1038/s41598-018-25966-9.
- Larson, S., Capel, P. and Majewski, M. (2019). *Pesticides in Surface Waters: Distribution, Trends and Governing factors (1<sup>st</sup> edition)*. CRC Press, Boca Raton. DOI: 10.1201/9780429062797.
- London, L. (1996) *The health hazards of chemical use in agriculture*. Republic of South Africa: University of Cape Town.
- London, L. and Baile, R. (2001). Challenges for improving surveillance for pesticide poisoning: policy implications for developing countries. *International Journal of Epidemiology*. 30 (3):564-70. DOI: 10.1093/ije/30.3.564.
- London, L., Flisher, A., Wesseling, C., Mergler, D. and Kromhout, H. (2005). Suicide and exposure to organophosphate insecticides: Cause or effect? *American Journal of Industrial Medicine*. 47(4):308-321. DOI: 10.1002/ajim.20147.
- Marks, C. and Van Hoving, D. (2016). A 3-year survey of acute poisoning exposures in infants reported in telephone calls made to the Tygerberg Poison Information Centre, South Africa. *South African Journal of Child Health*. 10(1):43-46. DOI: 10.7196/SAJCH.2016.v10i1.1045.

- Mlayeh, S., Annabi, K., Daly, A., Jedidi, M. and Dhiab, M. (2020). Pesticidepoisoning deaths: a 19-year retrospective study of medicolegal autopsies in center Tunisia. *Egyptian Journal of Forensic Sciences*. 10(1). DOI: 10.1186/s41935-020-00201-7.
- Mnif, W., Hassine, A., Bouaziz, A., Bartegi, A., Thomas, O. and Roig, B. (2010). Effect of Endocrine Disruptor Pesticides: A Review. *International Journal of Environmental Research and Public Health*. 8(6):2265-2303. DOI: 10.3390/ijerph8062265.
- Moriya, F., Hashimoto, Y. and Kuo, T. (1999). Pitfalls when determining tissue distributions of organophosphorus chemicals: sodium fluoride accelerates degradation. *Journal of Analytical Toxicology*. 23(3):210-215. DOI: 10.1093/jat/23.3.210.
- Mutlu, M., Cansu, A., Karakas, T., Kalyoncu, M. and Erduran, E. (2009). Pattern of pediatric poisoning in the east Karadeniz region between 2002 and 2006: increased suicide poisoning. *Human & Experimental Toxicology*. 29(2):131-136. DOI: 10.1177/0960327109357141.
- Naidoo, S., London, L., Burdorf, A., Naidoo, R. and Kromhout, H. (2010). Spontaneous miscarriages and infant deaths among female farmers in rural South Africa. *Scandinavian Journal of Work, Environment & Health*. 37(3):227-236. DOI: 10.5271/sjweh.3133.
- Nalwanga, E. and Ssempebwa, J. (2011). Knowledge and Practices of In-Home Pesticide Use: A Community Survey in Uganda. *Journal of Environmental and Public Health*. 2011:1-7. DOI: 10.1155/2011/230894.
- Nansen, C. and Thomas, J. (2013). The Performance of Insecticides – A Critical Review. *Insecticides - Development of Safer and More Effective Technologies*. IntechOpen: Rijeka. DOI: 10.5772/53987.
- National Health Act. (2003). *National Health Act No. 61 of 2003*. Pretoria, South Africa: Government Printers.
- National Institute for Occupational Safety and Health. (1997). *Pocket guide to chemical hazards. DHHS (NIOSH)*. 270:97-140. US Government Printing office: Washington DC.
- National Institute of Environmental Health Sciences. (2020). Pesticides. Available:<https://www.niehs.nih.gov/health/topics/agents/pesticides/index.cfm> [2020 , June 19].
- National Research Council of the United States. (1994). *Subcommittee to Review Permethrin Toxicity from Military Uniforms. Health Effects of Permethrin-Impregnated Army Battle-Dress Uniforms*. National Academies Press (US): Washington (DC). PMID: 25101418.

Nicolopoulou-Stamati, P., Maipas, S., Kotampasi, C., Stamatis, P. and Hens, L. (2016). Chemical Pesticides and Human Health: The Urgent Need for a New Concept in Agriculture. *Frontiers in Public Health*. 18(4):148. DOI: 10.3389/fpubh.2016.00148.

Nigam, M., Jain, B., Banerjee, U., Roy, D. and Chatterjee, S. (2013). Pesticide poisoning- an Epidemiological and Histopathological study. *Pacific Journal of Medical Science*. 12(1): 3-9.

Park, M., In, S., Lee, S., Choi, W., Park, Y. and Chung, H. (2009). Postmortem blood concentrations of organophosphorus pesticides. *Forensic Science International*. 184(1-3):28-31. DOI: 10.1016/j.forsciint.2008.11.008.

Pathomrattanasiri, W., Hountong, S. and Phuangphung, P. (2021). Determination of the reference range of whole blood cholinesterase activities in Thai postmortem cases. *Journal of Associated Medical Sciences*. 54(3): 1-10. Available at: <https://he01.tci-thaijo.org/index.php/bulletinAMS/article/view/247589> (Accessed: 29 September 2021).

Patience, M.(2018). *Retrospective analysis of suspected pesticide-related fatalities admitted to Salt River Mortuary in the West-Metropole of Cape Town*. Republic of South Africa: University of Cape Town.

Pesticide Action Network (2010). *PAN Pesticide database, 20.03.2011*. Available from <http://www.pesticideinfo.org>

Peter, J., Sudarsan, T. and Moran, J.(2014). Clinical features of organophosphate poisoning: A review of different classification systems and approaches. *Indian Journal of Critical Care Medicine*.18(11):735-45. DOI: 10.4103/0972-5229.144017.

Popp, J., Pető, K. and Nagy, J. (2012). Pesticide productivity and food security: A review. *Agronomy for Sustainable Development*. 33(1):243-255. DOI: 10.1007/s13593-012-0105-x.

Quinn, L., B, de, J., Fernandes-Whaley, M., Roos, C., Bouwman, H., Kylin, H. and Pieters, R. (2011). Pesticide Use in South Africa: One of the Largest Importers of Pesticides in Africa. *Pesticides in the Modern World - Pesticides Use and Management*. 1: 46-96. DOI: 10.5772/16995.

Ramchandra, A., Chacko, B. and Victor, P. (2019). Pyrethroid pesticides. *Indian Journal of Critical Care Medical*. 23(4):267-271.DOI: 10.5005/jp-journals-10071-23304.

- Ray, D. and Forshaw, P. (2000). Pyrethroid insecticides: poisoning symptoms, synergies, and therapy. *Journal of Toxicology: Clinical Toxicology*. 38(12):95-101. DOI: 10.1081/clk-100100922.
- Ray, D. and Fry, J. (2006). A reassessment of the neurotoxicity of pyrethroid insecticides. *Pharmacology & Therapeutics*. 111(1):174-193. DOI: 10.1016/j.pharmthera.2005.10.003.
- Razwiedani, L. and Rautenbach, P. (2017). Epidemiology of Organophosphate Poisoning in the Tshwane District of South Africa. *Environmental Health Insights*. 11:117863021769414. DOI: 10.1177/1178630217694149.
- Republic of South Africa: Department of Health. (2005). MRL of pesticides in foodstuff, 20.03.2011, Available from <http://www.DoH.gov.za/departement/foodcontrol/pesticides/chemical.zip>.
- Republic of South Africa: Department of Health. (2008). Pesticide poisoning statistics: 2008. <http://www.doh.gov.za/facts/index.html>. Accessed December 2009.
- Rivero, A., Vézilier, J., Weill, M., Read, A. and Gandon, S. (2010). Insecticide Control of Vector-Borne Diseases: When Is Insecticide Resistance a Problem?. *PLoS Pathogens*. 6(8):e1001000. DOI: 10.1371/journal.ppat.1001000.
- Robb, E. and Baker, M. (2021). *Organophosphate Toxicity*. In: StatPearls Publishing [Internet]. Treasure Island (FL): Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470430/>
- Ross, G. (2005). Risks and benefits of DDT. *The Lancet*. 366: 763-766. DOI: 10.1016/S0140-6736(05)67722-7.
- Rother, H. (2010). Falling through the regulatory cracks: street selling of pesticides and poisoning among urban youth in South Africa. *International Journal of Occupational Environmental Health*. 16 (2):202–213. DOI: 10.1179/107735210799160336.
- Rother, H. (2012). Improving poisoning diagnosis and surveillance of street pesticides. *South African Medical Journal*. 102(6):485. DOI: 10.7196/samj.5838.
- Rother, H. and London, L. (2009). Occupational health concerns with pesticides in agriculture and beyond. *Continuing Medical Education*. 27(11):506. Available from: <http://hdl.handle.net/10520/EJC63597>.

Sabino, B., Rozenbaum, H. and Oliveir, A. (2011). A Forensic View of Pesticide Poisonings in Brazil. *Pesticides in the Modern World - Effects of Pesticides Exposure*. 13: 5702-5722. DOI: 10.5772/16497.

Sacramento, C.A. (2008). What are the Potential Health Effects of Pesticides? Community Guide to Recognizing and Reporting Pesticide Problems. *Department of pesticide regulation: Sacramento*. 1:27–29.

Sakar, D., Shaheduzzaman, M., Hossain, M., Ahmed, M., Mohammad, N. and Basher, A. (2013). Spectrum of Acute Pharmaceutical and Chemical Poisoning in Northern Bangladesh.. *Asia Pacific Journal of Medical Toxicology*. 2:1-4. DOI: 10.22038/APJMT.2013.508.

Santos, A. and Flores, M. (1995). Effects of glyphosate on nitrogen fixation of free-living heterotrophic bacteria. *Letters in Applied Microbiology*. 20(6):349-352. DOI: 10.1111/j.1472-765x.1995.tb01318.x.

Silberman, J. and Taylor, A. (2020). *Carbamate Toxicity*. Treasure Island (FL): StatPearls Publishing. PMID: 29489157.

Soares, S., Rosado, T., Barroso, M., Vieira, D. and Gallardo, E. (2019). Organophosphorus pesticide determination in biological specimens: bioanalytical and toxicological aspects. *International Journal of Legal Medicine*. 133(6):1763-1784. DOI: 10.1007/s00414-019-02119-9.

Soloneski, S., Kujawski, M., Scuto, A. and Larramendy, M. (2015). Carbamates: A study on genotoxic, cytotoxic, and apoptotic effects induced in Chinese hamster ovary (CHO-K1) cells. *Toxicology in Vitro*. 29(5):834-844. DOI: 10.1016/j.tiv.2015.03.011.

Soycheva, M., (2011). *Pesticides in the Modern World: Effects of Pesticide Exposure*. IntechOpen: Rijeka. DOI: 10.5772/943. Available from: <http://www.intechopen.com/books/pesticides-in-the-modern-world-effects-of-pesticides-exposure>.

Swapan, K., Soumeek, C. and Parthapratim, M. (2021). A Study on the Histopathological Changes in Cases of Pesticide Poisoning and Proposed Diagnostic Algorithm. *Indian Journal of Forensic Medicine & Toxicology*, 15(2), 1042-1049. <https://doi.org/10.37506/ijfmt.v15i2.14457>.

- Swartz, A., Levine, S., Rother, H. and Langerman, F. (2018). Toxic layering through three disciplinary lenses: childhood poisoning and street pesticide use in Cape Town, South Africa. *Medical Humanities*. 44 (4): 247-252. DOI: 10.1136/medhum-2018-011488.
- Thatheyus, A. and Gnana Selvam, A. (2013). Synthetic Pyrethroids: Toxicity and Biodegradation. *Applied Ecology and Environmental Sciences*. 1(3):33-36. DOI: 10.12691/aees-1-3-2.
- Vale, A. and Lotti, M. (2015). Organophosphorus and carbamate insecticide poisoning. *Handbook of Clinical Neurology*. 1:149-168. DOI: 10.1016/b978-0-444-62627-1.00010-x.
- Van Hoving, D., Hunter, L., Lategan, H. and Marks, C. (2018). The burden of intentional self-poisoning on a district-level public Hospital in Cape Town, South Africa. *African Journal of Emergency Medicine*, 8(3):79-83. DOI: 10.1016/j.afjem.2018.03.002
- Veale, D., Wium, C. and Müller, G. (2013). Toxicovigilance I: A survey of acute poisoning in South Africa based on Tygerberg Poison Information Centre data. *South African Medical Journal*. 103(5):293. DOI: 10.7196/samj.6647.
- Wang, N., Jiang, Q., Han, L., Zhang, H., Zhu, B. and Liu, X. (2019). Epidemiological characteristics of pesticide poisoning in Jiangsu Province, China, from 2007 to 2016. *Scientific Reports*. 9(1). 8604-8612. DOI: 10.1038/s41598-019-44986-7.
- Wiese, I. and Bot, J. (1971). Pesticide regulation in South Africa. *Residue Reviews / Rückstands-Berichte*. 49-63. DOI: 10.1007/978-1-4612-9812-0\_4.
- Wilson, A., Morgan, E., Booth, M., Norman, R., Perkins, S., Hauffe, H., Mideo, N. and Antonovics, J. (2017). What is a vector?. *Philosophical Transactions of the Royal Society B: Biological Sciences*. 372(1719):20160085. DOI: 10.1098/rstb.2016.0085.
- World Health Organisation. (1990). *World Health Statistics Quarterly*.43:139–144. WHO: 20 Avenue Appia, 1211 Geneva 27, Switzerland.
- World Health Organization. (2005). Safety of Pyrethroids for Public Health Use: Communicable Disease Control, Prevention and Eradication WHO Pesticide Evaluation Scheme (WHOPES) & Protection of the Human Environment Programme on Chemical Safety (PCS). *World Health Organization*, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

World Health Organization. (2009). The WHO recommended classification of pesticides by hazard and guidelines to classification: 2009. *World Health Organization*, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

World Health Organization. (2002). *The World Health Report 2002: Reducing Risks, Promoting Healthy Life*. WHO; 20 Avenue Appia, 1211 Geneva 27, Switzerland.

World Health Organization. (2005).

The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2004, International Programme on Chemical Safety, p.16. *World Health Organization*, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

Yadav, I. and Devi, N. (2017). Pesticides Classification and Its Impact on Human and Environment. *Environmental Science and Engineering*. 1 (6):140 - 158. ISN: 1-62699-094-8.

Yonemitsu, K. and Pounder, D. (1993). Postmortem changes in blood tranylcypromine concentration: Competing redistribution and degradation effects. *Forensic Science International*. 59(2):177-184. DOI: 10.1016/0379-0738(93)90157-6.

Zhang, X., Zhang, T., Ren, X., Chen, X., Wang, S. and Qin, C. (2021). Pyrethroids Toxicity to Male Reproductive System and Offspring as a Function of Oxidative Stress Induction: Rodent Studies. *Frontiers in Endocrinology*. 12:656106. DOI: 10.3389/fendo.2021.656106.

## Chapter 2: Manuscript

A retrospective, descriptive analysis of pesticide-related deaths admitted to Salt River Mortuary, in Cape Town, South Africa (2016-2019)

### 2.1 Highlights

- A total of 92 pesticide-related fatalities were identified within this study cohort
- Approximately 60.8% of all identified pesticide cases were suspected suicides
- Terbufos was identified as the most frequently detected pesticide
- Male decedents predominate pesticide-related fatalities (59.8%)
- Most pesticide-related fatalities occurred in lower socio-economic areas

### 2.2 Abstract

Pesticide-related poisonings are a public health problem, especially in developing countries, or countries who face poverty, such as South Africa. The World Health Organisation (WHO) reported that 300 000 pesticide-related fatalities occur annually. Although strides have been made to ensure pesticide-related poisonings are documented, knowledge on the incidence and epidemiology of these poisonings in the South African context is lacking. Furthermore, the increased occurrence of illegally sold unlabelled pesticide formulations, known as street pesticides, make it more challenging to estimate the impact of pesticides on mortality and morbidity. Mortuary data could provide helpful clues in measuring pesticide-related mortality prevalence. This study therefore aimed to investigate pesticide-related deaths admitted to the Salt River Mortuary (SRM) in the West-Metropole of Cape Town.

A four-year retrospective, cross-sectional review of all unnatural death cases admitted to SRM between January 2016 and December 2019 (inclusive) was conducted to identify and describe pesticide-related deaths. Out of the 15,761 cases admitted to SRM; 92 (0.6%) were identified as being pesticide related. The majority of the pesticide cases were suspected suicides (60.8%). Male decedents predominated the study cohort (59.8%). The mean age of the cohort was 26.2 years (range: 2 months – 66 years) with the 11 to 20 (n=21, 22.8%) and 21 to 30 (n=20, 21.7%) year-old age groups having the highest case frequencies. Of the cases that had toxicological results (n=65), terbufos was detected most frequently (n=50, 77%). Toxicology results were outstanding in 21 cases at the time of the project conclusion. Overall, lower socio-economic areas were a hotspot for pesticide-related fatalities.

**Keywords:** Cape Town, mortality, organophosphate, pesticide, poisoning

## 2.3 Introduction

Pesticide-related poisonings have increased in low and middle-income countries (Balme *et al.* 2010). In the Republic of South Africa (RSA), over 3,000 pesticides are registered for use on agricultural crops (Dabrowski, 2015). There has been an increased shift in the use of agricultural pesticides for domestic purposes, particularly in lower socio-economic settings (Rother, 2010). The increase in domestic pesticide use in impoverished communities comes as a result of communities seeking out inexpensive, accessible and effective methods of maintaining pest-free environments (Balme *et al.*, 2010). The danger in this, is that the products used are often mixtures of highly hazardous pesticides, sold illegally in unknown formulations, known as street pesticides (Rother, 2012). These compounds may include toxic organophosphates, pyrethroids, and carbamates, and are typically sold in unlabelled containers comprised of either liquids, pellets, or granules (Balme *et al.*, 2010). The illegal sale or distribution of street pesticides places individuals at risk of being exposed to the acute and/or chronic effects of these compounds (Rother, 2012).

An effective monitoring system is essential for determining the role of pesticides in poisoning and death, especially since the impact of street pesticides on morbidity and mortality is unknown (Rother, 2012). Pesticide-related poisonings constitute a notifiable medical condition (NMC) in accordance with the National Health Act (Act 61 of 2003) of RSA. These cases fall under 'agricultural or stock remedy poisoning'. Studies have illustrated that notification and surveillance of pesticide morbidity and mortality in RSA is limited (London and Baile, 2001; London *et al.*, 1994; London 1992; Myers, 1990) and requires further interventions and improvement (Rother, 2012). According to London (2001), only 10% to 20% of all pesticide-related poisonings are successfully notified. Rother (2012) pointed out the importance of accurate diagnosis of pesticide-related poisonings in successful notification and surveillance initiatives. Unfortunately, the non- and misdiagnosis of these cases may impede case notification rates, which highlights the importance of training healthcare professionals to recognise and accurately diagnose cases. Transdisciplinary collaborations, intra-government co-operation, and improving the management and types of data collected were recommended to improve pesticide poisoning surveillance (London and Baile, 2001).

In RSA, there is limited data investigating the role and prevalence of pesticide toxicity in mortality specifically. The lack of mortuary data pertaining to pesticide mortality means

researchers are unable to accurately quantify the role of pesticides, particularly street pesticides, in local poisonings. Despite this, clinical information can help provide data for investigating mortality in cases where the deceased was hospitalised prior to death. The patient's clinical presentation and vital signs may assist in understanding the toxidrome that results in death. Many hospitals may test for pseudocholinesterase enzyme activity at hospital admission, as this is a biomarker for potential organophosphate pesticide poisoning. In RSA, there are no facilities available for rapid pesticide testing in hospitals, and pseudocholinesterase testing proves to be an important indicator in suspected organophosphate (OP) or carbamate pesticide poisonings. The pseudocholinesterase testing is done by the National Health Laboratory Service (NHLS) and should be conducted when patients present clinical symptoms associated with OP poisoning. Ante-mortem pseudocholinesterase levels are better indicators than those measured post-mortem. However, ante-mortem pseudocholinesterase testing is not always conducted. These should help eliminate certain suspicions surrounding death to provide more clear, accurate reflections of the actual circumstances leading up to death.

Limited pesticide mortality data has been published, however, a local study at the Salt River Mortuary (SRM) in the West Metropole of Cape Town, highlighted the usefulness of mortuary data in understanding acute pesticide poisoning deaths, especially in the form of case history, death scene and autopsy findings, as well as toxicology results (Patience, 2018). In that study, terbufos was found to be the most frequently detected pesticide in the cohort deaths between 2010 to 2015 (Patience, 2018). There were, however, outstanding toxicological results, limiting further understanding of the analytes involved. The study did, however, corroborate other research illustrating that acute pesticide poisoning occurred most frequently in lower socio-economic areas in Cape Town (Balme *et al.* 2010; Patience, 2018). This suggests a link between acute pesticide poisoning and the domestic use of pesticides, including more toxic street pesticides, in low socio-economic settings.

This study aimed to provide an updated and expanded investigation into pesticide-related deaths in the West Metropole of Cape Town. This information may be used in future to standardise an evidence-based protocol for investigating and monitoring pesticide deaths within RSA. Furthermore, this mortuary data may be useful to support policy development with regards to case notification practices or management of pesticide availability and use, and to guide future interventions to reduce poisonings and deaths.

## 2.4 Methods

### 2.4.1 Study context

In South Africa, all unnatural deaths must undergo a medico-legal autopsy, as per the Inquests Act (Act 58 of 1959) (Inquest Act, 1959). Forensic autopsies are performed by authorised medical practitioners within the Forensic Pathology Service (FPS), as governed by the National Health Act: Regulations rendering Forensic Pathology Service (National Health Act, 2018) and the Human Tissues Act (Act 65 of 1983) (Human Tissues Act, 1983). FPS falls within Western Cape Government, Department of Health, and works in conjunction with the South African Police Service (SAPS) to assist in medico-legal death investigation, with the ultimate aim of determining an individual's cause of death. The full judicial system process will determine the final manner of death (homicide, accident, suicide, or undetermined), with the magistrate using information from the post-mortem investigation and other evidence in an inquest or criminal trial. In this study, the *suspected* manner of death was recorded, as this is documented by the medical practitioner based on the history and autopsy findings.

SRM is one of 16 mortuaries in the Western Cape province (WCP) and is one of the busiest; receiving all unnatural death admissions from the West Metropole of Cape Town, which includes the Southern, Western, Klipfontein and Mitchells plain districts. SRM receives over 4,000 unnatural death admissions annually in an area whose total population is currently estimated to be 1,937,379 people (Statistics South Africa, 2011). The proportion of males to females within the West Metropole was 49.0% (n=949,592) for males and 51 % (n=987,787) for females. Approximately 21% of the metropole's population was within the 20- to 29-year-old age category (n = 407 965) (Statistics South Africa, 2011). This was the most recent formal census in the country.

### 2.4.2 Study design

The study design took the form of a retrospective cross-sectional records review of all unnatural death cases admitted to SRM between 1<sup>st</sup> January 2016 and 31<sup>st</sup> December 2019 (inclusive). A review of the Office Autopsy Database (OAD) (HREC ethics: R036/2014) housed within the Division of Forensic Medicine and Toxicology of the University of Cape Town, was conducted to identify cases of suspected pesticide-related toxicity. This database contains all routine

unnatural death case information from SRM cases as recorded by the medical practitioners performing the autopsies. All cases were screened on the database according to the circumstance, manner, method, and cause of death, to establish any possible relation to pesticide exposure. All cases that included a toxic exposure were included in the initial screen, to review further to determine the role of pesticides. Additional keywords were also used to search and identify cases, which included organophosphate, terbufos, pesticide, poison, carbamate, toxin, malathion, aldicarb and granules.

Once cases were preliminarily identified using the database, a detailed case review was conducted of the case files, which were also located within the Division of Forensic Medicine and Toxicology. The case files included death scene and autopsy records, hospital documents, and toxicology testing reports. Following the full review of the case file, cases were either included or excluded as being related to pesticide toxicity.

### **2.4.3 Research sampling**

#### *Inclusion and exclusion criteria*

Any decedents (of all ages) who were suspected to have died from pesticide-related toxicity based on the detailed case review, the pathologist's cause of death determination, and/or toxicological confirmation, were included in this study. This detailed case review involved a review of the available death scene and autopsy records, the forensic pathologists' post-mortem report, the FPS 100 form which includes summarised hospital notes if the individual was hospitalised before death, and the toxicology testing reports. All decedents admitted between 1 January 2016 to 31 December 2019 to the mortuary, and who adhered to the criteria above, were included.

All unnatural death cases relating to non-pesticide toxicity or other causes of death were excluded from this research study (e.g. stabbings, assaults, hangings, drownings, road-traffic collisions, drug-related or other toxicant deaths). The total number of cases admitted to the mortuary within the study period was recorded. In cases where an unknown toxin (i.e. traditional medicine or unknown chemical) may have contributed to the cause of death, these cases were excluded if there was no history of pesticide exposure and if there were no pathology or toxicology results to support pesticide involvement.

#### **2.4.4 Toxicological results**

Toxicological analyses were performed by the National Department of Health's Forensic Chemistry Laboratory in Cape Town and not by the researchers involved. It was recognised that the laboratory faces delays in processing toxicology, and therefore not all cases had analytical results at the time of the study conclusion. Pharmacological screening was performed by UCT's Division of Pharmacology and not directly by the researchers involved. This is a preliminary drug screen historically requested by medical practitioners, due to delays in formal toxicology by FCL.

The Division of Pharmacology has been performing preliminary drug screening using a SCIEX X500R LC-QTOF/MS for SRM. The method screens for over 600 prescription and recreational drugs and has been used on an ad-hoc basis by the FPS pathologists if require a preliminary drug screen. This would be in addition to requesting formal toxicological analyses with FCL. Pharmacology screened a few cases for pesticides, but subsequently stopped this work, thus the results are limited. These processes have changed recently however, with the implementation of the Forensic Toxicology Unit (FTU) within FPS/UCT, however, was still in use at the time of this study.

#### **2.4.5 Data collection and analysis**

The following data was collected from each case: case history (e.g., date and time of death and post-mortem, death scene and/or hospital findings, location of incident), demographic information (sex and age), autopsy findings (cause, manner of death and chief post-mortem findings), toxicology results (blood alcohol and/or toxicological results), and whether there was information concerning the notification of the case as an NMC. Information on the type of testing conducted for each case was also recorded. These tests include pseudocholinesterase testing, blood-alcohol testing, drug testing and pesticide detection or analysis.

All data was captured onto a database using Excel 2016 (Microsoft, USA) and analysed using IBM SPSS 26.0 (IBM SPSS Inc., Chicago, IL, USA). Statistical analysis included descriptive statistics describing the relationship and characteristic distribution of the demographic, geographical and age-related data for the included cases. Any specific trends pertaining to pesticide-related fatalities and the manner of death were described using figures and frequency tables. P-values were determined at the  $\alpha = 0.05$  level to determine significance

within the data using Fischer's Exact Test. In addition, clinical observations and chief post-mortem findings were collated to outline and describe any trends relating to the symptomology of pesticide-related fatalities.

The NMC notification record files housed within the Division of Forensic Medicine and Toxicology, were reviewed to identify which cases were notified. The total number of pesticide-related cases admitted to SRM per year as identified in the study was compared to the total number of cases identified in the NMC files for that year.

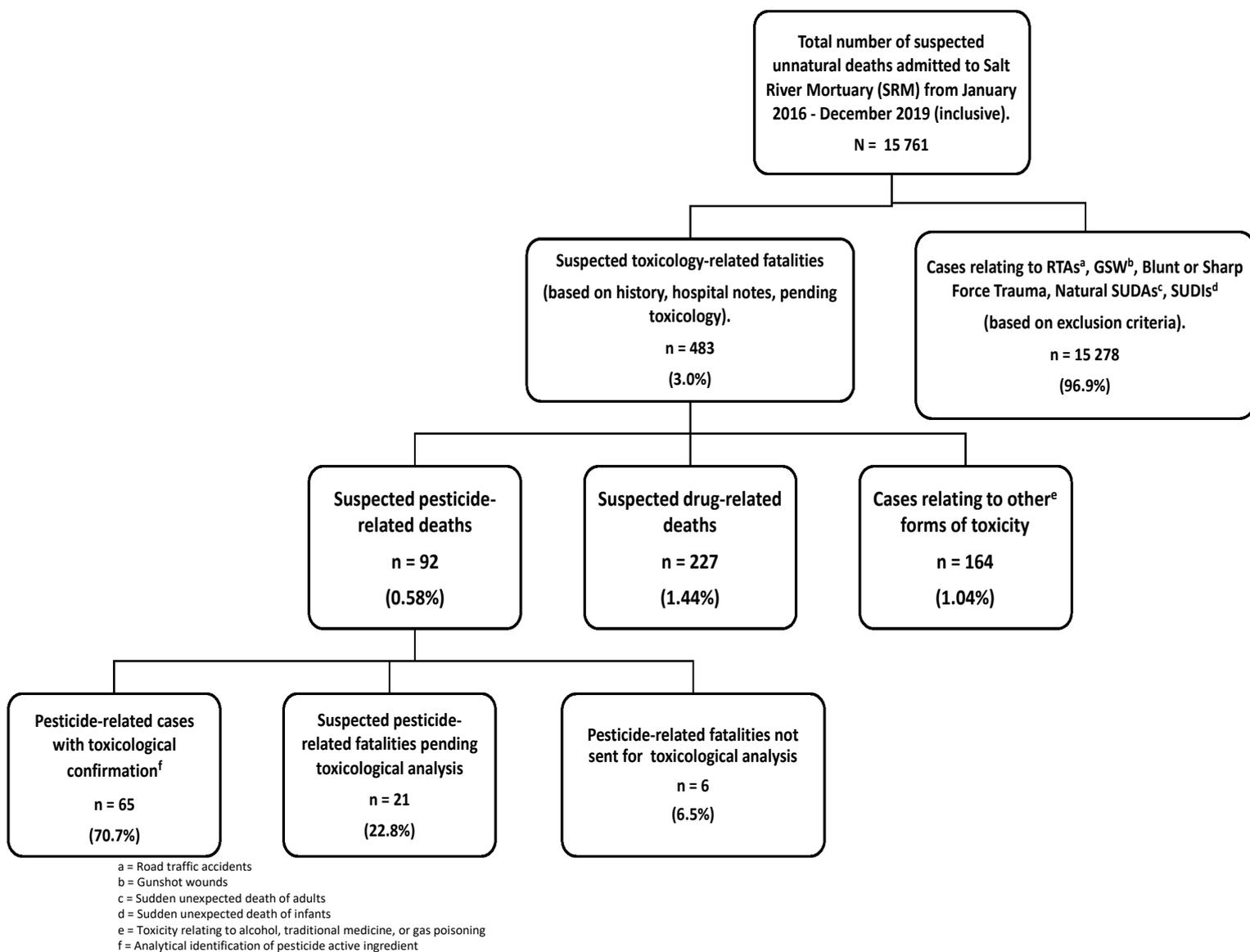
## **2.5 Ethics**

Ethical approval for this study was obtained from the Human Research Ethics Committee (HREC) of the University of Cape Town, Faculty of Health Sciences, with the reference: HREC: 246/2020.

## **2.6 Results:**

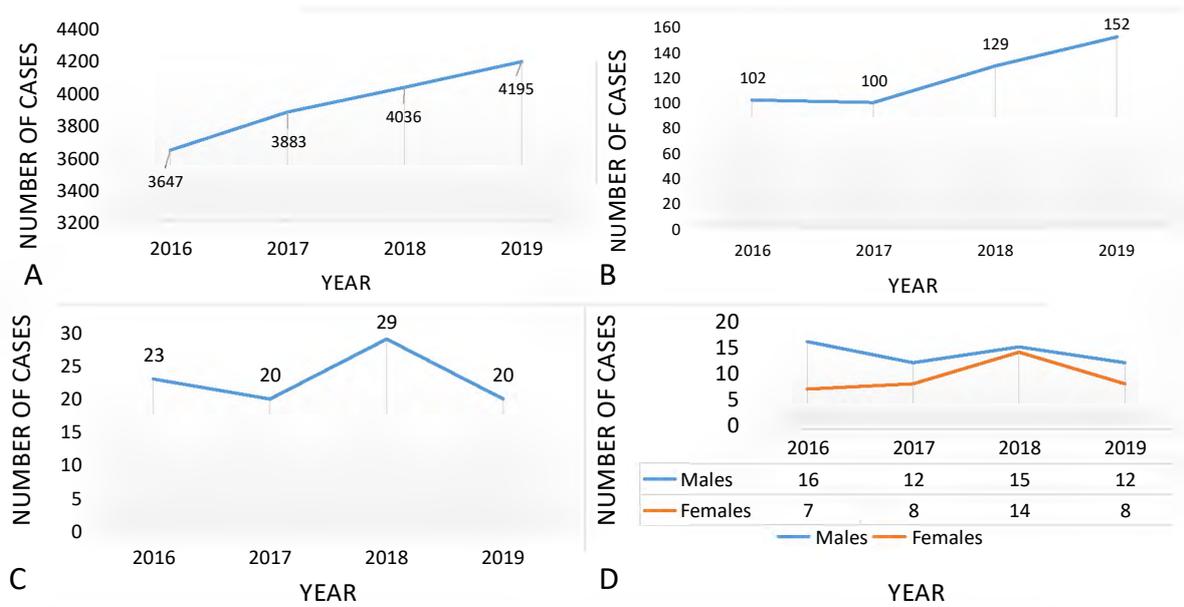
### **Case characteristics:**

A total of 15,761 unnatural death cases were admitted to SRM over the 4-year study period, with an annual average of 3,941 cases. From this total, the cause of death in 15,278 (96.9%) was non-toxicity related and in 483 (3.1%) cases was toxicity-related (Fig. 1). Ninety-two (0.6%) fatalities were deemed pesticide related and included for further analysis.



**Figure 2.** Flow of unnatural death cases admitted to SRM over four-year period and identification of pesticide deaths.

Of the 92 pesticide fatalities ( $\mu=23$  cases/annum), 55 cases (59.8%) were males compared to only 37 cases (40.2%) for females, with male deaths dominating over all four years (Figure 2D). The year 2018 saw the highest number of pesticide-related fatalities at 29 cases (Figure 2C). This can also be seen in the proportion of male and female pesticide-related fatalities for 2018 given in Figure 2D.



**Figure 3.** Unnatural death case distribution over 4-year study period **A.** Total number of unnatural death cases admitted to SRM per year **B.** Total number of toxicity-related deaths (deaths that relate to any form of poisoning) admitted to SRM per year **C.** Total number of pesticide-related cases admitted to SRM per year. **D.** Pesticide-related case distribution according to sex.

The included pesticide deaths were mostly suspected suicides ( $n=56$ ; 60.9%), but also included suspected accidental deaths ( $n=16$ ; 17.4%), homicides ( $n=4$ ; 4.3%) and cases that were still under investigation ( $n=16$ ; 17.3%) (Table 2). Most pesticide deaths involved individuals aged between 11 to 20 years old ( $n=21$ ), 21 to 30 years old ( $n=19$ ) and 31 to 40 years old ( $n=22$ ). According to the p-values, although the 31 to 40 year old group had the highest number of cases, there were no significant differences in the number of pesticide deaths between the groups when p-values or significance was calculated according to age and manner of death. Generally, suicides involved adults and teenagers/adolescents whilst accidents and homicides, although varied, were more frequently observed in toddlers and teenagers.

**Table 2.** Distribution of all pesticide-related death cases admitted to SRM over the four-year study period according to age, sex, and manner of death.

Manner of Death	Under Investigation (n = 16)		Suicide (n = 56)		Homicide (n = 4)		Accident (n = 16)		Total (N = 92)		P-values (significance between age groups)
	M	F	M	F	M	F	M	F	M	F	
Male (M) and female (F) distribution											-
Age distribution in years (years) (n)											-
0 – 10 yrs (15)	2(2.2)	2(2.2)	-	-	2(2.2)	1(1.1)	5(5.4)	3(3.3)	9(9.8)	6(6.5)	0.62
11 – 20 yrs (21)	1 (1.1)	2 (2.2)	4 (4.3)	10 (10.9)	1 (1.1)	-	2 (2.2)	1 (1.1)	8 (8.7)	13 (14.1)	0.02
21 – 30 yrs (19)	1 (1.1)	1 (1.1)	5 (5.4)	10 (10.9)	-	-	2 (2.2)	-	8 (8.7)	11 (11.9)	0.07
31 – 40 yrs (22)	3 (3.3)	-	14 (15.2)	4 (4.3)	-	-	1 (1.1)	-	18 (19.6)	4 (4.3)	1.00
41 – 50 yrs (7)	1 (1.1)	2 (2.2)	3 (3.3)	1 (1.1)	-	-	-	-	4 (4.3)	3 (3.3)	0.59
51 – 60 yrs (6)	1 (1.1)	-	3 (3.3)	-	-	-	2 (2.2)	-	6 (6.5)	0 (0)	1.00
61 -70 yrs (2)	-	-	2 (2.2)	-	-	-	-	-	2 (2.2)	0 (0)	1.00
<b>Total</b>	<b>9 (9.8)</b>	<b>7(7.6)</b>	<b>31(33.7)</b>	<b>25(27.2)</b>	<b>3(3.3)</b>	<b>1(1.1)</b>	<b>12(13.0)</b>	<b>4(4.3)</b>	<b>55(59.8)</b>	<b>37(40.2)</b>	<b>-</b>
p-values (significance according to manner of death)	<b>0.48</b>		<b>1.19</b>		<b>0.88</b>		<b>0.95</b>		<b>-</b>		<b>-</b>

On average, the months March, July, November, and December had the highest number of pesticide deaths over the four years, however, the numbers were too small to determine significance. Overall, the autumn season was found to have the highest pesticide death frequencies (n=29; 31.5%).

**Table 3.** Monthly distribution of pesticide-related cases over the 4-year study period

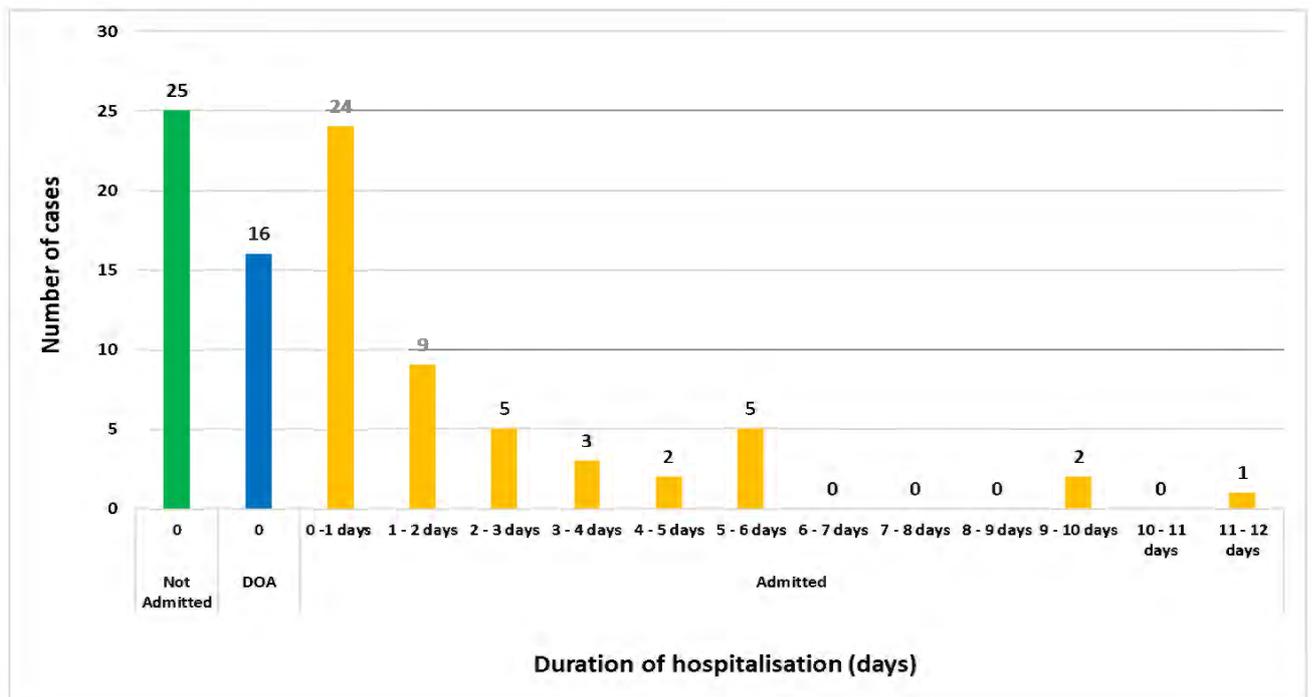
Season	Month	Number of cases (%)		
		Over 4-year period	Average Per annum	Per season
Summer	December	8 (8.7)	2 (8.7)	<b>17 (18.5)</b>
	January	5 (5.4)	1.25 (5.4)	
	February	4 (4.3)	1 (4.3)	
Autumn	March	15 (16.3)	3.75 (16.3)	<b>29 (31.5)</b>
	April	7 (7.6)	1.75 (7.6)	
	May	7 (7.6)	1.75 (7.6)	
Winter	June	5 (5.4)	1.25 (5.4)	<b>24 (26.0)</b>
	July	12 (13.0)	3 (13.0)	
	August	7 (7.6)	1.75 (7.6)	
Spring	September	6 (6.5)	1.5 (6.5)	<b>22 (23.9)</b>
	October	5 (5.4)	1.25 (5.4)	
	November	11 (11.9)	2.75 (11.9)	
<b>Total</b>		<b>92 (100)</b>	<b>23 (100)</b>	

Results indicate that Gugulethu (n=26, 28.3%), Nyanga (n=20, 21.7%), and Philippi (n=15, 16.3%), had the highest incidences of pesticide-related fatalities, as related to where the site of poisoning occurred. In addition, results from incident scene specifics indicated that in the

majority of cases, poisoning occurred in a domestic setting including informal housing areas (n=29, 31.5%), typically in the form of informal settlements, followed closely by formal house settings (n=22, 23.9%) (e.g. brick-walled structures).

**Hospitalisation:**

A total of 51 cases (55.4%) were admitted to hospital and survived for a period of time, whilst 16 cases (17.4%) were declared dead-on-arrival (DOA) to the hospital. Twenty-five (27.2%) cases were not hospitalised and died on scene. Figure 4 illustrates the hospitalisation cases over the four-year study period. The mean survival time for hospitalised cases (excluding DOAs) was 1.2 days ranging from 0.2 hours to 12 days. Approximately 26.1% of all hospitalised pesticide-related cases had a survival time of < 1 day. In addition, most hospitalised individuals were found to only survive a maximum of three days (n=38; 41.3%) with only 3 individuals surviving for longer than 9 days.



**Figure 4.** Figure illustrating the duration or survival time for suspected pesticide-related cases based on hospital admission status.

## Case history, hospital intervention and clinical observations:

The clinical observations associated with the cases are summarised in Table 4. Additionally, scene observations witnessed by those surrounding the deceased prior to death are included. Fasciculations (n=25, 27.2%), pin-point pupils (n=47, 51.1%), secretions (n=49; 53.3%), vomiting (n=28; 3.4%) and unresponsiveness (n=88; 95.7%) were most frequently reported on the scene and/or hospital documentation.

**Table 4.** Summary of reported clinical observations within the study cohort

Observations reported	Percentage frequency (%)			
	Admitted (n = 52)	Not Admitted (n = 25)	Dead on Arrival (n = 15)	Total (N = 92)
<b>Muscarinic effects</b>				
Pin-point pupils (dilated pupils)	36 (39.1)	0 (-)	11 (11.9)	47 (51.1)
Apnoeic	50 (54.3)	25 (27.2)	15 (16.3)	90 (97.8)
Foam around mouth	17 (18.5)	11 (11.9)	11 (11.9)	39 (42.4)
Salivating	15 (16.3)	3 (3.3)	3 (3.3)	21 (22.8)
Diarrhoea	14 (15.2)	0 (-)	1 (1.1)	15 (16.3)
Vomiting	18 (19.6)	4 (4.3)	6 (6.5)	28 (30.4)
Stomach Pain	5 (5.4)	0 (-)	2 (2.2)	7 (7.6)
Secretions	30 (32.6)	8 (8.7)	11 (11.9)	49 (53.3)
Sweating	10 (10.9)	1 (1.1)	2 (2.2)	13 (14.1)
<b>Nicotinic effects</b>				
Fasciculations (seizures)	21 (22.8)	2 (2.2)	2 (2.2)	25 (27.2)
Bradycardia	14 (15.2)	0 (-)	0 (-)	14 (15.2)
<b>Central Nervous System effects</b>				
Unresponsiveness	49 (53.3)	24 (26.1)	15 (16.3)	88 (95.7)
Dizziness	7 (7.6)	0 (-)	3 (3.3)	10 (10.9)
<b>Post-mortem signs</b>				
Congested organs	31 (33.7)	16 (17.4)	11 (11.9)	58 (63.0)
<b>History of Pesticide use</b>				
History of pesticide ingestion	36 (39.1)	8 (8.7)	7 (7.6)	51 (55.4)
Pesticide near deceased	2 (2.2)	2 (2.2)	0 (-)	4 (4.3)
<b>Medical Intervention</b>				
Atropine treatment	49 (53.3)	0 (-)	7 (7.6)	56 (60.9)
Hospital or medical intervention	52 (56.5)	0 (-)	9 (9.8)	61 (66.3)
<b>Pseudocholinesterase level<sup>a</sup> (&lt;8000 U/L)</b>				
Pseudocholinesterase level (measured ante-mortem)	23 (25.0)	0 (-)	1 (1.1)	24 (26.1)
Pseudocholinesterase level (measured post-mortem)	7 (7.6)	3 (3.3)	3 (3.3)	13 (14.1)

a = Normal range for pseudocholinesterase is 8 000 U/L – 18 000 U/L (Tietz, 2008)

## Toxicological results:

Out of the 92 pesticide-related cases within the cohort, formal toxicological analyses by FCL were requested in 86 cases whilst pharmacological screening was requested in only 39 cases. A summary of the results of both sets of analyses are given below (Table 5). Results from formal toxicological analysis indicated that terbufos was the most common pesticide detected, appearing in 50 cases, followed by methamidophos and malathion which appeared in only 4 and 2 cases respectively, whilst diazinon only appeared in 1 case within the study cohort. Formal toxicological results were not yet available in 21 cases. Blood alcohol concentration was requested in 42 cases (45.7%). From this, alcohol was positively

detected in only 9 cases (9.7%) (>0.01 g/100 mL) with a mean of 0.12 g/100 mL and values ranging from 0.02 g/100 mL to 0.22 g/100 mL.

**Table 5.** Results of formal toxicological analyses and pharmacological screening

<b>Toxicology results (from FCL)</b>	<b>Number of cases (%)</b>
Terbufos only	45 (48.9)
Terbufos and Carbendazim	1 (1.1)
Terbufos and drugs <sup>a</sup>	4 (4.3)
Diazinon	1 (1.1)
Malathion	1 (1.1)
Malathion and drugs <sup>b</sup>	1 (1.1)
Methamidophos	3 (3.3)
Methamidophos and drugs <sup>c</sup>	1 (1.1)
Drugs only <sup>d</sup>	7 (7.6)
No pesticides or drugs detected	1 (1.1)
Cases with outstanding results	21 (22.8)
Cases not sent for toxicology	6 (6.5)
<b>Total</b>	<b>92 (100)</b>
<b>Pharmacology results</b>	<b>Number of cases (%)</b>
Pesticide detected	1 (1.1)
Drugs detected <sup>e</sup>	19 (20.7)
No drugs detected	19 (20.7)
Cases with outstanding results	0 (-)
Cases not sent for pharmacological screening	53 (57.6)
<b>Total</b>	<b>92 (100)</b>

a = Drugs include atropine (1), carbendazim (1), efavirenz (1), isoniazid (1), metoclopramide (1), morphine (1) and propofol (1).

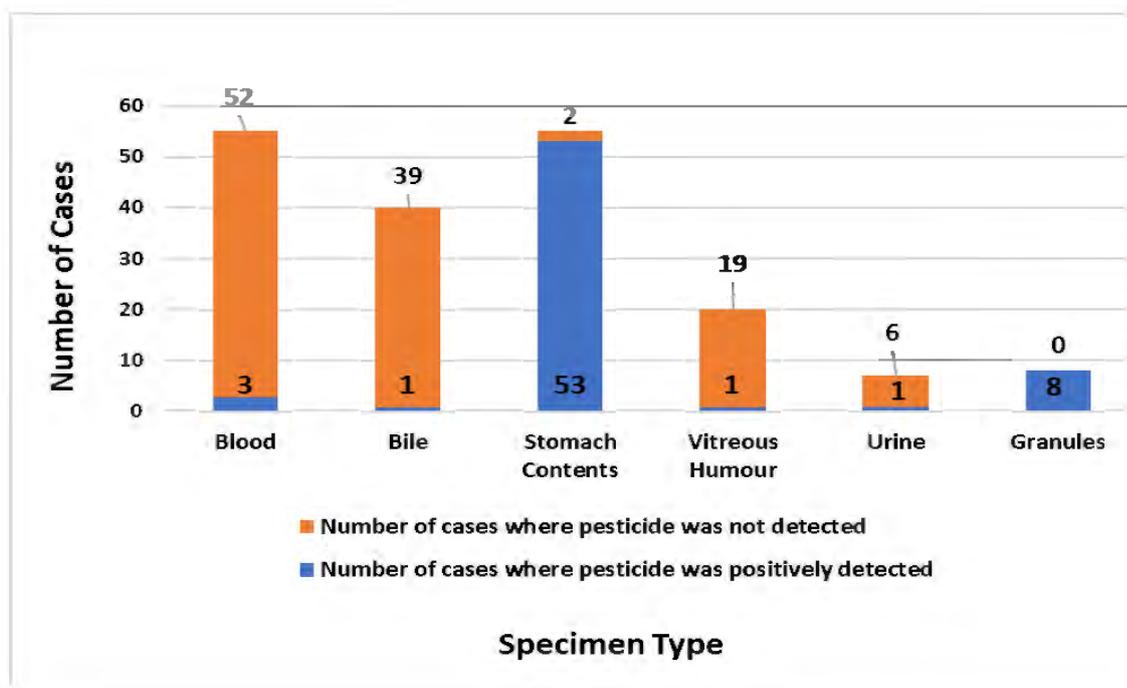
b = Terbutylazine (1)

c = Atropine (1) and verapamil (1)

d = Drugs include acetaminophen (4), carbamazepine (1), carbofuran (2), citalopram (1), cyclizine (1), efavirenz (1), 3-hydroxycarbofuran (1), ketamine (1), methamphetamine (1), metoclopramide (2), morphine (1) and phenytoin (2).

e = Drugs include acetaminophen (2), amphetamine (1), atropine (4), caffeine (1), citalopram (1), diazepam (1), diphenhydramine (1), doxylamine (1), efavirenz – (1), emtracetabine (1), gamma-Butyrolactone (2), 9-hydroxyrisperidone (1), isoniazid (1), lidocaine (1), methamphetamine (1), methaqualone (1), methcathionine (1), metronidazole (1), nevirapine (1), O-desmethylvenlafaxine (1), quetiapine (1), risperidone (1), tendovir (1) and venlafaxine (1).

In this cohort, blood, bile, stomach contents (which often included granules), vitreous humour and urine were typically submitted for toxicology whilst blood, bile, stomach contents and urine were submitted for pharmacology screening. Generally, detection of pesticides due to granules being present in the gastric content proved to be the most effective specimens for positive pesticide detection (as determined by FCL lab analysis), with a positive detection rate of 96.4% for stomach contents.



**Figure 5.** Graph illustrating specimens submitted for post-mortem toxicology in pesticide deaths and the positive detection rate of an active ingredient.

### Causes of death:

The causes of death were reported by the medical practitioners in the initial post-mortem report. Although varied in wording, these causes related to pesticide poisoning and the complications thereof, with a specific focus on organophosphates (OPs) (46.7%) (Table 6). Pesticide-associated causes of death amounted to 79.3% whilst 20.7 % were still under investigation at the time of the study, likely due to outstanding toxicology results.

**Table 6.** Categories of causes of death of all pesticide-related fatalities at SRM

Causes of Death	Number of cases (%)
Consistent with OP poisoning and resulting complications	43 (46.7)
Under investigation, undetermined, no anatomical cause of death	19 (20.7)
Consistent with pesticide poisoning or ingestion	25 (27.2)
Terbufos toxicity/poisoning	5 (5.4)
<b>Total</b>	<b>92 (100.0)</b>

### Notification

Although this was a four-year retrospective review, notification records could only be obtained in the division for the years 2018 and 2019 respectively. The notification rate was calculated

exclusively for 2018 and 2019 as these were the years with existing notification records. In total, 49 pesticide-related cases were identified for these years, 19 of which had been notified by forensic pathologists. This equates to a notification rate of 38.8% for the years 2018 and 2019. It must be noted that in cases where the patient was first hospitalised, the clinical doctor may have completed the notification.

## **2.7 Discussion**

Results from the four-year retrospective study indicate that the majority of unnatural death cases admitted to SRM related to non-toxicological causes of deaths. Using the Office Autopsy Database, 15,761 unnatural death cases were identified from 2016 – 2019 of which 438 were toxicity-related and 92 (0.6%) pesticide-related. In a prior investigation, out of the 16,543 cases admitted to SRM over 5 years (2011 to 2015) only 104 (0.6%) were related to acute pesticide toxicity (Patience, 2018). While there was variation in the number of cases per year, the average number of cases against the whole case load was constant over the two study periods.

Males predominate the number of pesticide deaths observed in this study cohort with a percentage frequency of 59.8 as compared to 40.2 in females. This aligns with research conducted by Razwiedani and Rautenbach (2017), which reported a higher occurrence of male decedents in pesticide deaths in Tshwane area of RSA.

In this study, the number of pesticide-related fatalities seen in females gradually increased per year whilst the numbers seen in males remained relatively constant. The gradual rise in female cases may be due to increased preference for pesticide-induced intentional poisoning by females as they often view this as a less painful method of self-harm (Gunnell and Eddleston, 2003). Male deaths were also more frequent between 31 to 40 years old (19.6% vs. 4.3%), while female deaths were more common between the ages 11 to 30 years (27.1% vs. 17.4%).

### *Suspected manner of death*

The suspected manners of death for this research cohort were separated into four categories, namely, accidents, homicides, suicides, and cases that were still under investigation (or undetermined). Most pesticide deaths were suspected suicides, accounting for 60.8% of the

study's cohort. It was purported that the ubiquitous availability of such toxic agricultural pesticides, provides the means for individuals to commit suicide. Nalwanga and Ssempebwa (2011) found that domestic pesticide users often know, by word of mouth, about the effectiveness or potency of pesticides as both pest repellents as well as harmful agents that may kill if ingested.

Accidental poisoning made up 17.4% of this study's cohort and mostly occurred in infants, children, and the elderly. These results are in keeping with London *et al.*'s (2005) deductions that accidental poisonings are more prevalent in children because of negligent storage of pesticides in the domestic setting. The negligent use or storage thus creates a breeding ground for unintentional poisoning as children assume that these compounds are safe for consumption. This highlights the need to provide end users of these compounds with more information on the hazards associated with incorrect pesticide use and the appropriate handling, storage and disposal procedures required.

#### *Age distribution*

The age distribution for the study cohort ranged from 2 months to 66 years old. Generally, ages within the female cohort fell on the lower end of the spectrum whilst the male cohort's ages seemed to be much older. A large number of pesticide fatalities were observed in the 31 to 40-year-old age category with a percentage frequency of 23.9 (n=22), followed by the 11 to 20-year-old age category at 22.8 (n=21) and lastly the 21 to 30-year-old age category at 20.7 (n=19). Overall, these percentage frequencies indicate that pesticide fatalities in this study cohort seemed to occur in teenagers, young adults and older adult populations. Furthermore, increased suicide frequencies were identified in the teenage and younger adult populations. This result is to be expected as teenagers and adults are the main participants involved in the handling, consumption, and distribution of pesticides with little safety information available at their disposal, making them at increased risk of exposure to the acute effects of these compounds. Moreover, according to Rother (2012), the youth are typically involved in the unregulated sale, distribution, transportation, storage, and domestic use of street pesticides, which remain largely unaccounted for. The ease of access and knowledge of toxicity of the compounds may thus increase their susceptibility to pesticide poisoning.

### *Seasonal trends*

A comparative review of pesticide-related fatalities per month was done to provide information on seasonal trends in pesticide deaths. Seasonally, pesticide-related fatalities mainly occurred during autumn followed by the spring and winter seasons respectively. This may be due to increased pest infestations, which would result in increased domestic pesticide use in these seasons (Dippenaar and Diedericks, 2005). The number of cases were however too small to infer significance. It should also be noted that investigating pesticide poisoning cases of patients who survive as well as calls to poison centres would provide a more holistic view of these poisoning cases in general, which may illustrate other patterns of use.

### *Hospitalisation and clinical observations*

The hospitalisation of pesticide poisoned patients provides important clues or information regarding the clinical presentation, as well as the general progression of individuals once admitted. Alewu and Nosiri (2010) highlighted the importance of observing and accurately diagnosing pesticide poisoning cases in accordance with the clinical manifestations observed. Many of the clinical symptoms (which included vomiting, pin-point pupils, foaming at the mouth, copious secretions and fasciculations) was observed in this cohort with higher frequencies in hospitalised cases (including DOAs) as compared to cases where individuals were not admitted to hospital. This cholinergic toxidrome is suggestive of OP and/or carbamate toxicity. In these cases, the measurement of pseudocholinesterase (PChE) levels is essential in further pointing towards organophosphate poisoning (Rao *et al.*, 2016). Acetylcholinesterase activity levels are useful to monitor a patient's response to treatment within hospital. Ante-mortem PChE levels are good indicators of the severity of poisoning and a predictor of duration of stay in hospital. Rao *et al.* (2016) found that PChE levels can indicate the type of medical intervention required for treating exposed individuals (such as mechanical ventilation and atropine treatment). This was observed within this current SRM study cohort where 60.9% of all pesticide-related cases required ventilation and atropine treatment. From this, it can be deduced that taking note of specific muscarinic, nicotinic and CNS effects in conjunction with the atropine and pseudocholinesterase levels can provide information that can assist in identifying organophosphate poisonings. In instances where decedents were not hospitalised, the medico-legal investigation often relies on the scene investigation and post-mortem signs observed during the autopsy such as congested organs (non-specific) and

pesticide odours and/or granules in the stomach contents. Although these signs are indicators of possible poisoning, they are typically non-specific thus, ancillary toxicology testing is required to confirm the analyte involved. Identification of the pesticide on scene is also a helpful addition to the investigation, as this can also be analysed to determine the analyte of interest in the case. Overall, hospital records, when used in conjunction with toxicology and information regarding history of pesticide ingestion, can provide conclusive evidence in pesticide-related deaths.

### *Incident area*

The incident areas where the poisonings occurred were assessed to better understand the circumstances surrounding the incidence of pesticide-related fatalities. In this cohort it was observed that township and informal settlement areas such as Gugulethu, Nyanga and Philippi had a high incidence of poisonings. An informal settlement is a housing area that is illegally built on municipal land using tin or other materials and lacks adequate structural architecture (Huchzermeyer *et al.*, 2014). These types of settlements are often characterised by lack of decent service delivery, no electricity, overcrowding and insufficient access to water and sanitation services (Huchzermeyer *et al.*, 2014). This coincides with results observed with the incident area distribution, which are lower socio-economic informal settlement areas. Low socio-economic areas are those characterised by high unemployment rates, poverty, social inequality, overcrowding, limited access to education and inadequate public health services (Ataguba *et al.*, 2011). This makes lower socio-economic areas a potential breeding ground for pest infestations, thereby creating an increased likelihood for domestic agricultural pesticide use within these areas. In the WC, individuals residing in townships like Gugulethu, Nyanga, Phillipi and Khayelitsha are considered low socio-economic groups, whilst individuals in more urban settings such as Tableview, Observatory, Mowbray and Rondebosch are considered middle to higher socio-economic groups.

Scene data suggested that 34.8 % of the pesticide-related fatalities occurred in informal housing structures, known as informal settlements. The higher proportions of pesticide-related fatalities in these structures also speaks to the accessibility of these compounds within informal environments such as taxi ranks and informal township tuck shops (informal convenience shop business, that is usually run from residential premises in South African townships (Kgaphola *et al.*, 2019), which are often close to informal housing structures in the township (Rother,

2010). These results suggest that pesticide exposure may be linked to socioeconomic status. Socio-economic status refers to the social and economic factors that impact an individual's quality of life (Darin Mattsson *et al.*, 2017). The correlation between pesticide exposure and socioeconomic status was also found in studies from Sri Lanka and China (Eddleston *et al.*, 2008; Zhang *et al.*, 2009).

### *Toxicology*

During medico-legal death investigation for cases involving drugs, pesticides or other toxicants, forensic pathologists in the local setting initially complete a preliminary post-mortem report based on autopsy findings and any available scene or hospital information where applicable. The cause of death as determined at autopsy is however preliminary and usually requires toxicological testing confirmation. This means that pathologists collect multiple post-mortem specimens for blood-alcohol and toxicological analysis. At SRM, the pathologists historically had access to a pharmacological screen and thus also collect specimens for pharmacology testing. This pharmacological screen typically provided more rapid insight into the drugs possibly involved in a case, however pesticide analysis was not typically part of this screen. The pesticide screening was thus part of the toxicological analysis conducted by FCL. Upon receipt of the blood-alcohol, toxicological and pharmacological results from FCL and UCT Pharmacology respectively, pathologists then completed a final report based on results from these analyses.

In this cohort, the cause of death in 79.3% of cases was associated with pesticide poison ingestion, of which 46.7 % related to OPs. These results indicate that OPs dominated pesticide fatalities. These results are consistent with research done by Abdullat *et al.* (2006) who found that OPs constitute the most frequently detected pesticide class in pesticide poisonings. Considering that many of these individuals in this study's cohort died in hospital and clinical symptomology suggested that of OP poisoning, the pathologist may have typically determined the cause of death based on clinical findings. The initial causes of death determinations, despite being inconsistent, indicate that OP poisoning deaths are easier to identify compared to deaths caused by other pesticide types. It should be noted however, that many symptoms of pesticide poisoning overlap. Amitraz may often be misdiagnosed as organophosphate poisoning for example (Veale *et al.*, 2013). This impedes efforts made to identify and measure the impact of

street pesticides (which may include carbamates, rodenticides, and other pesticides) on pesticide mortality.

According to the post-mortem toxicology results, terbufos, malathion, diazinon and methamidophos were detected in the various samples sent for analysis. In this four-year review, terbufos was found to be the most common pesticide associated with suspected pesticide-related fatalities, appearing in 50 (54.3%) cases overall. Similarly, previous work done by Patience (2018) identified terbufos as the predominating pesticide in deaths at SRM between 2011 to 2015. This class Ia granular insecticide is an OP used for pest control in the agricultural industry in RSA (Liang *et al.*, 2017). Its appearance in such high numbers may be indicative of its increased use domestically as a street pesticide where it may be sold illegally as granules in small plastic packets. However, since there is no information regarding where each of the decedents obtained the ingested pesticide compound, it is also possible that individuals legally purchased terbufos as it is sold commercially for agricultural purposes. The predominance of terbufos, an OP within this post-mortem cohort is similar to results of an acute poisoning survey conducted at the Tygerberg Poison Information Centre (TPIC), which found that pesticide exposures relating to cholinesterase inhibitors (OPs and carbamates) were the most common non-drug chemical exposures reported to the centre (Veale *et al.*, 2013). The toxicovigilance survey looked at TPIC data sourced from telephonic consultations made between 1 August 2008 to 31 July 2009 regarding poisoning exposures in humans specifically (Veale *et al.*, 2013). The study found that the most common pesticide-related exposures were cholinesterase inhibitors (25.3 %), anticoagulant rodenticides (20.5 %) and pyrethroids (14.4 %). The study also highlights how the TPIC was able to guide HCPs correctly identify amitraz (a tiazapentadiene insecticide/acaricide) poisonings often misdiagnosed and treated as an OP poisoning in 41 of 46 amitraz-related cases, again emphasizing the limited knowledge HCPs have diagnosing toxidromes related to other pesticide types (Eizadi-Mood *et al.*, 2011; Veale *et al.*, 2013).

The importance and suitability of certain specimens for pesticide detection was also highlighted. On average, stomach contents and granules (from gastric content) provided pesticide detection rates of 96.4% and 100% respectively (for which results were received), indicating that these specimens are the most suitable for analytically confirming pesticide ingestion in this setting. Out of the 55 case specimens pertaining to stomach contents, 53 case specimens returned positive test results whilst 2 case specimens did not. This equates to a detection rate of 96.4%. Similarly, all the 8 granular case specimens sent for toxicology

returned positive pesticide detection results. This translates to a pesticide detection rate of 100% for granular samples. The lack of detection in other specimens may be due to collection of blood in sodium fluoride, reported to increase organophosphate degradation, as well as the delays in toxicological testing by the National laboratories, taking years to analyse specimens.

A total of 55 cases had blood specimens collected for toxicological analysis for pesticide detection. Of these, only 3 cases (of 55 total cases or 5.5%) had positive pesticide detection within the blood samples whilst no pesticide was detected in the other 52 case samples. The decreased detection level in blood may be attributed to chemical instability of pesticides in post-mortem blood samples containing fluoride preservatives (Park *et al.*, 2009) and the delay in analysis. These preservatives lead to OP degradation, which, in addition to delays in analytical testing may render blood samples limited in use. Pesticide co-ingestion in this cohort was found to predominantly relate to medical drugs administered in attempt to treat pesticide exposure in patients.

At the conclusion of the study, there were still 22.8% of cases that had outstanding toxicology from the National Department of Health FCL (over all the years). This is significantly problematic as it means that cases may remain undetermined in terms of the cause of death, and it limits an up-to-date understanding of the type of pesticides involved in these cases. This is important to prevention strategies and public health and policy interventions. FPS has recently started a toxicology laboratory (the Forensic Toxicology Unit), who will soon perform pesticide analyses for the provincial mortuaries. If this testing is performed more timeously, it should support these developments in the country, especially with regards to more immediate notification of the analytes involved in poisoning cases. Overall, the role of forensic toxicology in medico-legal pesticide death investigation is crucial to accurately confirm pesticide exposure, especially in cases where incident scene information, hospital records and previous pesticide-related history is limited.

### *Notification*

In terms of the notification itself, if at autopsy there were clear signs of pesticide involvement in the cause of death (granules in the stomach and congested organs) along with accompanying hospital notes and scene information to corroborate suspected history of pesticide ingestion or poisoning, then a forensic pathologist may undertake notification of the suspected pesticide poisoning. However, if the pathologist is unsure at autopsy and there is no scene information or hospital information that indicates pesticide ingestion occurred, the pathologist may wait for

toxicological confirmation prior to making any final conclusions on the cause of death. The forensic pathologist will often categorise the death as undetermined awaiting toxicology. If toxicology is significantly delayed, so will be such a notification. This may however, be circumvented in hospitalised cases, where if there is a suspicion of pesticide poisoning, the clinician should also notify the case.

The notification rate in this study was identified as 38.8% for years 2018 and 2019 (19 of 49 cases over those two years). This result aligns with the deductions made by London (2001) who concluded that only 10% to 20% of all pesticide-related poisonings are successfully notified. The poor notification levels may suggest a disconnect between diagnosing and reporting these poisonings in death cases, especially if pesticide toxicity is only suspected. The problem is further exacerbated in cases where the deceased was not hospitalised and there was insufficient evidence to accurately determine cause of death. It must be noted that cases may have been notified by the hospital staff prior to death and may have been accounted for. The notification documentation obtained was stored in an ad-hoc manner internally, and it is possible that more cases had been notified, but the documentation was not stored internally. The NMC documents for 2016 and 2017 could not be allocated and therefore a full understanding of notification for these years could not be ascertained.

Research performed by Kabanda and Rother (2019) showed that healthcare professionals view notification as a time-consuming process that holds limited value. Kabanda and Rother (2019) suggest that improvements need to be made in training healthcare professionals whilst simultaneously advancing notification procedures to ease the burden on healthcare professionals. Recently, a mobile application was developed to allow notification to be performed through mobile phones. Further investigation of this form of notification is warranted to see if there are improvements in NMC numbers.

## **2.8 Limitations**

As this study was retrospective, it relied on the identification of cases through a secondary database source. A detailed review of case files was performed to ensure information in the OAD correlated with that contained in the actual case file. Missing information (incomplete scene information or hospital notes) was encountered during data collection, which points to possible underreporting of cases. Results of this study were specific to the West Metropole and

do not provide insight into cases within the rest of Western Cape, or RSA. In addition, this study did not investigate clinical pesticide poisonings or calls to poison centres. In these cases, however, the type of pesticide involved (terbufos) will not typically be known as such specific testing is not performed. Accurately measuring how many pesticide fatalities are associated with street pesticides may assist in ascertaining the impact of these compounds on pesticide poisoning prevalence. Collection of the exhibits or their containers on scene may assist in determining this, or alternatively questioning witnesses further about their use of the pesticide. The outstanding toxicological results also limits the understanding of the pesticides involved and indicates the problems associated with delay in case conclusion. Lastly the retrospective design of the study limits the ability for causal inference.

Future work should focus on collaborating with hospitals and poison centres to get a holistic view of poisoning cases or developing a protocol for investigating pesticide deaths and then monitoring the success of that protocol across the province.

## **2.9 Conclusion**

The Western Cape is an agriculturally rich region with extensive OP use. Domestic pesticide poisoning often occurs as a result of erroneous mixing, application and storage procedures of toxic pesticides. This was observed as evidenced by the frequent occurrence of pesticide-related incidences in informal housing settings. The accessibility, efficiency and cost effectiveness of street pesticides combined with negligent use resulted in frequent pesticide exposure, both intentionally and unintentionally. Furthermore, the intentional use of these compounds as a means of self-harm, especially among children, is of great concern. Individuals need to be informed at points of sale how to safely use, store, and dispose of pesticides to help prevent fatalities associated with negligent use. Risks posed by illicit street pesticides point to a need for the development of safer, more environmentally friendly alternatives for pest management. It is important to use a holistic approach in investigating pesticide-related fatalities. As can be seen in this study, incorporating scene information, hospital notes and forensic toxicology help provide a better understanding of the circumstances surrounding pesticide fatalities. Streamlining and enhancing mortuary data collection and toxicological services may assist in measuring the prevalence and more importantly identifying the pesticides involved in pesticide-related fatalities. Moreover, this information can help inform pesticide

policy making whilst simultaneously increasing the wealth of knowledge surrounding the epidemiology of pesticide use in SA.

## 2.10 References

- Abdullat, E., Hadidi, M., Alhadidi, N., AL-Nsour, T. & Hadidi, K. (2006). Agricultural and horticultural pesticides fatal poisoning; The Jordanian experience 1999–2002. *Journal of Clinical Forensic Medicine*. 13(6-8):304-307. DOI: 10.1016/j.jcfm.2006.06.011.
- Alewu, B. and Nosiri, C. (2010). Pesticides and Human Health. *Pesticides in the Modern World: Effects of Pesticide Exposure*. 1(12): 231-250. DOI:10.5772/18734.
- Ataguba, J. (2010). Health care financing in South Africa: Moving towards universal coverage. *Continuing Medical Education*. 28 (2): 74-77. ISSN 2078-5143. Available from: <http://www.cmej.org.za/index.php/cmej/article/view/1782>. Accessed%3A. Date accessed: 06 Oct. 2021.
- Ataguba, J., Akazili, J. and McIntyre, D. (2011). Socioeconomic-related health inequality in South Africa: evidence from General Household Surveys. *International Journal for Equity in Health*. 10(1):48. DOI: 10.1186/1475-9276-10-48.
- Balme, K., Roberts, J., Glasstone, M., Curling, L., Rother, H., London, L., Zar, H. and Mann, M. (2010). Pesticide poisonings at a tertiary children's hospital in South Africa: an increasing problem. *Clinical Toxicology*. 48(9):928-934. DOI: 10.3109/15563650.2010.534482.
- Dabrowski, J. (2015). Development of pesticide use maps for South Africa. *South African Journal of Science*. 111(1/2): 1-7. DOI: 10.17159/sajs.2015/20140091.
- Darin Mattsson, A., Fors, S. and Kreholt, I. (2017). Different indicators of socioeconomic position and their relative importance as determinants of health in old age. *Innovation in Aging*. 1(suppl\_1):93-94. DOI: 10.1093/geroni/igx004.385.
- Dippenaar, R. and Diedericks, R. (2005). Paediatric organophosphate poisoning--a rural hospital experience. *South African Medical Journal*. 95(9):678-81. PMID: 16327926.
- Eddleston, M., Buckley, N., Eyer, P. and Dawson, A. (2008). Management of acute organophosphorus pesticide poisoning. *The Lancet*. 371(9612):597-607. DOI: 10.1016/s0140-6736(07)61202-1.

- Eizadi-Mood, N., Sabzghabae, A., Yaraghi, A., Montazeri, K., Golabi, M., Sharifian, A. and Badri, S. (2011). Effect of antioxidants on the outcome of therapy in paraquat-intoxicated patients. *Tropical Journal of Pharmaceutical Research*. 10(1): 27-31. DOI: 10.4314/tjpr.v10i1.66537
- Gunnell, D. and Eddleston, M. (2003). Suicide by intentional ingestion of pesticides: a continuing tragedy in developing countries. *International Journal of Epidemiology*. 32 (6): 902-909. DOI: 10.1093/ije/dyg307.
- Huchzermeyer, M., Karam, A. & Maina, M. (2014). Informal settlements. *Changing Space, Changing City*. 154-175. DOI: 10.18772/22014107656.12.
- Human Tissue Act. (1983). *Human Tissue Act No. 65 of 1983*. Pretoria, South Africa: Government Gazette of South Africa.
- Inquest Act. (1959). *Inquest Act No. 58 of 1959*. Pretoria, South Africa: Union Gazette Extraordinary.
- Kabanda, S. and Rother, H. (2019). Evaluating a South African mobile application for healthcare professionals to improve diagnosis and notification of pesticide poisonings. *BMC Medical Informatics and Decision Making*. 19(1). DOI: 10.1186/s12911-019-0791-2.
- Kgaphola, M., Tawodzera, G. and Tengeh, R. (2019). Scope and Viability of Spaza Shops in a selected township in South Africa. *Amity Journal of Entrepreneurship*. 4(2):16-28. Available from: [http://www.researchgate.net/publication/340412879\\_Scope\\_and\\_Viability\\_of\\_Spaza\\_Shops\\_in\\_a\\_selected\\_township\\_in\\_South\\_Africa](http://www.researchgate.net/publication/340412879_Scope_and_Viability_of_Spaza_Shops_in_a_selected_township_in_South_Africa). Accessed 06 Oct. 2021.
- Liang, Y., Tong, F., Zhang, L., Li, W., Huang, W. and Zhou, Y. (2017). Fatal poisoning by terbufos following occupational exposure. *Clinical Toxicology*. 56(2):140-142. DOI: 10.1080/15563650.2017.1340647.
- London, L. (1992). Agrichemical hazards in the South African farming sector. *South African Medical Journal*. 81: 560-564.
- London, L. (2001). Challenges for improving surveillance for pesticide poisoning: policy implications for developing countries. *International Journal of Epidemiology*. 30(3):564-570. DOI: 10.1093/ije/30.3.564.

- London, L. and Baile, R. (2001). Challenges for improving surveillance for pesticide poisoning: policy implications for developing countries. *International Journal of Epidemiology*. 30 (3):564-70. DOI: 10.1093/ije/30.3.564.
- London, L., Ehrlich, R., Rafudien, S., Krige, F. and Vurgarellis, P. (1994). Notification of pesticide poisoning in the Western Cape, 1987-1991. *South African Medical Journal*. 84(5):269-272. PMID: 7809771
- London, L., Flisher, A., Wesseling, C., Mergler, D. and Kromhout, H. (2005). Suicide and exposure to organophosphate insecticides: Cause or effect?. *American Journal of Industrial Medicine*. 47(4):308-321. DOI: 10.1002/ajim.20147.
- Myers, J. (1990). Occupational health of farmworkers. *South African Medical Journal*. 78: 562-563.
- Nalwanga, E. and Ssempebwa, J. (2011). Knowledge and Practices of In-Home Pesticide Use: A Community Survey in Uganda. *Journal of Environmental and Public Health*. 2011:1-7. DOI: 10.1155/2011/230894.
- National Health Act. (2003). *National Health Act No. 61 of 2003*. Pretoria, South Africa: Government Printers.
- Park, M., In, S., Lee, S., Choi, W., Park, Y. and Chung, H. (2009). Postmortem blood concentrations of organophosphorus pesticides. *Forensic Science International*. 184(1-3):28- 31. DOI: 10.1016/j.forsciint.2008.11.008.
- Patience, M. (2018). *Retrospective analysis of suspected pesticide-related fatalities admitted to Salt River Mortuary in the West-Metropole of Cape Town*. Republic of South Africa: University of Cape Town.
- Rao, K., Rangappa, P., Jacob, I. and Hiremath, P. (2016). Pseudocholinesterase as a predictor of mortality and morbidity in organophosphorus poisoning. *Indian Journal of Critical Care Medicine*. 20(10): 601 -604. DOI: 10.4103/0972-5229.192052.
- Razwiedani, L. and Rautenbach, P. (2017). Epidemiology of Organophosphate Poisoning in the Tshwane District of South Africa. *Environmental Health Insights*. 11:117863021769414. DOI: 10.1177/1178630217694149.

Rother, H. (2010). Falling through the regulatory cracks: street selling of pesticides and poisoning among urban youth in South Africa. *International Journal of Occupational Environmental Health*. 16 (2):202–213. DOI: 10.1179/107735210799160336.

Rother, H. (2012). Improving poisoning diagnosis and surveillance of street pesticides. *South African Medical Journal*. 102(6):485. DOI: 10.7196/samj.5838.

Statistics South Africa. 2011. *2011 Census: Statistics South Africa*. Available: [http://www.statssa.gov.za/?page\\_id=3839](http://www.statssa.gov.za/?page_id=3839) [Accessed 14 March 2021].

Veale, D., Wium, C. and Müller, G. 2013. Toxicovigilance I: A survey of acute poisoning in South Africa based on Tygerberg Poison Information Centre data. *South African Medical Journal*. 103(5):293. DOI: 10.7196/samj.6647.

Zhang, J., Stewart, R., Phillips, M., Shi, Q. and Prince, M. (2009). Pesticide exposure and suicidal ideation in rural communities in Zhejiang Province, China. *Bulletin of the World Health Organization*. 87(10):745-753. DOI: 10.2471/blt.08.054122.

### **3.Appendix**

1. Funding statement Ethical approval letter
2. Ethical approval letter
3. Turnitin originality report

## **3.2 Funding statement**

The financial assistance of the National Research Foundation (NRF) towards this research is hereby acknowledged and expressed. The conclusions arrived at are those of the author and are not necessarily to be attributed to the NRF.



UNIVERSITY OF CAPE TOWN  
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15 July 2020

**HREC REF: 246/2020**

**Ms B Davies**

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Dear Ms Davies

**PROJECT TITLE: INVESTIGATING PESTICIDE-RELATED DEATHS AT A DEDICATED MORTUARY IN CAPE TOWN" FOR MPHIL CANDIDATE: MOLATELO PETER-sub-study linked to 220/2018**

Thank you for your response letter, addressing the issues raised by the Faculty of Health Sciences Human Research Ethics Committee (HREC).

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

**This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020.**

**Approval is granted for one year until the 30 July 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](http://www.health.uct.ac.za/fhs/research/humanethics/forms))

**The HREC acknowledge that the student: - Ms Molatelo Peter will also be involved in this study.**

**Please quote the HREC REF in all your correspondence.**

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

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.

HREC 246/2020sa

Yours sincerely

**PROFESSOR M BLOCKMAN**  
**CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE**

Federal Wide Assurance Number: FWA00001637.  
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NHREC-registration number: REC-210208-007

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (GMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.



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