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Is medical postmortem practice dying? An audit on postmortems in the department of anatomical pathology, university of the Witwatersrand, Johannesburg, South Africa.

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IS MEDICAL POSTMORTEM PRACTICE DYING? AN AUDIT ON POSTMORTEMS IN THE DEPARTMENT OF ANATOMICAL PATHOLOGY, UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG, SOUTH AFRICA.

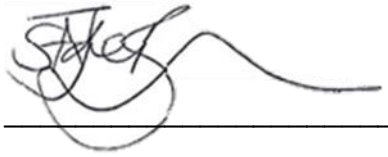
Jana Sophia Adriana De Bruin

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine (Anatomical Pathology).

Johannesburg, 2021

DECLARATION:

I, Jana Sophia Adriana De Bruin, declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Master of Medicine (Anatomical Pathology) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



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22nd day of February 2021 in Johannesburg.

DEDICATION:

This is dedicated to my parents, thank you for all your love and support.

ABSTRACT:

An audit of postmortems performed in the Division of Anatomical Pathology, University of the Witwatersrand, between January 2009 and December 2018 at Charlotte Maxeke Johannesburg Academic Hospital, and Chris Hani Baragwanath Academic Hospital was performed.

Background:

There is a worldwide downward trend in medical autopsies, however, autopsy remains the gold standard to determine the cause of death. There is presently limited data available on the practice of medical autopsies in South Africa.

Aims and Objectives:

Trends in the number of autopsies performed, demographic data and causes of death over a 10-year period between 2009 and 2018 were assessed.

Methods:

A retrospective, descriptive review of all postmortem reports over a ten-year time period.

Results:

A total of 889 autopsies were performed during the study period. The annual number of postmortems ranged from a maximum of 126 autopsies performed in 2009, the beginning of the study period, to a minimum of 68 in 2016 and 2018, towards the end of the study period. Adult autopsies comprised the majority of cases (66.25%), however, this age group showed a relatively larger decline from 91 (72.22%) cases in 2009 to 37 (54.41%) cases in 2018 compared to the paediatric and neonatal age groups. The most common immediate causes of death were related to the circulatory system (36%), infectious disease (29%) and unknown/indeterminate (16%). Diseases related to infections (23%),

the circulatory system (16%) and unknown/indeterminate (12%) were the most common underlying causes of death.

Conclusion:

This study shows a significant decline in autopsy numbers in our Division. It elucidates epidemiological data and the spectrum of causes of death and how these epidemiological patterns have changed over the 10-year study period.

ACKNOWLEDGEMENTS:

I would like to acknowledge my supervisors Ewen McAlpine and Gillian Davies, I appreciate your guidance through this process.

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LIST OF ABBREVIATIONS:

CAP: College of American Pathologists

CHAMPS: Child Health and Mortality Prevention Surveillance

CHBAH: Chris Hani Baragwanath Academic Hospital

CMJAH: Charlotte Maxeke Johannesburg Academic Hospital

CMSA: The Colleges of Medicine of South Africa

CoD: Cause of Death

CT: Computed Tomography

HIV: Human Immunodeficiency Virus

HJH: Helen Joseph Hospital

ICD: International Classification of Diseases

ICU: Intensive Care Unit

IQR: Interquartile Range

MIA: Minimally Invasive Autopsy

MPMCTA: Multiphase Postmortem Computed Tomography Angiography

MRI: Magnetic Resonance Imaging

NICD: National Institute for Communicable Diseases

NMC: Notifiable Medical Condition

PAD: Provisional Anatomic Diagnosis

PM: Postmortem

QA: Quality Assurance

RCP: Royal College of Pathologists

RMMCH: Rahima Moosa Mother and Child Hospital

TB: Tuberculosis

WHO: World Health Organisation

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CHAPTER 1

1 INTRODUCTION

Autopsy, the detailed examination of a body following death, is widely regarded as the gold standard for accurately determining the Cause of Death (CoD) (1). This practice was once accepted as routine to assess all in-hospital deaths because of its ability to reveal antemortem diagnostic errors before the availability of modern ancillary investigations. However, autopsy rates have experienced a steep worldwide decline over the past few decades, bringing into question its relevance in the 21st century (2,3,4,5). The reasons for the decline in autopsy rates are complex, but it has been postulated that this decline is closely associated with reduced quality assurance, medical knowledge and education (1,2,6).

In South Africa, a registrar in Anatomical Pathology is required to perform a specific number of autopsies to gain experience and competence in the practice (7). A significant decline in autopsy numbers which is associated with limited exposure to postmortem pathology, may result in substandard training in the field, compromise the quality of autopsies and result in an overall lack of skill and interest in the performance of autopsies by pathologists (8).

The field of Anatomical Pathology has progressed to a much more specialised histopathological and cytopathological discipline often referred to as *surgical pathology* which has been further shaped by the molecular era, personalised medicine, and digitisation. This is contrasted by autopsy practice following traditions and methods dating back to Virchow's techniques (9). Change and adaptability in autopsy practice is a prerequisite for its survival and for it to remain relevant in an advancing and modernising medical era. Alternative approaches to postmortem diagnosis have been sought and

implemented to make autopsies more acceptable to the public, clinicians, pathologists and mortuary staff and to optimally utilise time and resources (1,10,11).

Because of the decline in autopsy rates, and the complex causality of this, autopsy practice should regularly be re-evaluated to identify the role it plays in a dynamic medical field (6). However, autopsy reports are very rarely systematically evaluated, and the practice itself remains under-investigated. In addition to this, there is a lack of data to prove that autopsies improve the quality of patient care (12,13). Before autopsy practice can be accepted and implemented in clinical quality assurance it needs to be validated as a credible diagnostic procedure to prove that it impacts patient care.

There is limited data available on the actual practice of medical autopsies in South Africa, reflecting the scarcity of information on the value and role of autopsies in a local setting. In a study conducted at the Department of Anatomical Pathology, University of the Free State in Bloemfontein, South Africa, Venter et al, showed a definite decline in autopsy numbers in a milieu where the vast majority of clinicians deemed autopsies important (14). A similar audit of medical autopsies has not been performed at the University of Witwatersrand to date. It was deemed necessary to investigate the practice of autopsies at our institution to determine if similar trends exist.

To ensure the survival of autopsy practice change may be necessary; however, prior to this, the existing status quo needs to be established.

CHAPTER 2

2 AIMS AND OBJECTIVES

2.1 Aim of the study:

i. The aim of this study was to investigate the trend in the number of autopsies performed in the Division of Anatomical Pathology, University of the Witwatersrand over a ten year period and to assess the spectrum of CoD and other associated epidemiological data.

2.2 The study was undertaken with the following objectives:

i. To calculate the total number of autopsy cases performed in the Division of Anatomical Pathology at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and Chris Hani Baragwanath Academic Hospital (CHBAH) annually over a ten year time period (January 2009 - December 2018).

ii. To assess the following demographic and epidemiological factors associated with the autopsy cases: age, gender, race (where recorded), human immunodeficiency virus (HIV) status (where recorded), referring hospital.

iii. To assess the spectrum and change in CoD in the autopsies by:

- Assessing the first and last fifty completed autopsy reports in the study period.
- Describing the immediate CoD as well as the underlying CoD categorised into twelve classifications according to International Classification of Disease, 10th revision (2016).
- Determining in what proportion of cases a cause of death is unknown/indeterminate by autopsy.
- Determining the number of autopsy cases in which the CoD is related to an identifiable notifiable communicable disease as classified according to the National Institute of Communicable Diseases (NICD).

iv. To ascertain whether current autopsy numbers are sufficient to fulfil the requirements for registrar training in Anatomical Pathology.

CHAPTER 3

3 LITERATURE REVIEW

3.1 Autopsy practice then and now

The word autopsy, derived from the Greek autopsia, meaning “seeing for one’s self”, refers to the dissection of a dead body through a systematic approach observing macro- and microscopic pathological changes to determine the CoD. Other synonymous terms include “postmortem examination”, “necropsy” or “dissection” (1,15). The practice of autopsies has a checkered history dating back from ancient Egypt and has been documented throughout the dark ages and Renaissance period. It evolved as pioneers such as Rokitansky, Virchow and Osler modified and systematised the practice until it reached its peak in the 19th century. Autopsies became generally accepted as a quality indicator in medical practice and were performed in hospitals and public mortuaries as routine to assess all in-hospital deaths (1,17). In 1950 one in two patients dying in a United States hospital underwent postmortem examination; however, by the beginning of the 1960’s the practice of medical autopsies was already facing a decline (1,16,18).

The traditional autopsy found itself in a rapidly changing and advancing world of medicine. Experimental research became the focus to gain medical knowledge driven by financial support that demanded results and publications (17,18). In contrast, the autopsy could not keep up with the same trend as mortuaries were overburdened with routine work. Clinicians lost confidence in the practice as they felt reports often lacked judicious insight and they questioned the mass routine performance of autopsies that had little to show for all the data drawn from these cases. Additionally, medicine continued to advance in laboratory testing and radiological studies that improved diagnostic accuracy to such an extent that postmortem confirmation became less important (16). Autopsies also became less acceptable as modern medicine was striving to become less invasive with diagnostic and therapeutic approaches (18).

Later in the 20th century, the final blow was given by the Alder Hey organ retention scandal as the public suddenly grew awareness of the harsh reality and practice of autopsies (19). Autopsies were scrutinised by the public, the media, government and the medical profession, which marred confidence in postmortem pathologists and the practice (20,21). This led to the Human Tissue Act 2004 in the United Kingdom and The Royal College of Pathologists (RCP) in the United Kingdom responded by releasing the Updated Guidelines on Autopsy Practice. The RCP admitted that autopsy practice had been neglected and little had been done to uphold the standards of autopsies and reporting, whilst advancing sub-specialities in pathology such as histopathology and cytopathology had well maintained quality control. The guidelines also emphasised individual autonomy and the necessity of informed consent, placing the patient and family at the core of the practice (21).

Even though the practice had been poorly represented in certain ways, it still proved to significantly contribute to medical knowledge over the past few decades. One of many examples is how autopsy studies on HIV patients proved significantly useful in elucidating underlying preventable and treatable opportunistic infections (10). Today rapid molecular autopsies are used in research on the genomic evolution of tumours to apply knowledge in precision medicine (22). Most recently postmortem examination still proved its relevance in the SARS-CoV-2 pandemic by elucidating the CoD and provide insight into the pathogenesis of the novel virus (24,25,26).

The above brief history of autopsies shows that change and adaptability is a prerequisite for the practice to survive in an advancing and modernising medical era.

3.2 The role of autopsies

A postmortem examination can reveal diagnostic discrepancies and this quality can be utilised in quality assurance to improve patient care (1,17,26,27). In the past autopsies formed part of routine clinical practice and were used for hospital accreditation purposes to such an extent that the autopsy rate of a hospital reflected the quality of the hospital

(16). It can also function as an outcome measure to validate diagnostic tests, treatments and procedures (28–32). It has other virtues such as contributing to research, educating the medical community and providing accurate epidemiological statistics (1,6,10,33–35).

3.3 Autopsies in South Africa

In South Africa, there are two types of autopsies; medical/anatomical pathology autopsies and medico-legal/forensic autopsies. Medical autopsies are performed in academic institutions on patients that have died due to natural causes to establish the exact CoD and to advance medical education and research. Medico-legal autopsies are routinely performed under statutory provisions to investigate unnatural deaths to facilitate further legal decisions and proceedings (36). The former is performed after a request made by the attending physician and with family consent and the latter by forensic pathology services at the request of the police.

Under South African legislation medical autopsies are performed in terms of the National Health Act of 2003 (37). A pathologist can only conduct a medical autopsy if the following two requirements have been met; the deceased has died of a natural cause and appropriate consent has been obtained from the next-of-kin. In addition, pathologists can also be involved and assist in procedure-related deaths which are conducted by a Forensic pathologist in terms of the Health Professions Amendment Act 29 of 2007 (38).

3.4 Autopsy as a quality indicator

As mentioned above, postmortem examinations can function as a quality management tool by confirming unproven clinical diagnoses, discovering undiagnosed conditions and occasionally reveal antemortem diagnostic discrepancies. Past autopsy studies have mainly leveraged this ability to reveal clinical diagnostic errors to justify the role and importance of autopsies in current medical practice. To assess the clinical relevance of autopsies, some studies show reduced frequency of major discrepancies (2,12,29,39–41), while other studies show that major discrepancy rates remain unchanged (27,39,42,43).

In autopsy related research, a CoD is usually assigned according to the International Classification of Diseases (ICD) governed by the World Health Organisation (WHO) that provides tools to categorise morbid entities according to established criteria (44). The CoD is then further categorised according to the Goldman criteria (42). According to the Goldman criteria, a class I error is a major missed diagnosis, directly related to death and may have altered survival. A class II error is a major missed diagnosis, directly related to death and if detected would not have altered survival. Class III and IV are minor errors which are missed diagnoses not directly related to the CoD. The CoD of major errors (class I and II) have found to be mostly due to cardiovascular disease, followed by infections, neoplasms and central nervous system pathology (39,41,42). It should be noted that even though the term 'error' is ubiquitously used in autopsy literature, this should rather be viewed as clinical limitations in antemortem diagnoses in the face of atypical clinical presentations, as overall diagnostic performance relies on a combination of clinical acumen, experience and an institution providing suitable tests- including new and advancing investigations in the context of guidelines (2,39).

An unchanged discrepancy rate may be explained by many variables such as study design, selection of the study population and autopsy rates (39). Some argue that high discrepancy detection rates exist due to a selection bias of clinically problematic or complicated cases and results in an overestimation of diagnostic performance. In addition to this, most statistics are derived from studies performed in academic institutions which may also have an increased number of atypical cases that contribute to a high discrepancy rate (2). On the other hand, diagnostic overconfidence is the main factor leading to clinical diagnostic errors and the same reason autoptic verification of diagnoses is considered unnecessary by clinicians, and therefore these cases would not be reflected in autopsy studies (12,45). Also, lower autopsy rates are associated with higher rates of major diagnostic errors which will mask clinical performance because of selection bias towards unclear cases (39).

However, the overall error detection rate is declining, this is evidenced by an important meta-analysis of 53 autopsy series over a 40 year period published by Shojania et al. in

2003 showing a 9% median error rate for class I errors and 23.5% for major errors. In this period there was a relative decrease of 33% of class I errors and 20% for major errors per decade. In this study, it was estimated that in the year 2000 in an average United States hospital with a high autopsy rate of 100% (which would eliminate the effect of selection bias), class I errors would be detected in approximately 4% of cases and class II errors in an additional 4% (2).

The reduced frequency of major diagnostic errors is mostly ascribed to advances in clinical medicine, such as improved clinical skills and the expanding armamentarium of new diagnostic procedures over the past decades. Since 1960, groundbreaking investigations such as roentgenography, endoscopy, surgical explorations and biopsies were introduced, and since 1980 nuclear medicine, ultrasound and computed tomography (CT) have been utilised (42). Sonderegger-Iseli et al. assessed the diagnostic accuracy over 20 years (1972 to 1992) in which major discrepancies decreased from 30% to 14%. The increase in diagnostic accuracy was ascribed to a significant rise in non-invasive diagnostic procedures resulting in an improved specificity in cardiovascular diseases from 85% to 97% ($p=0.034$) and increased sensitivity for infectious diseases from 25% to 86% ($p=0.036$) (40). In a follow-up study a decade later, the same group observed a further significant reduction in major diagnostic errors from 14% to 7%. The specificity for cardiovascular diseases increased from 85-98% ($p<0.001$) and they correlated the significant rise in specificity for cardiovascular diseases with the introduction of sensitive laboratory tests such as d-dimers, troponin, and spiral CT angiography introduced from 1998 to 2000 (12).

Conversely, in intensive care units, the diagnostic error rate has not shown a decline which is mostly attributed to systemic infections with atypical presentations (46). In a systematic review of 31 observational studies examining autopsy-confirmed diagnostic errors in adult intensive care units (ICU), at least 1 misdiagnosis was found in 28% of autopsied ICU patients (47). Pulmonary embolus, myocardial infarction, pneumonia, and aspergillosis were the most common missed diagnoses. Tejerina et al. demonstrated the evolution in error rates in a medical-surgical ICU setting by comparing a previous study (1982-2007)

to a more recent study (2008-2015), finding that class I error rates remained similar 7.5% and 8.4% respectively (46). A study conducted by Sévaux et al. in a neonatal intensive care unit found major diagnostic errors in 48% of cases subjected to autopsies (48).

This shows that even though there is an overall reduction in the error detection rate, autopsy practice is well known for its benefits and these are sufficiently high to encourage ongoing use (2). This is supported by the fact that in less than 6% of cases, an adequate autopsy fails to establish a CoD and that autopsy usually successfully addresses clinical questions in up to 97% of the cases (2,27). Post-mortem case review as a substitute for autopsies has been shown to miss up to 85% of major diagnostic errors (12).

In light of the above, autopsies functioning as a quality measurement tool should not be viewed as a means to scrutinise clinical performance, but rather function as an educational feedback mechanism that eliminates uncertainty and strengthens the confidence in diagnostic workup in cases. Autopsies can therefore be a key player to reduce diagnostic errors and should be used to measure and confirm diagnostic performance (12). In addition to measuring clinical performance, the ultimate aim is to improve patient care, a goal in which the role of the autopsy has not been well established and research into this is required.

The following section will discuss some of the limitations in autopsy practice and why it is not fully embraced by current clinical practice.

3.5 Limitations in autopsy-based studies and autopsies

Although it has been shown that autopsies reveal diagnostic discrepancies, currently it is not utilised in hospital quality assurance, performance measurement or improvement programs (49). This is due to a lack of evidence-based research available to prove that conducting autopsies and publicising data directly contributes to improved patient care.

Routine autopsy reports and findings are not systematically analysed and, therefore, the data confined to these reports has not proven to contribute to patient care (6,8).

Horowitz and Naritoku surveyed pathology training programs and found that more than half of the programs did not analyse diagnostic discrepancies and did not further investigate factors that contributed to these discrepancies. They also found that most programs did not communicate discrepancy analyses with clinicians and that the reproducibility of diagnostic error analyses was assessed in very few programs (49).

Autopsy practice is also subject to errors as it is dependent on the pathologist's skill and use of ancillary studies, however, this is an under-investigated subject lacking studies that investigate error rates in autopsy diagnoses (6,49). A defined quality assurance program is advised by the College of American Pathologists (CAP) but often internal Quality Assurance (QA) and peer review processes are not utilised (49). For such reasons Shojania et al. concluded in the report 'The Autopsy as an Outcome and Performance Measure' that the healthcare system can greatly benefit from autopsies, however, evidence and research are deficient to confirm the quality of autopsies, technical adequacy in interpreting of autopsy findings, and reliability of the conclusions drawn from detected discrepancies (13).

Before autopsy practice can be accepted and implemented in clinical quality assurance it needs to be validated as a credible diagnostic procedure for this purpose. Furthermore, studies investigating the quality of autopsy accuracy, reproducibility and consistency in the categorisation of discrepancies are required (13,49).

3.6 The decline in autopsy rates

Without exceptions, international studies have shown a worldwide decline in medical autopsy rates (2). Declining autopsy numbers compromise autopsy training for Pathology trainees and is associated with limited experience and training in this discipline. This

decline has a complex causality, influenced by key players such as the pathologists who perform autopsies and uphold the standard of practice, the clinicians who initiate and drive the consent process, and the public who have the final say by giving consent for medical autopsies to take place (11,26).

3.7 Registrar training

In South Africa a trainee registrar in Anatomical Pathology is required to perform at least 50 autopsies; at least 35 adult autopsies and 15 paediatric autopsies, before qualifying (7). This has become the most significant sustaining factor in the performance of medical autopsies in academic institutions, as most of the autopsies are performed by registrars (11,49,50).

Due to decreasing medical autopsy numbers, training programs globally have difficulty in meeting the prescribed required number of autopsies for training. In some training programs autopsies are 'shared' by more than one registrar to amount to an adequate number, whilst others resort to rotating registrars to Forensic Pathology institutions where the supervision and educational value may be questionable (49,51). This raises concerns that registrars may not accumulate enough experience in general pathology, and will be deficient in practical skills, morphological and histological interpretations and ultimately competency in clinicopathological conclusions (49).

Daily pressures from routine surgical and clinical work, research and teaching duties take precedence, resulting in diminished quality in autopsy training. In some teaching programs, practical training relies on teaching from the prosector or more senior registrars (49,52). After multiple surveys, Horwitz concluded that newly qualified pathologists lack proficiency in gross and autopsy pathology and highlighted a lack of interest in the field (52).

3.8 The pathologist

The field of Anatomical Pathology has progressed and although some pathologists still regard autopsies as an integral part of their work, pathology training and professional development, others feel it is of little clinical value. There are therefore two opposing views on autopsies; the one viewing autopsies as outdated not adding value to medicine, and the other warning of serious consequences if completely omitted from practice (1,6,11).

Specific pathologists are seldom assigned to only do autopsies, and therefore the vast majority spend most of their time on routine surgical pathology, research and teaching which takes precedence over autopsies that can prolong their day (18,26). A survey conducted by the American Pathologists Autopsy Pathology education program showed that on average approximately 5.2 hours and 4.8 hours are spent on adult and foetal autopsies respectively (53). Many pathologists freely express their aversion and dislike towards autopsies and performing autopsies on infectious disease cases (8). For such reasons the RCP no longer includes competency in autopsy practice as a prerequisite to qualify as a pathologist (54,55).

Performing and interpreting a postmortem examination is one of the most complex technical procedures of the discipline, requiring high-level knowledge in anatomy, pathology and histopathology. To provide meaningful answers to clinical questions, a pathologist has to formulate relevant clinicopathologic conclusions drawn from sufficient pathophysiological knowledge (6,9,56). The decline in autopsy numbers is closely associated with diminishing pathologist experience in postmortem examination and will result in substandard practice and suboptimal services for clinical colleagues. Clinician's depreciation of postmortem examinations may result in reduced autopsy requests and perpetuate the cycle of declining autopsy rates (9).

3.9 The clinician

Clinicians play a critical role in the consent process and therefore affect autopsy rates as autopsies are more likely to be performed when strongly recommended by the clinician (57,58). A study by Burton and Underwood showed that the lowered autopsy rate is mostly attributed to clinicians not requesting autopsies. In cases where clinicians did request a postmortem, consent was obtained in 43.3% of cases (19). Clinicians can correctly inform family members and dispel false impressions that the next of kin may have, making a substantial difference in obtaining consent (59). Research as shown that as soon as clinicians are actively involved in autopsy programs, autopsy rates increase. By exposing junior physicians to formal training in the consent process and consistent motivation by senior registrars and department heads to perform autopsies are an effective means to increase autopsy rates (18).

In the South African context the main reasons for reduced autopsy request by clinicians in order of occurrence were: difficulty in obtaining consent from the deceased's next of kin, cumbersome administration involved in the consent process, the belief that medical autopsies are not performed on HIV positive patients and delay in autopsy reports (14). Another important factor that leads to reduced requests from clinicians is that since the Health Professions Act was amended in 2007, all procedure-related deaths are performed by forensic pathologists, and no longer seen as medical autopsies (38).

Some clinicians view autopsies as outdated and as no longer needed in clinical practice, as a result of their confidence in clinical diagnostic procedures increasing (6). Numerous advances in diagnostics capabilities of modern medicine depreciate autopsy as a gold standard to determine the CoD (49). The most common reasons for clinicians not to request an autopsy include: when they feel confident that the CoD is already known or that there is a 'do not resuscitate' order as the CoD is anticipated (4,12,45,59).

Today autopsies rarely form part of undergraduate medical training, therefore, as many graduates in medicine have not been exposed to autopsy practice it is not surprising that

they are unfamiliar with this practice and ignorant of its value (6,49,60). According to the investigator's knowledge, formal exposure to autopsies have been removed from the undergraduate medical curriculum at the University of the Witwatersrand.

Clinicians are not always satisfied with the quality of reports, long turnaround times and poor communication from the pathologists. Studies have shown that poor communication relating to when autopsies will be performed, delays in reporting and substandard communication with clinicians are frequent (8,11). The credibility of autopsy reports is questioned by clinicians as they often find them difficult to interpret, lacking clinicopathological correlation and failing to resolve initial diagnostic questions (51). Final autopsy reports are associated with a long turnaround time that can take weeks or months to be released, leaving the clinicians in a difficult position with families desperate for answers. A standard on reporting has been set by the CAP that requires the provisional anatomic diagnosis (PAD) to be submitted within 2 days and the final autopsy report to be completed within 30 working days to fulfil accreditation standards. The extended time intervals that clinicians have to wait for an autopsy report results in demotivation, loss of interest and relevance of cases, which feeds the negative cycle of the clinician's depreciation of autopsies (8,26,49,60).

Administrative complexity and time-consuming nature of the consent process also contribute to the infrequent recommendation. The administrative responsibility often falls on overburdened junior medical staff to just 'sign off' death certificates. These junior doctors might not see the need for an autopsy (14,58,60).

Some clinicians may also fear that information from postmortem investigations will be used as evidence of negligence in alleged malpractice lawsuits (18,61). Bove conducted a study showing that in about 20% of alleged negligence cases, autopsies proved to be helpful to the defendant clinician. Even if a treatable major diagnostic error was encountered at the time of postmortem, defendant physicians were usually exonerated. Medical negligence is based on the standard of care issues rather than the accuracy of

clinical diagnoses (61). The CAP reviewed court records of malpractice over 30 years and found that the defendant physician was exonerated of malpractice in 61% of cases where the autopsy favoured the plaintiff (detecting a major diagnostic discrepancy) and in 100% of cases that the autopsy favoured defendant (26).

Misconceptions and confusion in areas regarding autopsy practice and the consent process may hamper clinician participation. Clinicians might feel unequipped to fully explain the autopsy technique and other logistical issues to the next of kin and are, therefore, not keen to address the topic of consent (18). It has been shown that providing formal education and training to clinicians in the value autopsies and how to recommend and communicate with relatives improve autopsy rates (29,57–59,62–64).

3.10 The public

Research has shown that family refusal is the most important factor for not performing an autopsy (46). Clinicians also feel that the difficulty in obtaining consent contributes to declining autopsy rates (60). Blokker et al. analysed 1000 questionnaires on consecutive natural deaths and found that in 81% of cases the next of kin declined consent. The most important reasons for this is an assumed known CoD and that they feel it is unnecessary to further complicate a long period of illness of the deceased (59,65).

Contrary to this, an unknown CoD or finding another unexpected CoD are important drivers for next of kin to give consent (65). Family members are more willing to grant permission on younger patients, to find understanding or to contribute to medical knowledge (66). A German survey showed that up to 50% of the general public considered autopsy necessary and would be willing to request a postmortem examination and consent to one being performed (6).

But little is done to educate and inform the public and relatives on the importance and value an autopsy can offer to them. Studies have shown that with adequate information

and explanation, the public appreciates the value of autopsy (58,67). Free and accessible information on what a medical autopsy is, what to expect, and when to request a medical autopsy is not available to the public of South Africa. It is advised to use evidence-based communication tools to change public opinion regarding the value autopsies offer towards research and routine data collection (10).

Poor communication and long turnaround times also affect the relatives of the deceased as it delays burial or cremation, causing apprehension to consent to an autopsy (59). Studies have shown that next of kin don't always receive feedback regarding the autopsy (58,68).

The public's cultural and religious perspectives also influence consent. Mutilation of the body of a loved one prevents open-casket viewing which may be important to certain cultures (65,68). Various religious views may cause refrain, for example, Islam and Judaism require burial within 24 hours unless otherwise specified by law, and therefore, delayed burial caused by an autopsy would not be permitted (26,58). The African culture views organs as crucial parts to continue existence in the afterlife and consent should be subject to not only the next of kin but rather granted on a community basis complicating the consent process (69).

The family's opinion after the loss of a loved one is paramount and echoes the emphasis made by the RCP in 2000 after the aforementioned tissue retention scandal. The patient and family should be centrally placed, sufficiently informed and granted full autonomy of choice. Given the above-mentioned importance of the public opinion, alternative options in postmortem examination to determine a CoD which may be more culturally acceptable should be available to family members.

3.11 Alternative approaches

Alternative approaches in the field have been sought and implemented to make autopsies not only more acceptable to the public, clinicians, pathologists and mortuary staff, but also optimise time efficacy and resources. The type of postmortem investigation can be adapted to the autopsy indication, needs of the next of kin, and availability of resources and expertise. Following the same trend as modern medicine, autopsies are becoming less invasive with diagnostic approaches. Full autopsies may not be feasible or acceptable in certain settings requiring adaptability to apply a suitable intervention that can still provide robust aetiological data (1,10). The various alternative options will be discussed briefly.

Verbal autopsies are well accepted but prove to provide limited accuracy. This postmortem investigative method is utilised in low and middle-income countries in which vital registration system and data on mortality are substandard. Information is collected from contacts of the deceased to formulate a diagnosis, this is useful in cases of trauma or easily identifiable medical conditions. It is by far inferior to conventional autopsy and lack sensitivity and specificity to detect other diseases (10).

Boulle et al. have shown that artificial neural networks can be used to classify the data obtained by a verbal autopsy to establish a CoD. Gajalakshmi and Peto reported that verbal autopsies performed in India reduced the proportion of deaths of unknown causes from 54% to 23% in urban areas and from 41% to 26% in rural areas. The verbal autopsy had a 95% sensitivity and specificity of 50% for the identification of deaths caused by cancer when compared with records held in a cancer registry. However, some articles report the sensitivity to be as low as 30% (11).

A range of minimally invasive autopsy (MIA) techniques have been developed and are widely used in research, including: needle aspirates and percutaneous needle biopsies. These techniques show 83% to 85% concordance rate with conventional autopsies respectively (11). MIA comprises a series of postmortem tissue biopsies and body fluid

samples taken as soon as possible after death. These specimens are then submitted for histopathological and microbiological assessment to determine a CoD (70). MIA is considered more acceptable by the community and health care providers, potentially also has reduced risk of infection for pathologists and mortuary workers (10,35,70). It is a less complex procedure, more cost and time effective and does not cause significant disfigurement to the deceased. It can also detect microorganisms which are seldom possible in conventional autopsy due to contamination (70). MIA has specifically been utilised in paediatric research exemplified by the multicountry Child Health and Mortality Prevention Surveillance (CHAMPS) project, aiming to investigate the leading causes of death and disease trends in low socio-economic environments (10). Although this method offers many advantages, it has a high false-negative rate and often results in non-contributory results. The main drawback of MIA is that these techniques are limited to detecting focal lesions, and is most useful in detecting pathology that diffusely affects large viscera (11).

Postmortem radiological techniques also referred to as the virtual autopsy or virtopsy have shown recent drastic improvements in detecting CoD, and can be used as diagnostic procedures or as adjuncts to MIA. Advantages to the virtopsy include; low maintenance cost, short examination time, ease of operation and optimisation of human resources (11). Importantly, virtopsy is not suitable for low-income countries where technology is sparse and where there is limited skilled personnel (10). Radiological alternatives include techniques such as: endoscopic autopsies, echopsy and imaging autopsies that includes postmortem CT, multiphase postmortem CT angiography (MPMCTA) and postmortem magnetic resonance imaging (MRI) (71,72).

Currently, the best results are still obtained when combining radiology as an adjunct to an autopsy, however, postmortem imaging which is mostly explored in Forensic medicine has made extraordinary progress in recent years. Grabher et al. showed that postmortem CT angiography is superior to autopsy for all findings especially in detecting vascular and skeletal disease but proves to be inferior in detecting soft-tissue lesions. Combining CT angiography with postmortem CT increases sensitivity for detecting pathologic findings

from 64% to 81%, comparable to conventional autopsy (83%). Presently MPMCTA shows a sensitivity that is comparable to conventional autopsy in detecting sudden cardiac death such as disruption of coronary arteries, vascular obstruction and fatal haemorrhages and in addition to this, a specific form of MPCTA developed to investigate coronary artery pathology offers near-histologic levels of myocardial, coronary and valvular lesions (72). As these modalities advance, it may ultimately replace the need for conventional autopsy (71).

The molecular autopsy is a form of postmortem genetic testing that involves DNA sequencing analysis of specific genes related to a specific disease. One of the applications is to establish a CoD in cardiomyopathies (73). Genomic studies have also been applied in research on cancer tissue obtained during rapid autopsies in which the aim is to perform the autopsy within one hour after death to accurately investigate clonal evolution and heterogeneity of tumours for the development of targeted therapies(22). The most novel is the liquid autopsy in which cell-free DNA is used in conjunction with the rapid autopsy in cancer research (73,74).

3.12 Change is required

Change and adaptability in autopsy practice is a prerequisite for its survival in an advancing and modernising medical era. The conventional medical autopsy cannot remain unchanged for more than a century. Langer et al. published an article on how a modernised postmortem diagnostic unit was implemented to rejuvenate autopsy practice, as it was felt that a change of culture in postmortem diagnostics may contribute to a better reputation of postmortem examinations from a perspective of clinicians and affected relatives. Important changes were implemented such as investing financially, restructuring aspects such as work-flow, transforming autopsy rooms into operating rooms, implementing case discussions with clinicians and students, minimally invasive approaches and integration of digitalisation. Following modern medicine which emphasises sub-specialisation, a limited number of pathologists were dedicated to postmortem diagnostics and separated from normal histology service. This showed enthusiasm from pathologists to change current practice which proved to halt the

decreasing autopsy number trend in that unit. Only recently have pathologists started questioning their contribution to reversing this decline (9).

We are at a crossroads in the area of autopsy pathology. The autopsy should not be preserved in a conventional form but rather developed as a valuable tool in medicine and research. The onus falls on pathologists to take leadership in the evolution of the autopsy and prove its relevance and value to patient care in modern medicine (26,49).

3.13 Evaluation of current practice

Because of the decline in autopsy rates, with its complex causality, autopsy practice should be regularly re-evaluated to identify the role it plays in a dynamic medical field (29). However, the practice itself remains under-investigated (6,13,75).

CHAPTER 4

4 MATERIALS AND METHODS

4.1 Study design and sample

A retrospective, descriptive review on the quantitative data of all autopsies performed in the Department of Anatomical Pathology at CMJAH and CHBAH over a ten-year time period (January 2009 to December 2018) was performed by reviewing autopsy reports.

4.2 Inclusion criteria

All medical autopsies performed at Division of Anatomical Pathology at CMJAH and CHBAH over the ten years from January 2009 to December 2018.

4.3 Exclusion criteria

All autopsies performed at the forensic pathology mortuary or for forensic purposes. All natural death autopsies referred by the forensic pathology service and performed at CMJAH.

4.4 Methods

The cases reported during the study period were obtained from autopsy registers in the Department of Anatomical Pathology at CMJAH and CHBAH, respectively. Demographic data for all autopsies conducted over the study period were obtained from the autopsy registers, if available, and from autopsy reports, if not recorded in the registers. The following details were recorded for each case:

- Age at the time of death
- Gender
- Race

- HIV status (where recorded in the autopsy report). HIV positive cases were recorded if the patient tested positive for HIV. HIV exposed cases were recorded if a foetus or paediatric patient was born to a mother that was HIV positive and the HIV status of the foetus or paediatric patient was either negative or unknown.
- The year in which the autopsy was performed
- The referral hospital and whether it was a state or private hospital

In addition, causes of death were obtained from autopsy reports for the first and last 50 postmortems conducted in the study period. The provisional anatomical reports and final autopsy reports were reviewed, and the relevant data was extracted.

The first 50 cases and last 50 cases were utilised as samples taken from the beginning of the study period and at the end of the study period. From these cases the following additional details were recorded:

- The date that the autopsy was performed
- The immediate and underlying causes of death were grouped into 11 classifications according to the International Classification of Disease, 10th revision (2016) as shown in Table 4.1 (44).
- Where the autopsy failed to establish a CoD, the final diagnosis was rendered as unknown/indeterminate.
- Where the immediate or underlying CoD was related to a communicable disease, the specific disease was classified according to the National Institute for Communicable Diseases (NICD) classification of notifiable diseases (NMC) shown in Table 4.2 (76).

Table 4.1: Classification of cause of death (45).

International Statistical Classification of Disease 10th Revision		
	Cause of Death	Code
1.	Infectious diseases	(A00-B99)
2.	Neoplasms	(C00-D48)
3.	Diseases of blood and blood forming organs and certain disorders involving the immune mechanisms	(D50-D89)
4.	Endocrine, nutritional and metabolic diseases	(E00-E90)
5.	Diseases of the nervous system	(G00-G99)
6.	Diseases of the circulatory system	(I00-I99)
7.	Diseases of the respiratory system	(J00-J99)
8.	Diseases of the digestive system	(K00-K93)
9.	Diseases of the genitourinary system	(N00-N99)
10.	Congenital malformations, deformations and chromosomal abnormalities	(Q00-Q99)
11.	Injury, poisoning and certain other consequences of external causes	(S00-T98)

Table 4.2: Categorisation of Notifiable Medical Conditions (76).

Notifiable Medical Conditions				
	Category 1	Category 2	Category 3	Category 4
1.	Acute flaccid paralysis	Agricultural or stock remedy poisoning	Ceftriaxone-resistant Neisseria gonorrhoea	Carbapenemase-producing Enterobacteriaceae
2.	Acute rheumatic fever	Bilharzia (schistosomiasis)	West Nile virus, Sindbis virus, Chikungunya virus	Vancomycin-resistant enterococci
3.	Anthrax	Brucellosis	Dengue fever virus, other imported arboviruses of medical importance	Staphylococcus aureus: hGISA and GISA
4.	Botulism	Congenital rubella syndrome	Salmonella spp. other than S. Typhi and S. Paratyphi	Colistin-resistant Pseudomonas aeruginosa
5.	Cholera	Congenital syphilis	Rubella virus	Colistin-resistant Acinetobacter baumanii
6.	Diphtheria	Haemophilus influenzae type B	Shiga toxin-producing Escherichia coli	Clostridium difficile
7.	Enteric fever (typhoid or	Hepatitis A	Shigella spp.	

	paratyphoid fever)			
8.	Food borne disease outbreak	Hepatitis B		
9.	Haemolytic uraemic syndrome	Hepatitis C		
10.	Listeriosis	Hepatitis E		
11.	Malaria	Lead poisoning		
12.	Measles	Legionellosis		
13.	Meningococcal disease	Leprosy		
14.	Pertussis	Maternal death (pregnancy, childbirth and puerperium)		
15.	Plague	Mercury poisoning		
16.	Poliomyelitis	Soil transmitted helminths (Ascaris Lumbricoides, Trichuris trichiuria, Ancylostoma duodenale, Necator americanus)		
17.	Rabies (human)	Tetanus		
18.	Respiratory disease caused by a novel respiratory pathogen	Tuberculosis: pulmonary		
19.	Rift valley fever (human)	Tuberculosis: extra-pulmonary		
20.	Smallpox	Tuberculosis: multidrug-resistant (MDR-TB)		
21.	Viral haemorrhagic fever diseases	Tuberculosis: extensively drug-resistant (XDR-TB)		
22.	Yellow fever			

4.5 Ethics

Approval for the study was given by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, under ethics number M190309 (Appendix 1).

4.6 Data analysis

Statistical analysis of the data was performed using appropriate statistical analysis techniques and software. A Microsoft Excel Spreadsheet was used to store the data, as well as to calculate descriptive statistics. The data was expressed quantitatively as summary statistics and visually as graphs and tables.

The frequency of autopsies performed per year was calculated. Numerical data was described by using the median as a measure of center, the minimum, maximum and interquartile range (IQR) as measures of variation.

Descriptive statistics were used to describe the demographic information. All cases were grouped into specific age groups and the patient age was categorised as follows:

- Foetal/neonatal (stillborn to < 1 month)
- Paediatric (1 month to 11 months) and (1 year to 16 years)
- Adult (≥ 17 years)

The paediatric age group was separated into two groups for practical purposes. Numerical data was described by using the median as a measure of center, the minimum, maximum and IQR as measures of variation.

The number of autopsy cases performed per year was used to determine the number of registrars that could be accommodated for autopsy training per year according to the prescribed Colleges of Medicine of South Africa (CMSA) training requirements. For adequate experience and training, a registrar in Anatomical Pathology is required to perform 50 autopsies that comprise at least 35 adult autopsies and 15 paediatric autopsies

of which foetal autopsies should not account for more than 5. For a registrar to comply with the prescribed requirements an average of 8-9 adult, 2-3 paediatric and 1-2 foetal or neonatal autopsies should be performed per year (7). To calculate the number of registrars that can be accommodated in our training programme, the annual number of autopsies were categorised according to foetal/neonatal, paediatric and adult autopsies. The number of autopsies per category was then divided by the number of autopsies required per registrar annually for that specific age group.

The hospital bed number was used as a surrogate marker to indicate the size or capacity of the major referring teaching hospitals relative to the number of annual referrals from these hospitals.

CHAPTER 5

5 RESULTS

5.1 Sample size

A total of 889 postmortems were performed over the 10-year study period – 604 (67.94%) at CMJAH and 285 (32.05%) at CHBAH.

5.2 Number of autopsies performed

Of the total number of autopsies performed, a maximum number of 126 autopsies was performed in 2009 and a minimum number of 68 performed in 2016 and 2018. The median number of autopsies performed was 84.5 and the interquartile range (IQR) was 29. At CMJAH the maximum number of autopsies performed was 78 in 2009 and the minimum was 37 in 2018. The median number of autopsies was 63 and the IQR was 14.5. At CHBAH the maximum number of autopsies performed was 48 in 2009 and the minimum 15 in 2014 and 2016. The median number of autopsies was 29.5 and the IQR was 18.5. The total number of postmortems performed per year is presented in Table 5.1 and illustrated graphically in Figure 5.1.

Table 5.1: Postmortems performed at CMJAH and CHBAH annually.

		CMJAH		CHBAH	
Year	Total number of postmortems	Number of postmortems	% of annual postmortems	Number of postmortems	% of annual postmortems
2009	126	78	61.90	48	38.10
2010	107	67	62.62	40	37.38
2011	108	69	63.89	39	36.11
2012	91	60	65.93	31	34.07
2013	88	68	77.27	20	22.73
2014	81	66	81.48	15	18.52
2015	72	54	75.00	18	25.00
2016	68	53	77.94	15	22.06
2017	80	52	65.00	28	35.00
2018	68	37	54.41	31	45.59

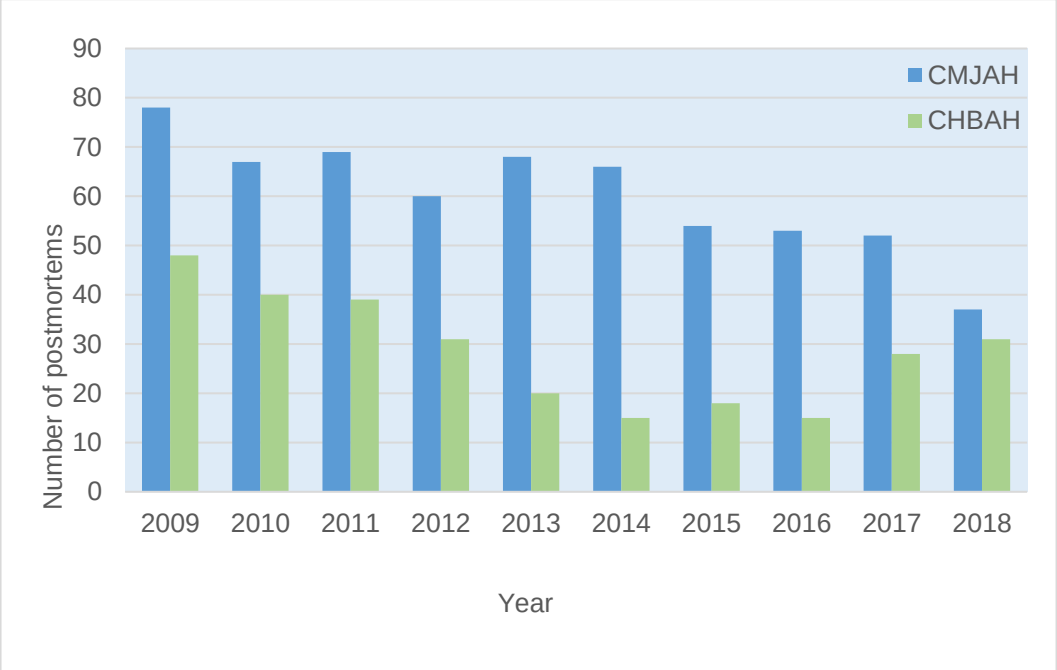

Figure 5.1: A bar chart of the number of postmortems performed at CMJAH and CHBAH annually.

5.3 Gender

Male patients accounted for 454 (51.06%) of postmortems in the study period and females, 431 (48.48%). The gender was not recorded in 3 (0.34%) postmortem reports. One (0.11%) postmortem was performed on a patient with sirenomelia in which there was no gender predominance.

5.4 Age

The age of the study population ranged from stillborn to 93 years of age. Within the neonatal age group (1 day to < 1 month) the median age was 3 days and the IQR was 4.25 days. Within the first paediatric group (1 month to 11 months), the median age was 4.93 months and the interquartile range was 4.67 months. Within the second paediatric group (1 year to 16 years) the median age was 6.83 years and interquartile range was 9.7 years. The median age for the adults was 47 years and the interquartile range was 28 years. The number of postmortems per age group is graphically represented in Figure 5.2.

Of the total number of cases, 589 autopsies (66.25%) were performed on adult patients, followed by 191 (21.48%) autopsies performed in the pediatric age group (1 month to ≤16 years) and 109 (12.26%) of autopsies performed on foetuses and neonates (0 to < 1 month). Figures 5.3 to 5.5 depict the number of postmortems performed per age group at CMJAH and CHBAH respectively.

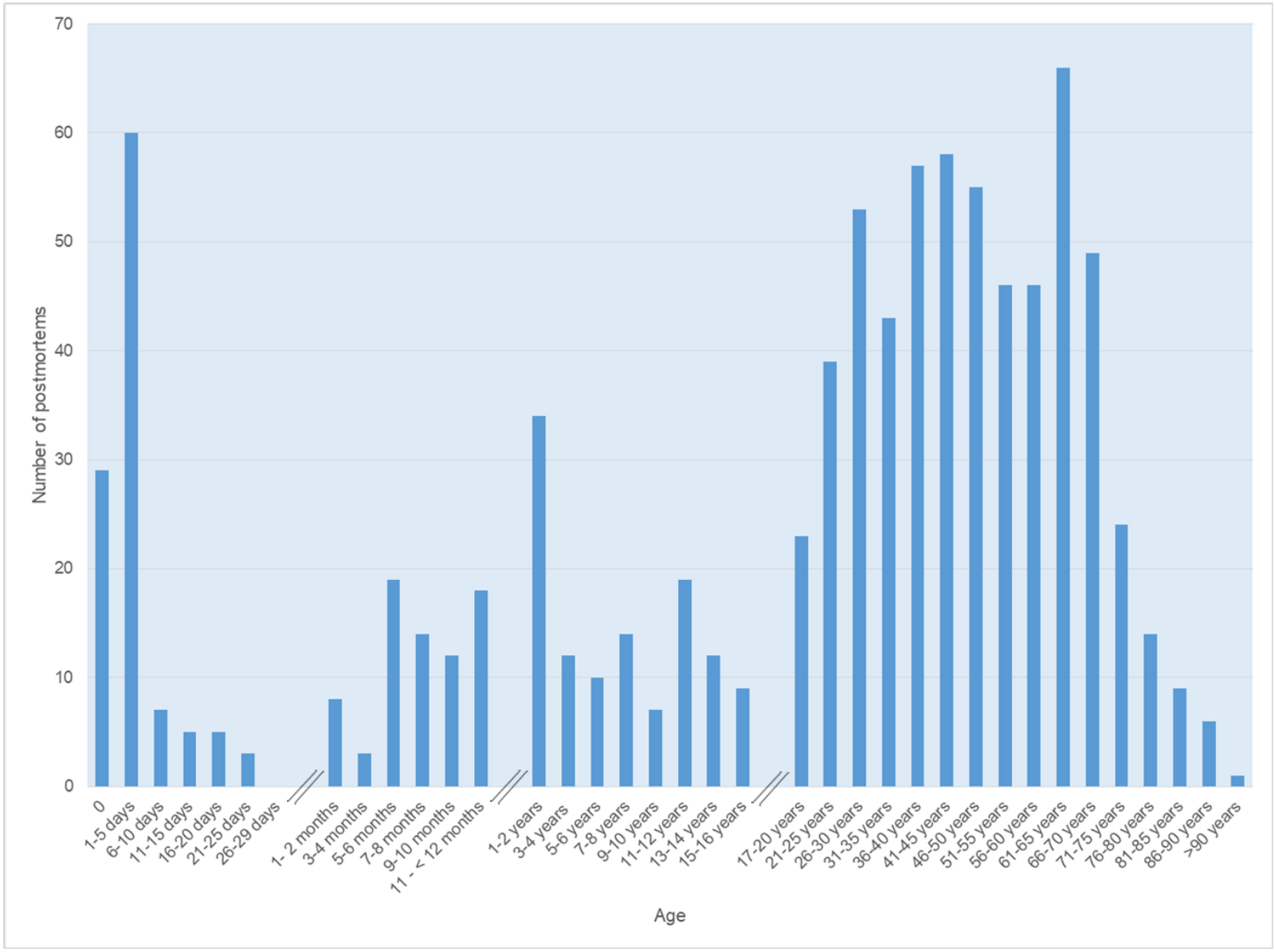

Figure 5.2: A histogram of the number of postmortems performed in all age groups. '0' indicates stillborn.

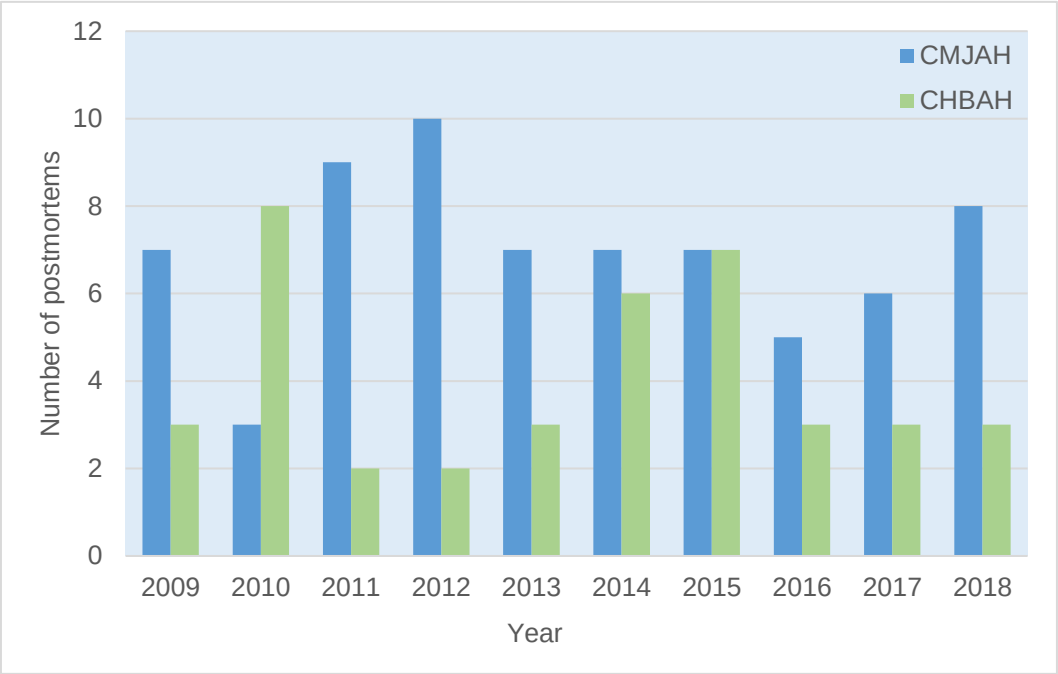

Figure 5.3: A histogram of the number of postmortems performed on foetuses and patients under a month of age.

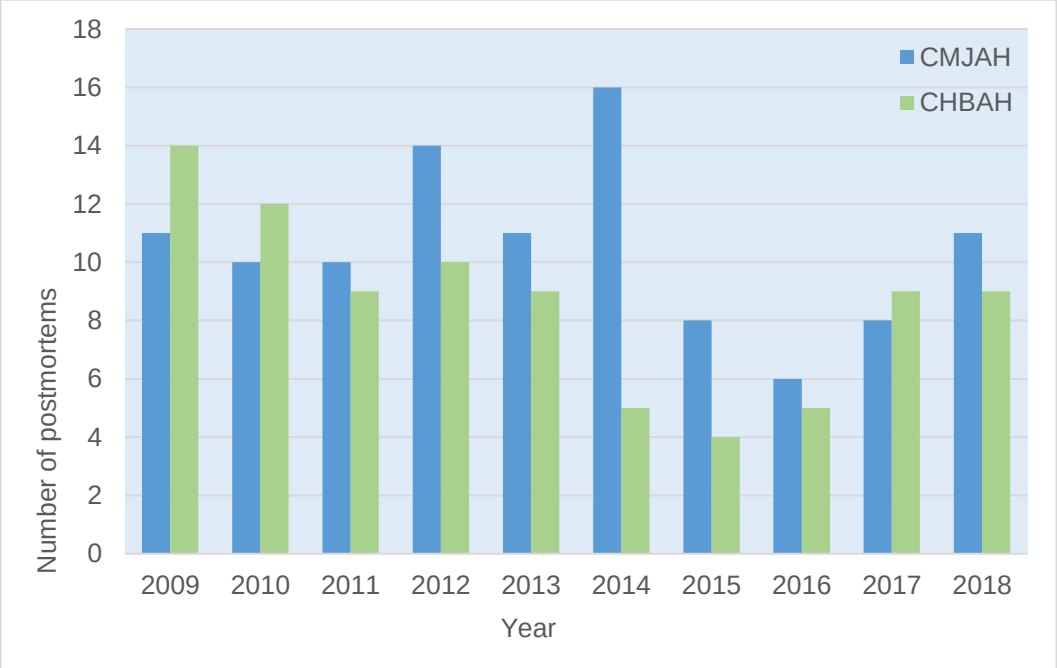

Figure 5.4: A histogram of the number of postmortems performed on paediatric patients (1 month to 16 years).

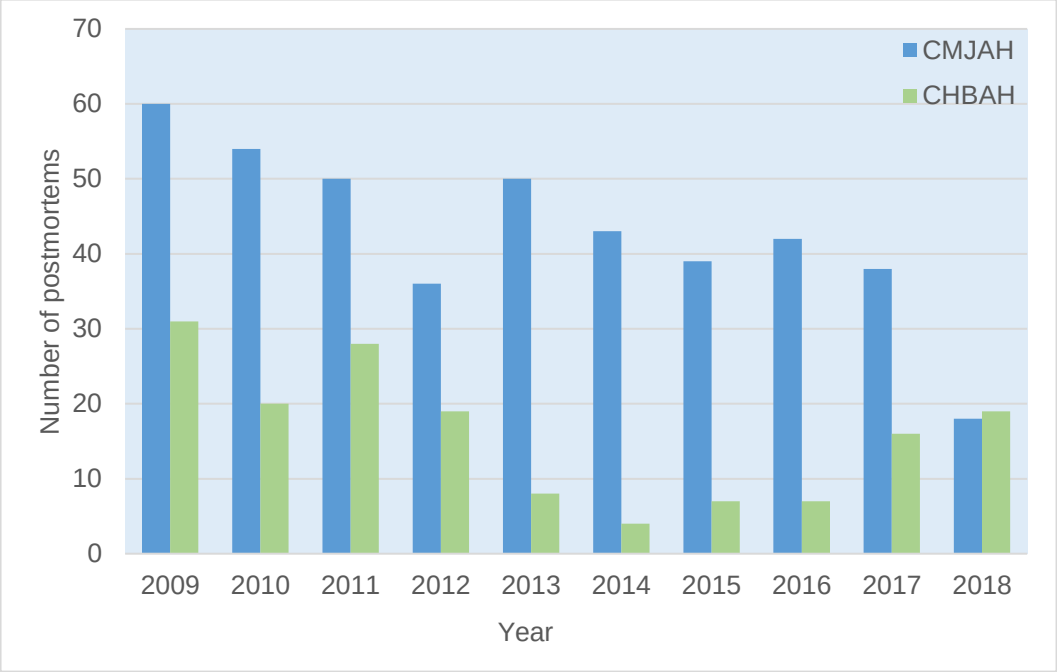

Figure 5.5: A histogram of the number of postmortems performed on adults (>16 years).

5.5 Race

A total of 628 (70.64%) cases were African patients, 212 (23.85%) White, 32 (3.6%) Coloured and 12 (1.35%) Indian. In 5 (0.56%) cases, race was not reported.

5.6 HIV status

The HIV status of the study population is summarised in Table 5.2. HIV status was unknown in 688 (77.39%) of the cases. Of the cases where HIV status was recorded, the total number of recorded HIV-positive cases was 90 (10.12%) and HIV exposed cases was 8 (0.90%). The total number of HIV-negative cases was 103 (11.59%). During the study period, the number of unknown HIV statuses did show a decline.

Table 5.2: HIV statuses on postmortems performed.

HIV status				
Year	HIV-positive (%)	HIV-exposed (%)	HIV-negative (%)	Unknown HIV status (%)
2009	11 (8.73%)	2 (1.59%)	5 (3.97%)	108 (85.71%)
2010	14 (13.08%)	0	14 (13.08%)	79 (73.83%)
2011	7 (6.48%)	3 (2.78%)	9 (8.33%)	89 (82.41%)
2012	9 (9.89%)	0	6 (6.59%)	76 (83.52%)
2013	9 (10.23%)	0	15 (17.05%)	64 (72.73%)
2014	6 (7.41%)	0	12 (14.81%)	63 (77.78%)
2015	10 (13.89%)	0	13 (18.06%)	49 (68.06%)
2016	6 (8.82%)	0	7 (10.29%)	55 (80.88%)
2017	9 (11.25%)	2 (2.5%)	11 (13.75%)	58 (72.5%)
2018	9 (13.24%)	1 (1.47%)	11 (16.18%)	47 (69.12%)
Total	90 (10.12%)	8 (0.9%)	103 (11.595)	688 (77.39%)

5.7 Referral hospitals

The number of cases referred by hospitals from within the state sector was 839 (94.38%). The number of cases referred from the state sector declined from 122 in the year 2009 to 62 in the year 2018. The number of cases referred by private hospitals was 50 (5.62%) in total. The number of privately referred autopsies stayed relatively unchanged throughout the study period and ranged from 4 (3.17%) cases in 2009 to a maximum of 7 (7.95%) cases in 2013 and 6 (8.82%) cases in 2018.

5.8 Autopsies performed per hospital bed capacity

The majority of autopsies performed at CMJAH was referred from CMJAH (1018 beds), Helen Joseph Hospital (HJH) (485 beds) and Rahima Moosa Mother and Child Hospital (RMMCH) (338 beds number) comprising 486 (80%) of 604 autopsies performed at CMJAH over the study period. The combined bed capacity of these three hospitals is 1841 in total (77). As seen in Table 5.3 there is a marked relative decline of autopsy

referrals from these three hospitals throughout the study time period. In the beginning of the study period CMJAH, HJH and RMMCH referred 46, 18 and 7 autopsy cases per year respectively, the referrals reduced to 8, 2 and 4 respectively at the end of the study period.

Table 5.3: Major referral hospitals to CMJAH mortuary and their respective autopsy requests.

Major referral hospitals to CMJAH mortuary				
Year	Referrals from CMJAH (1018 beds)	Referrals from HJH (484 beds)	Referrals from RMMCH (338 beds)	Total number of autopsies performed at CMJAH
2009	46	18	7	78
2010	36	15	9	67
2011	40	7	13	69
2012	38	7	6	60
2013	37	10	9	68
2014	31	15	12	66
2015	35	4	4	54
2016	24	8	9	53
2017	18	6	8	52
2018	8	2	4	37

The majority of autopsies performed at CHBAH were referred directly from CHBAH comprising 278 of the 285 (97.54%) total autopsies. CHBAH is the third-largest hospital in the world with a 3200 beds capacity (78). Table 5.4 shows that autopsy referrals followed an overall downward trend at CHBAH at the start of the study period, however, there has been a relatively slight increase in postmortems performed at CHBAH in the final two years of the study period.

Table 5.4: Major referral hospital to CHBAH mortuary and its autopsy requests.

Major referral hospitals to CHBAH mortuary		
Year	Referrals from CHBAH (3200 beds)	Total number of autopsies performed at CHBAH
2009	48	48
2010	39	40
2011	39	39
2012	31	31
2013	20	20
2014	15	15
2015	18	18
2016	15	15
2017	26	28
2018	27	31

5.9 Immediate CoD

The most common immediate causes of death were from the circulatory system (36%), infectious disease (29%) and unknown/indeterminate (16%). The immediate causes of death are summarised in Tables 5.5 and 5.6 as well as illustrated graphically in Figures 5.6 and 5.7.

With regards to the first 50 recorded cases:

The most common immediate causes of death recorded in the first 50 cases were related to the circulatory system accounting 48% of the cases, followed by 14 infectious cases (28%), and 6 unknown/indeterminate (12%). In contrast, nervous system, digestive system and neoplastic related causes of death were the least common among the first 50 autopsies in the study period- comprising 2% each. Diseases related to the following categories were not recorded; genitourinary tract, diseases of blood and blood forming organs and certain disorders involving the immune mechanisms, endocrine, nutritional

and metabolic diseases, genitourinary system, congenital malformations, deformations and chromosomal abnormalities, injury, poisoning and certain other consequences of external causes.

Table 5.5: Immediate causes of death in the first 50 cases.

First 50 recorded cases			
	Immediate Cause of Death	Number	%
1.	Diseases of the circulatory system	24	48
2.	Infectious diseases	14	28
3.	Unknown / Indeterminate	6	12
4.	Diseases of the respiratory system	3	6
5.	Neoplasms	1	2
6.	Diseases of the nervous system	1	2
7.	Diseases of the digestive system	1	2
8.	Diseases of blood and blood forming organs and certain disorders involving the immune mechanisms	0	0
9.	Endocrine, nutritional and metabolic diseases	0	0
10.	Diseases of the genitourinary system	0	0
11.	Congenital malformations, deformations and chromosomal abnormalities	0	0
12.	Injury, poisoning and certain other consequences of external causes	0	0

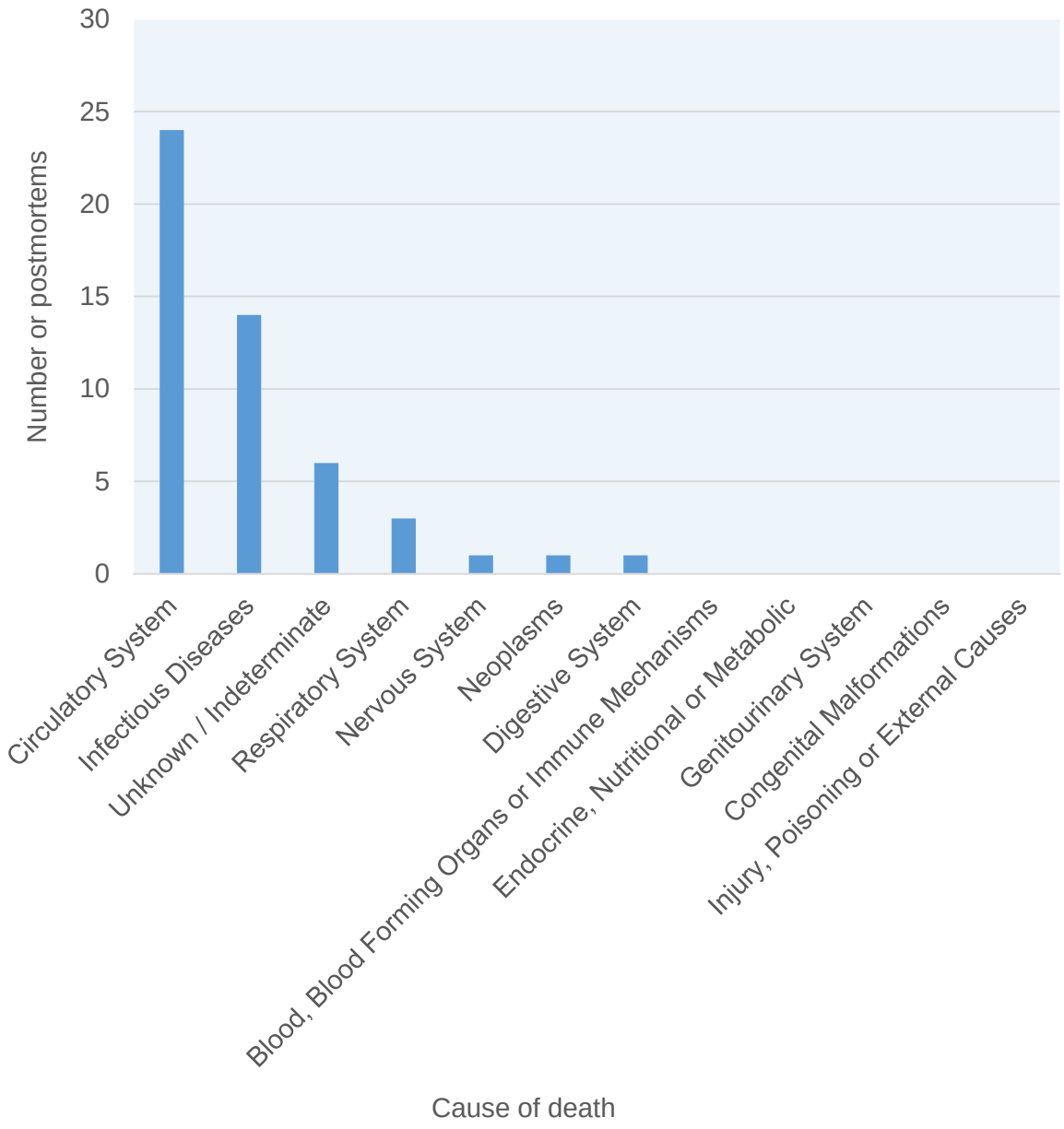

Figure 5.6: A bar chart of the immediate causes of death in first the 50 cases.

Regarding the last 50 recorded cases:

The most common immediate causes of death recorded in the last 50 cases were infectious in aetiology accounting for 15 of the cases (30%), 12 were from the circulatory system (24%), and 10 were unknown/indeterminate (20%).

The least common CoD was of the nervous system, digestive system and related to neoplasia which remained unchanged at 2% as well as endocrine, nutritional and metabolic diseases which accounted for 2%.

Diseases related to the following categories were not recorded: genitourinary system, and injury, poisoning and certain other consequences of external causes.

Table 5.6: Immediate causes of death in the last 50 cases.

Last 50 recorded cases			
	Immediate Cause of Death	Number	%
1.	Infectious diseases	15	30
2.	Diseases of the circulatory system	12	24
3.	Unknown / Indeterminate	10	20
4.	Diseases of the respiratory system	4	8
5.	Congenital malformations, deformations and chromosomal abnormalities	3	6
6.	Diseases of blood and blood forming organs and certain disorders involving the immune mechanisms	2	4
7.	Neoplasms	1	2
8.	Diseases of the nervous system	1	2
9.	Diseases of the digestive system	1	2
10.	Endocrine, nutritional and metabolic diseases	1	2
11.	Diseases of the genitourinary system	0	0
12.	Injury, poisoning and certain other consequences of external causes	0	0

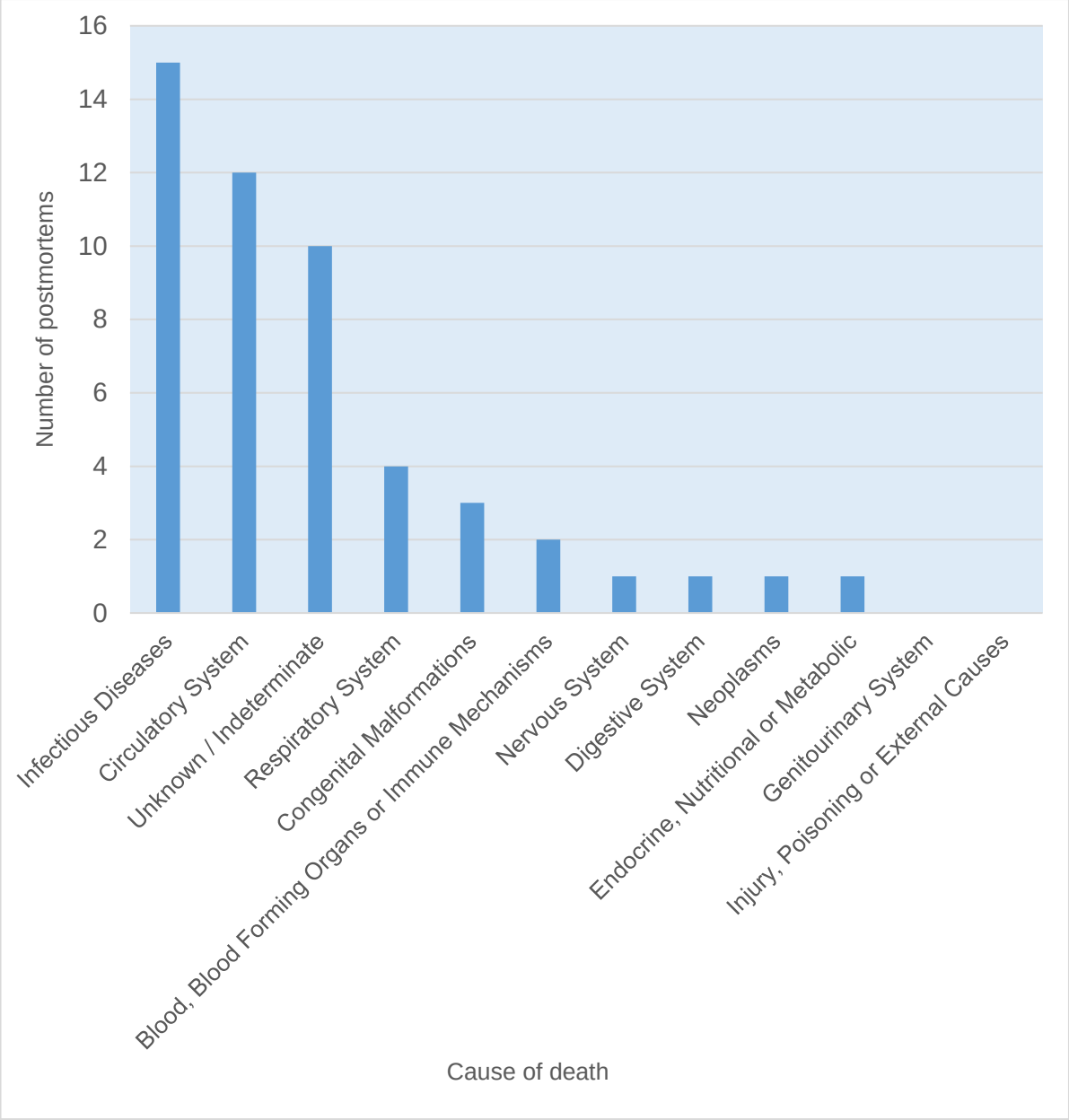

Figure 5.7: A bar chart of the immediate causes of death in the last 50 cases.

5.10 Underlying CoD

The most common underlying causes of death were from disease related to infections (23%), circulatory system (16%) and unknown/indeterminate (12%). The underlying causes of death are summarised in Tables 5.7 and 5.8 as well as illustrated graphically in Figures 5.8 and 5.9

Regarding the first 50 recorded cases:

The most common underlying causes of death recorded in the first 50 cases were from the circulatory system accounting for 11 (22%) of the cases, followed by 8 (16%) infectious disease cases and 8 (16%) cases related to neoplasia. Least commonly recorded underlying causes of death were from the nervous system, genitourinary system and related to injury or external which were 2% respectively.

Table 5.7: Underlying causes of death in the first 50 cases.

First 50 recorded cases			
	Underlying Cause of Death	Number	%
1.	Diseases of the circulatory system	11	22
2.	Infectious diseases	8	16
3.	Neoplasms	8	16
4.	Unknown / Indeterminate	4	8
5.	Endocrine, nutritional and metabolic diseases	4	8
6.	Congenital malformations, deformations and chromosomal abnormalities	4	8
7.	Diseases of blood and blood forming organs and certain disorders involving the immune mechanisms	3	6
8.	Diseases of the digestive system	3	6
9.	Diseases of the respiratory system	2	4
10.	Diseases of the nervous system	1	2
11.	Diseases of the genitourinary system	1	2
12.	Injury, poisoning and certain other consequences of external causes	1	2

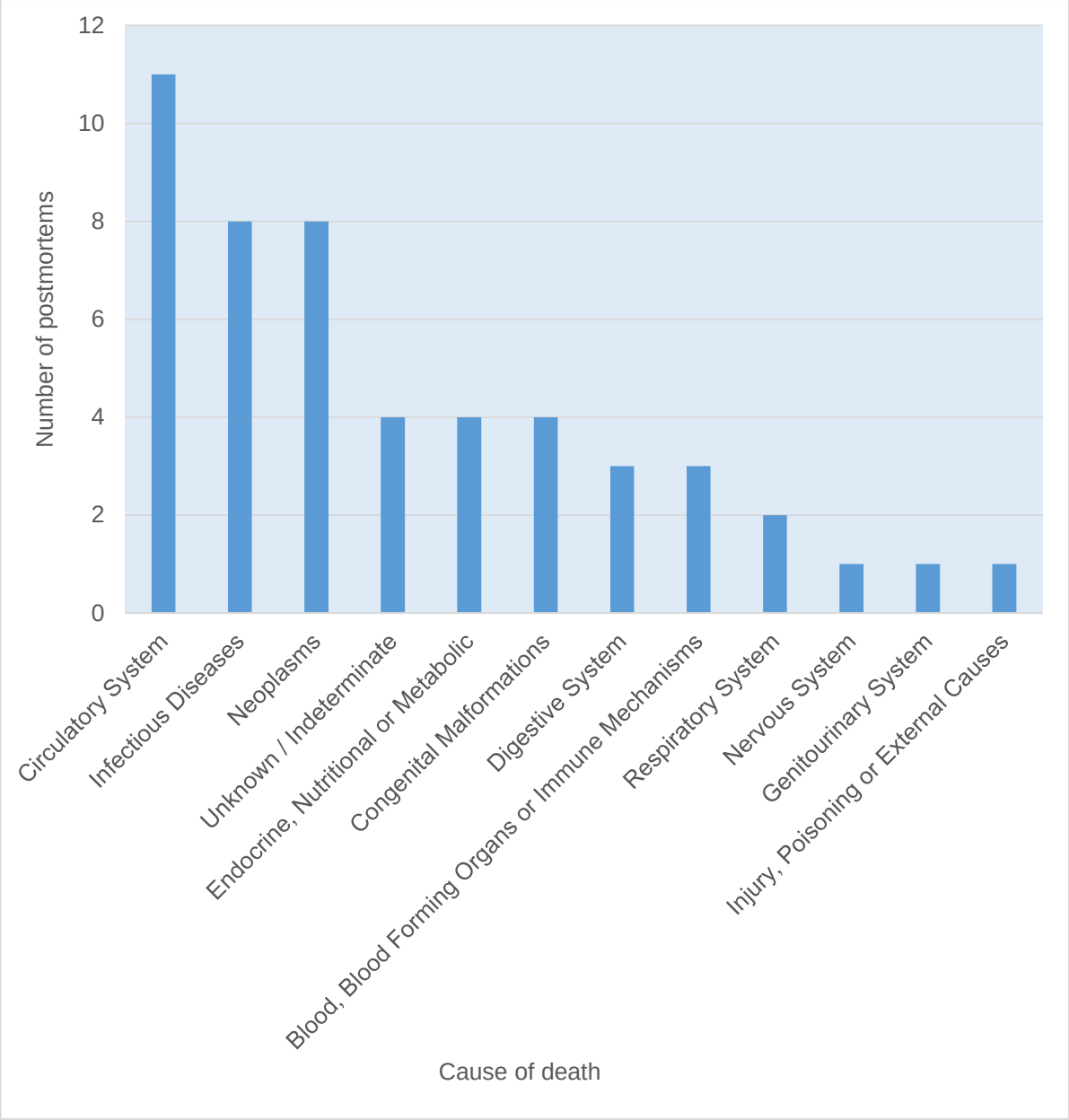

Figure 5.8: A bar chart of the underlying causes of death in the first 50 cases.

Regarding the last 50 recorded cases:

The most common underlying causes of death recorded in the last 50 cases were infectious in aetiology accounting for 15 (30%) of the cases, 8 (16%) were unknown/indeterminate and 6 (12%) were related to diseases of blood and blood forming organs and certain disorders involving the immune mechanisms. Underlying CoD related to the pulmonary system was the least common accounting for 1 (2%) case. Diseases

related to the following categories were not recorded; nervous system, genitourinary system and external causes.

Table 5.8: Underlying causes of death in the last 50 cases.

Last 50 recorded cases			
	Underlying Cause of Death	Number	%
1.	Infectious diseases	15	30
2.	Unknown / Indeterminate	8	16
3.	Diseases of blood and blood forming organs and certain disorders involving the immune mechanisms	6	12
4.	Diseases of the circulatory system	5	10
5.	Congenital malformations, deformations and chromosomal abnormalities	5	10
6.	Diseases of the digestive system	4	8
7.	Neoplasms	2	2
8.	Endocrine, nutritional and metabolic diseases	2	4
9.	Injury, poisoning and certain other consequences of external causes	2	4
10.	Diseases of the respiratory system	1	2
11.	Diseases of the nervous system	0	0
12.	Diseases of the genitourinary system	0	0

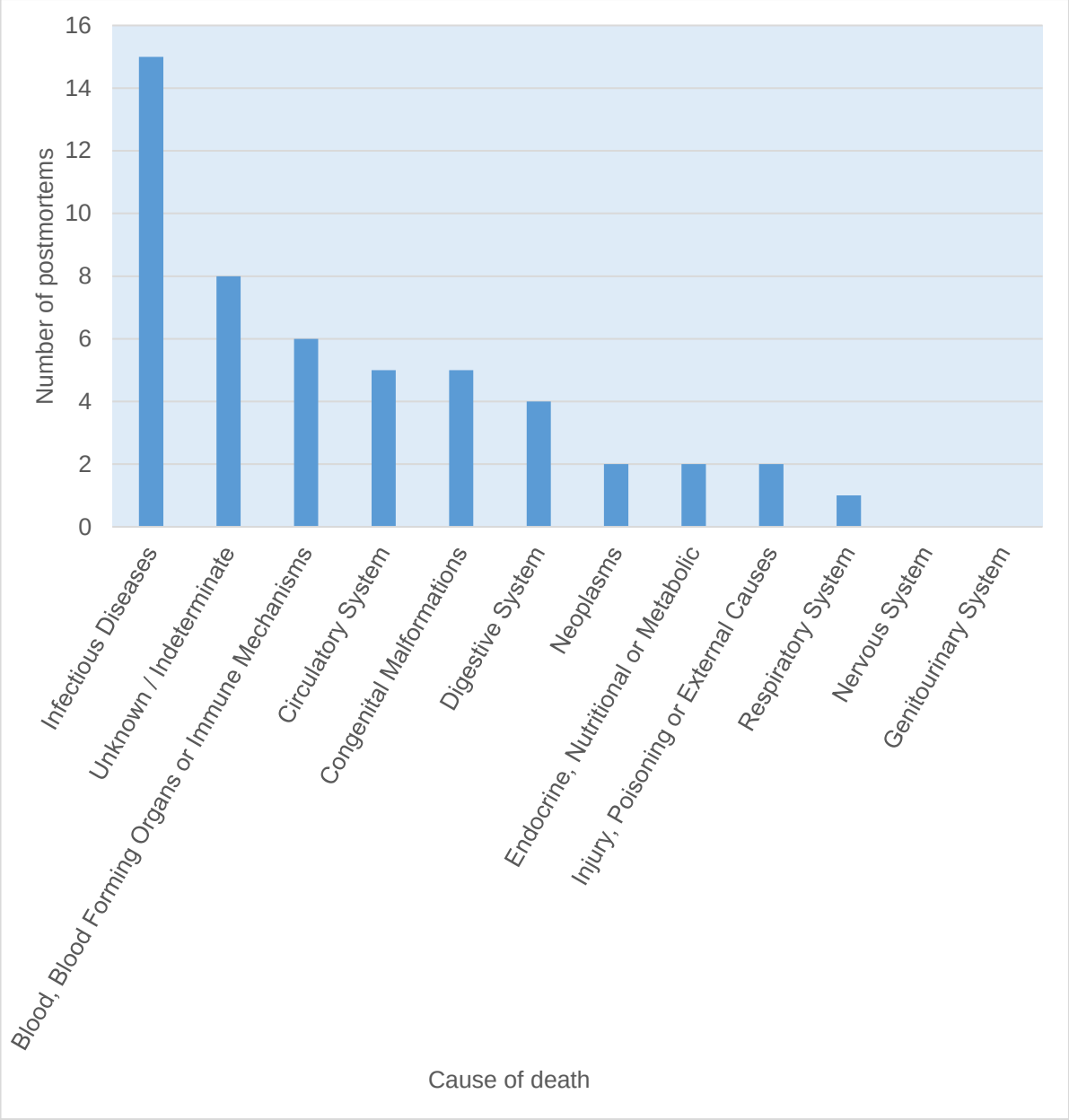

Figure 5.9: A bar chart of the underlying causes of death in the last 50 cases.

5.11 Infectious diseases

Of the first 50 and last 50 cases, a total of 38 cases (38%) the immediate or underlying CoD was related to infectious disease. A total of 10 cases (10%) were NMC2 as a result of tuberculosis and one case (1%) a NMC4 due to pseudomembranous colitis. The infectious related causes of death and associated NMC is shown in Table 5.9 and depicted in Figure 5.10.

Table 5.9: Infectious related causes of death and their associated NMC.

Infectious diseases in the first 50 and last 50 cases				
	CoD related to infectious disease (immediate/underlying)	% of CoD related to infectious disease	Number of NMC's	NMC category
First 50 cases	18	36%	5	NMC2 = 4 NMC4 = 1
Last 50 cases	20	40%	6	NMC2 = 6

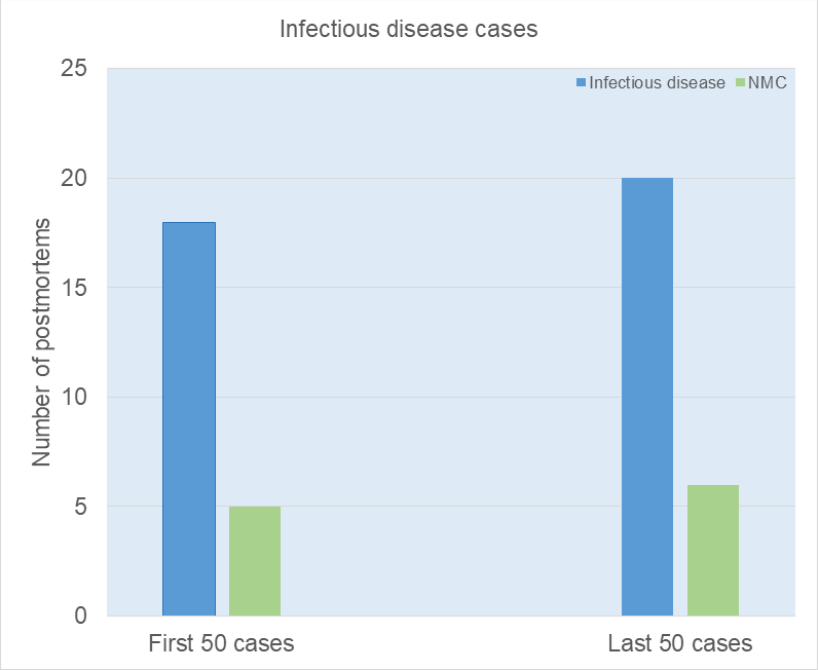

Figure 5.10: A bar chart of the infectious related causes of death and their associated NMC.

5.12 Autopsies and registrar training

The findings show that the declining number of autopsies results in a decrease in the number of registrars to be adequately trained. In the year 2009 the annual number of autopsies were sufficient to provide training for 10 registrars for that year, and in 2018 for only 4. Table 5.10 summarises the number of registrars that could be by trained according to the number of autopsies performed. The results show a relative increase in foetal, neonatal and paediatric autopsies at both CMJAH and CHBAH. Although there is an increase in the number of adult autopsies at CHBAH, a striking decline is seen in adult autopsies at CMJAH.

Table 5.10: Training capacity for registrars.

The number of postmortems according to age group and associated registrar training positions.						
Year	Number of adult postmortems	Number of potential registrars who could be adequately trained	Number of paediatric postmortems	Number of potential registrars who could be adequately trained	Number of foetal and neonatal postmortems	Number of potential registrars who could be adequately trained
2009	91	10.11	25	8.33	10	5.00
2010	74	8.22	22	7.33	11	5.50
2011	78	8.67	19	6.33	11	5.50
2012	55	6.11	24	8.00	12	6.00
2013	58	6.44	20	6.67	10	5.00
2014	47	5.22	21	7.00	13	6.50
2015	46	5.11	12	4.00	14	7.00
2016	49	5.44	11	3.67	8	4.00
2017	54	6.00	17	5.67	9	4.50
2018	37	4.11	20	6.67	11	5.50

CHAPTER 6

6 DISCUSSION

The aim of this study was to conduct an audit on autopsies performed within the Division of Anatomical Pathology, University of the Witwatersrand, Johannesburg and, to this end, significant insight has been gained into current trends. The study confirms that the total number of medical autopsies performed in our department decreased over the 10 year study period. The decline is seen at both CMJAH and CHBAH where a decline from 126 autopsies in 2009 to 68 in 2018 was observed. A more prominent reduction in numbers was seen at CMJAH where autopsies performed declined from 78 in 2009 to 37 in 2018 compared to CHBAH where 48 autopsies were performed in 2009 and 31 in 2018. Autopsy numbers at CHBAH did show a relative increase from 2016 towards the end of the study. The Division of Anatomical Pathology at the University of the Witwatersrand is the largest Anatomical Pathology training facility in the country and, therefore, this may represent similar trends in other departments elsewhere in South Africa.

The declining autopsy numbers seen in our department is in line with global trends, supporting the theory that our institution is facing similar challenges as other institutions around the world (2–5). This decline is also supported by a study conducted by Venter et al, at the University of the Free State in Bloemfontein, South Africa (14). Factors such as lack of quality control, reduced training with associated impaired diagnostic competencies, lack of interest in the field and diminishing autopsy-based research have been associated with declining autopsy numbers in the literature and these factors are also likely to play a role in the decline in local autopsy rates (1,2,6).

The declining numbers predominantly result from reduced referrals from the major teaching hospitals. CMJAH was the leading referral hospital in 2009 but became the second least contributing hospital in 2018. Similarly, HJH and RMMCH showed diminishing referrals over the study period. Despite the fact that CHBAH has the largest bed capacity it showed the least contributing referrals per bed number over the study

period. Teaching hospitals are expected to have the highest medical autopsy rates, however, our data shows that autopsy referrals in academic institutions are very low and on the decline (2).

Declining autopsy rates will have a significant impact on registrar training in the future. Adult autopsies have shown to contribute mostly to the declining numbers, therefore, the scarcity of adult autopsies will be the most limiting factor to attain qualification requirements. The numbers of postmortems available will either allow for a reduced number of registrars being trained at any one time or postmortems from alternative sources (e.g. forensics) should be made available to allow for adequate numbers for registrar training. This situation is not unique to this department and often encountered in other training institutions where adaptations are made to comply with training requirements. This does, however, raise concern for substandard training and exposure in the field of general pathology (49,51). To uphold the practice, alternatives have been implemented at other institutions globally. To maintain adequate autopsy numbers, registrars can 'share' autopsies or fulfil the requirement by rotating at a Forensic Pathology institution. In some histopathological training institutions, such as the RCP, autopsies form part of training but are not a requirement for graduation, allowing pathologists the choice to become 'autopsy pathologists' by obtaining a certificate of higher autopsy training (54,55). Alternatively, in line with modern medicine, medical autopsies can become part of a sub-speciality in anatomical pathology or one can become competent in autopsies by obtaining a diploma through Forensic Pathology (6,17).

Data from this study points to factors that influence autopsy requests and consent. These are important to be aware of as they affect autopsy rates. Our data shows the gender does not affect bias in autopsy requests as the number of male and female autopsies were similar, comparable gender ratios have also been documented in other studies (65,66). Contrarily, age has shown to play an important discriminator in autopsy requests. Overall, most autopsies were performed on adult patients (17 years of age and older). Paediatric (1 month to ≤16 years) autopsies were the second most commonly performed and foetal/neonatal (0 to < 1 month) the least commonly performed type of autopsy. By

looking at trends within these age groups, the number of foetal and neonatal autopsies stayed relatively unchanged, however, there has been a relative increase in paediatric postmortems in the final two years of the study period. The most noticeable decline in numbers was noted within the adult age group. These findings are overall consistent with data from other studies that also show a decrease in autopsy rate with increasing patient age (14,65,66). The increase in autopsies on younger patients may reflect the need for clinicians and family members to find understanding in the premature CoD or to contribute to medical knowledge (66).

Race and culture also impact autopsy requests and consent. The majority of autopsies documented were conducted on African patients which reflects the population distribution in South Africa (79,80). There was, however, a relative increase among White patients and a decrease among the other races which might be explained by cultural and religious beliefs with regards to autopsy consent. In the context of African culture, multiple factors may complicate the consent process and therefore result in decreased autopsies performed- such as delayed burial and complex community influences in granting consent (69). Furthermore, religions such as Islam and Judaism require burial within twenty-four hours and do not approve tissue retention (11).

Insight has also been gained into the spectrum of diseases autopsies reveal by investigating the causes of death and the implications thereof. The first fifty cases and last fifty cases were utilised as samples taken from the beginning and end of the study period to represent the study population.

Overall the 3 most commonly recorded immediate causes of death remain the same over the study period and were related to the circulatory system (36%), infectious disease (29%) and unknown/indeterminate (16%). Initially, in the first fifty cases, the causes of death related to the circulatory system (48%), followed by infectious disease (28%) and unknown/indeterminate (12%) were most commonly recorded. In the last fifty cases, the frequency changed as infectious diseases (30%) becomes the leading CoD, followed by

causes of death related to the circulatory system (24%) and unknown/indeterminate (20%).

Diseases related to infections (23%), the circulatory system (16%) and indeterminate (12%) were most commonly recorded as underlying causes of death. Within the first fifty cases, the most common underlying causes of death were related to the circulatory system (22%), due to infections (16%) and neoplasia (16%). In the last fifty cases, causes of death related to infection (30%) became more prevalent followed by the unknown/indeterminate (16%) and causes of death related to haematological or immune systems (12%).

The main immediate and underlying causes of death elucidated by this study is similar to the leading causes of death in other autopsy studies which are related to the circulatory system, neoplasia and infectious disease, however, diseases related to the CNS is less commonly found in our division (39,41,42). This may reflect clinical diagnostic confidence or may represent lower diagnostic sensitivity to these conditions.

Interestingly, of the entire sample size, a significant number- 16 cases (16%) of the immediate CoD and 12 cases (12%) of the underlying CoD are concluded as unknown or indeterminate. This diagnosis was more often made in both the immediate and underlying last fifty cases compared to the first fifty. An unknown diagnosis may negatively impact the clinicians understanding of the value of autopsies and affect subsequent autopsy requests, perpetuating the cycle of decreasing autopsy requests. The percentage of failure rate to establish a CoD is higher as compared to other studies which report a 1-5% failure rate to establish a CoD (2,27). This may be explained by limited diagnostic competence or may reflect the limited use of ancillary studies and molecular techniques that may increase diagnostic abilities.

Our data shows that infectious diseases play an important role in both immediate and underlying causes of death over the study period. Of the first and last fifty cases, infectious diseases were related to the immediate or underlying CoD in 38 cases (38%). In addition to this, a noteworthy percentage (10%) were NMC2 due to tuberculosis and one case (1%) a NMC4 due to pseudomembranous colitis. It is essential to be aware of specific Notifiable Medical Conditions as they are infectious diseases that are of public health importance and poses risks that can result in disease outbreaks or epidemics with high case fatality rates. Tuberculosis is an important NMC and exposure to it may contribute to the reluctance of pathologists, registrars and mortuary staff to engage in autopsies. Tuberculosis is estimated to be the leading cause of HIV/AIDS-related deaths globally (81). South Africa is rated as a high tuberculosis burden country according to the WHO and, therefore, it would be expected to have a significant number of deaths due to tuberculosis and even multidrug-resistant tuberculosis. Literature has shown that autopsy personnel are significantly at risk of TB infection during an autopsy and demonstrated that an autopsy unit had a much higher concentration of infectious particles compared to a clinical tuberculosis ward and that brief exposure puts one at high risk of transmission and subsequent infection (82,83).

Furthermore, in the majority of cases (77.39%), the HIV status was unknown, while the remaining 22.60% had a known HIV status at the time of autopsy. The HIV statuses recorded is expected to be higher in a hospital setting and does not correlate with national statistics. In the year 2009, the HIV prevalence among adults (15–49 years) in South Africa was 10.3% which is similar to our HIV status numbers, and in the year 2018, it was 20.4% which is much higher than the HIV statuses recorded, indicating that our data underrepresents the true number of HIV positive cases (84). The lack of known HIV status poses multiple issues in performing autopsies. Firstly, HIV is a hazardous infectious agent in itself and increases exposure to other related and opportunistic infections especially tuberculosis as discussed. Secondly, a masked HIV status diminishes the interpretation of CoD and limits comprehensive clinicopathologic conclusions.

This highlights the prominent role infections play in the CoD in our setting. As the HIV status and possible concomitant infections are not always known during an autopsy, required precautions should always be taken. All autopsies should be performed in a facility with adequate air handling systems and by personnel wearing appropriate personal protective equipment (85).

This descriptive study provides baseline information on autopsy practice at our institution and can function as a platform for further studies.

This present study is limited in its design in that an autopsy rate in relation to hospital mortalities was not calculated as per other studies. The hospitals' mortality rates were not pursued as this data is not provided to our Department and not readily available. Clinical diagnostic discrepancies were not evaluated as these were not always stated in the reports, a study assessing diagnostic discrepancies or error rates can also give greater insight into autopsy practice in our local setting. A follow-up study is proposed where autopsy rates and clinical diagnostic discrepancies can be assessed to compare with other international studies. Additionally, this audit can also be refined to act as a quality control method assessing the overall quality of autopsy practice in our institution by looking at the following aspects; autopsy performance, reporting, communication with clinicians, intradepartmental peer-reviewing of cases and quality of the mortuary facility.

As many other studies previously performed provide vast amounts of information on reasons for the decline from different stakeholders, this has not been done in our department and would also prove useful as a further study. Furthermore, there are significant areas in the field that are under-investigated such as the impact of autopsies on medical education and training, contribution to research, quality control, and impact on patient care which can be further investigated. Most importantly, there is an overall lack in data and evidence on the impact of autopsies on patient care, a study addressing this topic in our unique setting may be useful to illustrate the value of autopsies in South Africa.

CHAPTER 7

7 CONCLUSION

This study was undertaken as an audit on autopsies in our division to investigate the trend in autopsy numbers, assessing the demographical data and reviewing the spectrum of the cause of death. It has shown that there is a definite decline in the number of autopsies performed over the ten year study period. This institution is the largest of its kind in the country and therefore may represent similar trends in other departments elsewhere in South Africa.

The declining autopsy numbers in our department is in line with global trends implying that our institution is facing similar challenges to international institutions. Factors such as lack of quality control, reduced training with associated impaired diagnostic competencies, lack of interest in the field and diminishing autopsy-based research are associated with declining autopsy numbers internationally.

Importantly, the declining autopsy numbers limit registrar training in the field, as the available autopsy number provide for a decreasing number of registrars to have adequate training. This situation is not unique to this department and is often encountered in other training institutions where adaptations are made to comply with training requirements, however, this raises concern for substandard training and exposure in the field of general pathology. Quality registrar training is essential as trainees will become the ones who will uphold and further develop the practice in the future.

The demographic data shows that the majority of autopsies were performed on adults but there is a change in the trend with a relative increase in the number of autopsies performed on paediatric patients. This reflects the age group in which there is most commonly uncertainty regarding the CoD necessitating autopsy as a further investigation.

The spectrum of CoD elucidated shows that infectious diseases including HIV play an important role and impacts autopsy practice in our local setting.

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APPENDICES:

Appendix 1- Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr J De Bruin

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M190309

NAME: (Principal Investigator)	Dr J De Bruin
DEPARTMENT:	School of Pathology Department of Anatomical Pathology National Health Laboratory Service
PROJECT TITLE:	Is medical post mortem practice dying? An audit on post mortums in the Department of Anatomical Pathology, University of the Witwatersrand, Johannesburg, South Africa
DATE CONSIDERED:	2019/03/29
DECISION:	Approved unconditionally
CONDITIONS:	Reissued on 2019/08/26 - conditions removed
SUPERVISOR:	Drs G Davies and E McAlpine
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2019/04/05

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. I agree to submit a yearly progress report. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **March** and will therefore reports and re-certification will be due early in the month of **March** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

26/08/2019
Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

Appendix 2- Turn it in report

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ORIGINALITY REPORT

6%	3%	5%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Eva E. Tejerina, Rebeca Padilla, Elena Abril, Fernando Frutos-Vivar et al. "Autopsy-detected diagnostic errors over time in the intensive care unit", Human Pathology, 2018 Publication	1%
2	Burton, J.L.. "Clinical, educational, and epidemiological value of autopsy", The Lancet, 20070428/0504 Publication	1%
3	www.nature.com Internet Source	1%
4	worldwidescience.org Internet Source	<1%
5	"Proceedings of the 20th Congress of the International Ergonomics Association (IEA 2018)", Springer Science and Business Media LLC, 2019 Publication	<1%
6	Rupert Langer, Alexandra Tröhler, Beat Schnüriger, Mafalda Trippel et al.	<1%