A Clinical Audit of the Utilisation of Red Blood Cell products in Elective Total Hip Replacement Surgery

By

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DECLARATION

I, Yvonne Grace Peters, declare that the contents of this dissertation/thesis represent my own unaided work, and that the dissertation/thesis has not previously been submitted for academic examination towards any qualification. Furthermore, it represents my own opinions and not necessarily those of the Cape Peninsula University of Technology.

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Signature: …….. Date: ……

Abstract

Title: A clinical audit of red cell transfusion in elective total hip replacement surgery.

Background:

Previous international studies have documented a marked variation in transfusion practice for Total Hip Replacement (THR) surgery. This is despite widespread dissemination of clinical guidelines for the use of blood products. The cost and potential wastage of blood products as well as concerns regarding patient care and outcomes are important drivers of optimal blood management.

The aim of this study was to audit red cell product utilisation for THR surgeries at two tertiary referral hospitals.

Methods:

A retrospective clinical audit was conducted at two tertiary hospitals in the Western Cape. The audit involved patient folder review and the review of computer records of the respective blood banks. The folders of two hundred and seven consecutive patients undergoing elective THR surgery from January 2013-December 2013 from each hospital were reviewed. Baseline data relating to age, gender, clinical observations, indications for surgery, pre and post-operative haemoglobin, comorbidities, length of hospital stay and transfusion history was recorded.

Data was then uploaded from individual data collection sheets onto IBM SPSS version 22 statistical package for analysis.

Results:

The two institutions were coded Hospital Green (HG) and Hospital Yellow (HY). Of the two hundred and seven patients who had THR surgery, eighty seven were excluded from the analysis, leaving one hundred and twenty eligible for review, which were equally split between the two hospitals. The transfusion rate at HY (41.6%) was significantly higher than that at HG (10%). The mean post-operative haemoglobin (Hb) in the transfused patients at HG was 8.3g/dL, compared to HY with a mean of 9.1g/dL. Females had a significantly higher transfusion rate (33%) than males (15%) ($p < 0.05$) and the mean age of transfused patients was significantly greater than untransfused patients ($p < 0.005$). Although patients with co-morbidities had a higher transfusion rate

than those without, this did not reach statistical significance. One hundred and thirteen (94%) patients had a blood order from the blood bank, the vast majority, one hundred and two (85%), were group and screen requests of which twenty nine(24%) were converted to a full crossmatch.

Conclusions:

The transfusion rates for the two hospitals for elective THR were significantly different although both are well within the wide ranges documented in the literature. Although there are no bench marks, several studies support a restrictive transfusion regimen strategy with a guideline “trigger” Hb level of 7-8 g/dL. In this study HG had a transfusion rate of 10% with a mean post-operative Hb of 8.3g/dL in the transfused population, compared to 9.1g/dL at HY which had a transfusion rate of 41.6%. This suggests that a benchmark of 20% would not be unreasonable and together with rational blood ordering policies (group and screen rather than a full crossmatch) would lead to significant savings.

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Dedication

To my husband Donovan and children, Robin, Michaela and Alexander my biggest cheerleaders, for your love and endless patience. A huge thank you for your practical, emotional and unconditional support as I added work, study and personal development to the ever competing roles of wife and mother.
To Captain and Dee this is for you.

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Abbreviations

AABB	American Association of Blood Banks
ACD	Acid Citrate Dextrose
ATP	Adenosine Triposphate
ASA	American Society of Anaesthesiologists
AVN	Avascular Necrosis
CAP	College of American Pathologists
CABG	Coronary Artery Bypass Surgery
CPUT	Cape Peninsula University of Technology
C/T ratio	Cross match / transfusion ratio
vCJD	variant Creutzfeldt - Jakob disease
CMV	Cytomegalovirus
DVT	Deep Vein Thrombosis
GA	General Anaesthesia
GMP	Good Manufacturing Practice
G&S	Group and screen
GVHD	Graft versus Host Disease
HCT	Haematocrit
HG	Hospital Green
Hb/Hgb	Haemoglobin
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
HT	Hypertension
HTLV1	Human T-Cell Lymphotropic Virus I

HTLV2	Human T-Cell Lymphotropic Virus II
HY	Hospital Yellow
ICCTO	International Consensus Conference on Transfusion Outcomes
ICU	Intensive Care Unit
ISTMI	Italian Society of Transfusion Medicine and Immunohaematology
LIS	Laboratory Information Systems
LOS	Length of Hospital Stay
MSBOS	Maximum/Maximal Surgical Blood Ordering Schedule
NHLS	National Health Laboratory Services
NHS	National Health Services (United Kingdom)
PRBC	Packed Red Blood Cell
RBC	Red Blood Cell
RBCC	Red Blood Cell Concentrate
RCC	Red Cell Concentrates
RSA	Republic of South Africa
RTHR	Revision Total Hip Replacement
SANBS	South African National Blood Service
SD	Standard Deviation
TB	Tuberculosis
TKR	Total Knee Replacements
THR	Total Hip Replacement
THA	Total Hip Arthroplasty
TACO	Transfusion Associated Circulatory Overload
TRALI	Transfusion Related Acute Lung Injury

TTD	Transfusion Transmissible Diseases
WNV	West Nile Virus
WPBTS	Western Province Blood Transfusion Service
UK	United Kingdom
XM	Cross Match
YRS	Years

1 Chapter One: Introduction

As a result of recent advances in the diagnostic technology developed to screen for transfusion transmissible diseases (TTD), pathogen inactivation measures and improvement in good manufacturing practice (GMP), the risk of transmission of TTD is currently extremely low. In the Republic of South Africa (RSA) no Human Immunodeficiency Virus (HIV) infection from a blood component has been documented for more than a decade (C. Ingram, personal communication, 15 April 2015). According to Toy (1996:1) and Murphy et al., (2013:3) transfusions still carry risks for patients even though these are minimal. In addition, because they are costly, increased focus on appropriate blood management with the publication of clinical guidelines and audits have occurred over the last decade. Clinical audits serve as a tool to identify areas of practice which can be improved and thus form part of quality improvement initiatives that serve to enhance patient outcomes, improve safety as well as minimising cost by ensuring the best transfusion practice.

Florence Nightingale was one of the first audit pioneers (Lee et al., 2013: 245). During the Crimean War of 1854-1856 she was appalled by the poor standards of hygiene which led to high mortality rates amongst the injured. She sought to improve these standards and the mortality rates subsequently improved. It became evident that by auditing current practice and making changes where deficiencies were observed, standards could be greatly improved. This ultimately led to better quality of care, treatment and service provided to patients.

Medical audits are a vital component of quality assurance and quality improvement in health care delivery (Pinkerton, 1995:283). Medical audit has been defined as a systematic approach by peer review of medical care, in order to identify opportunities for improvement as well as to realise them. From an economic point of view, audits can also improve resource management. Thus transfusion medicine audit is part of the larger field of medical audit which also involves resource and management as well as of product quality audits (Pinkerton, 1995: 283).

Variability in transfusion practice in association with coronary artery bypass grafting (CABG) and other surgery is well documented both in the United States and Europe. (Goodnough et al., 1991; Sanguis Study Group, 1994) However, the reasons for these variations are not well established. In addition, numerous audits of blood use have been published identifying variations in clinical transfusion practice as well as inappropriate practice (Velicchi et al., 2011; Boralessa et al., 2009; Joy & Bennet, 2012). These studies have suggested that further investigation and standardisation is required in this area of transfusion medicine.

1.1 Problem Statement

International studies have demonstrated large variations in transfusion practice for patients undergoing Total Hip Replacement (THR) surgeries, even though guidelines for transfusions are in place. This could potentially have a direct impact on patient care and cost. (Spencer, J et al., 2005; Gombotz et al., 2007; Jans, O et al., 2011).

In South Africa very few studies of blood usage practice have been conducted. Therefore, because blood is a valuable and scarce resource, information regarding its usage in the Western Cape is necessary.

1.2 Aim

The primary aim of this study was to evaluate the utilisation of red blood cell products in THR surgery in two tertiary referral hospitals in the Western Cape by means of a retrospective clinical audit.

1.3 Objectives

The objectives of the study were to:

- Audit transfusion practice for elective THR at two tertiary referral hospitals in the Western Cape Province of South Africa.

- Investigate compliance with the current clinical guidelines for the utilisation of red blood cell products for THR surgery.

- Correlate this information with pre-operative clinical and laboratory data (transfusion triggers).

2 Chapter Two: Background and Literature Review

2.1 History of audits

Medical audits began during the Crimean War (1854-1856), when Florence Nightingale was appointed to the position of nursing administrator. She was appalled by the poor standards of hygiene which led to high mortality rates and sought to improve standards of hygiene which resulted in a significant drop in the mortality rates (Lee et al., 2013:245). This was the first clinical audit and it became evident to many that by examining current practice and initiating changes, standards could be improved. This would ultimately improve patient care and the quality of the service provided to them. Florence Nightingale therefore became known as the pioneer of the clinical audit process.

2.2 History of Blood Transfusion

In 1667 the first blood transfusion was unsuccessfully attempted and this resulted in a patient's death shortly after a transfusion with animal blood. Although the patient's physician was eventually exonerated, a peer review committee (the Faculty of Medicine of Paris) issued a decree stating that performing a blood transfusion was a criminal act unless it was sanctioned by the Faculty. The science of blood transfusion dates back to the 19th century when in 1818, Dr James Blundell, a British obstetrician, performed the first transfusion of human blood, for the treatment of postpartum haemorrhage (Giangrande, 2000:758). After a number of attempts with variable results, blood transfusions as a viable therapeutic procedure only became possible after Landsteiner's pioneering experiments in establishing the ABO blood group system (Watkins, W.M, 2001:243-265). In World War 1 transfusions with preserved blood were utilised for the first time in major trauma inflicted on the battlefields (Robertson, 1918:691). However it was not until 1937 that the first blood bank was established and it was at this time that it was officially acknowledged that a transfusion committee was required to guide transfusion practices (Fantus, 1984:647-649). World

War 2 was a catalyst for the development of an acid-citrate dextrose (ACD) solution enabling blood storage for up to twenty one days (Loutit & Mollison, 1943:744).

In South Africa, blood transfusions were first used in the 1920's. The first Blood Transfusion service was established in Johannesburg in 1937 and in Cape Town in 1938. In 1943 the first blood bank in Cape Town was opened (De Benedictis & Gibbs, 1987:6). Currently two Blood Services exist in South Africa and operate independently but work in close collaboration. The South African National Blood Service (SANBS) provides an essential service within South Africa and operates across all of South Africa, with the exception of the Western Cape.

The Western Province Blood Transfusion Service (WPBTS) is a non-profit independent organisation operating throughout the Western Cape. Its goal is to supply safe blood and blood products to the Western Cape Province. Both Transfusion Services rely on voluntary, unpaid donors and have a commitment to provide the best possible service to the community. In the Western Cape a blood bank is located at all major hospitals to service the needs of patients. Smaller hospitals and community clinics are serviced by a blood bank situated within a hospital closest to them. Each of these smaller hospitals or community health clinics has a supply of emergency blood (group O Positive and O Negative) in the event that blood is urgently needed. The Clinical Guidelines for the use of Blood Products in South Africa, 5th Edition was compiled by the Medical Directors and medical staff of both Transfusion Services, together with input from clinicians who frequently prescribe blood products.

Historically whole blood was the product of choice to treat all patients requiring red cell transfusions. With advances in modern technology as well as transfusion medicine knowledge, the concept of blood component therapy was introduced where red cell concentrates with minimal amounts of plasma are used. Other blood components (e.g. platelets) were also introduced (Ingram, Bellairs & Bird, 2014:17).

Red Cell Concentrates (RCC's) are prepared by the removal of most of the plasma from a unit of whole blood. The buffy layer which is rich in leucocytes and platelets is removed and a preservative solution is added to the residual red cells. RCC's and other cellular components can also be further filtered to remove practically all remaining leucocytes. In most well-resourced countries this is now standard practice.

The transfusion of RCC's is indicated to restore the oxygen carrying capacity after tissue oxygenation has been impaired by either haemorrhage or by symptomatic anaemia.

One unit of RCC (at a dose of 4mL/kg) can be expected to increase the haemoglobin (Hb) level of an average (70kg) adult by approximately 1-2g/dL. (Ingram, Bellairs & Bird, 2014:15).

2.3 The Clinical Audit

A clinical audit is defined as a quality improvement process that seeks to improve patient care and outcomes through a systematic review of care against explicit criteria and the implementation of change (Hine & Rawlins, 2002). Aspects of the structure, processes, and outcomes of care are selected and systematically evaluated against established criteria. Clinical audits form part of quality improvement plans to improve, enhance as well as to ensure the highest standard of current practices. This process can be described as a cycle in which systematic procedures of establishing best practice, measuring care against criteria, taking action to improve care and continued monitoring to sustain improvement, take place (Hine & Rawlins, 2002:3). This is a continuous process and each cycle aspires to a higher level of quality. Multi-institutional audits play a useful benchmarking role and when followed by targeted education and re-audits they can improve transfusion practice.

Figure 1. A flowchart of the Audit Cycle (Warburton: 2012)

A clinical audit is one of the most important tools used to establish whether the best methodologies or systems are being used in practice as it compares actual practice to a standard of practice. This system identifies gaps between what is done and what should be done, and can therefore be used to rectify any deficiencies in the actual process of care (Seddon, 2006:1-2).

An example of a clinical audit was undertaken by Jack Wennberg of Dartmouth University who was the first to challenge unexplained variations in the frequency of common surgeries in neighbouring regions of the United States. He found that the frequency of some surgeries e .g tonsillectomies in children, varied as much as tenfold between hospitals in the same states. These differences could not however be explained and it was concluded that most of the variations could be attributed to training, time since graduation and historical practice patterns (Wennberg & Gittelsohn, 1982: Seddon, 2006:2).

2.4 Transfusion Audits

The increasing value of transfusion audits can be demonstrated by a Medline computer search done in 1974 which failed to reveal any articles on transfusion and audits (Toy, 1996:1). In contrast however, more than seventy articles were found for the period 1993-1998. The interest in audits has subsequently increased even further over the last decade (Toy, 1999:592; Wallis et al., 2002:5-6; Frank et al., 2013:3052, 3057). These reports highlight the importance and relevance of utilising a clinical audit to identify problems in current practice and to propose strategies to improve systems.

The auditing of transfusion data may be gathered retrospectively, prospectively or concurrently (Wallis et al., 2002:4; Nel, 2008:65).

Prospective audits entail the review and validation of the decision to transfuse at the time it is made, and then comparing it to the agreed clinical guidelines. It is therefore a review of data collected prior to the transfusion. This approach to audits is limited in that it requires increased resources in comparison to the retrospective approach. A prospective audit requires carefully structured order forms which need to be completed by the ordering physician. It also necessitates review by a physician, registered nurse or blood transfusion technologist with transfusion knowledge and experience. In addition access to laboratory results via Laboratory Information Systems (LIS) would be required on a continuous basis. Prospective audits have however been shown to be both practical and valuable. (Wallis et al., 2002:4, Nel, 2008:65)

Retrospective audits are the most practical and involve the review of data post transfusion, post-surgery and post hospital encounter. Retrospective audits do not have an impact on the treatment of the patient as the review takes place after the event. The major disadvantage of retrospective audits is that they are reliant on the appropriate and accurate recording of all necessary information by hospital personnel. The advantage of this type of audit is that it is very effective in yielding information on

current practice and can serve as a tool to establish whether current transfusion practices are adequate and acceptable in terms of the agreed guidelines.

It also has the ability to determine whether established blood product guidelines are of an acceptable standard and meet the requirements of the clinical setting (Nel, 2008:69).

Concurrent audits require the collection of information on transfusion related episodes and feeding it back to the clinician within a time scale which is usually before the patient is discharged from hospital. The advantage of concurrent audits is that the data is accurate and the outcome can be provided to the decision making clinician while it is still relevant to the specific episode (Nel, 2008:69). This allows appropriate action, such as cancelling the unit requested for cross match.

Elective surgeries are the most common target of transfusion audits, probably due to the fact that they have the advantage of providing well-defined patient groups. It has been suggested that the clinical use of red cells is a very relevant area for audits even though current practice is based on uncertain evidence (Wallis, 2002:1-9).

The utilisation of audits is to reduce unnecessary transfusions and the discarding of outdated blood (i.e. better inventory management). This will become more important as the world faces diminishing blood supplies due to stricter donor requirements as well as a decline in public willingness to donate blood. It has been shown that in practice, implementation of an audit with follow up monitoring can significantly reduce the use of allogeneic blood products resulting in considerable cost savings and decreased reliance on conventional blood donation. (Pinkerton, 1995:284)

2.5 Hawthorne effect

A major flaw of conducting an audit is the disregard for the Hawthorne Effect (Kanter, 1998:69). The Hawthorne Effect was derived after a number of important experiments were conducted in industrial history. Hawthorne established that the performance of employees was influenced by their surroundings and by the people that they were working with as much as by their own innate abilities (Franke & Kaul: 1978:624).

When conducting an audit or introducing a new process, people involved in the study tend to do a better job than expected. If clinicians were aware that a clinical audit was being performed they may be more cautious with regards to the ordering of blood products and blood products. A retrospective study or audit has the advantage of excluding this phenomenon and is therefore often the method of choice.

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2.6 Hip Replacements

Total hip replacement surgery is an elective procedure commonly performed on patients suffering from hip joint damage which in over 80% of patients is caused by osteoarthritis. It is a procedure commonly performed on elderly patients (Jans et al., 2011:374).

2.7 Variations in Transfusion Practice

In major elective orthopaedic procedures blood loss is common, leading to decreased haemoglobin levels post-operatively. This often results in the transfusion of allogeneic red blood cells to treat intra-operative and post-operative anaemia. It has been documented that orthopaedic surgery is the leading elective surgical indication for transfusion in Europe (Shander et al., 2012:55) and accounts for approximately 10% of all RBC units transfused. THR surgeries accounts for 4.6% of this amount. (Boralessa et al., 2009:99).

The reasons for the variation in transfusion practice in orthopaedic surgery are not well understood, but it has been suggested that two factors consistently influence the use of RCC transfusions. These are a decreased haemoglobin and age. Other important factors found to influence the use of RCC transfusions were, increased surgical complexity (e.g. revision vs. primary THR), low body weight, presence of additional comorbidities and the female sex (Barr, 2011:304,316).

It has been estimated that a 2-3g/dL of haemoglobin is the anticipated blood loss during THR or total knee replacement (TKR) surgery (Spahn, 2010:484).

2.8 Risks of Blood Transfusions

The risks associated with blood transfusions include viral, bacterial and parasitic infections as well as the risk of the patient developing various adverse transfusion reactions. These include the following: allergic, febrile, haemolytic reactions, Transfusion Related Acute Lung Injury (TRALI), Transfusion Associated Circulatory Overload (TACO), Immunomodulation and Graft versus host Disease (GvHD) (Murphy et al., 2013:3,113).

The most commonly transmitted viral diseases include Hepatitis B and C, HIV I and II, HTLV - I, HTLV- II, the West Nile Virus (WNV) as well as the Cytomegalovirus (CMV) (Murphy et al., 2013:3,113).

Parasitic infections such as malaria and Chagas Disease can also be transmitted via a blood transfusion (Murphy et al., 2013:134).

Transmission of other diseases caused by prions includes variant Creutzfeldt - Jakob disease (vCJD) (Vamvakas and Blajchman 2009: 3406-3412). Although these risks

are minimal, they cannot be completely eradicated and therefore blood transfusions as a therapeutic option still remain a risk.

2.9 Transfusion Guidelines

Guidelines exist to assist medical personnel in making transfusion decisions. These decisions have to be made with the view that the benefit of a transfusion will outweigh the potential risks. Integral to all audits are structured practice standards or practice guidelines. In transfusion medicine the major motivation for the development of transfusion guidelines was the perceived need to define the indications for transfusion and to try to confine treatment to those situations where it is absolutely necessary (Ghali et al., 1994:1449-54). According to this article, applications of the American College of Physicians guidelines to red cell transfusion practice in a Canadian teaching hospital suggested that in spite of the long standing concept of guidelines and audits, and publicity surrounding the hazards of transfusion, a substantial proportion of red cell transfusions was carried out without any clinical justification (Pinkerton, 1995: 283).

Transfusion practice guidelines are recommendations based on a combination of clinical practice consensus and scientific evidence. The guidelines should allow for clinical flexibility and be specific and totally unambiguous. Furthermore they must include specific recommendations about thresholds for transfusion accompanied by laboratory data that are relevant to transfusions requirements. However, the decision to transfuse should allow for clinical judgement and not be completely dependent on laboratory parameters. The guidelines should be reviewed periodically and modified as new data regarding the appropriateness of blood transfusion become available (Girish et al., 1997:141-146).

2.9.1 The College of American Pathologists.

Guidelines from the College of American Pathologists focus on surgical and non-surgical acute anaemia as well as chronic anaemia. These guidelines propose that the most important factors to consider when making transfusion decisions for patients with acute anaemia are: the Hb level before blood loss, the extent of the blood loss and the presence of medical conditions that may adversely affect the tolerance of the anaemia. Based on these considerations, RBC transfusions are almost always indicated if the Hb level is < 6g/dL, and rarely indicated if the Hb is > 10g/dL. Decisions regarding patients who have a Hb level between 6-10 g/dL, depends on the extent of the blood loss, the presence of any underlying cardiac disease and the overall clinical status of the patient. The guidelines propose that an acute blood loss of more than 40% of the total blood volume usually indicates the need for RBC transfusion in almost all patients. These guidelines also indicate that after the final decision to transfuse has been made, the response should be monitored using indicators of peripheral tissue oxygenation (peripheral perfusion index, oxygen saturation levels). In routine practice as well as in the absence of these parameters, attention should be directed towards the clinical signs and symptoms including heart rate and blood pressure, Hb levels, co-morbidities, prior medical history and whether bleeding is active or controlled.

A transfusion based purely on Hb or haematocrit (hct) levels is discouraged and the reliance on vital signs in anaesthetised patients may be inadequate because of the effects of anaesthetic agents and the possibility of “silent” ischaemia (Shander et al., 2013:195; Simon, Alverson, AuBuchon et al., 1998:130-138).

2.9.2 The American Society of Anaesthesiologists (ASA).

The ASA transfusion guidelines are focused on transfusion indications in the perioperative setting. A pre-operative evaluation of the patient should include a complete medical history, family history and relevant laboratory workups to identify risk factors for ischemia and bleeding. These guidelines propose that the patients be prepared for surgery by optimisation of RBC mass using pharmacological interventions

and adjustment of anticoagulant therapy. During and immediately after surgery, Hb/hct levels, perfusion status and indicators of ischaemia should be monitored using parameters such as blood pressure, heart rate, oxygen saturation, urine output, and electro cardio graphic changes.

In the perioperative setting, RBC transfusion is usually indicated if the Hb is < 6g/dL, and rarely indicated if Hb is >10g/dL. In patients with Hb's of 6-10 g/dL, evidence of organ ischaemia, rate and amount of bleeding, intravascular volume status, and risk factors for complications of inadequate oxygenation should be considered to guide transfusion decisions (Nuttal et al., 2006; 198-208).

2.9.3 The Italian Society of Transfusion Medicine and Immunohaematology.

Italian guidelines address the perioperative period and propose that the factors to consider when initiating the decision to transfuse include Hb, the amount and rate of blood loss, the clinical condition of the patient and symptoms of reduced oxygen delivery. (Liumbruno et al., 2011:21).

They recommend the use of point-of-care automated Hb or hct analysers to monitor patients. This would provide consistent monitoring and therefore improved transfusion practice. It is also suggested that in acute haemorrhage, there may be a delay before the systemic Hb or hct levels adjust to blood loss and therefore the amount of acute blood loss in addition to the clinical condition of the patient should be the main determinants of transfusion decisions.

In cases of an acute blood loss of 15% of the total blood volume (750 ml), a RBC transfusion is not usually deemed necessary unless there is evidence of a pre-existing anaemia. An acute blood loss of between 15-30% of the total blood volume (750-1,500 mL) would also not be considered as an indication for a RBC transfusion unless a pre-existing anaemia or cardiopulmonary disease is evident. However, in cases of acute blood loss of 30-40% of the total blood volume, (1,500-2,000mL) RBC transfusion would be indicated. RBC transfusion would become a lifesaving therapy in the event of

an acute blood loss of >40% of the total blood volume. Guidelines based on the Hb levels for acute anaemia are as follows. Haemoglobin levels of < or = 6 g/dL, are almost always an indication for a RBC transfusion.

Intermediate Hb levels of 6-8g/dL, in the absence of risk factors such as coronary heart disease, heart failure, electrocardiographic signs of ischaemia and lactic acidosis is not a consideration for a RBC transfusion and when the Hb level is >8-10g/dL, a RBC transfusion is only indicated when signs of tissue hypoxia are present. RBC transfusion is not indicated when the Hb is >10 g/dL (Liumbruno et al., 2011:320-335,189-217, 19-40).

2.9.4 A Compendium of Transfusion Practice Guidelines.

This set of guidelines was published by the American Red Cross and combines red blood cell utilization guidelines for both peri-operative and peri-procedural surgeries. It is recommended that RCC's are indicated for patients with a symptomatic deficiency of oxygen-carrying capacity or tissue hypoxia due to an inadequate circulating red cell mass. RCC's are usually not required when the Hb concentration is >10g/dL and when Hb concentrations are between 6-10g/dL. RCC transfusion should be based on any on-going indication of organ ischemia, potential or actual on-going bleeding (rate and magnitude), the patient's intravascular volume status, and the patient's risk factors for complications of inadequate oxygenation. These risk factors include a low cardiopulmonary reserve and high oxygen consumption. (Quraishy et al., 2010:14; 15).

2.9.5 The British Orthopaedic Association's Blood Conservation in Elective Surgery.

British guidelines agree with previous recommendations that propose that if the Hb concentration is >10g/dL patients should not be transfused. However if the Hb concentration is <7 g/dL a transfusion is recommended and essential when the Hb concentration decreases to 5g/dL. Hb concentrations of between 8g/dL and 10 g/dL are generally safe, even for patients with significant cardiorespiratory disease. Patients

with symptoms of dyspnoea, angina, tachycardia, orthostatic hypotension and syncope that can only be attributed to anaemia and not to any other pathophysiological process should be transfused. The guidelines also recommend that it is appropriate to use only one unit of RCC to exceed transfusion threshold if necessary. (Joy & Bennet, 2012:202).

2.9.6 The American Association of Blood Banks (AABB).

In general, the AABB Guidelines made three recommendations:

- Adhering to a restrictive transfusion strategy (7 to 8 g/dL) in hospitalised, stable patients;
- Adhering to a restrictive strategy in hospitalised patients with pre-existing cardiovascular disease and considering transfusion for patients with symptoms or a Hb level of 8 g/dL or less; and
- Considering symptoms as well as Hb concentration during transfusion decisions.

The AABB Guideline could not however recommend a liberal or restrictive transfusion strategy for hospitalized, haemodynamically stable patients with acute coronary syndromes.

Healthy adult patients with a normal Hb level who are undergoing elective surgical procedures do not require blood replacement if there is less than 1000mL of blood loss, provided that intravascular volume is maintained with crystalloid or colloid solutions (Triulzi, 1999:59; Carson et al., 2012: 49-58).

2.9.7 Clinical Guidelines for the use of Blood Products in South Africa (5th Edition, 2014).

This is available to all medical staff in South Africa. The aim of this publication is to provide useful basic information about blood products available to South African clinicians and includes brief guidelines for their optimum use. The Clinical Guidelines also serve as a standard against which transfusion practice can be assessed.

The standards are based on published peer reviewed studies and other guidelines such as those summarised above. Their recommendations are similar to many other recently published guidelines and reviews and serve as the basis standard against which transfusions in this audit were regarded as appropriate.

These standards recommend that a RBC transfusion is usually indicated if Hb levels are <6g/dL and rarely indicated if Hb is >10g/dL. For patients with Hb levels between 6-10g/dL other factors such as age, co-morbidities, intensive care, risk of ischaemia and rate and volume of blood loss should be considered. A transfusion is usually indicated if Hb <7g/dL in post operative patients, in critically ill patients with the risk of end stage organ ischaemia or if symptoms of hypoxia are present. In surgical patients or patients with pre-existing cardiovascular disease, a transfusion is recommended when the Hb is <8g/dL. These guidelines also state that the trigger for patients with acute coronary syndrome is equivocal as there is limited evidence available to recommend a transfusion to a patient with a Hb of >8g/dL. Thus a decision should be made on a clinical basis to transfuse to >8g/dL where indicated. Therefore, for each patient, depending on co-morbidities, a transfusion threshold for red cell transfusion should be determined (Ingram, Bellairs & Bird, 2014:11).

In summary, published guidelines recommend a restrictive transfusion strategy as opposed to a more liberal one. This decision has been reached by a number of researchers who reported that a restrictive strategy was associated with equal or better clinical outcomes when compared to a more liberal transfusion strategy (Carson et al., 2012; Bracey et al., 1999). All of the above guidelines do however highlight the

point that the use of a rigidly applied transfusion trigger should be avoided and that all clinical factors should be taken into account before making a decision to transfuse.

2.10 Maximum Surgical Blood Ordering Schedules (MSBOS)

A maximum surgical blood ordering schedule can improve the utilisation of blood resources and decrease patient care costs by eliminating unnecessary cross matches. The schedule is usually developed after the analysis of blood usage for each specific elective surgical procedure. By comparing the number of units cross matched to the number of units transfused, the cross match/transfusion (C/T) ratio can be calculated. Surgical procedures that have C/T ratios of greater than 2.5 are considered to have had an excessive number of units of blood units ordered and cross matched. The goal of the MSBOS is to limit the number of units cross matched to the usual number transfused. In surgical procedures associated with a less than 10% likelihood of requiring blood transfusions, a type and screen instead of a cross match is recommended (Triulzi, 1999:59).

2.11 Variations in Transfusion Practice - Previous Audits and Findings

A multicentre study performed in Europe covering ten countries and forty three teaching hospitals assessed the use of blood products and artificial colloids in six commonly performed elective surgical procedures, including THR. They reported significant differences in the number and type of products used for the same patient category. For example, an elderly patient in a European Union country who needed a THR had a 30-100% chance of receiving a blood transfusion depending on which hospital performed the surgery (Sanguis Group 1994:251-266).

Further variations in transfusion rates were confirmed by studies performed in the United Kingdom in 2002 (Sharma et al., 2002:269-272; Roberts, 2000:44-48) and again in 2009, the NHS Blood and Transplant group, together with the Royal College

of Physicians undertook a national audit of transfusion practice and found transfusion rates for THR varied among hospitals from between 1-100% (Boralessa et al., 2009).

In California a study involving twenty four institutions also noted variability in transfusion rates for CABG and concluded that variability is not confined to THR surgeries, but to other disciplines as well (Stover et al., 1998:327-33).

Further studies confirming and reporting similar variations were done in Denmark in 2010 (Jans et al., 2011:374-380) as well as in Italy (Verlicchi et al., 2011:383-387).

In an audit conducted in South Africa at a Kimberly Hospital Complex it was reported that there was a relatively low percentage of non-concordant transfusions. This study aimed to audit the haemoglobin levels at which patients at the Kimberley Hospital Complex were being transfused as well as the indications for RCC transfusions. Only eight percent of transfusion episodes were found to be entirely non- concordant with the guidelines. This figure was low when compared to the results obtained from other studies. Thirty two percent of transfusions were considered entirely concordant based on national guidelines and forty-eight percent were non-concordant either due to over or under transfusion. Ten percent of the cases could not be assessed due to lack of information (Bidmos & Nel, 2011:191-196).

Emphasis on the proper usage of this scarce and valuable resource cannot be more relevant than it is today. With the focus on Patient Blood Management to improve transfusion safety and ultimately improving patient outcomes, audits as a way of monitoring proper blood usage need to be done to ensure positive patient outcomes.

3 Chapter Three: Design and Methodology

3.1 Type of study

This retrospective clinical audit was conducted at two tertiary referral hospitals within the Western Cape. The two hospitals which granted permission to be part of the research were HY and HG. Both of these hospitals are tertiary academic institutions and were assigned a unique colour code in order to be able to distinguish between the two. The retrospective audit involved patient folder review.

3.2 Patient selection

The study population consisted of consecutive patients each of whom had undergone elective total hip replacement (THR) surgery. The patients' folders were examined consecutively to avoid selection bias. The folder reviews were conducted on patients operated on between January 2013 and December 2013. Patients were excluded from the study if they had been admitted with a fracture to the hip area due to trauma, undergone more than one surgery, had a malignancy or had been admitted to the trauma unit with injuries to the hip area requiring emergency surgery.

3.3 Data collection

Retrospective reviews of the computer records of the Blood Banks at the two hospitals were performed. Both Blood Banks are managed by the Western Province Blood Transfusion Service (WPBTS). A data collection form was devised as a tool in order to fulfil the criteria necessary for the audit. See Addendum 1.

The patients' folder numbers were used to cross reference the WPBTS blood bank computer records and to access information with regards to the number of red blood

cells concentrates (RBCC) requested, the number of RBCC cross matched, and the number of RBCC issued as well as the type of blood bank order.

Each patient was assigned a unique number for the purpose of the audit. This number was entered on the data collection form. The hospitals unique colour code was also entered on the data collection form. Information included in the data collection form consisted of demographic data relating to age, length of hospital stay, gender of the patient, type of surgery (primary or revision THR) as well as pre and post-surgery haemoglobin values. Other data included clinical information and observations, as well as the type of blood bank order, the amount of red blood cell products requested and the amount of red blood cells transfused. (See Addendum 1).

The folders were requested from the medical records department of the respective hospitals and reviewed. The information was recorded as required on the data collection form.

The patients who had undergone THR surgery during the review period were identified from the operating lists of the respective orthopaedic departments.

The audit at Hospital Green (HG) was conducted by manual folder review while at Hospital Yellow (HY) it was conducted via manual folder review as well as accessing computerised records.

The following co-morbidities present at the time of surgery were documented: diabetes, hypertension, cardiac disease, bleeding disorders, asthma, tuberculosis (TB), cancer and hypercholesterolemia. These were of interest and importance to the study as existing co-morbidities could have an effect on the amount of blood the physician would request. It has been recommended that patients with pre-existing cardiac conditions and co-morbidities should have a higher transfusion threshold, although in a study by Carson et al in 2011 it was concluded that it was reasonable not

to transfuse patients who had undergone surgery, in the absence of symptoms of anaemia or a drop in haemoglobin of below 8g/dL, even in elderly patients with underlying cardiovascular disease or risk factors.

The indications for surgery were documented and included: osteoarthritis, rheumatoid arthritis, post traumatic arthritis, osteonecrosis - also known as avascular necrosis (AVN), childhood hip disease (Legg-Calve-Perthes Disease). A check box was designated to include any reason for surgery which did not fall into the categories listed.

All information on the initial pre-operative blood transfusion request was collected. This included a blood group and antibody screen (G&S) or a blood group and antibody screen and a cross match.

Data on transfusion episodes were recorded from day one of surgery and was concluded on the day of discharge or day thirty post surgery, whichever came sooner.

Post-operative complications were documented but were not limited to the following: Infection, deep vein thrombosis (DVT), ventilation, other and none. “Other” referred to complications not listed in the data collection sheet but which were significant enough to be analysed in the study.

Performance indicators for the purpose of this study included: the percentage of patients transfused per hospital, the number of RBCC transfused per hospital as well as the “trigger” haemoglobin levels at which the patient was transfused.

Haemoglobin values were recorded for both pre and post-surgery and in situations where more than one value existed, the lowest value was used.

Information for the study was retrieved from the admission checklist, nursing notes, surgery notes, fluid chart notes, physiotherapist’s notes and discharge notes found in the patient’s folder.

3.4 Ethical and Legal considerations:

All information captured during the audit was treated as confidential and did not reveal the identity of the respective hospital, hospital personnel or patients. Complete anonymity was achieved by assigning a colour code to each hospital, as well as a unique study number to each patient. Hard copies of the data collection form were securely stored in a locked filling cabinet on the premises of WPBTS. This was to ensure that unauthorized personnel not involved in the study would not have access to the information. Informed consent from individual patients was not required due to the anonymity of the study and because no new data would be required.

Approval was obtained from the Cape Peninsula University of Technology's Ethics Committee (Ethics number CPUT/HW-REC2013/H38, see Addendum 2). Once ethics approval was given, permission was obtained from the management of the relevant hospitals. Responses from the relevant hospitals are not included in the addendums to ensure confidentiality of the hospitals but are available on request.

3.5 Statistical analysis

Data from individual data collection sheets was uploaded onto IBM SPSS version 22 statistical package for analysis. From this, frequency tables, contingency tables as well as descriptive analysis for numeric variables using mean, standard deviation and standard error were deduced.

Summary statistics are given as means and standard deviations (SD) and average values were presented as a mean or median where deemed appropriate.

Performance indicators included the number of patients transfused per hospital as well as the number of units transfused per hospital.

The Chi-square test was used to identify significant differences between two or more groups pertaining to categorical variables or to test for a significant association between two categorical variables.

The student t-test was used in this study to compare the means of a numerical variable between two groups. (Mean female Hb vs. Mean male Hb).

p Values are given to test the null hypothesis thus testing the validity of a claim made about this population.p Values were given for information purposes and a p value of <0.05 was considered significant and would reject the null hypothesis.

4. Chapter Four: Results

4.1 Study population

A retrospective audit by folder review was conducted on two hundred and seven consecutive patients admitted for elective Total Hip Replacement (THR) to two tertiary referral hospitals in the Western Cape province of South Africa from January 2013 to December 2013. Twenty four patients were excluded as there had been recent trauma to the hip, one patient was excluded due to the presence of an underlying primary malignancy in the hip and sixty two patients were excluded owing to incomplete data in the folder. This left one hundred and twenty patients eligible for review, which were equally split between the two hospitals (Table 1).

Table 1: Demographics and Baseline Characteristics

	All patients	Male	Female
Total no.	120	48	72
Age (Mean)	64.2	61.0	66.0
Procedure			
Primary Unilateral THR	97	42	55
Revision THR	16	4	12
Primary bilateral THR	7	2	5
Indication for THR			
Osteoarthritis	86	31	55
Rheumatoid arthritis	3	0	3
Trauma (>12 months)	5	2	3
Osteonecrosis	7	6	1
Childhood hip disease	1	1	0
Other *	12	6	6
Data unavailable	6	2	4
Co-morbidities	91	31	60
Hypertension(HT)	45	11	34
Diabetes	1	1	0
Diabetes & HT	10	4	6
HT & **other diseases	20	8	12
Tuberculosis(TB)	2	1	1
Cardiac	4	3	1
*** Other	9	3	6

***** Ankylosing spondylitis, scoliosis, painful hip

** Cancer (in remission), asthma, TB, hypercholesterolemia, Parkinson's disease

******* Myasthenia gravis, Parkinson's disease, ulcerative colitis, chronic obstructive pulmonary disease, epilepsy, diverticulitis, Paget's syndrome, restrictive lung disease.

4.2 Transfusion Rates (see Figure 2)

Of the total sample population, thirty one (25.8%) patients were transfused with red cell concentrates either intra-operatively or within twenty four hours post-operatively. Of these six (5%) were at HG and the remaining twenty five (21%) at HY, while the remaining eighty nine (74%) received no blood products. The average number of units transfused to each patient was 2.7. All transfused patients received allogeneic standard buffy coat depleted Red Cell Concentrates (RCC's). Pre-deposit autologous donations are not offered at the two hospitals.

There was a significant difference between the transfusion rates at the two hospitals ($\chi^2_{=}$ 15.701, p-value < 0.001). Also of note is the significantly higher (33% vs. 15%) transfusion rate in females ($\chi^2_{=}$ 5.285, p-value < 0.05). Patients with co-morbidities were more likely to receive blood than those without co-morbidities, however this was not statistically significant (Figure 2).

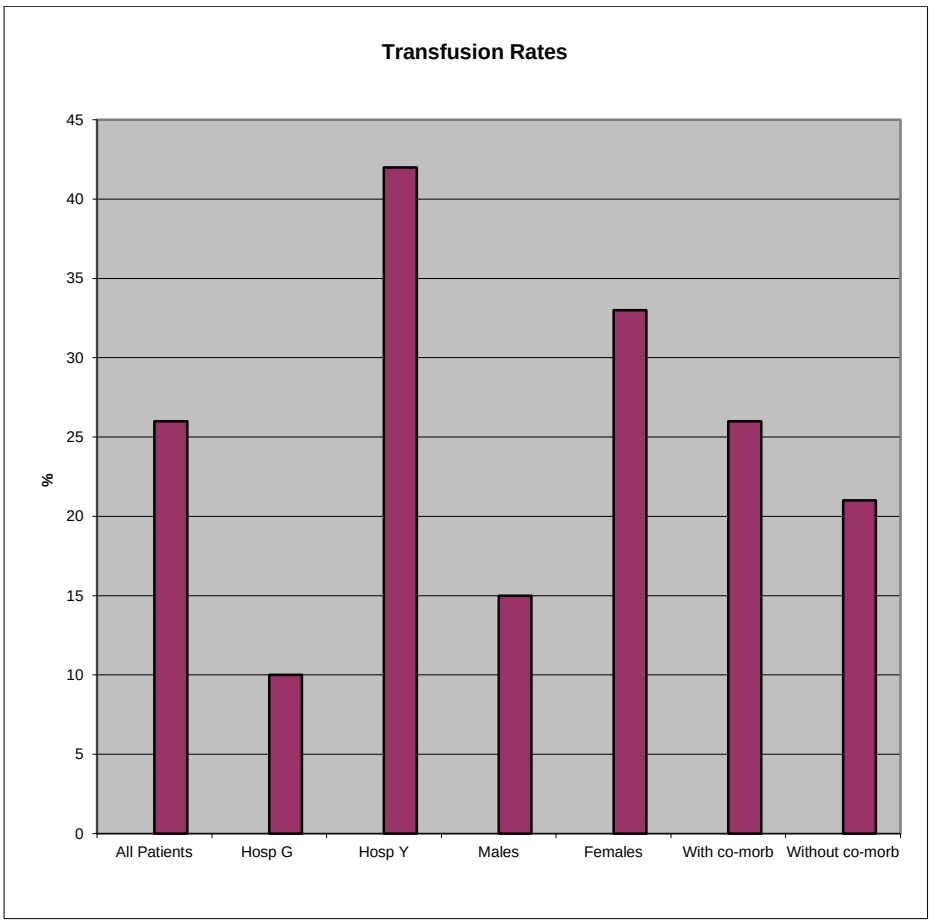

Figure 2: This graph demonstrates the significant difference between the transfusion rates at the two academic hospitals (p-<0.001) and between males and females (p<0.05). There is no significant difference between those with and without co-morbidities.

Figure 3 summarises the pre and post-surgery Hb levels for all patients (Addendum 3) and is further broken down into those who were transfused compared with those who received no red cell concentrates. On average the post-operative Hb was 2.7g/dL lower than the pre-operative Hb in all patients. The transfused patients had significantly lower mean Hb's than those who were not transfused. (Pre-Surgery Hb t-value = 4.821, p-value < 0.001; Post-Surgery Hb t-value = 5.225, p-value < 0.001).

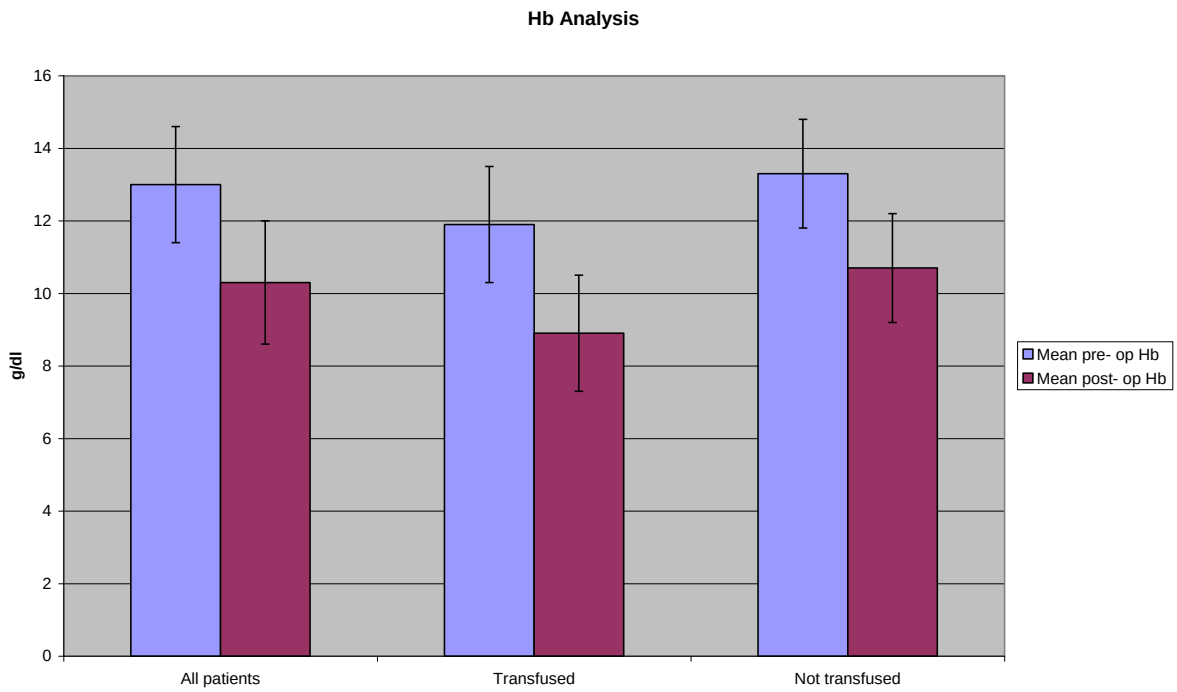

Figure 3: Transfused patients had significantly lower mean Hb than those who were not transfused ($p<0.001$)

4.3 Blood Bank Ordering Analysis (Figure 4)

Blood was cross matched for forty (33%) patients: seventy three (61%) had a Group and Screen (G&S) procedure, twenty nine ((24%) had a G&S converted to a full cross match, eleven (9%) had a full pre-operative cross match while seven (6%) had no blood bank order. In summary, one hundred and thirteen (94%) of the sample population had a pre-operative blood bank order. In total, one hundred and sixteen RCC's were cross matched and eighty four RCC's were transfused giving a cross match/transfusion ratio of 1.4.

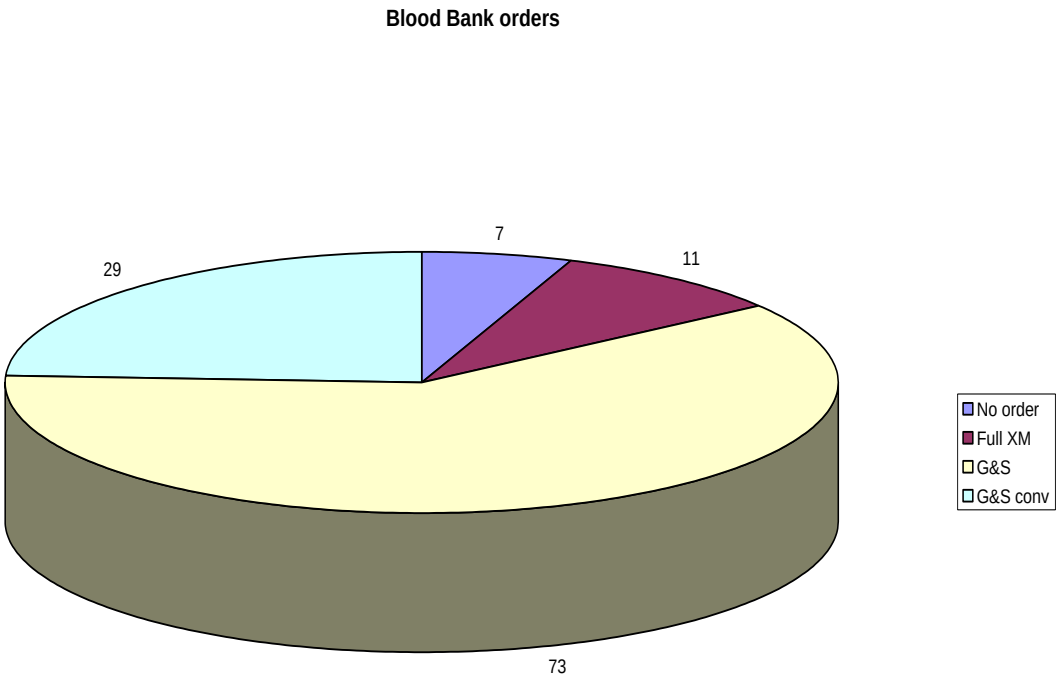

Figure 4: One hundred and thirteen (94%) of patients had a pre-blood bank order. This diagram demonstrates the breakdown of these orders. Seven (6%) had no blood bank order.

4.4 Age Group Analysis and Transfusion rates (Figure 5)

Not surprisingly, given the nature of the underlying pathology, the majority of patents were > 60 years (yrs). Of note is the significantly increased transfusion rate with increasing age. The mean age of those not having received a transfusion was 62.16, with a standard deviation of 11.75, while the mean age of those having received a transfusion was 70.03 with a standard deviation of 10.01. This difference was statistically significant (t-value = 3.33, p-value < 0.005).

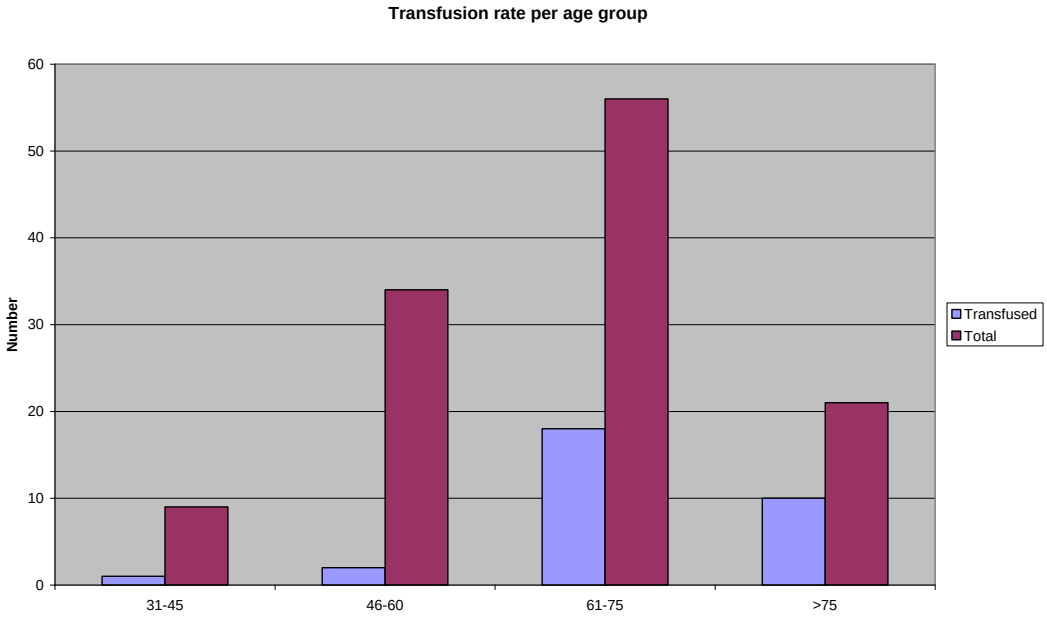

Figure 5: This diagram demonstrates that the transfusion rate increases with increasing age.

4.5 Length of Hospital Stay (LOS) (Figure 6)

The majority of the patients were discharged by day ten. None of the patients discharged by day five received a transfusion. There was a significant statistical association between receiving a transfusion and LOS ($p<0.01$).

The length of hospital stay could be associated with a number of factors including anaemia and pre existing co-morbidities. In our study however the presence of a co-morbidity was not associated with an increased transfusion rate. The finding of an association between having a transfusion and LOS has been previously described (Jans et al., 2011).

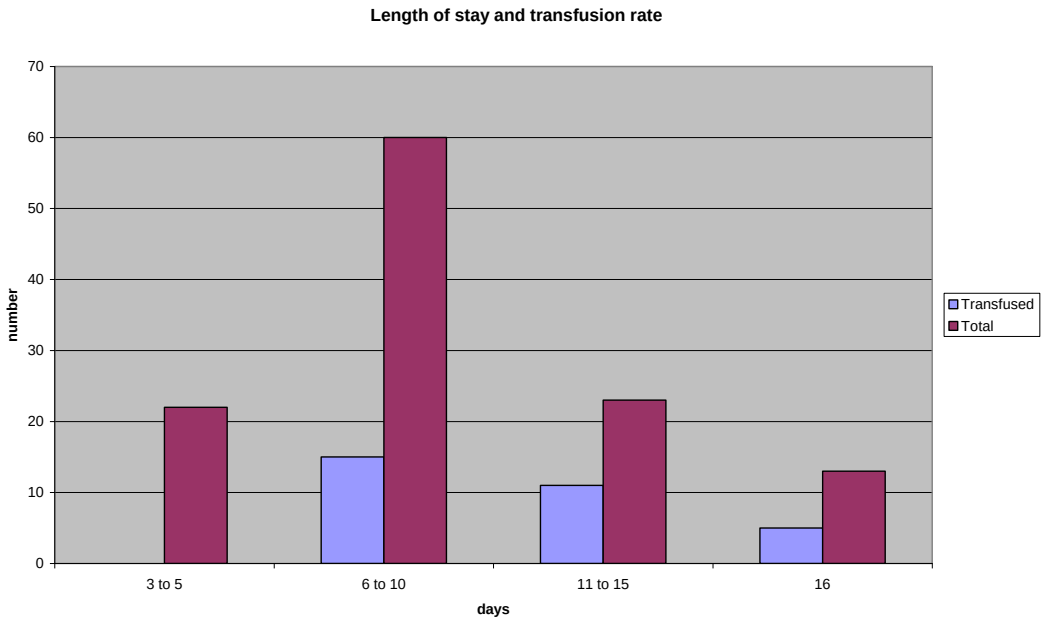

Figure 6: This graph demonstrates the significant association between length of hospitals stay and transfusion rate ($p<0.01$).

4.6 Post-operative Complications:

A total of one hundred and seven (89.2%) had no post-surgery complications. Of the remaining thirteen, one (0.8%) developed Deep Vein Thrombosis (DVT) complications despite the application of DVT stockings and three (2.5%) developed infections and were given antibiotics. Nine (7.5%) developed complications listed as other. This included acute urinary retention, allergy/itching, rash (due to general anaesthesia), severe vomiting, a cardiac episode and temperature spikes.

Of the six patients transfused at HG none had post-operative complications. Of the twenty five patients transfused at HY, five had post-operative complications. These included infection, DVT, cardiac episode, acute urinary retention and a rash following general anaesthesia.

4.7 Comparative Analysis of the Two Centres

As noted earlier there was a significant difference in the transfusion rates between the two centres and therefore the data from each hospital was analysed separately.

4.7.1 Haemoglobin values (Raw Hb values attached: see Addendum 3)

Figure 7 shows that most transfused patients post-operative Hb levels were close to the generally recommended restrictive "trigger" Hb level of 8g/dL. This is particularly seen at HG whereas at HY, the mean Hb trigger is closer to 9.0g/dL. Although the numbers are small, at HG three (50%) patients were transfused with post-operative Hb of > 8.0 g/dL, whereas at HY seventeen (68%) of transfused patients had post-operative Hb levels of > 8.0 g/dL.

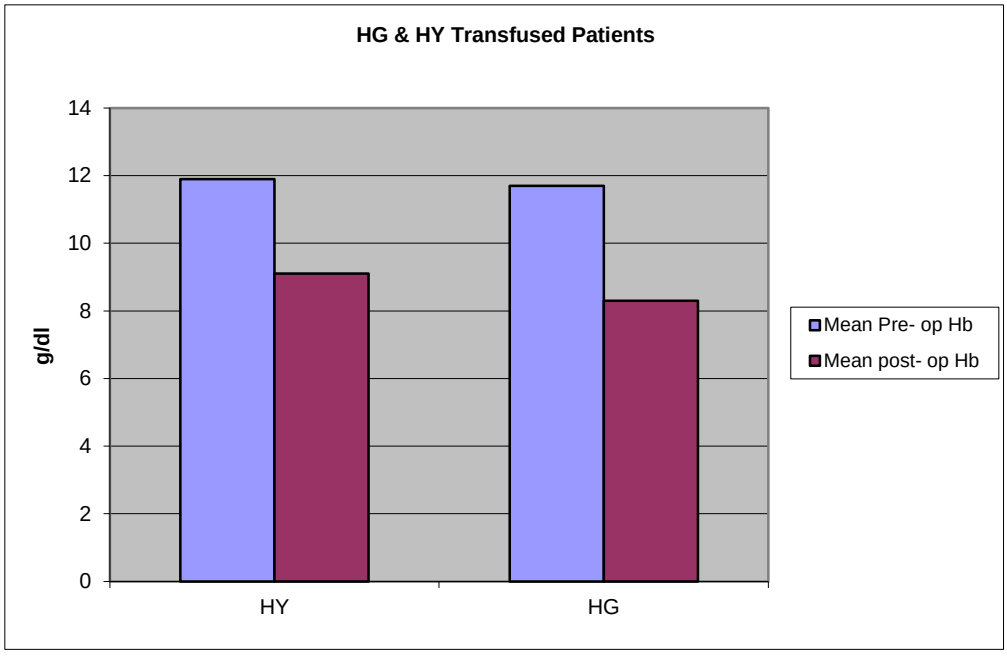

Figure 7: The mean haemoglobin levels pre and post-surgery at the two hospitals.

4.7.2 Co-morbidities

It has been shown earlier that the transfusion rate for patients with co-morbidities was higher than those without co-morbidities, but this did not reach statistical significance. When broken down to the individual hospitals, HG had forty two patients with co-morbidities of which four (10%) were transfused, while HY transfused twenty one of forty nine (43%) patients with co-morbidities. There was a significant difference between the two hospitals in the transfusion rates of patients with co-morbidities ($p<0.001$).

4.7.3 Gender

As shown in Table 1 and Figure 2, the majority of patients were female, particularly at HY where forty one (68%) of the patients were female. At HG they were split more or less evenly and thirty one (51.7%) were female. The transfusion rate was significantly higher in female patients ($p<0.05$).

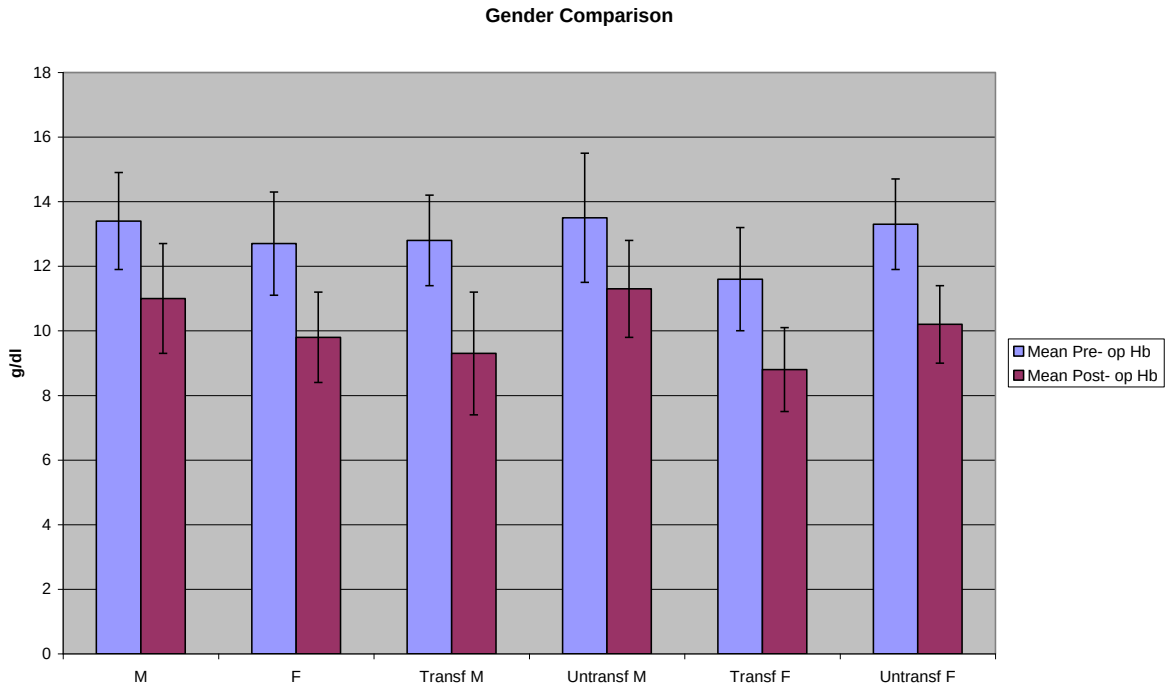

Figure 8: Gender differences in haemoglobin levels between male and female patients.

Figure 8 reflects the gender difference in Hb levels normally seen in the general population. Transfused patients, both male and female, had significantly lower mean Hb levels than those patients who were not transfused.

Table 2: Pre and post-surgery haemoglobin in male and female patients.

Group Statistics

	Gender	N	Mean	Std. Deviation	Std. Error Mean	t-value	p-value
Pre-surgery haemoglobin	Female	72	12.699	1.6379	.1930	2.366	<0.05
	Male	48	13.404	1.5416	.2225		
Post-surgery haemoglobin	Female	72	9.818	1.4316	.1687	4.118	<0.001
	Male	48	11.017	1.7403	.2512		

4.7.4 Blood ordering analysis

Figures 9a and 9b show a comparison of the blood ordering analysis at the two hospitals. Both hospitals used the G & S as the default order (fifty four at HG; forty eight at HY). Not unexpectedly, given the higher transfusion rate, HY had a larger number converted to a full cross match and the number of full cross matches ordered pre-operatively was three to four fold greater than at HG.

HG requested full cross matches for ten patients (total of twenty-two units) of whom six were transfused with eleven RCC's resulting in a cross match/transfusion ratio of 2 and an average of two units per patient transfused. At HY blood was cross matched for thirty patients (total of ninety four units) of whom twenty five were transfused with seventy three RCCs, giving a cross match/transfusion ratio of 1.3 and an average of three units per patient.

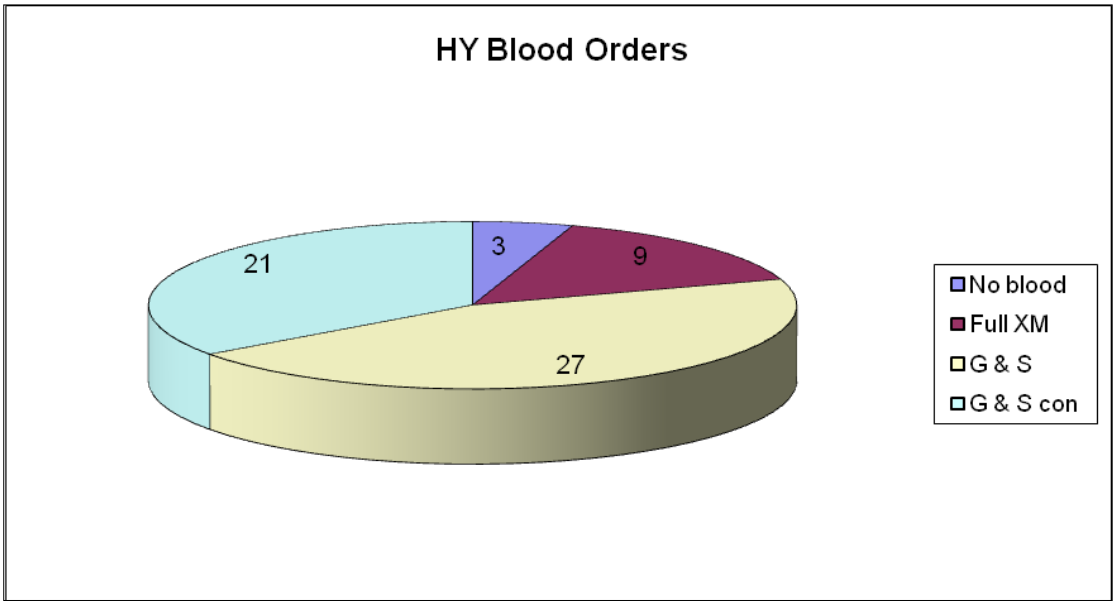

Figure 9a: Blood orders for HY

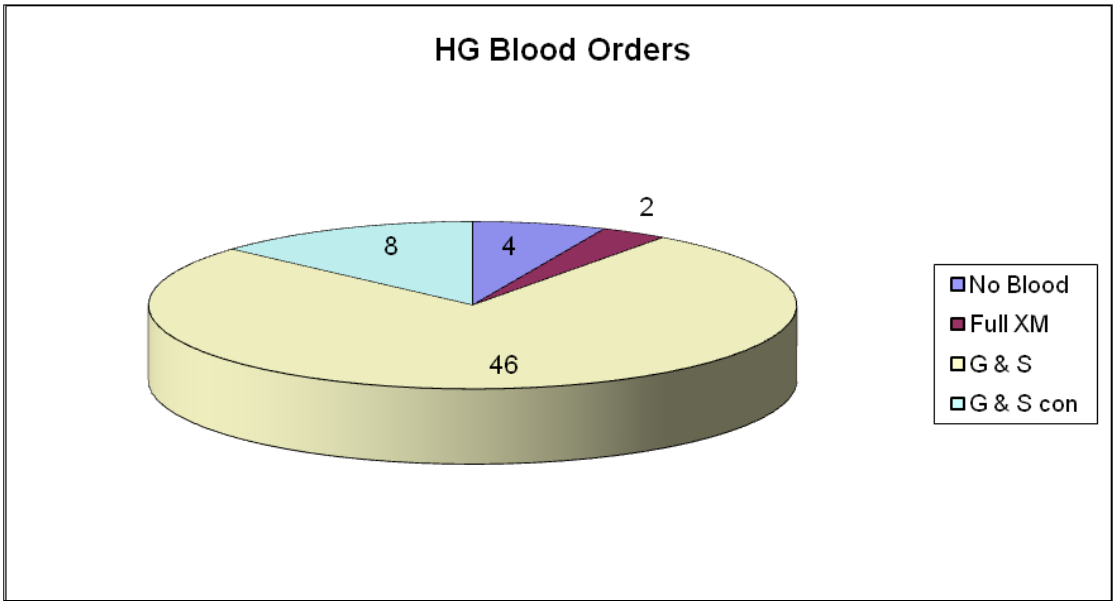

Figure 9b: Blood orders for HG

4.7.5 **Age Group comparison** (figure 10)

The mean age at HG was 62.6 yrs (range 33-88); while at HY the mean age was 65.8 yrs (range 38-84). This difference was not statistically significant (t-value = 1.485, p-value >0.05). This has been demonstrated graphically below in Figure 10 where the age groups are compared in age group categories.

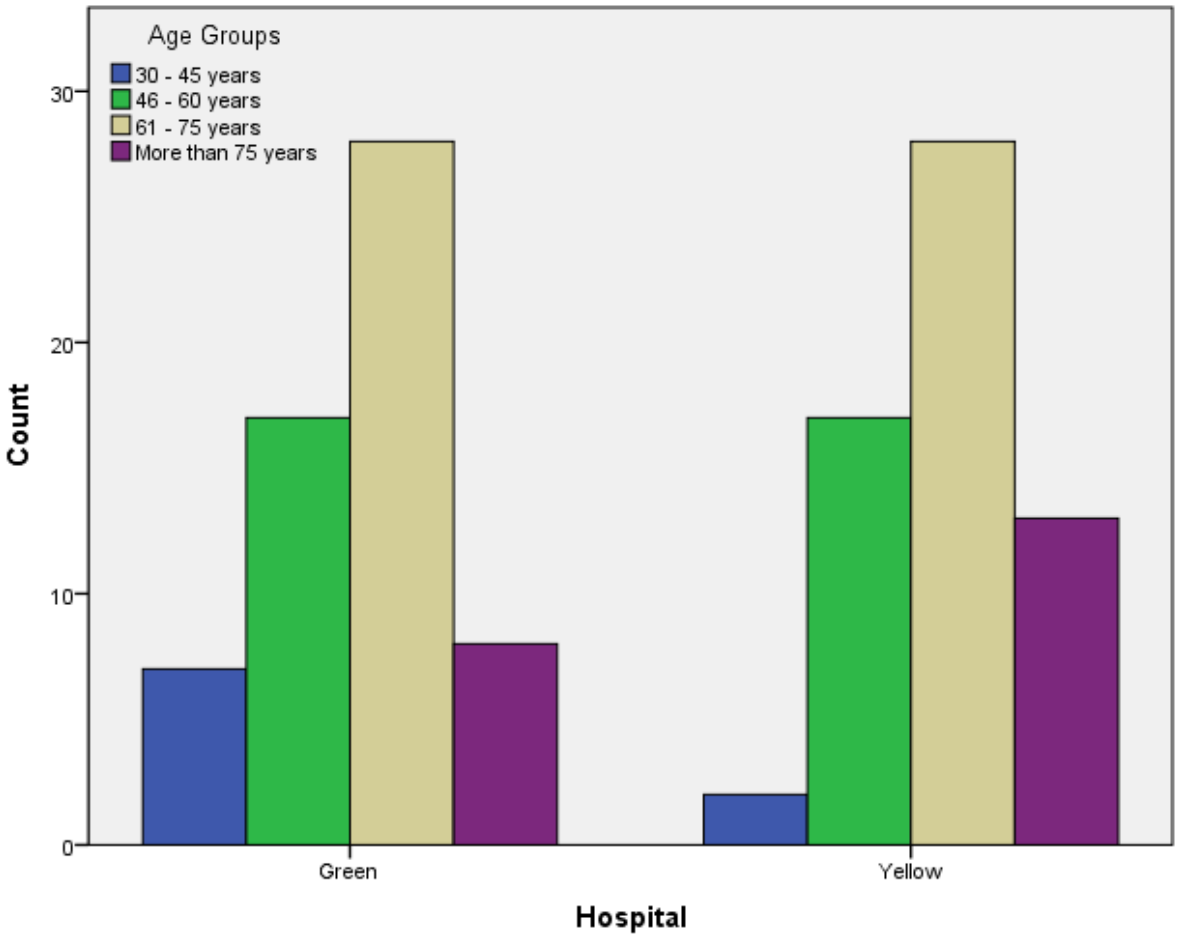

Figure 10: There was no significant difference between the age groups of patients receiving THR between the two hospitals.

4.7.6 Length of Hospital Stay (LOS)

The length of hospital stay is markedly different between the two hospitals (see figure 11). This difference did not appear to be associated with post-operative complications as the prevalence of the latter was low. However, those patients who had a hospital stay of more than five days had a far higher transfusion rate than those discharged within five days.

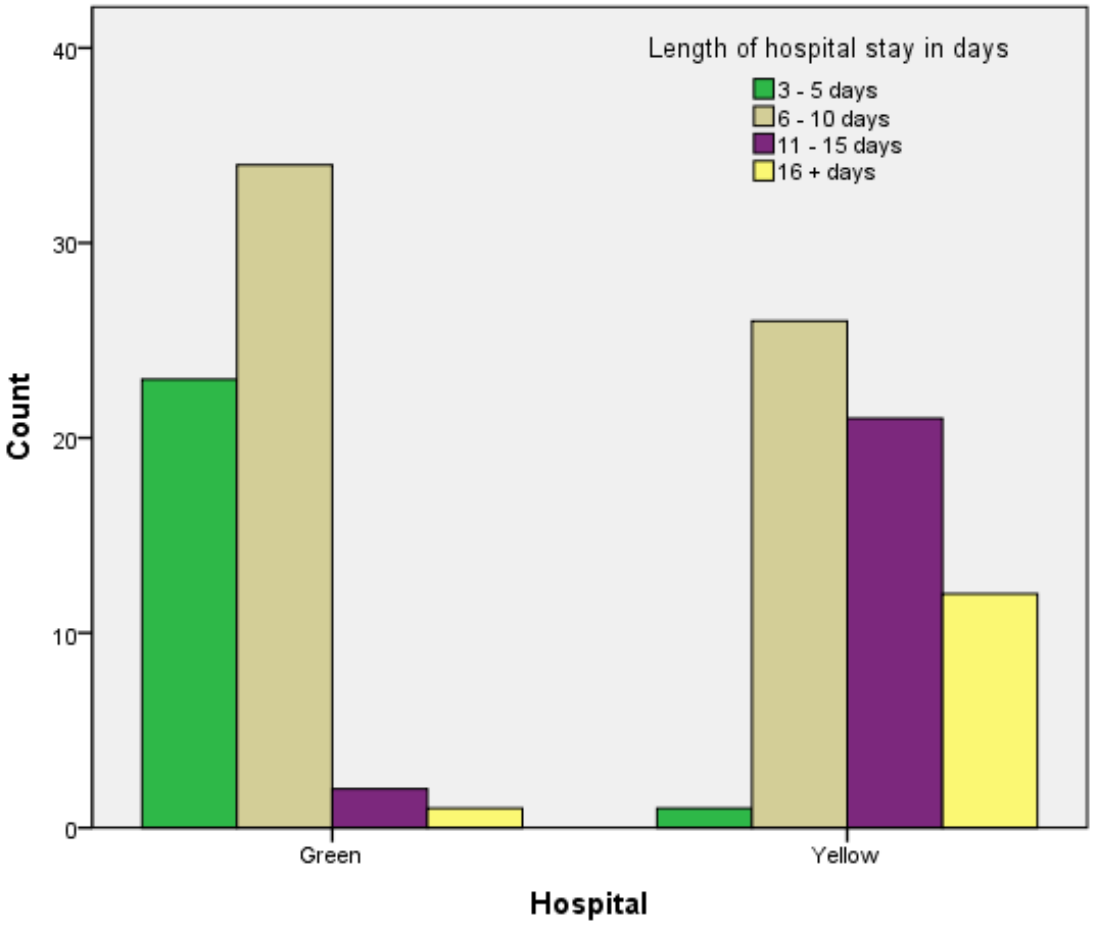

Figure 11: This graph demonstrates the significant difference between the hospital stays at the two hospitals. ($p < 0.001$).

5. Chapter Five: Discussion

International studies have revealed wide variations in red blood cell transfusion practice for elective surgery including total hip replacement (THR). In addition, these studies have also reported the impact of varying transfusion practices on patient care and financial resources (Mallet, 2000:1003-1024; Spencer et al., 2005:28-30; Jans et al., 2011:374-380). Blood products are a valuable resource and because no such study has been performed in the Western Cape, the aim of this project was to evaluate the utilisation of red blood cell products in THR surgery at two tertiary referral hospitals in the Western Cape by means of a clinical audit.

5.1 Transfusion Rates

According to Wallis et al (2001) an audit of compliance with a recommended transfusion trigger is possible in well-controlled circumstances. However where widely varying clinical factors are present and the decision to transfuse must be made during varying states of blood loss, this type of audit may be difficult to perform. For this reason only patients undergoing elective THR were selected to participate in the study. In addition, for the same reason patients with bleeding abnormalities were noted and excluded from the study.

The international variability in transfusion rates was highlighted by a nationwide Danish study by Jans et al (2011). This audit reported that the transfusion rates varied between seven and seventy one percent for THR surgery. A further article published by the Sanguis Group in 1994 noted that in Europe if an elderly patient needed a THR, depending on the hospital of choice, the chances of receiving a transfusion varied from between thirty to one hundred percent (Sanguis Study Group, 1994).

In our current study the overall transfusion rate was less than 50% for both hospitals combined. Hospital HG had a transfusion rate of 10% which was significantly lower

when compared to hospital HY which had a transfusion rate of 41.6%. This finding is consistent with international studies where transfusion rates ranged from 3%-100%, (Sanguis Study Group, 1994; Gombotz et al., 2007; Boralessa et al., 2009; Joy & Bennet, 2012; Jans et al., 2011). (Europe, Austria, U.K., Denmark).

The difference in transfusion rates between the two hospitals cannot be explained however hospital HG has had previous audits which possibly resulted in signage reminding clinicians to order G&S for certain procedures as opposed to ordering blood. The distribution and availability of the clinical guidelines was similar at both hospitals.

It is, therefore, difficult to set a benchmark based on the published work owing to the wide variation in transfusion rates. Nevertheless, it has been recommended that each centre should review its transfusion policy for this procedure and follow a restrictive transfusion regimen which has been shown to be equally efficacious when compared to a more liberal one (Carson et al, 2011). Carson et al., reported a study in which patients who were considered at high risk for cardiovascular disease were assigned to a liberal transfusion arm and were transfused at a Hb trigger of 10g/dL, while in the restrictive group, patients were transfused if there were symptoms of anaemia or a trigger of 8g/dL. Patients in the liberal arm received a mean of two units of red cells per patient whereas those in the restrictive group received no blood. The results demonstrated that there was no significant difference between the two groups in terms of mobility, mortality or cardiovascular events at sixty days post-operative follow up and it was therefore concluded that a more restrictive transfusion policy is equally effective. (Carson et al., 2011).

5.2 Gender

The transfusion rates for females were significantly higher than that of males (See Figure 2). Similar findings have been demonstrated in other studies (Jans et al., 2011; Tellisi et al., 2007; Rosencher et al., 2003).

In a study by Gombotz, conducted in Austria, the transfusion rates for females were found to be 52%, whereas for males it was 29.6%. This was a prospective observational study and included eighteen randomly selected public hospitals. A total of one thousand four hundred and one patients undergoing primary unilateral THR were analysed (Gombotz et al., 2007).

A similar finding was reported in the United Kingdom. The aim of this study was to review transfusion practice in primary hip arthroplasty in order to produce guidelines to help reduce the consumption of allogeneic blood. This audit consisted of seventy two patients who received blood transfusions. Of these, thirty nine (54%) were females while the remaining thirty three (46%) were male (Tellisi et al., 2007).

Our project demonstrated that the mean pre-operative Hb for all female patients was 12.7g/dL, which is just within the National Health Laboratory Service (NHLS) reference range (12g/dL-15g/dL). Nineteen (26%) females were anaemic in terms of the reference range. Male patients had a mean pre-operative Hb of 13.4g/dL which is also at the lower limit of the NHLS reference range for males (13g/dL-17g/dL). In total, 16 (33%) of the male patient group were anaemic. Despite this, the transfusion rate for females was significantly greater than for male patients. This suggests that factors other than Hb levels were considered when making the decision to transfuse in this group of patients.

Our results therefore support previous studies which suggest that the transfusion rate in female patients is significantly higher than that for male patients.

5.3 Co-morbidities

Patients with co-morbidities had a higher transfusion rate than those without. This however did not reach statistical significance. Hospital HG had a similar number of patients with co-morbidities when compared to HY yet despite this, fewer patients were transfused. The presence of co-morbidities in this study therefore was not associated with an increased transfusion rate.

In the study by Tellisi et al., (2007) out of a total of seventy two transfused patients, ten presented with hypertension and ten with cardiac disease. In the non-transfused group, which represented twenty one patients, four had hypertension and one had cardiac disease. In this study the co-morbidities were merely mentioned and it was not stated whether co-morbidities had influenced transfusion rates or not.

In a further study by Carson, patients with cardiovascular disease were studied as cardiovascular disease is the most significant co morbidity associated with anaemia and potential transfusions. The results of this audit proved that a restrictive regime was as effective as a liberal transfusion regime (Carson et al., 2011).

5.4 Age

In a study done in Denmark the mean age of the patients undergoing elective surgery was sixty nine years (Jans et al., 2011). A further article by the Sanguis Study Group, which monitored the use of blood products for this type of surgery in forty three European hospitals, reported a similar mean age of sixty six years (Sanguis Study Group, 1994). Our study targeted a similar group of patients and the mean age of the study population was sixty four years. In addition, our audit also revealed that that there was no significant difference between the mean age of the patients at both hospitals and that the age categories of the two hospitals were similar. In the age group category 46-60 years, both hospitals had seventeen patients while in the age group category 61-75 years, both hospitals had twenty eight patients.

Of significance however was the mean age of the patients who received a transfusion which was seventy years. This was significantly increased when compared to those patients who did not receive a transfusion who had a mean age of sixty two years (p value < 0.005).

Similar findings have been reported in Italy and the United Kingdom. In these countries the mean age for receiving a blood transfusion in their cohorts of patients was 77.4 and 71.45 years respectively. (Verlicchi et al., 2011;Tellisi et al., 2007). In the study

done by Verlicchi in Italy a total of three hundred and eighteen patients undergoing THR surgery at four public hospitals were evaluated. Included in this study were one hundred and seventy nine patients undergoing THR surgery at private hospitals. This study, although inclusive of THR surgeries, also included patients undergoing knee replacement surgery and compared private and public transfusion rates. The authors concluded that patients undergoing surgery at public institutions were more likely to be transfused than those patients at private institutions Verlicchi et al., 2011).

In summary therefore, the mean age group of the study population in our audit receiving red cell concentrates was significantly higher than those who did not and this confirms the findings of similar studies in the current literature.

5.5 Haemoglobin Analysis and transfusion triggers

Post-surgery there was a mean drop in Hb levels of 2.7g/dL .The transfused patients had a significantly lower pre and post-surgery Hb than those who were not transfused. This finding is consistent with other published reports (Ratcliffe et al., 2013; Guerin et al., 2005).A study carried out by Guerin et al., included a total of one hundred and twenty patients who were analysed with the aim of identifying predictors of total blood loss in THR surgery. The results of this work suggested that the decrease in the haemoglobin level in patients less than seventy years of age was 2.77g/dL. However, in patients older than seventy it was slightly higher, at 3.53g/dL (Guerin et al., 2005). Therefore the use of haemoglobin level as a “trigger” appears to be important when making the decision to transfuse.

In a further study, patients undergoing THR in thirty hospitals in Canada were evaluated. Transfusion triggers were set at Hb levels of less than 7g/dL, where a transfusion was likely to be appropriate, between 7 and 10 g/dL, if accompanied by symptoms and inappropriate if the Hb was > 10g/dL. In this project a comprehensive blood conservation programme was implemented via the use of this algorithm. The study concluded that patients were less likely to be transfused at hospitals that implemented this programme than patients treated at other institutions (Wong et al., 2007).

The trigger to transfuse in our study appears to be at a Hb level of 8g/dL at hospital HG and 9g/dL for hospital HY (see Figure7). Three (50%) of the patients transfused at HG had a Hb of > 8 while at HY seventeen (68%) of the twenty five patients were transfused with a Hb of >8g/dL. This finding probably explains the differences in transfusion rates between the two hospitals. Current guidelines support a trigger Hb of 7-8 g/dL (Carson et al, 2012; Ingram, Bellairs and Bird, 2014; Joy and Bennet, 2012 (AABB, SA, British). Exceptions to this would be patients with severe cardiac ischemia. However, this has been challenged by studies which have demonstrated that a restrictive regimen was equally as safe as a liberal policy in patients with a high risk for cardiovascular disease (Shander et al., 2012; Carson et al., 2011).

5.6 Blood ordering analysis

A group and screen (G&S) was the order of choice which is appropriate considering the transfusion rates. Both hospitals utilized this request appropriately and were therefore compliant with the Clinical Guidelines. A G&S was ordered for seventy three (61%) of patients, of which twenty nine were converted to full cross matches. HY had a higher conversion rate of G&S to cross matches (21 vs. 8) which was not surprising, given the higher transfusion rate at this hospital.

An example of an MSBOS published by the AABB recommends that up to three units of blood should be cross matched pre operatively for THR surgery. (Roback et al., 2011). However, institutional practices regarding the number of units to be cross matched varies. In one study, a G&S was recommended for 5 of 12 elective orthopaedic procedures and if blood was to be cross matched, a maximum of 2 units was recommended for some elective surgeries. (Subramanian et al., 2010).

The results of our study suggest that routine pre-operative orders for cross matched RCC’s are unnecessary and that a G&S is sufficient.

The cross match transfusion ratio of both hospitals taken together was 1.4, which is acceptable. Cross match transfusion ratios of more than 2 would indicate excessive cross match orders and would imply a potential wastage of 50%.

This audit revealed that HG had a low transfusion rate but with a cross match transfusion ratio of 2. This result indicated a 50% return rate with potential wastage. The number however is small given the low transfusion rate. In contrast HY had a higher transfusion rate but a cross match transfusion ratio of 1.3. This finding demonstrates that C/T ratios should be interpreted in the context of transfusion rates, trigger Hb's and other factors.

Previous guidelines have supported the practice of ordering multiple units of blood which are transfused consecutively without an assessment of the patient's condition between units (Audet et al., 1996). Recent data, however, has suggested that this is not optimal (Audet et al., 1998). It was recommended that patients have single unit transfusions and that for subsequent units, the patient should be assessed before the next unit is transfused. (Audet et al., 1998).

5.7 Length of Hospital Stay (LOS)

International studies have reported that the average LOS for patients receiving a transfusion was six days and for those who did not receive a transfusion, four days (Jans et al., 2011). Other audits have suggested that an increased LOS was associated with anemia on admission, post-operative anaemia and the transfusion of RCC's (Spahn et al., 2010:889).

In the study by the Sanguis Group (1994), where forty three European hospitals were evaluated for their blood use in elective surgeries, the mean post-operative LOS for patients undergoing THR surgery was found to be fourteen days. The total number of patients in this study was one thousand, six hundred and forty seven patients and a

transfusion rate of 80.8% was reported (Sanguis Group, 1994). The high transfusion rate could possibly explain the long LOS.

A further audit performed in six European countries analysed the LOS of two thousand six hundred and forty patients. The investigators limited the number of patients to twenty patients per centre and the LOS was found to be twelve days. An additional finding was that the transfusion rate was 68%, which is also considerably higher than the transfusion rate in our study (Rosencher et al., 2001).Therefore it appears that in both these studies a high transfusion rate is linked to a longer hospital stay.

In contrast, a large randomised trial conducted in twenty nine hospitals in Ontario, Canada, revealed a much shorter LOS. The aim of this study was to evaluate a blood conservation algorithm in patients undergoing total hip joint arthroplasty. A total of sixty patients were studied and the mean LOS was 6 days (Wong et al., 2007).

Our study appears to favour a slightly more conservative transfusion rate and a shorter LOS rather than a higher LOS and the transfusion rates reported in European countries.

Our audit demonstrated a significant difference between the two institutions (HY and HG) with regard to those categories of patients staying in hospital for more than six days. All of the patients at HG who were transfused had a hospital stay of between 6-10 days, while at HY most of the transfused patients had a LOS of more than six days. In this study therefore, it appears that transfusion is also associated with a longer period of hospitalisation.

5.8 Post-surgery complications

In the study by Wong et al., a total of 1.2% of the total patients who had undergone THR surgery developed major complications that were potentially attributable to postoperative anaemia and were listed as follows, myocardial infarction, stroke or death (Wong et al., 2007). This study did not evaluate patients for minor complications such as the ones included in our study.

In our study of the thirteen patients who had post operative complications, five were transfused at hospital HY, while none of the transfused patients at HG developed any post operative complications.

6 Chapter Six: Conclusions, Recommendations and Limitations

6.1 Conclusions

In conclusion this study has found that:

a) The mean transfusion rates for both hospitals combined was 25.8%, which compares favourably with other publications even though published data indicates a wide variation in transfusion rates (Sanguis Study Group,1994; Boralessa et al.,2009; Jans et al., 2011; Spahn, 2010). HY had a transfusion rate of 41.6%, which was significantly higher than HG at 10%.

b) The mean pre-operative Hb levels were significantly lower in transfused patients when compared to those who did not receive blood.

c) The mean Hb trigger for transfusion at HY was 9.1g/dL as compared to a more restrictive trigger of 8.3g/dL at HG.

d) Transfusion rates were significantly higher for female patients (33% vs15%) despite the findings that their mean pre-operative Hb values were within the reference range and that significantly fewer females were anaemic compared to males patients.

e) Patients who had co-morbidities had a higher transfusion rate than those without, but this did not reach statistical significance.

f) The mean age of transfused patients was significantly higher than non-transfused patients.

g) Length of hospital stay was associated with a greater likelihood of transfusion.

h) G&S is the appropriate pre-operative blood order for elective primary THR.

These findings are largely in agreement with other studies where age, Hb levels, weight and estimated blood loss at surgery were predictors of transfusion (Rosencher et al., 2003; Guerin et al., 2005; Garrioch, et al., 2004).

In this study we did not record weight nor did we document estimated blood loss from the folder notes. There was a mean drop in Hb of 2, 7 g/dL, which is similar to other studies and therefore it is likely that the blood loss in THR at the two centres was not very different to that seen in other studies (Guerin et al., 2005; Ratcliffe et al., 2013; Gombotz et al., 2007).

The increased transfusion rate in females has been reported in other audits (Jans et al., 2011; Tellisi et al., 2007; Rosencher et al., 2003), but it is difficult to explain the reason for this finding, especially in the light of the greater prevalence of pre-operative anaemia amongst males.

In the blood ordering analysis a G&S was the favoured order which is appropriate given the transfusion rates. The standard recommendation for THR in some centres was a pre-operative cross match of 2-3 RCC's. This study does not support this and a G&S order is safe and more cost effective. (R 172.00 vs. R1092 per RCC cross matched).

It could be argued that at an institution where there is an onsite blood bank, the requirement for a G&S could be waived since RCC's can be rapidly cross matched and dispatched. While calculating the cross match /transfusion ratio is helpful, it must be assessed in the light of the transfusion rate and the guideline "trigger" Hb.

6.2 Recommendations

Each centre should have a policy for blood management which should include:-

- A recommended “trigger” Hb. A number of studies have confirmed that a restrictive transfusion regimen (in THR and other elective surgeries) is safe and Hb levels of 7-8 g/dL are acceptable limits before considering a transfusion (Shander et al., 2012; Carson et al., 2011).

- Continual monitoring of transfusion rates and comparison with published data is important. Although it is difficult to set a benchmark given the variation in practice, maintaining a transfusion rate of 10 – 20% appears to be reasonable. If the transfusion rate increases, factors influencing the transfusion rate should be investigated – e.g. possible increased age of the patient population as well as possible increased prevalence of pre-operative anaemia.

- The recommended pre-operative blood order is a G & S.

Ideally the blood management programme should include a pre-operative assessment of anaemia and appropriate management (e.g. oral iron therapy if hypochromic, microcytic anaemia is present) to treat the underlying cause of anaemia. Optimal management of anaemia in this setting is influenced by long waiting lists and distances patients have to travel. In a middle income developing country such as South Africa this is a practical difficulty as opposed to better resourced countries where follow up is easier and waiting lists are shorter. Nevertheless, anaemia assessment and management could be initiated at the booking visit.

Preoperative anaemia is associated with longer hospital stays, increased rates of transfusion, and greater morbidity and mortality (Spahn, 2010, Shander et al., 2012, Boralessa et al., 2009). To achieve consistency and accuracy in estimating the Hb, it is recommended that Hb measurements are carried out by the National Health Laboratory Services (NHLS) since point of care testing done by ward haemoglobinometers are rarely part of a formal Quality Assurance system. The

booking and admission Hb should be part of a full blood count (FBC) in order that a better assessment of anaemia can be made.

In order to complete the clinical audit cycle, the findings of this study will be presented to the respective orthopaedic departments at each hospital. This will be followed by another audit to document any improvements.

Further audit of elective surgical procedures is recommended and should preferably be prospective including private hospitals on a comparative measure. There is also a need to monitor whether there is underutilisation of blood products in patients who might benefit from transfusion. There are, however, few studies addressing this. Two studies that investigated this did not find that patients with low Hb levels or platelet counts were inappropriately under transfused (Waters & Yazer, 2015:701; Hibbs, et al., 2015:909).

To make prescribers of blood aware that active blood management should be part of good clinical practice and therefore encourage evaluation of departmental blood transfusion policies with reference to the current clinical guidelines. This would ensure that blood donations are optimally utilised and that our blood requests would be appropriate and essential.

6.3 Limitations

This was a retrospective folder review study and therefore data extraction was time consuming and labour intensive. Ideally in this type of audit a well-structured information system for patient records would be ideal.

6.4 Summary

Active blood management should be part of good clinical practice. Audits of blood usage should be conducted in order to compare current practice with local or international standards. This would ensure that blood wastage and unnecessary expenditure is kept to a minimum. Furthermore, blood donations would be optimally utilised and blood bank requests would be appropriate and essential.

7 Glossary-Clarification of basic terminology

Haemoglobin (hb) trigger - The point at which a transfusion is recommended.

Elective surgery -	Surgery that is scheduled in advance as it is not a surgical emergency.
Benchmark -	A standard or reference point by which something can be compared to or measured.
Clinical audit -	The measurement of practice against agreed standards and implementing change to ensure all patients receive the same care to that same standard.
Group and Screen Conversion -	Group and screen order with a cross match added.
Cross match -	A compatibility screening procedure whereby a patient's plasma is used to test against donor red cells to ensure that there is a serological match between the blood product and the patient.
Cross match form -	Documentation to be completed when blood products are required for a patient.
Red Cell Concentrate -	Also referred to as packed cells, red cells, packed red blood cells. This is indicated to restore oxygen carrying capacity when tissue oxygenation has been impaired by haemorrhage or symptomatic anaemia. This product can be leucocyte depleted to reduce the number of white cells in a red cell concentrate.
Group and screen Procedure -	The group of a patients sample is determined as well as a screening procedure to test whether any irregular blood group antibodies exist. No blood is

cross matched. It is usually ordered as a preliminary test before the patient goes to surgery and is valid for 48 hours. It is also known as Type and Screen or Type and Hold.

Cross match Transfusion ratio - This is a measurement of cross matched blood divided by number of units of blood transfused.

Legg Calves Perthes Disease - Childhood Hip Disease.

8 Addendums

Addendum 1 Data collection form

Addendum 2 Ethics Approval

Addendum 3 Raw Data Hb Values

Addendum 1: Data Collection form

STUDY NUMBER: ☐

FOLDER NUMBER: ☐ ☐

CODE:

1) **Hospital:** ☐ Private ☐ State
2) **Gender:** ☐ Female ☐ Male
3) **Age:** _____
4) **Primary (P) or Revision (R):** ☐ P ☐ R
5) **Length of hospital stay**: _____ days
6) **Presurgery Hgb:** _____
7) **Post surgery Hgb:** _____
8) **Blood bank encounter:** ☐ Yes ☐ No
9) **Number of red cell products requested:** _____
10) **Number of red cell products transfused:**_____
(One month from day of surgery)
11) **Reason for surgery:**

☐ Osteoarthritis ☐ Rheumatoid arthritis ☐ Post traumatic arthritis

☐ Osteonecrosis ☐ Childhood hip disease (Legg-Calve-Perthes disease) ☐ Other

12) **Comorbidities:**

☐ Diabetes ☐ hypertension ☐ diabetes and hypertension

☐ Cardiac disease ☐ Bleeding coagulopathies

☐ Other

13) **Initial blood bank request:** _____
14) **Patient on waiting list:** ☐ Yes ☐ No ☐ NA
15) **Complications:**

☐ Infections ☐ DVT ☐ Ventilation

☐ None ☐ Other :

Addendum 2: Ethics Approval

Cape Peninsula
University of Technology

HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE (HW-REC)
Registration Number NHREC: REC- 230408-014

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3 October 2013
CPUT/HW-REC 2013/H38

Faculty of Health and Wellness Sciences – Biomedical Sciences Department

Dear Ms Yvonne Grace Peters

APPLICATION TO THE HW-REC FOR ETHICAL CLEARANCE

Approval was granted on 20 September 2013 by the Health and Wellness Sciences-REC to Yvonne Grace Peters for your Ethical Clearance application. This approval is for research activities related to an MTech: Biomedical Technology at this Institution.

Title: Clinical Audit of the utilisation of red blood cell products in total hip replacement surgery.

INTERNAL SUPERVISOR: Dr GM Davison

EXTERNAL CO-SUPERVISOR: Dr. Greg Bellairs

Comment:
Approval will not extend beyond 3 October 2014. An extension should be applied for 6 weeks before this expiry date should data collection and use/analysis of data, information and/or samples for this study continue beyond this date.

Note:
The investigator(s) should understand the conditions under which they are authorized to carry out this study and they should be compliant to these conditions. **It is required that the investigator(s) complete an annual progress report that should be submitted to the HW-REC in December of that particular year, for the HW-REC to be kept informed of the progress and of any problems you may encounter.**

Kind Regards

Zuleika Nortjé
CHAIRPERSON – ETHICS RESEARCH COMMITTEE
FACULTY OF HEALTH AND WELLNESS SCIENCES

Addendum 3: Raw Data-Hb Values

Pre-op Hb All	Post-op Hb All	Pre-op Hb Transf	Post-op Hb Transf	Pre-op Hb Not Transf	Post-op Hb Not Transf
15	15	10.2	9.9	15	15
13.1	11.9	9.5	6	13.1	11.9
11.6	10.1	11.3	9.9	11.6	10.1
11.9	9.9	14.2	9.1	11.9	9.9
14	10.4	12.6	7.5	14	10.4
15.4	11.4	11.8	7.4	15.4	11.4
12.3	9.4	12	8	12.3	9.4
13.1	9.2	9.5	8.6	13.1	9.2
13.4	8.2	10.6	9	13.4	8.2
15	10.2	12.1	8.5	15	10.2
15.3	9.4	9.8	8.6	15.3	9.4
10.7	10	11.4	8.4	10.7	10
12.1	11.2	10.7	11	12.1	11.2
13.8	11	12.7	7	13.8	11
12.9	11	13.5	9.6	12.9	11
13.7	8.8	12	10	13.7	8.8
15.2	13.7	10.9	8.9	15.2	13.7
14.3	13.7	11	9.8	14.3	13.7
11.2	9.5	12	8	11.2	9.5
14.7	10.2	13.1	8.7	14.7	10.2
14.5	11.1	12.4	10.5	14.5	11.1
12.5	11.1	10	8	12.5	11.1
15.1	11	13.6	6.6	15.1	11
13.4	10.3	13.4	7.4	13.4	10.3
15.9	9.9	12	8.8	15.9	9.9
12.7	10.2	12.2	9.4	12.7	10.2
13.7	11.8	14.5	12.9	13.7	11.8
15	13	14.2	10.3	15	13
14	9.9	14.7	10	14	9.9
17.8	13.1	8.5	8.5	17.8	13.1
13.3	10.1	12.6	10.5	13.3	10.1
14	12			14	12
15	13			15	13
13.2	11.2			13.2	11.2
13.9	11.5			13.9	11.5
13	12.7			13	12.7
15.3	11			15.3	11
12.2	10.3			12.2	10.3
11.7	8.3			11.7	8.3
15.7	13.5			15.7	13.5
12.4	13.3			12.4	13.3
14.3	11.5			14.3	11.5
11.5	10.5			11.5	10.5
13.4	9.8			13.4	9.8
14.1	12.6			14.1	12.6

11.1	9.4			11.1	9.4
15.4	10.6			15.4	10.6
13	11.2			13	11.2
15.4	14			15.4	14
13.7	13			13.7	13
12.6	9.5			12.6	8.5
14.5	12.6			14.5	12.6
15	12.9			15	12.9
13.6	9.3			13.6	9.3
12	10			12	10
13.5	12			13.5	12
13.1	12.2			13.1	12.2
15.9	13			15.9	13
13	9.5			13	9.5
14.5	9.5			14.5	9.5
12.6	10			12.6	10
11.5	9			11.5	9
12.4	9.2			12.4	9.2
9.9	9			9.9	9
15.4	9			15.4	9
13	10			13	10
12.3	11.5			12.3	11.5
12.8	10			12.8	10
13	11			13	11
13.5	9.5			13.5	9.5
14.2	9			14.2	9
13.9	11.5			13.9	11.5
13	10			13	10
13.6	10.5			13.6	10.5
12.4	9.8			12.4	9.8
10.5	9.9			10.5	9.9
13.5	10			13.5	10
13.2	9.8			13.2	9.8
13	10.7			13	10.7
10.5	10.5			10.5	10.5
15.1	10			15.1	10
13.7	9.5			13.7	9.5
11.9	10.8			11.9	10.8
11	10			11	10
13.3	8.5			13.3	8.5
12.6	8.6			12.6	8.6
11	11			11	11
13	10.7			13	10.7
11.5	10			11.5	10
10.2	9.9				
9.6	6				
11.3	9.9				
14.2	9.1				
12.9	7.5				
11.8	7.4				
12	8				
9.5	8.6				

10.6	9				
12.1	8.5				
9.7	5.7				
11.5	8.4				
10.7	11				
12.7	7				
13.5	9.6				
12	10				
10.9	8.9				
11	9.8				
12	8				
13.1	8.7				
12.4	10.5				
10	8				
13.6	6.6				
13.4	7.4				
12	12				
12.2	9.4				
14.5	12.9				
14.2	10.3				
14.7	10				
8.5	8.5				
11	10.5				
12.98083	10.26417	11.90323	8.929032	13.36966	10.71461
1.630863	1.690298	1.590699	1.419905	1.46104	1.46104

Pre-op Hb	Post-op Hb	Pre-op Hb	Post-op Hb	Pre-op Hb	Post-op Hb	Pre-op Hb	Post-opHb	Pre-op Hb	Post-op Hb	Pre-op Hb	Post-op Hb
Male	Male	Female	Female	Transf	Transf	Transf	Transf	Non transf	Non transf	Non transf	Non transf
				Male	Male	Female	Female	Male	Male	Female	Female
15	15	11.6	10.1	10.9	8.9	12	8	15	15	11.6	10.1
13.1	11.9	14	10.4	13.1	8.7	9.5	8.6	13.1	11.9	14	10.4
11.9	9.9	12.3	9.4	12.2	9.4	10.6	9	11.9	9.9	12.3	9.4
15.4	11.4	13.1	9.2	14.5	12.9	12.1	8.5	15.4	11.4	13.1	9.2
15.3	9.4	13.4	8.2	14.7	10	9.8	8.6	15.3	9.4	13.4	8.2
10.7	10	15	10.2	12.6	7.5	11.4	8.4	10.7	10	15	10.2
12.1	11.2	11.2	9.5	11.8	7.4	10.7	11	12.1	11.2	11.2	9.5
13.8	11	14.7	10.2			12.7	7	13.8	11	14.7	10.2
12.9	11	14.5	11.1			13.5	9.6	12.9	11	14.5	11.1
13.7	8.8	12.5	11.1			12	10	13.7	8.8	12.5	11.1
15.2	13.7	13.4	10.3			11	9.8	15.2	13.7	13.4	10.3
14.3	13.7	15.9	9.9			12	8	14.3	13.7	15.9	9.9
15.1	11	12.7	10.2			12.4	10.5	15.1	11	12.7	10.2
13.7	11.8	14	9.9			10	8	13.7	11.8	14	9.9
15	13	13.2	11.2			13.6	6.6	15	13	13.2	11.2
17.8	13.1	13.9	11.5			13.4	7.4	17.8	13.1	13.9	11.5
13.3	10.1	15.3	11			12	8.8	13.3	10.1	15.3	11
14	12	12.2	10.3			14.2	10.3	14	12	12.2	10.3
15	13	11.7	8.3			8.5	8.5	15	13	11.7	8.3
13	12.7	12.4	13.3			12.6	10.5	13	12.7	12.4	13.3
15.7	13.5	14.3	11.5			10.2	9.9	15.7	12.5	14.3	11.5
14.1	12.6	11.5	10.5			9.5	6	14.1	12.6	11.5	10.5
15.4	10.6	13.4	9.8			11.3	9.9	15.4	10.6	13.4	9.8
13	11	11.1	9.4			14.2	9.1	13	11.2	11.1	9.4
13.7	13	15.4	14					13.7	13	15.4	14
15	12.9	12.6	9.5					15	12.9	12.6	9.5
13.6	9.3	14.5	12.6					13.6	9.3	14.5	12.6
13.5	12	12	10					13.5	12	12	10
13.1	12.2	15.9	13					13.1	12.2	15.9	13
12.6	10	13	9.5					12.6	10	13	9.5
11.5	9	14.5	9.5					11.5	9	14.5	9.5
13	10	12.4	9.2					13	10	12.4	9.2
13.9	11.5	9.9	9					13.9	11.5	9.9	9
12.4	9.8	15.4	9					12.4	9.8	15.4	9
10.5	9.9	12.3	11.5					10.5	9.9	12.3	11.5
13	10.7	12.8	10					13	10.7	12.8	10
10.5	10.5	13	11					10.5	10.5	13	11
11.9	10.8	13.5	9.5					11.9	10.8	13.5	9.5
12.6	8.6	14.2	9					12.6	8.6	14.2	9
11	11	13	10					11	11	13	10
13	10.7	13.6	10.5					13	10.7	13.6	10.5
10.9	8.9	13.5	10							13.5	10
13.1	8.7	13.2	9.8							13.2	9.8
12.2	9.4	15.1	10							15.1	10
14.5	12.9	13.7	9.5							13.7	9.5
14.7	10	11	10							11	10
12.6	7.5	13.3	8.5							13.3	8.5

11.8	7.4	11.5	10							11.5	10
		12	8								
		9.5	8.6								
		10.6	9								
		12.1	8.5								
		9.8	8.6								
		11.4	8.4								
		10.7	11								
		12.7	7								
		13.5	9.6								
		12	10								
		11	9.8								
		12	8								
		12.4	10.5								
		10	8								
		13.6	6.6								
		13.4	7.4								
		12	8.8								
		14.2	10.3								
		8.5	8.5								
		12.6	10.5								
		10.2	9.9								
		9.5	6								
		11.3	9.9								
		14.2	9.1								
13.39792	11.00208	12.71944	9.765278	12.82857	9.257143	11.63333	8.833333	13.49512	11.28049	13.2625	10.23125
1.544309	1.713959	1.626596	1.397196	1.390101	1.862666	1.568346	1.297042	1.955863	1.490003	1.374637	1.208508

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