PROSPECTIVE COHORT STUDY TO DETERMINE IF PERIOPERATIVE MORTALITY AT THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA HAS CHANGED COMPARED TO HISTORICAL DATA FROM 1987

BY

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Dissertation submitted to the University of Zambia in partial fulfilment of the requirements for the degree of Masters of Medicine in Anaesthesia and Critical Care

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DEDICATION

This dissertation is dedicated to my parents who have always taught me the value of hard work and encouraged me to aim higher. To my wife, for her encouragement, support and patience, can’t thank you enough. To my children, with dedication and hard work you can achieve anything in life.

DECLARATION

I, Dr. Henry Nchimunya hereby declare that this dissertation herein presented for the degree of master of medicine in anaesthesia and critical care has not been previously submitted either in whole or in part for any other degree at this or any other university, nor being currently submitted for any other degree.

SIGNED

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APPROVAL

This Masters dissertation of Dr. Nchimunya Henry is approved as fulfilling part of the requirement for the award of the degree of Master of Medicine in Anaesthesia and Critical Care by the University of Zambia.

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ABSTRACT

Despite low-income and middle-income countries (LMIC) being the regions of the world with the greatest gap in access to safe surgical and anaesthetic services, there are fewer published data for these countries on perioperative mortality indices. Global trends are that perioperative mortality has declined over the last five decades. Zambia has had two published studies over the last 30 years. The initial study conducted by Heywood, Wilson and Sinclair in 1987 revealed an overall sixth day inpatient perioperative mortality rate (POMR) of 7.55 per 1000 operations which was more than three times the current rate of high income countries. Surgical avoidable POMR was highest at 1.93 per 1000 operations, followed by administrative avoidable POMR at 0.85 per 1000 operations and then anaesthetic avoidable POMR lowest at 0.53 per 1000 operations. Some of the recommendations from this study resulted in the establishment of a trainining programme in anaesthesia and critical care, and procurement of modern anaesthetic and monitoring equipment. It was the lack of more recent knowledge to ascertain whether the quality of the Zambian surgical and anaesthetic services have improved in keeping with global trends that made it imperative to conduct a perioperative mortality study in the largest teaching hospital in Zambia as a follow up to the initial study.

Over a six months period we prospectively identified all patients who died within six days of surgery, having undergone a surgical procedure by either a general, regional or combined anaesthesia at the University Teaching Hospital in Lusaka. All demised patients had their records analysed by a specialist surgeon and anaesthetist to determine factors contributing to their death by consensus. The causes of death were classified as avoidable, partially avoidable and unavoidable. The deaths categorised as avoidable and partially avoidable were further categorised into contributing factors, namely anaesthetic, surgical, administrative cause or a combination thereof. The data on denomenator was collected from the surgical and recovery room registers. The numerator was the total number of all inpatient deaths within six days of the surgical procedure, with date of surgery being day one. A total of 9775 cases were captured with 449 of these being lost to follow up. The denominator was therefore made of 9326 cases. Seventy nine patients were detected to have died during the study period. The overall sixth day inpatient perioperative mortality rate (overall POMR) was found to be 0.85% (95% CI: 0.68-1.06) and the sixth day inpatient avoidable mortality rate (avoidable POMR) was found to be 0.42% (95% CI: 0.30-0.57). The sixth day inpatient anaesthetic POMR, surgical POMR and administrative POMR were found to be 0.04% (95% CI: 0.01-0.079), 0.19% (95% CI: 0.12-0.31) and 0.19% (95% CI: 0.12-0.31) respectively. Compared to the historical indices from 1987 by Heywood, Wilson and Sinclair the chi-square test revealed a difference of no statistical significance (x^2=0.411 with 1df, p=0.522). With regard to the 24 hour inpatient perioperative mortality indices, the overall POMR was found to be 0.30% (95% CI: 0.21-0.44). The 24hr inpatient avoidable mortality rate (avoidable POMR) was 0.17% (95% CI: 0.10-0.28). The 24hr inpatient anaesthetic, surgical and administrative avoidable POMR were 0.02% (95% CI: 0.00-0.08), 0.07% (95% CI 0.03-0.16) and 0.08% (95% CI: 0.03-0.16) respectively. The perioperative mortality indices at UTH have not reduced in comparison to the historical data from 30 years ago. This is contrary to global indices which have shown a downward trend over the last five decades.

Keywords: perioperative, mortality, numerator, denominator, avoidable

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ABBREVIATIONS

ASA	American Society of Anesthesiologists
CI	Confidence Interval
CO	Clinical Officer
CEPOD	Confidential Enquiry into Peri-Operative Death
DOT	Death on the Table
ENT	Ear, Nose and Throat
GCS	Glasgow Coma Scale
GRZ	Government Republic of Zambia
HICs	High Income Countries
ICU	Intensive Care Unit
LMICs	Low- and Middle- Income Countries
MICU	Main Intensive Care Unit
MOH	Ministry Of Health
Obs/Gynae	Obstetrics and Gynaecology
PCO	Principal Clinical Officer
POMR	Peri-Operative Mortality Rate
RTA	Road Traffic Accident
SHO	Senior House Officer
SMS	Short Message System
THET	Tropical Health and Education Trust

UTH	University Teaching Hospital
USA	United States of America
UNZABREC	University of Zambia Biomedical Research Ethics Committee

STUDY DEFINITIONS

24 hour inpatient perioperative mortality (24 hour overall POMR) was defined as death occurring from induction of general anaesthesia or the performance of a local procedure up to 24 hours after the anaesthetic was initiated.[8]

Sixth day perioperative mortality (sixth day overall POMR): a death occurring from the induction of general anaesthesia or regional anaesthesia up to the sixth day post operatively (with day one being the day of the operation).[6]

Avoidable death: a perioperative death for which consensus is made that there was evidence of mismanagement of a type and degree sufficient to account for the death.[6]

A probably avoidable death: was defined as a case where the consensus was that it was likely but not certain that the patient would have survived if the quality of care was improved.[7]

An "unavoidable death" (unavoidable POMR) was defined as a case where the consensus was that the patient would have died regardless of the quality of care.[7]

Avoidable perioperative mortality rate (avoidable POMR) was calculated by combining the deaths by consensus that were declared to be avoidable and probably avoidable.

An anaesthetic contribution to avoidable perioperative mortality (anaesthetic POMR) was defined as a death where improved care by the anaesthetic or surgical team could have prevented death, using currently available resources.[6,7]

A surgical contribution to avoidable perioperative mortality (surgical POMR) was defined as a death where improved care by the surgical team could have prevented the death, using currently available resources.

Administrative/systems of care contribution to avoidable death (administrative POMR) was when avoidability fell outside of the immediate remit of these teams and included organizational issues, nursing care and the availability of essential resources.[6,7]

CHAPTER ONE: INTRODUCTION

1.1 Background

The Lancet Commission on Global Surgery was launched in January 2014 to look into crucial gaps in knowledge, policy and action pertaining to improving access to safe surgical and anaesthetic services in low-income and middle-income countries (LMIC).[1] Access to safe surgical and anaesthetic services is vital to reduce mortality and morbidity for patients with disease conditions requiring surgical intervention.[1,9,20,21,24] The commission came up with six key indicators to assess surgical and anaesthetic safety, both at facility and national level. Perioperative mortality rate (POMR) was one of the key indicators considered to be easily measurable and was already being collected by most countries worldwide.[1, 9,24]

Perioperative mortality data has been collected for more than 150 years since the first recorded anaesthesia related death in Newcastle, United Kingdom involving a 15 year old girl who died within three minutes of induction for a minor procedure, a toenail removal.[2,3] High income countries (HIC) have databases where perioperative mortality data is collected continuously, for example the National Confidential Enquiry into Peri-Operative Deaths (NCEPOD) in the United Kingdom, which were necessary also gives case-by-case feedback to parties involved in patient mismanagement.[4]

There has been a global reduction in perioperative mortality which can be attributed to multiple factors including improvements in monitoring, human resources, equipment, access to operating theatres, understanding of modern anaesthetic drugs, to mention but a few.[5] Most LMICs however have little or no published data on perioperative mortality indices despite being the regions where the gaps in access to safe surgical and anaesthetic services are the greatest[5, 20,24]. Most studies show that the perioperative mortality indices are two to three times higher in LMICs compared to HICs.[5,24]

To date, available data in published articles and official reports on perioperative mortality indicate that the risk of death related to anaesthesia has declined over the years[3]. This limitation supports the need for ongoing audits and peer review of all of the complications relating to anaesthesia.

In Zambia, there have only been two perioperative mortality studies over the last 30 years. In other countries, especially the western world, studies have shown a significant decrease in perioperative mortality rates over the last five decades. The Heywood, Wilson and Sinclair[6] study carried out in 1987 at the University Teaching Hospital was the first published data with regards to perioperative mortality in Zambia.[6] The study focused on perioperative deaths that occurred within six days of the operation over a period of seven months and categorized the causes into avoidable and unavoidable.[6] This was done prospectively by reviewing the surgical records and mortuary records. The avoidable causes were further categorized into surgical, anaesthetic and administrative causes.[6] The sixth day overall perioperative mortality rate was found to be 7.55 per 1000 operations. The recommendations that were made after the study include: (i) setting up an academic anaesthesia department to encourage Zambian medical graduates to join the specialty; (ii) improving staffing levels especially in the anaesthesia department; (iii) improving recovery facilities and equipment maintenance; (iv) improving communication channels; (v) improving the blood transfusion facilities; (vi) emphasizing the need for combined surgical and anaesthetic audits. Of these, a postgraduate program in Anaesthesia has been set up and has been running for the last six years under the University of Zambia with support from the Tropical Health and Education Trust (THET) and some new modern anaesthetic equipment have been procured by the hospital.[7,19] However, low staffing levels across the board and erratic supply and misuse of blood products still remain a challenge. This made it imperative to conduct a follow-up study to assess the UTH's performance now 30 years on, taking into consideration the above changes as well as global declining perioperative mortality trends.

In 2012 a retrospective follow-up study on perioperative mortality at UTH was carried out by Lillie et al.[7] It indicated that perioperative mortality in Zambia had not changed in 25 years and concluded that the results may have been an underestimate as a significant number of patient mortality folders were not available for review during the study.[7]

In South Africa, the most recently published audits on anaesthetic related deaths were conducted by Harrison et al who surveyed deaths attributed to anaesthesia from 1956-1987, and also Coetzee et al who examined perioperative deaths from 1987 to December 1990.[4,8] Harrison defined death associated with anaesthesia as “death occurring during or within 24hrs of the anaesthesia or failure of the patient to regain consciousness after anaesthesia.”[4] The choice of the 24 hours period was arbitrary.[4]

A consensus meeting was held involving representatives of surgical and anaesthetic colleges and societies to obtain an agreement about which indicators were the most appropriate, and a credible measure for access to safe surgery and anaesthesia.[3,9] It was recommended that Perioperative Mortality Rate (POMR) be introduced as the health indicator of the quality and safety of surgical and anaesthesia services.[9] POMR is not only a measure of safety but also an indirect measure of access to surgical and anaesthetic services.[9] Poor access to safe surgical and anaesthetic services will result in delayed presentations which will reflect as both a higher mortality rate and a smaller number of procedures. More valuable information on access to surgical services may be gained by reporting the number of procedures per 10,000 or 100,000 populations.[9] It was also recommended to define POMR in two main time periods. That is death occurring on day of surgical procedure (or within 24 hours of the surgical procedure) and death occurring before discharge or within 30 days of operation - if means are available to follow up these patients.[9] Finally, interpretation of POMR for hospitals and at national level was to be done using simple measures of risk adjustment limited to four variables. These are urgency of procedure, age of patient, the condition being treated or procedure being performed and the American Society of Anaesthesiologists (ASA) status of the patient.[9]

For this study we decided to do an inpatient follow-up to the sixth day postoperatively in keeping with the Heywood, Wilson and Sinclair study to allow direct comparison[4]. The data analysis was primarily for sixth day inpatient perioperative mortality and secondarily for 24 hour perioperative mortality indices.

1.2 Statement of the problem

Perioperative mortality indices serve as a monitoring and evaluation tool for surgical and anaesthetic specialties to achieve improvement in clinical care. To do this, evidence has to be collected from clinical studies and audits, then appropriate feedback and recommendations should be implemented. In some developed countries, data on perioperative deaths is collected continuously and reports on the overall perioperative indices are produced annually, for example, the Confidential Enquiry of Perioperative Deaths (CEPOD) in the United Kingdom, which involves individual case follow-up and feedback to parties involved in the management of the cases. Unfortunately, this has not been the case for Zambia seeing that there have just been two published perioperative mortality studies done in the last three decades.

1.3 Study justification

The study of perioperative mortality is particularly important in the surgical and anaesthetic specialties. It is one of the key indicators used to measure access to safe anaesthetic and surgical services.[9] Heywood A.J. et al conducted the initial study on perioperative mortality at UTH, Zambia in 1987 and the sixth day inpatient perioperative mortality was found to be 7.55 per 1000 operations (OMR) and particular recommendations were made.[6] Global trends in the last 50 years have shown a reduction in perioperative mortality rate. Unfortunately, UTH has had a greater than 28 years gap on accurate data regarding perioperative mortality since the initial study. So, it was imperative that a follow up study be conducted to determine whether there has been a reduction in perioperative mortality which would be in keeping with the global trends. We hoped to fill this gap by conducting a prospective cohort study to determine the 24hr inpatient perioperative mortality as well as the current sixth day inpatient perioperative mortality rate at the University Teaching Hospital as a follow up to the initial study. The knowledge acquired from this study will be invaluable for many teaching hospitals in low- and middle-income resource settings to determine a tailored approach for data collection of perioperative mortality indices. This is in the quest to attain more accurate and more consistently collected data with the possibility of case to case feedback as is done with CEPOD. The study will help identify areas that need improvement, in order to reduce avoidable perioperative mortalities. The study will provide new knowledge on perioperative mortality indices for the academia and students of research which will be an invaluable contribution to the proposed Lancet Commission on Global Surgery pilot study on perioperative mortality in Zambia.

1.4 Research question

Has the perioperative mortality rate reduced at the University Teaching Hospital in keeping with the global trends?

1.5 Objectives

1.5.1 Main objective:

To determine the sixth day inpatient perioperative mortality rate at UTH.

1.5.2 Specific objectives:

1. To determine the 24 hour inpatient perioperative mortality rate at UTH.

2. To determine the inpatient avoidable perioperative mortality rate at UTH.

3. To determine the proportion of avoidable perioperative deaths attributed to anaesthetic, surgical or administrative factors.

4. To compare the 24 hour perioperative mortality rate at UTH with those from studies done within the region and internationally.

CHAPTER TWO: LITERATURE REVIEW

This literature review aims to firstly look at the global trends of perioperative indices by reviewing systematic reviews of perioperative studies, and secondly to review 24 hour perioperative studies available both internationally and regionally. Lastly we review available data on sixth to seventh day perioperative mortality data to compare with the initial sixth day inpatient perioperative mortality study .[6]

With regard to global trends, Bainbridge et al sought to determine whether the risk of perioperative mortality around the world had declined in the last fifty years and whether there were differences in temporal risk in high-resource versus low-resource settings.[5] The researchers reviewed all studies on perioperative mortality published before February 2011 that included more than 3,000 patients who underwent anaesthesia in a hospital setting. Of the 3,162 abstracts reviewed, 177 articles were retrieved and 87 studies representing 12.4 million administered anaesthetics were included in the study.[5] This study revealed that the risk of anaesthetic sole mortality in the first 48 hours post induction has decreased progressively over the last five decades from 0.357 per 1000 operations before the 1970s to 0.052 per 1000 operations in the 1970s-1980s and 0.034 in 1990s-2000s ($p=0.000001$).[5] The overall perioperative mortality declined over the decades from 10.603 per 1000 operations (95% CI: 10.423-10.784) before the 1970s to 4.533 per 1000 operations (95% CI: 4.405-4.664) in the 1970s-1980s and 1.176 per 1000 operations (95% CI: 1.148-1.205) in the 1990s-2000s ($p<0.0001$ across subgroups).[5] (Find studies reviewed in the Bainbridge et al study in appendix 2. Courtesy of Bainbridge.) A systematic review of mortality in anaesthesia was conducted by Brazilians Braz et al by reviewing perioperative studies published between 1954 and 2007, which also revealed a decline in anaesthesia related deaths to less than 1 per 10 000 anaesthetics in the last two decades.[10] Decline in the overall perioperative mortality rate was to less than 20 per 10 000 anaesthetics in developed countries but Brazilian studies revealed overall POMR of 19-51 per 10 000 anaesthetics in the same period.[10] This was in agreement with the Bainbridge study which revealed a two to three times risk of death after an anaesthetic in LIMC as compared to HICs.[5,10] Near home, Harrison et al conducted a 30-

year surveillance (1956-1987) study of anaesthetic mortality associated with 0.75 million anaesthetics administered at Groote Schuur Hospital, Cape Town.[4] The overall 24 hour anaesthetic mortality rate was found to be 0.19 per 1,000 anaesthetics.[4] "There was a six-fold decrease in the incidence, computed quinquennially, from 0.43 per 1000 anaesthetics in the first quinquennium to 0.07 per 1000 anaesthetics in the last".[4] This latter figure portrays a standard of safety in anaesthesia for patients equal to that in the developed countries.[4] It also demonstrates much faster improvements in anaesthetic safety with institution of the appropriate intervention, in agreement with the Braz et al study where the rate of decline in anaesthetic related mortality is higher than the overall mortality.[4,10]

With regard to 24 hour perioperative mortality, Arbous et al conducted a study entitled: Mortality associated with anaesthesia: a qualitative analysis to identify risk factors.[11] This study was conducted prospectively from 1 January 1995 to 1 January 1997 in three out of the twelve provinces in Holland (Zuid-Holland, Utrecht and Gelderland).[11] This accounted for 51 anaesthetic departments operating in 64 different hospitals and performing a third to half of the total surgical procedures in Holland.[11] The study population was 869,483, and all consecutive patients (n=811) who died within 24hrs of the operation or remained comatose unintentionally 24hrs after the anaesthesia were scrutinized to determine a relationship with anaesthesia.[11] The incidence of 24 hour overall perioperative mortality per 1000 anaesthetics was 0.88, that of perioperative coma was 0.05 and anaesthetic related deaths accounted for 0.14.[11] These values were comparable to both the Bainbridge et al and the Braz et al study.[5,10,11] Of the anaesthesia related deaths, 52% were associated with poor cardiovascular management, 48% with other anaesthetic management, 10% with ventilatory management and 10% with patient monitoring.[11]

McKenzie et al conducted a study in Zimbabwean Hospitals in 1992 whose objective was to determine and analyze perioperative mortality rate in the hope that the information obtained would lead to an improvement in standards of service delivery.[12] It was carried out at Harare Central and Parirenyatwa Hospitals, which are both referral centres; at the time of the study they had 1087 and 1031 operational beds respectively.[12] Both were serviced by a single anaesthetic department and had several surgical firms. The anaesthetic department then comprised of nine consultants, ten registrars, 15 senior house officers and 12 nurse anaesthetists.[12] The surgical services were provided by several surgical firms each comprising of a consultant, registrar, senior house officers and pre-registration house officers (interns).[12] Out of the 34,553 subjects who presented for a surgical procedure between 1st January and 31st December 1992 there were 89 deaths within 24 hours post the anaesthetic.[12] These patient records were scrutinized and further information was obtained from mortality meetings and confidential discussions. The main outcomes included incidence of Anaesthesia Associated Deaths (AAD), Avoidable Peri-Operative Mortality Rate (Avoidable POMR) and classification of avoidable into Surgical, Anaesthetic and Administrative factors.[12] AAD in this study was defined as death within 24 hours of anaesthesia or failure of a previously conscious patient to regain consciousness.[12] According to its definition AAD is equivalent to 24 hour Overall Perioperative Mortality Rate (Overall POMR). The incidence of AAD per 1000 anaesthetics was 2.58. This value was comparable to the studies from Brazil (1.9-5.1 per 1000 anaesthetics) but was more than the studies from HICs (<2 per 1000 anaesthetics).[10] The avoidable POMR was 1.34 per 1000 operations. Avoidable POMR was defined as deaths where there was mismanagement of a degree to have contributed the mortality. The surgical, anaesthetic and administrative POMR per 1000 operations were 0.80, 0.33 and 0.21 respectively.[12] The anaesthetic avoidable POMR was much higher (three times) as compared to the global trends as well as the Harrison et al study.[4,5,10] The commonest avoidable factors in order of frequency were uncontrolled haemorrhage, poor post-operative management and anastomotic dehiscence.

Coetzee et al in 1992 in South Africa published a study in the Southern African Medical Journal entitled; Perioperative mortality in the Anaesthetic service at Tygerberg Hospital, over a three and half year period from July 1987.[8] The aim of this study was to: (1) identify perioperative deaths associated the anaesthesia; (2) use the information to improve patient care; (3) identify problems associated with the evaluation process and thereby improve system of peer review.[8] In this study, a perioperative death was defined as death occurring from induction of general anaesthesia or the performance of a local procedure up to 24 hours after the anaesthetic was initiated.[8] Anaesthesia related death was defined as a death in which the anaesthetic technique could have contributed to the death but was not the sole cause of the death.[8] An anaesthetic death was defined as a death caused solely by the anaesthetic management.[8] Of the 94,945 procedures performed during the study period, there were 113 deaths within 24 hours.[8] The anaesthesia related mortality rate was 2.3 per 10,000 procedures.[8] The anaesthetic mortality rate was 1.1 per 10,000 procedures, just slightly over the values in developed countries (< 1 per 10 000 anaesthetics).[8,10] The 24 hour overall perioperative mortality was 11.9 per 10,000 procedures and was comparable to that in developed countries (< 20 per 10 000 anaesthetics).[5,8,10] The majority of the deaths (8.5/10,000) were attributed to a combination of trauma and haemorrhagic shock.[8]

Maman et al conducted a 24 hour inpatient perioperative mortality study over a six month period in 2002 in a tertiary hospital in Togo to determine the anaesthetic death rate, the causes of death and avoidable mortality of consecutive anaesthetics.[13] The anaesthetic service was provided by one physician anaesthetist and 74 nurses who have a three year basic training and thereafter an on the job training as anaesthetists. Of 1464 anaethetics performed, 30 patient died within 24 hours of their operation.[13] This revealed an overall 24 hour POMR of 2.57%, avoidable POMR of 1.5% and anaesthetic, surgical and administrative avoidable POMR of 0.75%, 0.07% and 0.68% respectively.[13] This was an extremely high overall mortality rate of greater than 13 times the global trends and the anaesthetic avoidable mortality rate is worse at greater than 75 times the global trends.[5,10,13] This was noted to be due to inadequately trained anaesthetic providers (most anaesthetics were administered by nurses) and lack of continuous monitoring as well lack of essential drugs for rapid sequence inductions (e.g. suxamethonium).

Hansen, Gausi and Merikebu also conducted a 24 hour perioperative study over a six month period at Lilongwe Central Hospital (LCH) in Malawi.[14] Of 3022 consecutive anaesthetics administered, 14 patients died within 24 hours of the operation.[14] The anaesthetic service was provided by a single physician anaesthetist, five clinical officers and four medical assistants. It revealed an overall 24 hour POMR of 4.63 per 1000 anaesthetics, avoidable POMR of 3.64 per 1000 anaesthetics and anaesthetic, surgical and administrative avoidable POMR of 1.99, 0.33 and 1.32 per 1000 anaesthetics respectively.[14] The overall POMR is two to three times greater than global trends and 1.5 times greater than the Zimbabwean study but almost five times less than the Togolese study.[5,10,11,13] The anaesthetic avoidable POMR was 20 times greater than global trends but three times less than the Togolese study.[5,10,13] What was common about the Malawian and the Togolese studies, was how less qualified anaesthetic providers correlated to a significantly higher anaesthetic mortality rate and hence overall mortality rate.[10,13,14] Part of the reason why these two studies had higher anaesthetic avoidable POMR could have been that the less qualified anaesthetic providers could not have a level headed discussion on the cause of death with their more senior surgical colleagues and ended up taking more of the blame. The lack of agreement of POMR indices between the Heywood, Wilson and Sinclair 1987 study and the Malawian study was probably because firstly the Heywood, Wilson and Sinclair study was a sixth day perioperative study while the Malawian study was a 24 hour perioperative study. Secondly the Heywood, Wilson and Sinclair study had better (not the best) qualified anaesthetic providers than the Malawian study.[6,14]

With regard to sixth day inpatient perioperative mortality, we had a challenge finding perioperative studies which went up to the sixth to seventh day postoperatively other than the two initial studies (Heywood, Wilson and Sinclair and Lillie et al), as most studies typically do 24 hour and/or 30 day postoperatively as recommended by most authorities on the subject.[1,3,5,9] Heywood, Wilson and Sinclair[6] in 1987 at the University Teaching Hospital (our study site) conducted the first perioperative mortality study in Zambia.[6] It was done over a period of seven months and captured 10,592 consecutive surgical procedures performed at the institution.[6] In the study, Perioperative Mortality was defined as an inpatient death occurring within six days of the operation with day one being the day of the operation.[6] Deaths were classified as either avoidable or unavoidable.[6] Avoidable deaths were those for which there was evidence of mismanagement of a type and degree sufficient to account for the death.[5] The causes of the avoidable deaths were further classified into surgical, anaesthetic and administrative factors.[6] The researchers prospectively followed up, reviewed and scrutinized patient files and sometimes mortuary records of all deaths within six days of the operation during the study period.[6] At the time of the study, UTH had a total bed space of 1,500, served the Lusaka District population of approximately one million and admitted referrals from all over the country (population of eight million).[6] There were five general surgical firms and four gynaecological and obstetric firms, each comprising of a consultant, senior registrar or registrar, one or two pre-registration house officers and sometimes an SHO.[6] The anaesthetic services depended heavily on clinical officer anaesthetists (COA). COA training includes an initial three year basic training as a clinical officer followed by a period of general duties.[6] Then a further one year of anaesthetic training to become a qualified COA and later more senior Principal COA. During this study, the Department of

Anaesthesia comprised of only 1 Consultant, 2 senior registrars, 1 SHOs, 3 Principal COAs, 12 qualified COAs and 8 student COAs. Eighty deaths in total during the study period occurred within six days of the operation resulting in an Overall Mortality Rate (OMR) of 7.55 per 1000 operations which was three times more than that of HICs currently and 1.5 times of the higher end of the index from the Brazilian studies.[5,6,10] There were 35 avoidable deaths giving an Avoidable Mortality Rate (AMR) of 3.3 per 1000 operations.[6] It was noted that major emergency cases were associated with both a higher OMR and AMR. Surgical AMR was highest at 1.93 per 1000 operations, followed by administrative AMR at 0.85 per 1000 operations and then anaesthetic AMR lowest at 0.53 per 1000 operations. The anaesthetic AMR was greater than five times that currently in HICs, as well as the Brazilian studies and the Harrison et al study.[4, 5, 10]

Lillie et al conducted a retrospective cohort study, identifying perioperative deaths by comparing the theatre and mortuary registers for the calendar year 2012 at the University teaching hospital in Lusaka, Zambia.[7] Patient records were reviewed when available by multiple independent raters from anaesthesia and surgery/obstetrics to identify avoidable causes of death.[7] The study revealed that of the 18,010 surgical patients operated on in 2012, 114 were identified as having died within six days of the surgery resulting in an estimated sixth day perioperative mortality rate of 0.63%.[7] This was not significantly different from the 1987 study. It was however noted that a large number of the patient records could not be retrieved to verify patient details and outcomes, and hence the 2012 perioperative rates were thought to underestimate actual perioperative rates.[7] The key factors leading to avoidable deaths were noted to include; delays in surgery, lack of readily available blood/blood products and poor postoperative care.[7] Of note is that the mortality rates were expressed in different ways for the different papers reviewed, but for direct comparison they were all converted to per 1000 procedures in the following table.

Table 1: The table below shows a summary of the literature review.

Year	Author	Post-op period follow up	Denominator	Numerator	Overall POMR /1000	Anaesthetic avoidable POMR/1000
2012	Bainbridge et al[5] (Meta-analysis)	48hrs	12.5M	Before 1970s	10.603	0.357
				1970s-1980s	4.533	0.052
				1990s-2000s	1.176	0.034
2012	Lillie et al[7] (Zambia)	6 days	18 010	114	6.3	1.05
2002	Maman et al[13] (Togo)	24hrs	1 464	30	25.7	7.5
2000	Hansen, Gausi and Merikebu[14] (Malawi)	24hrs	3 022	14	4.63	1.99
1997	Arbous et al[11] (Holland)	24hrs	0.87M	811	0.88	0.14
1992	Mckenzie[12] study (Zimbabwe)	24hrs	34 553	89	2.58	0.33
1992	Harrison[4] study (South Africa)	24hrs	750 000			0.19 (0.43-0.07)
1987	Coetzee[8] study (South Africa)	24hrs	94 945	113	1.19	0.23
1987	Heywood, Wilson and Sinclair[6] study (Zambia)	6 days	10 590	80	7.6	0.53

CHAPTER THREE: METHODOLOGY

3.1 Study site

Our study site is the University Teaching Hospital (UTH), in Lusaka, Zambia. Zambia in 2016 had a population estimated at 16.6 million and a high birth rate of 44 per 100 per year.[15] The country continues to have a low life expectancy of 60.8 years due to a number of factors including poor health services, high HIV/AIDS prevalence, and high infant and maternal mortality rates.[15] The UTH is the largest hospital in Zambia with one of the country's state-owned medical schools with a post-graduate program. It services the capital city Lusaka (estimated population 2,198,999 by 2010 census[16]) and also functions as the main referral centre for the entire country. The hospital's bed space has remained at 1,673 over the years despite the rise in the population, culminating in floor beds and congestion due to high patient turnover.[16, 17] This results in demand for safe anaesthetic and surgical services far outstripping the capacity of the institution. The patient burden is worsened by the fact that the hospital currently functions with less than 50% of the required nursing staff and only 60% of the required doctors.[13, 14]

3.2 Surgical and Anaesthetic Staff

The anaesthetic department at UTH consists of four permanent consultants plus two visiting consultants, 17 registrars, five senior house officers, three principle clinical officer anaesthetists, three clinical officer anaesthetists and four intern clinical officer anaesthetists. This is a slight increase in the number of staff as compared to the initial study in 1987. However, the staffing level is still inadequate for the surgical population. This is attributed to an increase in the population and also increase in the number of surgical firms at the institution. There are five general surgical firms, five orthopaedic firms, two urology firms and five obstetrics/gynaecology firms. Other specialties with a firm each include ophthalmology, maxillofacial, ENT, paediatric general surgery, spinal surgery and neurosurgery. Each firm is composed of a consultant(s), senior registrars, registrars, senior house officers and interns (pre-registration house officers).

3.3 Study Design

This was a prospective cohort study that involved the follow up of all consecutive surgical procedures and review of inpatient deaths between the administration of anaesthesia, up to the sixth day postoperatively. The inpatient follow ups to establish perioperative mortality were done prospectively but the file review of all inpatient deaths to establish causality and avoidability were done retrospectively. All consecutive surgical procedures were followed up prospectively up to the sixth day postoperatively during a six months study period. Trained research assistants retrieved patient records of deaths within the inclusion criteria that occurred during the period of the study. The patient records were then used to enter relevant information on to the data collection proforma. This was done by both a designated specialist surgeon and anaesthetist to classify avoidability, causality (surgical, anaesthetic, administrative or combination of the above), in keeping with the 1987 study. Information regarding the grading of the primary surgeon and anaesthetist involved were recorded. The identifying markers for both patients and medical staff involved in cases were left out. Further information was obtained by reviewing mortality meeting minutes, mortuary records and interviewing parties involved (i.e. surgeons, anaesthetists and nurses) in the cases if the form was deemed inadequate to come up with a conclusion on the cause of death.

3.4 Study Population

3.4.1 Denominator: The absolute number of all consecutive surgical procedures, defined as the incision, excision, or manipulation of tissues that required regional or general anaesthesia or profound sedation to control pain, undertaken in an operating room[4, 6], at UTH in the six months study period. This formed the cohort of the study population. This data was collected from the surgical registers and the recovery room registers. There were 9,775 cases that were performed at UTH that fitted the denominator description. There were approximately 4000 manual vacuum aspirations that were performed during the study period which were not included as part of the denominator because they were not done in an operating theatre. 449 cases were lost to follow up and were removed resulting in 9326 cases being used as the denominator for calculation of POMR indices.

3.4.2 Numerator: All inpatient deaths within six days of the surgical procedure with date of surgery being day one. This was the primary outcome.

3.4.3 Numerator Inclusion criteria:

Patients who had died between the administration of anaesthesia up to the sixth day postoperatively, whose procedures were performed in an operating room.

3.4.3 Numerator Exclusion Criteria:

- Patients who had died within the study period but whose surgical procedures were not performed in an operating room.
- Patient who had died on the surgical ward within the study period but did not undergo any surgical procedure.

3.5 Numerator Detection

- For death on the table (DOTs): The theatre nurse in charge reported DOTs to the chief investigator.
- Main intensive care unit (MICU): The principle investigator followed up all post-operative admissions to MICU.
- For surgical ward patients: A method of triangulation was employed to improve the detection of inpatient perioperative deaths during the study period. This was done by:

1. Involving ward clerks to separate mortality records meeting the inclusion criteria and informing the principle investigator.

2. Using research assistants who followed up and collected records for patient deaths identified from theatre registers that fit the numerator inclusion criteria. The patient folders were kept in a safe designated area pending record review.

3. Reviewing mortuary records for deaths from the surgical wards, then tracing the patient records to ascertain if the death fits the inclusion criteria.

3.6 Data Collection Process

The surgeons, anaesthetists, theatre nurses and other theatre staff as well as nursing staff on the wards were informed about the study. All consecutive patients that underwent a surgical procedure in an operating room were followed up to sixth day post operatively (with day one being the day of the procedure) or discharge, whichever came first. The records of the inpatients that died within this period were retrieved by the research assistants and stored in a designated, safe place until a set date for the review of the records. The principle investigator with a designated specialist surgeon and specialist anaesthetist, with the use of a data collection proforma reviewed the records to identify and categorize the causes of avoidable deaths by consensus into surgical, anaesthetic, administrative or combination of two or all three.

Data for the denominator was collected from the surgical patient registers and compared with the recovery room patient registers. The patient follow ups were triangulated by ward clerks, who communicated to the principle investigator using a Short Message System (SMS). The clerk checked each death on the surgical ward, whether the deceased had a surgical operation in the last six days leading to their death. They then sent an SMS of the record file number and the ward on which patient died to the principle investigator.

3.7 Variables

3.7.1 Primary outcome variables include:

- Mortality within six days of the operation

- Patient discharged within six days of the operation

3.7.2 Secondary outcome variables include:

- Age
- American Society of Anesthesiologists (ASA) score
- Urgency of operation
- Type of operation
- Grade of anaesthetist
- Grade of surgeon

3.8 Data Analysis

Based on the previous publication of perioperative mortality data, it was analyzed as:

- Demographic data of study population
- Number of deaths
- The spectrum of operations and specialties represented
- The grade of the operating surgeons involved
- The grade of the anaesthetist involved
- Avoidable deaths and related factors (categorized as surgical, anaesthetic or administrative)
- Age distribution of the perioperative deaths
- ASA score of the perioperative deaths
- Urgency of the surgical procedures for the perioperative deaths
- Access to surgical and anaesthetic services at UTH to the surrounding Lusaka population.

Primary analysis: The overall perioperative mortality rate was analyzed to predict a difference between the historical data from the 1987 Heywood, Wilson and Sinclair[6] study to the current rate using the chi-square test with a p-value of 0.05.

Secondary analysis: Data on the avoidability of the perioperative deaths was by detailed expert qualitative analysis based on case note review until consensus was reached with input from specialist anaesthetists, surgeons and obstetricians with data being summarized descriptively with a thematic analysis.

3.9 Ethical and Adminstrative Issues

All research leads were up-to-date with Good Clinical Practice[22] and the research was carried out adherent to the principles of the Declaration of Helsinki.[23]

To clarify issues relating to this study specifically:

- No patient, caregiver/relative or staff involved with any patient was contacted by the research team.
- No patient or person directly or indirectly involved in the care of the patients is identifiable in the final report.
- The research team made no contribution, extraction or alteration to the medical records of patients whose data was collected for the study.
- Opinions and judgments for categorization of data was not biased by anyone outside of the research study, or by any prior or additional knowledge of individual cases outwit what was held on the study forms and medical records.

All electronic data will be kept on encrypted data storage devices, and paper data will be archived for ten years.

3.10 Study Limitations

i. The study focused mainly on inpatient perioperative mortality and hence did not yield data on outpatient perioperative mortality.

ii. The study did not yield any data on the postoperative quality of life and/or level of disability following the surgical procedure.

iii. A thirty day perioperative mortality study as recommended by most authorities would have yielded more comprehensive data but however it comes at a very high cost for the follow ups.

CHAPTER FOUR: RESULTS

In a period of six months from 19th January to 18 July 2016, a total of 9,775 operations were followed up prospectively from all the theatres at the UTH. These included Phase V (the emergency and trauma theatre), Phase III (the elective theatre), D-block (the paediatric surgery theatre) and C-block (the obstetrics and gynaecology theatre). Of the 9,775 cases followed up, 449 cases (4.59%) were lost to follow up and these cases were mainly from phase V, the emergency theatres, where the registers had some missing pages, the post-op ward for this theatre block had one of its registers missing, all confounded by very poor and incomplete documentation. Lost to follow up meant that the theatre register showed that a case was done but record of where the patient went after the operation is not clear and hence the patient outcome could not be determined. This resulted in our denominator being reduced to 9326 procedures, that is minus the patients lost to follow up, for the purpose of mortality rate calculation.

Through triangulation, by follow up of individual cases prospectively using research assistants, an SMS alert system of perioperative deaths by ward clerks, review of theatre critical incident forms, mortuary records and MICU records, a total of 79 patients were suspected to have died as inpatients within six days after having surgery in any of the four theatre blocks. Of these cases, we were only able to retrieve 66 patient records for further review. Among these 66 cases, three were not actual files but the critical incident forms were the only record that was retrieved. These three files were classified as undetermined because there was not enough information from the critical incident forms to determine the contributory factors and final cause of death. Refer to Figure 1.

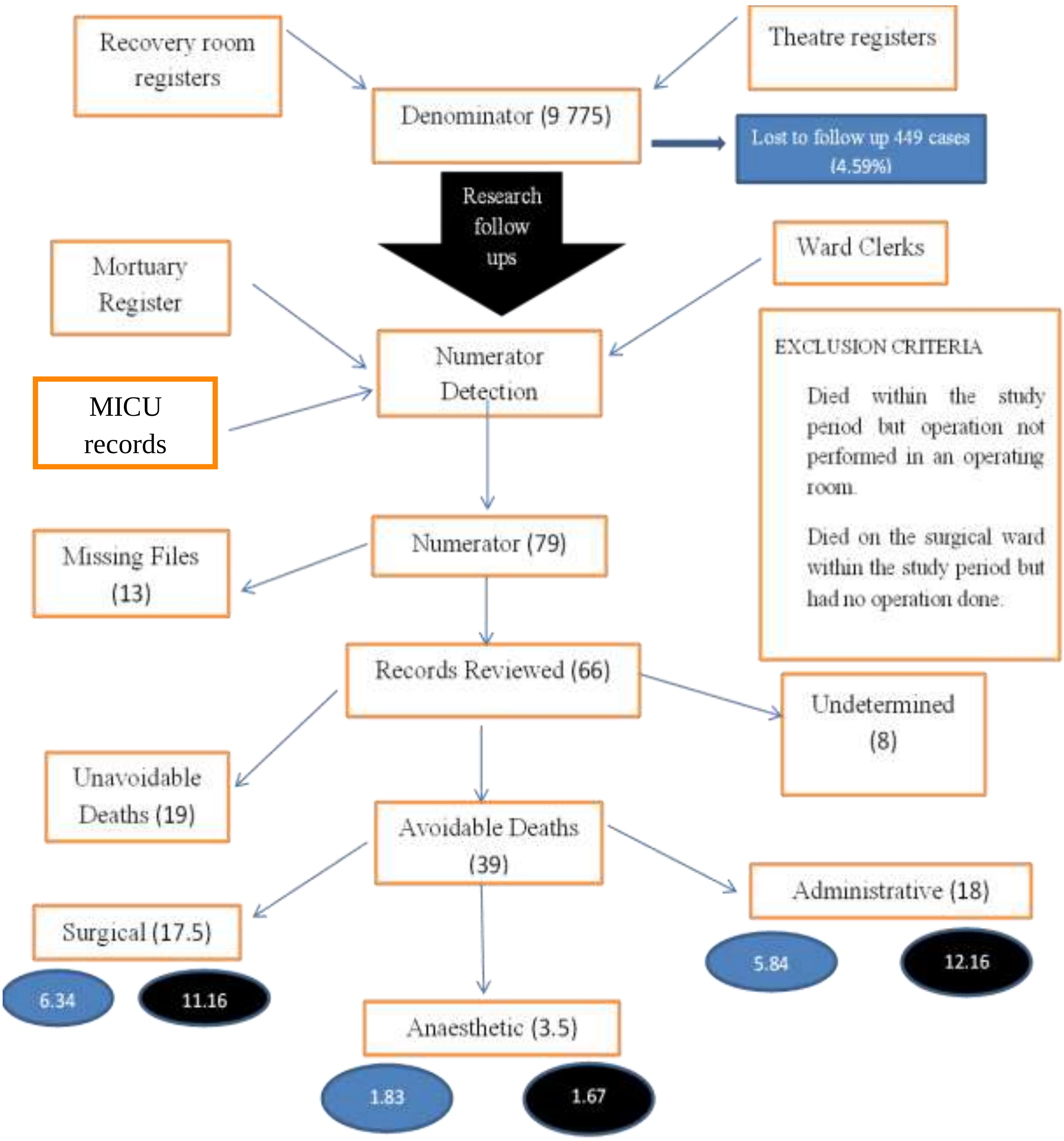

Figure 1. Showing flow chart for a prospect cohort study on perioperative mortality at the University Teaching Hospital in Lusaka, Zambia. Lighter shade (blue) is totally avoidable and the darker shade (black) is partially avoidable.

This made it difficult on further review to ascertain the causality of the deaths because of lack of adequate information pertaining to the events that lead to the patient's demise. During this study the patient record retrieval rate was found to be 84% (66 out of 79 records recovered for further review) which was much better compared to the 2012 sixth day inpatient mortality study by Emma Lillie et al which was conducted retrospectively and had a patient record retrieval rate of 52%.

Patient characteristics were shown in Table 2 and also illustrated in Figures 2 and 3. Among the reviewed perioperative mortality records, 43.9% of the cases involved a consultant surgeon/obstetrician (consultant was defined as a senior doctor who completed a locally or internationally recognized specialty training program[14]), while only 34% of cases involved a consultant anesthesiologist. Forty-five deaths involved patients who were less than forty years of age accounting for 68.2% (refer to Figure 2).

Table 2: Showing demographic data on mortalities and the cohort group.

	Numerator	Denominator
Gender		
• Male	43 (65%)	4777 (48.9%)
• Female	23 (35%)	4998 (51.1%)
Age distribution		
• 0-9	20 (30%)	2069 (21.2%)
• 10-19	3 (4.5%)	1104 (11.2%)
• 20-29	5 (7.6%)	2313 (23.7%)
• 30-39	17 (26%)	2106 (21.5%)
• 40-49	7 (11.6%)	949 (9.7%)
• 50-59	4 (6.1%)	484 (5.0%)
• 60-69	3 (4.5%)	309 (3.2%)
• 70-79	3 (4.5%)	159 (1.6%)
• >80	0	50 (0.5%)

• Not documented	4 (6.1%)	232 (2.3%)
Urgency		
• Elective	12 (18%)	2574 (26.3%)
• Emergency	54 (82%)	7201 (73.7%)
Type of Surgery		
• Minor	1 (1.5%)	4676 (47.8%)
• Major	65 (98.5%)	5040 (51.6%)
• Not documented	0	59 (0.6%)
Surgical specialty		
• General surgery	30 (45%)	3474 (35.5%)
• Paediatric surgery	14 (21%)	627 (6.4%)
• Obs/Gynae	4 (6.1%)	2421 (24.8%)
• Neurosurgery	11 (16.7%)	218 (2.2%)
• ENT	1 (1.5%)	177 (1.8%)
• Orthopaedic surgery	2 (3%)	2223 (22.7%)
• Cardiac	4 (6.1%)	38 (0.4%)
• Urology	0	246 (2.5%)
• Ophthalmology	0	166 (1.7%)
• Plastic	0	108 (1.1%)
• Renal surgery	0	29 (0.3%)
• Spinal surgery	0	14 (0.1%)
• Maxillofacial surgery	0	32 (0.3%)
• Not documented	0	2 (0.0002%)
ASA Score		
• I	4 (6.1%)	
• II	4 (6.1%)	
• III	23 (34.8%)	

• IV	34 (51.5%)
• V	1 (1.5%)
Most senior surgeon present	
• Consultant/senior registrar	29 (43.9%)
• Registrar	28 (42.4%)
• SHO/intern	9 (13.6%)
• CO	0
Most senior Anaesthetist present	
• Consultant/Snr registrar	23 (36.5%)
• Registrar	23 (36.5%)
• SHO/intern	0
• CO	11 (16.7%)
• None	8 (12.1%)
• Not documented	1

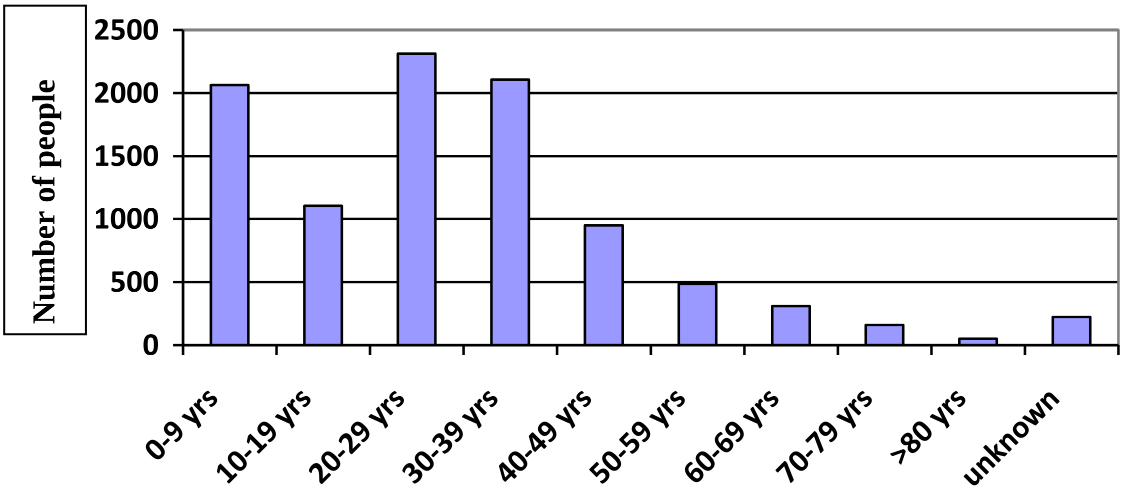

Figure 2: Age distribution of the surgical population at UTH during the study period of six months.

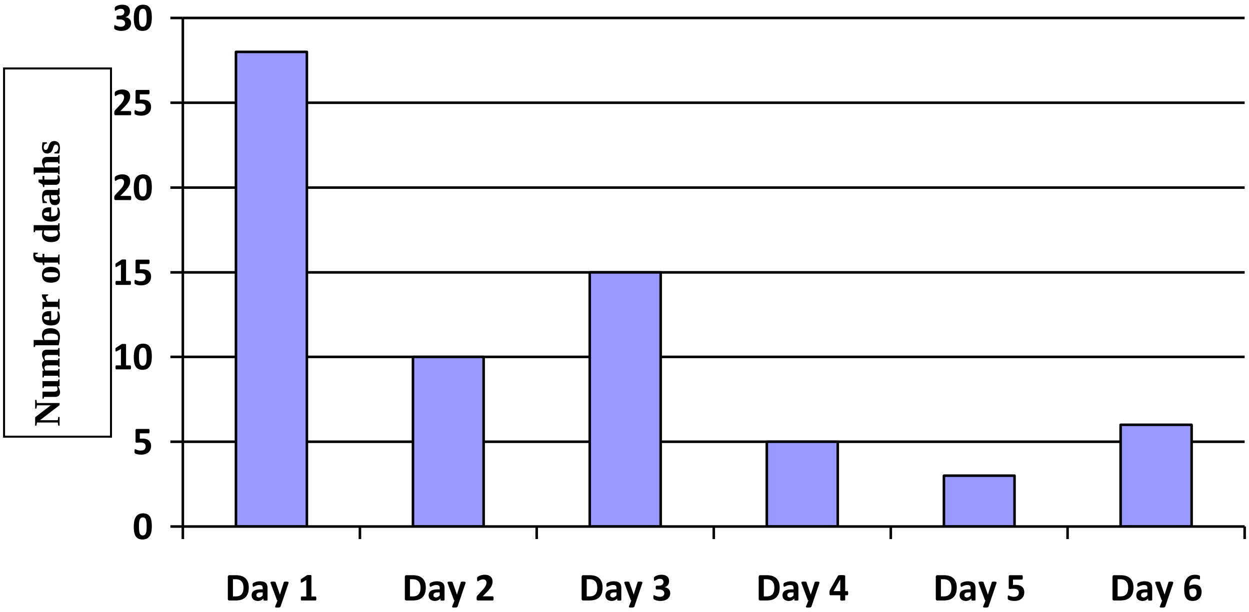

Figure 3: Number of perioperative deaths by post-operative day.

When it came to determining the causality and avoidability of the perioperative deaths, two reviewers (consultant surgeon and consultant anaesthetist) from the group of consultant that agreed to take part in the study, sat together per case record review. Consensus was reached on causality for 63 of the records, while the remaining three mortalities were declared as undetermined based on the fact that only the critical incident forms were recovered which were deemed to not have enough information to reach a consensus on causality of the deaths.

Thirty-nine cases were considered as avoidable (59.1%). Of these 14 cases were considered definitely avoidable (21.2%) and 25 cases were probably avoidable (37.9%). Nineteen cases (28.8%) were thought to be unavoidable and 8 cases (12.1%) were declared as undetermined (Patient records were deemed to not have enough information to reach a consensus on causality of the deaths) as shown in Table 3 and factors contributing to the 39 avoidable deaths were shown in Table 4. Refer to Figure 1 as well.

Table 3. Showing causes of death and number of unavoidable, avoidable and partially avoidable of each cause.

CLINICAL CAUSE OF DEATH	Unavoidable (n=19)	Avoidable (n=14)	Partially avoidable (n=25)
Abdominal/pelvic sepsis	6	1	10
Head injury	2	1	3
Haemorrhage	2	5	0
Bowel obstruction	0	0	3
Respiratory failure (excluding aspiration	1	4	2
Metabolic/renal/electrolyte disorder	0	2	1
Malignancy	4	1	1
Aspiration vomitus/pus	0	0	1
Others	4	0	4

*unclear/undetermined=8 cases

Table 4. Factors contributing to the 39 avoidable deaths.

SURGICAL AVOIDABLE CAUSES	
• Delayed surgical treatment	17
• Poor preoperative management	7
• Poor postoperative management	9
ANAESTHETIC AVOIDABLE CAUSES	
• Poor airway management	1
• Poor preoperative management	6
• Poor perioperative management	2
• Poor care during recovery	1
ADMINISTATIVE AVOIDABLE CAUSES	
• Insufficient/ no blood products	4
• Poor communication	2
• Poor recovery facilities/ward	14
• Lack of emergency essential supplies	2
• Equipment failures	0
• Lack of laboratory support	6
• Delayed access to operating rooms	5
• Delayed or lack of access to intensive care facilities	3

n> 39 because some patients were affected by more than one factor of a different type.

Box 1 shows summarized de-identified examples of avoidable perioperative deaths that were reviewed for purpose of assigning a cause of death and avoidabilities of the patient deaths and the categorical contributory factors were illustrated in figure 4.

Box 1: includes de-identified examples of avoidable deaths.

Avoidable mortality attributed to surgery (and systems of care)

A five day old neonate (ASA III) with duodenal atresia who underwent laparotomy. Operation went well but postoperatively the baby was prescribed a dose of pethidine that was four times greater than the maximum advised dose per body weight by the surgical team. The baby died in the immediate post-op period. Delayed access to surgery was the commonest surgical complication. E.g. Neurosurgical patient admitted with a GCS 11/15 after an assault was only reviewed by neurosurgeons two hours post admission at which time the GCS was 6/15 and a Diagnosis of Epidural Haematoma in traumatic brain injury after CT scan. Operation was done ten hours post admission at when the GCS was 3/15 and it remained so till his death on the sixth day postoperatively. By day two postoperatively he was declared to have had brainstem death.

Avoidable mortality attributed to anaesthesia (and surgery)

A three year old child (ASA III) with recurrent laryngeal papilloma for direct larygoscopy and excision. An inhalation induction was started then 20mg propofol was given which lead to airway obstruction (can't intubate, can't ventilate scenario), four failed attempts were made at intubation with different sized tube. Tracheostomy was performed with an incomplete tracheostomy set with a lot of difficulty that resulted in bilateral pneumothoraces and hypoxic arrest. Child was resuscitated but died three days later from brainstem death. Consensus was that the intubation should have been attempted while the child was still spontaneously breathing on the inhalation anaesthetic without the propofol which leads to apnoea.

Avoidable mortality attributed to systems of care (administrative and surgery)

A male unknown adult admitted as RTA victim with severe head injury and multiple fractures. He was reviewed by surgical unit 8 hours post admission, neurosurgical unit 9 hours post admission. Diagnosis of subdural haematoma was made and the operation was done 15hrs post admission due to lack of a readily available neurosurgical set. There was no intensive care unit space available both preoperatively and postoperatively despite having GCS<5 since admission. Patient only received one unit blood preoperatively and died on day three postoperatively due to brainstem death and multiple organ failure.

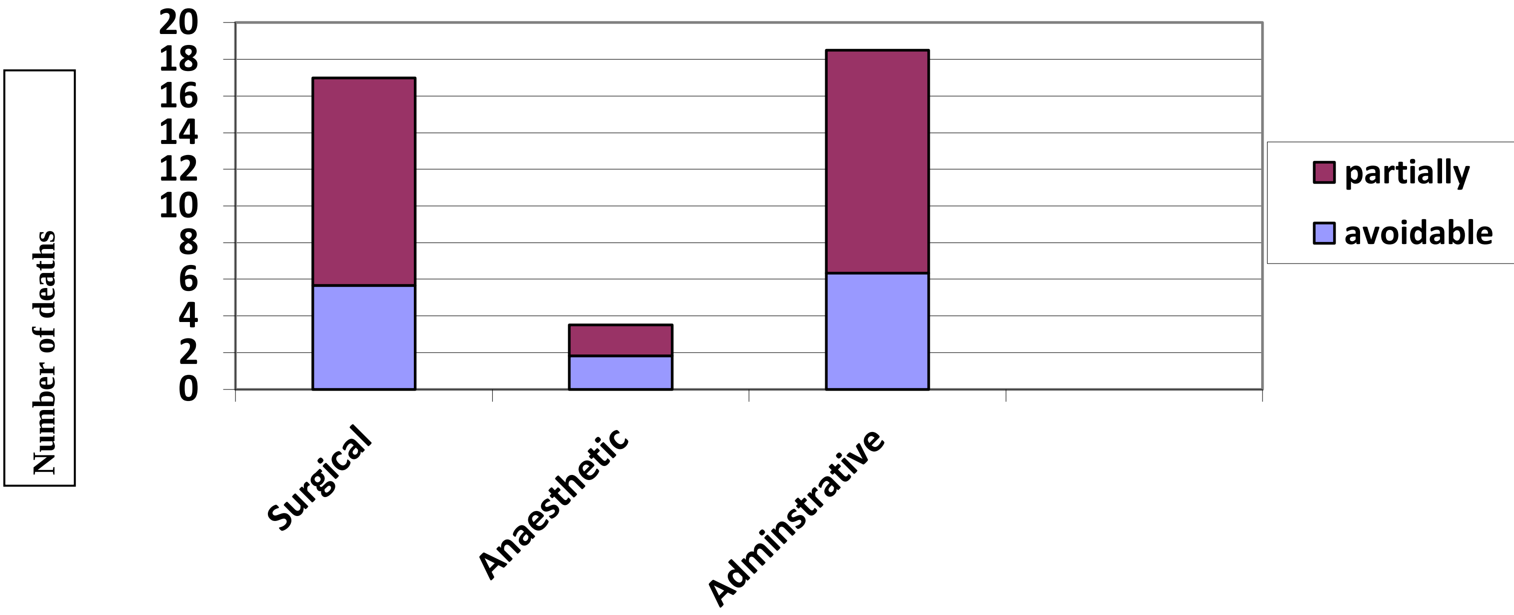

Figure 4: Illustrates the contribution of surgery, anaesthesia and administrative or systems of care to the avoidable deaths.

The overall sixth day inpatient perioperative mortality rate was found to be 0.85% (95% CI: 0.68-1.06) and this excluded patients that were lost to follow up. Of the avoidable and probably avoidable deaths combined, 21 cases (53.85%) had contributory factor/factors from one party (either anaesthetic, surgical or administrative cause/s), 15 (38.46%) had two parties as contributory factors (combination of two) and only 3 (7.69%) had all three parties as contributory factors. In cases were only one party was identified as cause of death e.g. anesthetic cause, it was assigned one point. If two parties were identified e.g. anaesthetic and surgical causes, they were each assigned one half of a point. If all three parties were involved, they were each assigned one third of a point. This is the reason why some figures in figure 1 are fractions. The sixth day inpatient avoidable mortality rate (AMR) was found to be 0.42% (95% CI: 0.30-0.57). The sixth day inpatient avoidable anaesthetic POMR, surgical POMR and administrative POMR were found to be 0.0% (95% CI: 0.01-0.079), 0.19% (95% CI: 0.12-0.31) and 0.19% (95% CI: 0.12-0.31) respectively. Compared to the historical indices from the 1987 study by Heywood, Wilson and Sinclair[6] which had an overall sixth day inpatient mortality of 0.75%, the chi-square test revealed a difference of no statistical significance (x^2=0.411 with 1df, p=0.522).[6] The avoidable POMR, anaesthetic POMR, surgical POMR and administrative all with the chi-square test revealed a difference of no statistical significance as shown in Table 5.

Table 5. Shows a comparison of 6th day inpatient perioperative mortality indices.

STUDIES	POMR Indices (rates)	denominator	numerator	Overall POMR	Avoidable POMR	Anaesthetic POMR	Surgical POMR	Administrative POMR
Current study 6th day POMR (2016)	POMR Indices	9 326	79	0.85%	0.42% (39)	0.04% (3.5)	0.19% (17.5)	0.19% (18)
Historical study: Heywood, Wilson and Sinclair[6] study 6th day POMR (1987)	POMR indices	10 592	80	0.75%	0.33% (35)	0.053% (5.5)	0.193% (20.5)	0.088% (9)
	X^2 with 1 df			0.411	0.801	0.013	0.007	3.505
	P- value			0.522	0.371	0.908	0.933	0.061
	Statistical significance			none	none	none	none	none
Lillie et al[7] study 6th day POMR (2012)	POMR indices	18 010	114	0.63%				
	X^2 with 1 df			3.662				
	P-value			0.056				
	Statistical significance			none				

With regard to the 24 hour in patient perioperative mortality indices, the overall 24 hour inpatient perioperative mortality rate was found to be 0.30% (95% CI: 0.21-0.44) as seen in Table 6. Of the 28 24hr inpatient perioperative deaths, 6 (21%) were totally avoidable, 10 (36%) were probably avoidable, 6 (21%) were unavoidable, 6 (21%) were unclear/indeterminate due to insufficient documentation to determine the causality. The combined 24hr inpatient avoidable mortality rate was 0.17% (95% CI: 0.10-0.28). The 24hr inpatient anaesthetic, surgical and administrative avoidable perioperative mortality rates were 0.02% (95% CI: 0.00-0.08), 0.07% (95% CI 0.03-0.16) and 0.08% (95% CI: 0.03-0.16) respectively. Table 6 shows the comparison of the 24 hour inpatient POMR indices with studies done internationally and regionally with appropriate chi-square test and p-values for assessment of differences of statistical significance.

Table 6. Showing the comparison of 24 hour inpatient perioperative mortality indices to regional and international 24 hour inpatient perioperative mortality studies.

STUDIES	POMR Indices (rates)	denominator	Numerator	Overall POMR	Avoidable POMR	Anaesthetic POMR	Surgical POMR	Administrative POMR
Current study 24hr POMR (2016, Zambia)	POMR indices	9 326	28	0.30%	0.17% (16)	0.02 % (2.17)	0.07% (6.67)	0.08% (7.17)
Maman et al[13] study 24hr POMR (2002, Togo)	POMR indices	1464	30	2.57%	1.5% (22)	0.75% (11)	0.07% (1)	0.67% (10)
	X^2 with 1 df			67.549	59.150	49.730	0.008	25.795
	P-value			0.0001	0.0001	0.0001	0.930	0.0001
	Statistical significance			Extreme	Extreme	Extreme	None	Extreme
Hansen, Gausi and Merikebu[14] study 24hr POMR (2000, Malawi)	POMR Indices	3022	14	0.46%	0.36% (11)	0.20% (6)	0.03% (1)	0.13% (4)
	X^2 with 1 df			1.329	3.024	11.692	0.142	0.320
	P-value			0.249	0.082	0.004	0.707	0.571
	Statistical significance			None	None	Extreme	None	None
Mckenzie[12] study 24hr POMR (1992, Zimbabwe)	POMR indices	34 553	89	0.26%	0.134% (46)	0.033% (11.4)	0.080% (27.6)	0.021% (7.3)
	X^2 with 1 df			0.353	0.519	0.032	0.033	5.298
	P- value			0.553	0.471	0.859	0.856	0.021
	Statistical significance			none	None	None	None	Present
Arbous et al[11] study 24hr POMR (1997, Holland)	POMR indices	869 482	811	0.09%		0.014% (114)		
	X^2 with 1 df			30.011		0.051		
	P- value			0.0001		0.821		
	Statistical significance			Extreme		none		

CHAPTER FIVE: DISCUSSION

Patient characteristics on age distribution, as shown in Table 2, revealed that the patients who presented for surgery during the study period were of a young age in common with the historical data but in contrast to HICs where the majority of the patients are older. 78% of the cases followed up were below 40 years of age; this was also reflected in the mortality group (numerator) as 69% and in the avoidable mortality group as 69%. This was in agreement with other studies done in African countries including the African Surgical Outcomes Study (ASOS) which showed a younger age of patients dying postoperatively in comparison to HICs.[5, 12, 13, 24] Despite the age group for patients enrolled to the ASOS study being over 18 years, the median was found to be 38.5 signfying a surgical population with a younger age group.[24] The male to female ratio revealed that twice as many males died but the ratio was equal in the follow up group or cohort (denominator). This was in agreement with the Arbous et al study where twice as many men died postoperatively but in contrast with the McKenzie study where an approximately equal sex ratio of the patients died postoperatively.[11,12] This could be reflective of poor maternal services in the later study with a documented 2.75 rise in maternal mortality during the study period. In this study, 88% of mortalities had an ASA score of III and over, which was comparable to the Lillie et al study where 68% had a score of III and over. The overall mortality rate in the emergency cases was almost twice as much as elective cases (0.75% vs. 0.47%) which is in agreement with most studies in high-income countries as well as LMICs.[5, 9, 11, 12] Amongst the fatalities, there was only one minor case and this was a one year six months old child with burns who had a general anaesthetic for a venous cut-down for failed intravenous access and died on the third day postoperatively of suspected hypothermia and hypoglycemia. The major case overall sixth day POMR and minor case overall sixth day POMR were 1.289% and 0.021% respectively, of which the major overall POMR was high compared to the McKenzie study (0.74%). The was obviously because the McKenzie study was 24 hour POMR and this study was sixth day POMR.[12]

The commonest cause of death was abdominal/pelvic sepsis accounting for 25.8% of mortalities followed by haemorrhage and respiratory failure both accounting for 10.6% and

10.6% respectively. Abdominal/pelvic sepsis and haemorrhage were the two top causes of avoidable mortality. Abdominal/pelvic operations are very common procedures done with life saving intent which carry a substantial mortality rate which is also two to three times higher in LIMCs compared to HICs.[25]

Surgical causes of avoidable perioperative mortality were mainly preoperative in nature and included delayed decision to operate and inadequate preoperative resuscitation. Postoperative mismanagement mainly included failure to recognize a deteriorating patient and infrequent postoperative reviews. They were some intraoperative mismanagements for abdominal procedures where junior surgeons failed to make colostomies in patients post primary anastomosis of bowel who would have had a clear benefit from one.

Anaesthetic causes of avoidable perioperative mortality were firstly perioperative mismanagement of patient and secondly inadequate patient preparation preoperatively. The case of a sole anaesthetic avoidable cause of death involved an inappropriate decision to do a major elective case within a week of the patient being treated for pneumonia. Patient died due to severe hypoxia immediately post induction as a complication of suspected bronchospasm before knife to skin. Poor airway management did not seem to be a big concern in our study as compared to other African studies, maybe this was because of a slightly higher grade in qualification of the anaesthetic providers in our study.[12, 13, 18]

Administrative causes of avoidable perioperative mortality most frequently encountered were inadequate postoperative patient monitoring followed by inadequate laboratory support, then unavailability of blood products and no or delayed access to intensive care services as well delayed access to theatres.

With regard to our primary objective which was sixth day POMR indices, there was a challenge in making comparisons to other studies from other countries apart from the systematic review studies because most studies are either 24 hour POMR or 30 day POMR as recommended by most authorities.[5,9,10] Its been well documented that it is difficult to compare perioperative mortality studies due to differences in a lot of factors including level of training, availability of drugs, equipment, level of hospital e.t.c.[3] The overall sixth day inpatient POMR was found to be 0.85% (shown in Table 5) which was four times the rates in high-income countries.[5,10] This value excluded the 449 (4.59%) lost to follow up from the total of 9 775 procedures bringing the denominator down to 9326 procedures.

Compared to the 2012 Lillie et al study with a sixth day inpatient overall POMR of 0.63%, the chi square test also revealed a difference of no statistical significance (x^2=3.662 with 1df, p=0.056).[7] The sixth day inpatient avoidable mortality rate (Avoidable POMR) was found to be 0.42%. This value as shown in Table 5, when compared to the avoidable mortality rates of the 1987 study, does not translate to any statistically significant difference as evidenced from the chi-square test (0.33% in 1987, x^2=0.801, p=0.371). The sixth day inpatient anaesthetic POMR, surgical POMR and administrative POMR were found to be 0.04%, 0.19% and 0.19% respectively as seen in Table 5. All showed no difference of statistical significance when compared to the historical data. The sixth day anaesthetic avoidable POMR in the current study was still four times greater than that in HICs (4 vs. <1 per 10 000 anaesthetics).[5,10]

The sixth day inpatient mortality indices from this study were believed to be more accurate compared to the ones in the 2012 Lillie et al study for two main reasons.[7] Firstly the file retrieval rate was much higher during this study at 84% with 13 files out of 79 deaths not being available for review vs. 52% in the Lillie et al study were 55 files out of 114 deaths were not available for review. Record retrieval challenges were not only unique to these two studies; the McKenzie study was a prospective study which had a record retrieval rate of 75.3% and hence comparable to our current study.[12] And secondly, the numerator detection rate was also higher in this study (0.85% vs. 0.63%). However there is also the possibility that the mortality rate has just increased.[7] More recently, Biccard et al[24] conducted the African Surgical Outcomes Study (ASOS) published in 2018 was a multicenter prospective observational cohort study involving 25 African countries.[24] The overall POMR was two and half times greater than in our study (2.1% vs 0.85%).[24] This may have been because the ASOS study was a 30 day POMR while ours was a sixth day POMR. The ASOS study concluded that despite a low risk profile (lower ASA scores) and fewer complications, patients in Africa were twice as likely to die after surgery when compared to the global average for postoperative deaths.[24]

The secondary objective of this study was to determine the 24 hour inpatient perioperative mortality rate at the University Teaching Hospital. Of the 28 cases that were detected to be our numerator with regard to 24 hour inpatient perioperative mortality, 25 records were traced and retrieved for further evaluation. For the other three, only the critical incident reports could be traced. The overall 24 hour inpatient perioperative mortality rate was 0.30%. The avoidable mortality rate (Avoidable POMR), Anaesthetic POMR, Surgical POMR and Administrative POMR were 0.17%, 0.02%, 0.07% and 0.08% respectively as shown in Table 6 with the relevant chi-square test in comparison to other 24 hour studies. The 24 hour POMR indices in this study were closely in agreement with the McKenzie study done in Zimbabwe with a slightly lower anesthetic avoidable POMR (0.02% vs. 0.03%). The overall 24 hour POMR was one and a half times, while the anaesthetic avoidable POMR was two times the values seen in HICs (30 vs. 20 per 10 000 anaesthetics and 2 vs. <1 per 10 000 anaesthetics).[5, 10] The 24 hour POMR indices revealed by this study were better than those from the Hansen, Gausi and Merikebu study (Malawi) and Maman et al (Togo) study, whose values were very high, especially the Anaesthetic avoidable POMR as shown in Table 5.[13, 14] This may have been because both their anaesthetic services were provided mostly by low level inadequately (job on training; some without adequate medical background e.g. medical assistants and nurse anaesthetist with no formal anesthetic training) trained anaesthetic providers coupled with the lack of adequate monitoring and drugs. Part of the reason why the anaesthetic contribution to mortality was high in these two studies may have been that the anaesthetic providers did not have sufficient knowledge to argue the cases with the more senior surgeons. Compared to the more recent 24 hour overall POMR from the ASOS study (2018), ours was more than two times higher (0.30% vs. 0.13%) but this was because the ASOS study only included cases done on patients that were 18 years and over.[24] The 24 hour overall POMR was comparable, though slightly higher after adjustment by removal of cases done on patients under 18 years from our study (0.20% vs. 0.13%) .[24] The chi-square test revealed a difference of no statistical significance (x^2=1.495 with 1df, p=0.221) with regard to the adjusted POMR..The overall 24 hour POMR from the ASOS study was comparable to the indices from studies in HICs.[24] This shows that our study site has a lot of work to do with regards to improving access to safe surgical and anaesthetic services. The South African studies stand as a symbol of hope for African countries to strive to higher levels of care with anaesthetic avoidable POMR comparable to those in developed countries (0.7 per 10 000 anaesthetics).[4]

The strengths of this study include that it was prospectively done which resulted in a higher patient record retrieval rate as compared to the 2012 study which was retrospective. This study also included 24 hour perioperative mortality indices that were compared with other studies from the region and internationally. We also employed a triangulation method involving ward clerks, research assistants, MICU theatre admissions, theatre Death on table records and mortuary records to improve the numerator detection. Both the consultant surgeon and consultant anaesthetist had to sit down together including the principle investigator to categorize the causes of death based on consensus.

The weaknesses of this study included poor record keeping which made file retrieval very difficult. Even in instances where the files were found, some charts were either missing or incompletely filled. Of note were missing anaesthetic charts for a good number of the records retrieved. Missing drug charts, patient monitoring charts and fluid balance chart as well as patient notes were not uncommon. There was no follow up information on the sixth day outcome for patients discharge before the sixth day postoperatively. Lack of funds and human resource limited the study to the sixth day inpatient postoperative period compared to the recommended standard 30th day postoperative period for perioperative mortality follow ups.

It would be desirable to do a continuous thirty day perioperative mortality study with individualized case by case feedback to parties involved as it is with the CEPOD (confidential enquiry into perioperative deaths) in the United Kingdom. This would greatly improve the quality of both the surgical and anaesthetic services and define the recurring administrative factors leading to poor surgical outcomes. Most causes of death were due to pelvic/abdominal sepsis, and it may be worthwhile conducting a research on the effects on surgical outcomes of delays to surgical access for patients requiring laparotomies.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

It is alarming to note that the sixth day inpatient overall perioperative mortality at the University Teaching Hospital has not reduced; this is out of keeping with global trends which show decline. The mortality rate has remained high and involves mainly patients of a younger age group as compared to HICs. The leading cause of death was still abdominal sepsis. Poor postoperative care was noted to be a major contributory factor to perioperative mortality.

The 24 hour inpatient overall perioperative mortality rate has not reduced; it is currently 0.30% at UTH, which is comparable to fellow developing countries from 20 years ago. In contrast, anaesthetic avoidable mortality was found to be comparable with that in HICs from 10 years ago. This signifies an appreciable improvement in this particular perioperative mortality index.

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6.2 Recommendations

1. UTH management to improve postoperative care by increasing nurse to patient ratio and providing monitoring equipment in established postoperative care units on ward.
2. Blood bank services to improve blood product stocks and prioritization of emergencies.
3. Multi-disciplinary approach to establishing post-operative care protocols.
4. Training on paediatric prescribing.
5. UTH/MOH to establish simulation training programs (e.g. emergency, identifying the critically unwell) as a form of continuous medical education.
6. MOH to set up a Mortality review committee that can even give individual feedback to medical practitioners involved in cases resulting in avoidable deaths.

REFERENCES

1. Meara JG, Leather AJ, Hagander L, Alkire BC, Alonso N, Ameh EA et al. Global surgery2030: evidence and solutions for achieving health, welfare and economic development. Thelancet[internet]. 2015 Apr [cited 2016 nov 18]: 1-56. Available from: www.thelancet.com. http://dx.doi.org/10.1016/S0140-6736(15)60160-X

2. Knight PR, Bacon DR. An Unexplained Death Hannah Greener and Chloroform. Anesthes [internet]. 2002 May 1;96(5):1250–3. Available from: http://anesthesiology.pubs.asahq.org/pdfaccess.aspx?url=/data/journals/jasa/931217/

3. Lundgren Christina(2012). Editorial. S AfriJAnaesthAnalg. 2012; 18(1): 3-4. Available from: http://www.sajaa.co.za/index.php/sajaa/article/view/922/1050

4. Harrison GG. Deaths due anaesthesia at Groote Schuur Hospital, Cape Town---1956-1987. S Afri Med J .1990 Apr;77(8): 416-21.

5. Bainbridge D, Martin J, Arango M, Cheng D. Perioperative and anaesthetic-related mortality in developed and developing countries: systemic review and meta-analysis. Lancet. 2012 Sep 22; 380(9847): 1075-1081. Doi:10.106/S0140-6736(12)60990-8.

6. Heywood AJ, Wilson IH, Sinclair JR. Perioperative Mortality in Zambia. Ann R CollSurgEngl 1989 Nov; 71 (6): 354-8

7. Lillie EM, Holmes CJ, O'Donohoe EA, Bowen L, Ngwisha CL, Ahmed Y et al. Perioperative mortality at the University Teaching Hospital, Lusaka, Zambia: a retrospective cohort study. Canadian Journal of Anesthesia. 2015 Dec;62(12):1259-67. doi: 10.1007/s12630-015-0483-z

8. Coetzee A. Mortality associated with anaesthesia. South Afri Med J 1996; 86:973-6.

9. Watters DA, Hollands MJ, Gruen RL, Maoata K, Perndt H, McDougall RJ et al.Perioperative mortality rate (POMR): a global indicator of access to safe surgery and anaesthesia. World J Surgery. 2015 Apr;39(4):856-64. Doi: 10.1007/s00268-014-2638-4.

10. Braz LG, Braz DG, Da Cruz DS, Fernandes LA, Modolo NS, Braz JR. Mortality in Anaesthesia: a systematic review. 2009 Oct; 64(10): 999-1006. Doi: 10.1590/S1807-59322009001000011

11. Arbous MS, Grobbee DE, Van Kleef JW, De Lange JJ, Spoormans HH, Touw P et al. Mortality associated with anaesthesia: a qualitative analysis to identify risk factors. Anaesthesia. 2001 Dec; 56(12): 1141-53.

12. Mckenzie AG. Mortality associated with anaesthesia at Zimbabwean Teaching Hospitals. S Afr Med J. 1996; 86:338-42

13. Maman AO, Tomta K, Ahouangbevi S, Chobli M. Deaths associated with anaesthesia in Togo, West Africa. Trop Doct. 2005 Oct; 35: 220-2.

14. Hansen D, Gausi SC, Merikebu M. Anaesthesia in Malawi: complications and deaths. Trop Doct. 2000; 30:146-149.

15. Demographic Dividend. Investing in human capital, Zambia. 2018, October 18. Available from http://www.demographicdividend.org/country_highlights/zambia/

16. Mashikolo N, Mbangweta P. UTH and the population explosion. The voice of the Hospital. 2013 May; 4: 10

17. TIME PUBLISHED. Congestion continues at UTH despite first level Hospitals. *The Lusaka Times.*2011 Oct 13. *Retrieved from http://www.lusakatimes.com*

18. Paiva H (2003) Perioperative Mortality in Papua Guinea. Mmed Thesis. University of Papua Guinea.

19. Kinnear JA, Bould MD, Ismailova F, Measures E. A new partnership for anesthesia training in Zambia: reflections on the first year. Canadian Journal of Anesthesia. 2013;60(5):484-91.

20. Meara JG, Hagander L, Leather AJ. Surgery and global health: a Lancet Commission.The Lancet. 2014;383(9911):12-13.

21. Grimes CE, Henry JA, Maraka J, Mkandawire NC, Cotton M. Cost-effectiveness of surgery in low-and middle-income countries: a systematic review. World journal of surgery. 2014;38(1):252-263.

22. [Internet]. Apps.who.int. 2005 [cited 12 January 2016]. Available from: http://apps.who.int/iris/bitstream/handle/10665/43392/924159392X_eng.pdf;sequence=1

23. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013 Nov 27;310(20):2191-4. doi: 10.1001/jama.2013.281053.

24. Biccard BM, Madiba TE, Munlemuo DM, Madzimbamuto FD, Basenero A, Gordon CS et al. Perioperative patient outcomes in the African Surgical Outcomes Study; a 7-day prospective observational cohort study. *Lancet*. 2018 Apr 21;391(10130):1589-1598. Doi: 10.1016/S0140-6736(18)30001-1

25. GlobalSurg Collaborative. Mortality of emergency abdominal surgery in high-, middle- and low-income countries. *Br J Surg*. 2016 May; 103(8):971-88. Doi.org/10.1002/bjs.10151

APPENDICES

Appendix 1: Data collection Proforma

Data Collection Proforma

Perioperative Mortality UTH

Analysts:	
Case Number:	
Study Number:	

Patient Demographics:

Sex	
Age	
ASA	
Co-morbidity	

Presenting complaints:

Date of Admission:						
Date of Surgery:						
Time of Surgery:						
Duration of surgery:						
Date of Death:						
P Time of death:						
Days Post	**D1**	**D2**	**D3**	**D4**	**D5**	**D6**

Operation:	

Defn: with day 1 being the day of the surgical procedure.

Surgical Specialty:

Operation: Indication:

Surgical category:

Elective	Urgent	Emergency

Definitions:

Elective surgery when the surgical procedure is scheduled in advance because it does not need to be performed immediately[14].

Urgent surgery when the surgical procedure can wait until the patient is medically stable, but should be done today or tomorrow[14].

Emergency surgery when the surgical procedure must be performed without any delay[14].

Grade of surgery: Definition

Major	Intermediate	Minor

Cause of Death:

(Explain cause of death and other relevant information.)

Avoidable	Partially Avoidable	Unavoidable

If Avoidable what was the cause:

(Can tick multiple boxes)

Surgical	Anaesthetic	Administrative

(Explain the contributions of the cause of death in the appropriate cell or cells)

Surgical:

Anaesthetic:

Administrative:

Grade of Surgeon:

(Can tick multiple boxes)

	Clinical Officer
	Intern
	Registrar
	Consultant
	Not Documented

Grade of Anaesthetist:

	Clinical Officer
	Registrar
	Consultant
	Not Documented

Appendix 2: Studies in the Bainbridge et al perioperative systemic review study.

Year	Author	Post-op period follow up	Denominator	Numerator	Overall POMR /1000	Anaesthetic avoidable POMR/1000
1997	Arbous et al (Holland)	24hrs	0.87M	811	0.88	0.14
1983-1987	Aubas (France)		102 468	168	1.64	
1948-1952	Beecher (USA)	<7 days	599 548	7 977	13.31	
1954-1959	Bomar (USA)		68 918	31	0.45	
1983-1984	Bradley (Australia)	<7 days	11 925	81	6.79	
1986-2005	Braz (Brazil)		53 718	118	2.2	
1962-1973	Bodlander (Australia)	<7 days	21 130	408	19.31	
2003-2004	Charuluxannan (Thailand)	<7 days	163 403	462	2.83	
1952-1962	Clifton (Australia)	<7 days	205 640	162	0.79	

1987	Coetzee study (South Africa)	24hrs	94 945	113	1.19	0.23
1988	Cohen (Canada)	<7 days	100 007	714	7.14	
1943-1954	Dornette (USA)	<7 days	63 105	108	1.71	
1992-1995	Dupont (France)	<7 days	52 654	170	3.23	
1996-2000	Fasting (Norway)	<7 days	83 844	42	0.5	
1984-1985	Forrest (USA)	<7 days	17 201	19	1.1	
1991-1999	Hamel (USA)	<7 days	594 911	18054	30.35	
2000	Hansen (Malawi)	<7 days	3022	14	4.63	
1956-1960	Harrison (South Africa)	<7 days	177 928	2026	11.39	
1967-1976	Harrison (South Africa)	< 7 days	240 483	2442	10.15	
2007-2008	Haynes (Various)	30 days	7 688	88	11.45	

1987	Heywood, Wilson and Sinclair study (Zambia)	6 days	10 590	80	7.6	0.53
1945-1954	Hingson (USA)	<7 days	136 043	127	0.93	
1960-1984	Holland (USA)	<7 days		2516		
1975	Hovi-viander (Finland)	<7 days	338 934	626	1.85	
1947-1954	Jacoby (USA)	<7 days	54 000	34	0.63	
1999	Kawashima (Japan)	<7 days	793 840	570	0.72	
2001	Kawashima (Japan)	<7 days	1 284 957	824	0.64	
1994-1998	Kawashima (Japan)	<7 days	2 363 083	1 696	7.18	
1992-2003	Khan (Pakistan)	<7 days	111 289	35	0.31	
1992-2003	Kubota (Japan)	<7 days	95 506	140	1.47	
1964-1977	Langrehr (USA)	<7 days	37 924	115	3.05	

1992-1994	Legasse (USA)	<7 days	146 548	232	1.58	
1995-1999	Legasse (USA)	<7 days	11 705	17	1.45	
2000-2001	Lindenauer (USA)	30 days	663 635	13 454	20.27	
1999-2001	Liu (Singapore)	<7 days	31 000	7	0.23	
1965-1969	Marx (USA)	<7 days	34 145	645	18.89	
1992	Mckenzie (Zimbabwe)	<7 days	34 553	89	2.61	
1955-1964	Memery (USA)	<7 days	69 291	1 027	14.82	
2000	Morita (Japan)	<7 days	910 757	652	0.72	
1998-1999	Niskanen (Finland)	<7 days	25 091	122	4.86	
1986-1987	Pedersen (Denmark)	30 days	7 306	3	0.41	
1976-1987	Pitt miller (Trinidad)	<7 days	129 107	186	1.44	

1963	Pohjola (Finland)	<7 days	137 145	78	0.57	
1952-1956	Schapira (USA)	<7 days	22 177	200	9.02	
1980-1992	Tan (Malaysia)	<7 days	155 000	125	0.81	
1986	Tikkenen (Finland)	<7 days	325 585	570	1.75	
1964-1966	Vacanti (USA)	<7 days	68 388	266	3.89	
1988-1990	Warner (USA)	<7 days	38 598	2	0.05	
1989-1993	Wolter (Germany)	30 days	6 286	237	37.7	
1959-1962	NHS 1966 (USA)	30 days	856 500	16 840	19.66	