Chapter 1

Introduction

Nyashadzaishe Mafirakureva
INTRODUCTION

Blood transfusion is a routine, life-saving medical intervention which is generally regarded as safe when done appropriately\(^1\). Without blood, the management of many medical conditions such as trauma, cardiac surgeries, organ transplantation, malaria and obstetric haemorrhage, would have been difficult or nearly impossible. However, this life-saving procedure is often associated with significant clinical risks, which can be broadly classified as infectious or non-infectious complications\(^2\). The main challenges inscribed throughout the history of blood transfusion were centred on adequacy and safety of the blood supply. Attempts to resolve these challenges led to the evolution of blood transfusion into a multidisciplinary field, beyond issues related to blood procurement and storage\(^3\). Blood transfusion now involves several aspects, including but not limited to, adequate and safe blood supply, appropriate use of blood & blood products, development of novel cellular therapies, manipulation and prevention of immune responses and economic evaluation. The blood supply is now much safer largely due to conversion from paid to voluntary non-remunerated blood donors, improvements in donor screening, improvement of assays that detect transfusion-transmissible infections in donor blood, regular quality control on blood units, leucoreduction techniques, blood management, hospital transfusion committees and haemovigilance\(^3-6\). Although strategies to improve supply and minimise transfusion risk have been fully implemented with successful results in most developed countries, they are considered to be too expensive to implement in most resource-limited settings. As such, most resource-limited settings are still confronted with challenges in terms of limited access to blood transfusion or the provision of safe blood\(^7\). Most of the countries in the African Region collect about 4 units per 1000 population, less than half of the World Health Organisation recommendation of 10 per 1000, compared with an average of over 30 per 1000 population in developed countries\(^8\).

In resource-limited countries, blood transfusion is mainly used for complications of pregnancy, anaemia, infectious diseases, cancer, and gastrointestinal diseases\(^9-11\). The majority of blood and blood component use in sub-Saharan Africa (SSA) is for emergencies, hence unavailability may result in loss of lives. Although there is striking evidence of limited access to blood transfusions, there is very little information on actual utilization patterns prompting suspicions of irrational use. Blood component utilisation data is widely available for a variety of countries globally\(^12-21\) while it’s limited to a few studies in Africa\(^9-11,22-24\). These studies demonstrate substantial variations in transfusion practices, arising from differences in population age structures, prevalence of conditions requiring transfusion, and levels of health care provision\(^16,25,26\). Most developed countries are characterised with ageing populations, chronic non-infectious diseases and advanced surgical technologies\(^12,13,17,18,21\), all of which may result in different patterns of blood component use when compared with developing countries. In contrast, the population in developing countries is predominantly young and blood utilisation patterns are likely to be very different. Information on blood utilisation will assist in conducting cost-effectiveness analyses\(^17,\)
establishing clinical practice guidelines, planning efforts for recruitment of new blood donors and streamlining resources for the therapeutic benefit of patients\textsuperscript{19,25}. In light of these potential differences in utilization patterns and the importance of utilisation data in decision making; it is imperative that developing countries in SSA collect their own data of profiles of transfusion recipients and the patterns of blood and blood component usage in order to correctly inform decision making in their settings.

In addition to studying the demographics of blood transfusion recipients and utilization patterns, it is equally important to establish the outcomes following transfusion. These may include risks (infectious and non-infectious), length of hospital stay and mortality following a blood transfusion. Continuous surveillance of the whole transfusion chain, which includes assessing information on unexpected or undesirable effects resulting from the use of blood transfusions and preventing their occurrence and recurrence, is a necessary activity for any country\textsuperscript{27,28}. The major transfusion-transmissible infections (TTIs) of clinical importance in Africa are mainly the human immunodeficiency virus I and II (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV). Although variable, the residual risk of HIV, HBV and HCV transmission by blood transfusion has been substantially described for countries in SSA\textsuperscript{29-34}. Variability may be due to the adoption of different screening technologies by different countries, application of different methodologies in the estimation process and therefore emphasizes the need for additional data on TTI incidence and prevalence and residual transfusion risk in Africa. Information on the number of TTIs verified to have been transmitted via transfusion is lacking due to the difficulties that exist in tracking of patients and blood components. As a result, there are very few functional transfusion-transmissible infection 'lookback' programmes in SSA. In addition to these infectious risks, the significance of non-infectious risks in transfusion medicine is on the rise and these risks are often associated with significant morbidity and mortality\textsuperscript{35-38}. This information is very important for performing meaningful risk assessment and assessing the effectiveness of blood transfusions. There is a general paucity of information on non-infectious risks associated with blood transfusions in SSA, despite its significance.

Further to the challenges in terms of limited access to blood transfusion or the provision of safe blood, blood transfusion services in SSA are required and expected to comply with stringent regulatory demands, implement quality management systems, and comply with internationally recognized standards of ethics and practice\textsuperscript{39,40}. Technologies and advancements required to ensure such compliance may require a great deal of investments subsequently resulting in higher costs of producing blood\textsuperscript{41-43}. In resource-limited settings, such increases may threaten adequate supply of blood hence access as well as the safety of the supply. There is a limited number of published data on the costs and cost drivers for the provision of blood in SSA. Cost estimates from several studies performed in developed countries\textsuperscript{44-46} are not readily transferable
to countries in SSA, hence the need for locally derived data. Cost analysis data is useful for budget planning, policy analyses, economic evaluations and decision making.

Economic evaluations are increasingly being used to support decisions related to resource allocation in the health care field\textsuperscript{47-49}. Three fundamental economic principles highlight the need for economic evaluations; scarcity of resources, need for making choices and consideration of opportunity costs. Because there are limited resources, decision makers have to make choices on the interventions to be implemented; and at the same time they have to take into consideration the value of forgone benefits because resources are not available for their best alternative use. The main purpose of economic evaluations is to provide decision makers with quantitative measures of the efficiency of health care interventions necessary to guide resource allocation\textsuperscript{50}. Two most common types of economic evaluations are cost-effectiveness analysis (CEA) and cost-utility analysis (CUA). CEA describes a set of methods where results are expressed in natural units, as a ratio of cost to health benefits e.g. infections prevented or life year saved. CUA is a subset of CEA which accounts for both morbidity and mortality when measuring health benefits by making use of preference weights assigned to relevant health states. Results of CUA are frequently expressed as costs per quality adjusted life year (QALY) or disability adjusted life year (DALY) saved/gained. Decision making on policies and adoption of technologies in transfusion medicine are complicated by the implications on public health, legal and liability issues, as well as political, regulatory and public expectations regarding blood safety\textsuperscript{50-52}. These issues, plus the general desire to achieve ‘zero’ risk have limited the application of economic evaluations in transfusion decision making. Economic evaluations are considered an important aspect of risk based decision modelling, particularly when comparing competing interventions\textsuperscript{52,53}.

Nucleic acid testing (NAT), a highly sensitive and specific method for virus detection; is a blood safety strategy introduced to reduce the window period (WP) of TTIs and thus further reduce the risk of infection by blood transfusion. It is widely implemented in developed countries (Europe and North America) but little used in most of SSA, essentially because of its cost. However, NAT has been associated with low returns at high costs resulting in unfavorable cost-effectiveness ratios in most developed countries where economic evaluations were performed\textsuperscript{54-57}. On the contrary, favorable cost effectiveness was demonstrated for Ghana\textsuperscript{54}, a developing country in SSA. Outcomes of economic evaluations of NAT are dependent on factors such as the incidence of infections in the donor population, donor deferral and follow up practices and the demographic characteristics of blood transfusion recipients\textsuperscript{58}. The epidemiology of disease in the donor population determines the cost-effectiveness profile of infectious disease screening\textsuperscript{50,51}. Economic evaluations of new blood safety strategies should therefore be done for each respective setting where they will be implemented.
OBJECTIVES AND THESIS OUTLINE

This thesis consists of a series of papers which sought to close in on the information gaps highlighted in the preceding paragraphs. The main objective of the thesis was to determine the health and economic consequences of introducing Nucleic Acid Testing Technology as a blood safety strategy in a developing country. This attempted to answer the questions: Can a resource-limited setting (Zimbabwe) afford implementing NAT as a blood safety strategy? Does implementing NAT offer value for money? In order to populate the economic model, several papers were developed to obtain the required parameters and are described.

Data on donor and donation characteristics is readily available at the National Blood Service Zimbabwe (NBSZ), however information on the demographics of transfusion recipients and utilization patterns of blood and blood components is lacking. This is despite the usefulness of such data in conducting cost-effectiveness analyses, establishing clinical practice guidelines, planning efforts for recruitment of new blood donors and streamlining resources for the therapeutic benefit of patients. The demographics of transfusion recipients and the patterns of blood and blood components usage are described in Chapter 2. Similarly, information about the risks of transfusion in resource-limited settings is limited. In Chapter 3, we report data on the incidence and pattern of transfusion-related adverse events reported by hospitals in Zimbabwe.

If a blood strategy implemented at the blood service misses an infected unit of blood, the transfusion recipient may become infected. Health related quality of life (HRQoL) is increasingly becoming an important patient outcome which can be incorporated into economic evaluations. In Chapter 4, we present an assessment of the HRQoL in patients infected with HIV. The costs of antiretroviral therapy in patients infected with HIV are presented in Chapter 5.

The costs of producing a unit of blood are not widely described for SSA. We describe the costs of producing a unit of blood in Zimbabwe in Chapter 6. Data on implementation of NAT demonstrated low returns at high costs resulting in unfavorable cost-effectiveness ratios in most developed countries where economic evaluations were performed. This could be attributed to the low incidence of TTIs. The risk of TTIs is relatively high in sub-Saharan Africa and transfusions recipients are much younger. This may subsequently enhance the benefits of introducing NAT in these settings, yet limited economic evaluations are available. In Chapter 7, data generated from the preceding chapters is collapsed into an economic model that estimates the cost-effectiveness and budget impact of adding NAT screening to blood donations in Zimbabwe. Recognizing the reported critical lack of African researchers and research outputs as the main reason behind the total unavailability, or availability of poor quality evidence to guide blood safety decisions in SSA, we undertook a systematic review, assessing the NBSZ’s research capacity as a way of guiding its research strategy in Chapter 8.
REFERENCES


