Chapter 9

General Discussion
INTRODUCTION

The provision and maintenance of an adequate, high quality and safe blood supply is a key component of any sound health system. The inclusion of whole blood and its components on the World Health Organization's (WHO) essential medicines list underscores the important role blood transfusions play in public health. An adequate and safe blood supply is integral to the WHO HIV/AIDS plan to accelerate the prevention of HIV infection and to the achievement of the health-related Sustainable Development Goals aiming to reduce child mortality, improve maternal health, combat HIV and develop global partnership for development.

Blood transfusion services and systems in developing countries are faced with several challenges that threaten the successful fulfilment of their missions. Some of these challenges include inefficient blood supply structures; blood shortages, inequitable access and increasing needs; weak quality systems, high risk of transfusion transmissible infections and inappropriate or unnecessary use of blood components. These challenges threaten the goal of ensuring universal access to safe blood and blood products. The WHO recommends an integrated strategy for blood safety and availability which includes: establishment of a national blood system with well-organized and coordinated blood transfusion services; collection of blood, plasma and other blood components from low-risk, regular, voluntary unpaid donors through the strengthening of donation systems; quality-assured screening of all donated blood for transfusion-transmissible infections (TTIs); rational use of blood and blood products to reduce unnecessary transfusions and minimize the risks associated with transfusion; and step-wise implementation of effective quality systems. Barriers to maintaining an adequate and safe blood supply in developing countries are often multifaceted. Key to these are infrastructure and resources. Efforts to meet stringent regulatory demands, implementation of quality management systems, and need for compliance with internationally recognized standards of ethics and practice often lead to increases in the production costs of blood and blood components. Meeting internationally recognized standards is an expectation of all countries, especially as countries adopt the Resolutions agreed at the annual World Health Assembly Meetings, of the WHO. In addition, the introduction of advanced technologies to ensure safety from new and emerging infectious agents is particularly desirable in sub-Saharan Africa (SSA) where the residual risks of TTIs is considerably high. All these requirements are subject to periodical increases in operational, administration, and overhead expenses, resulting in an increase in the service fees for blood. The limited availability of resources coupled with the never ending competing needs in SSA requires careful assessment of the costs and benefits of adopting such standards and interventions.

Therefore, this thesis presents the health economics and safety of blood transfusion in a resource-limited setting, with the aim of helping decision-makers understand the cost-effectiveness of introducing a blood safety measure, nucleic acid testing (NAT). In particular, it discusses the
chronic challenges in the collection, availability and quality of empirical data; and their impact in informing a health economic model and subsequently decision making relating to blood safety. This chapter summarizes the main results, findings and provides some insights into future perspectives.

**SUMMARY OF RESULTS**

In Chapter 2, the demographic characteristics of blood transfusion recipients, the utilisation patterns of blood and blood components and discharge diagnoses are described. In addition, the outcomes following blood transfusions were also provided. Transfusion recipients in Zimbabwe are generally young, with a mean age of 35 (SD; 20) years. The majority of transfusion recipients studied were female (63.2%), most of whom (65.3%) were in the reproductive age group, i.e. 15-49 years. More than ninety percent of the recipients received a red blood cell transfusion. The top diagnoses associated with blood transfusion were pregnancy and childbirth (22.3%), diseases of blood and blood-forming organs (17.5%), neoplasms (10.1%), infectious and parasitic diseases (9.0%) and diseases of the digestive system (8.2%). The median time spent in hospital was 8 days (range, 0-214) and in-hospital mortality was 15.4%.

Chapter 3 reviewed the transfusion-event records reported to the national blood service by hospitals in order to estimate their incidence and pattern of occurrence following blood transfusion. The incidence of suspected transfusion adverse events, 0.46 per 1,000 blood components distributed, was generally low. The majority (61.6%) of the recipients who experienced a transfusion-related adverse event were female. The most striking finding was the disproportionate association of whole blood with transfusion adverse events. Two-thirds (66.6%) of the adverse events occurred following transfusion of whole blood, although only 10.6% of the blood was distributed as whole blood. On the other hand, red blood cells which accounted for 75% of blood components distributed, were associated with 20.1% of the events. Under-reporting of transfusion events was highly suspected in Zimbabwe where a passive reporting system was in place. The general quality of the assessed reports was graded as low, because most of them were incomplete making classification difficult.

An assessment of the patient-reported Health Related Quality of Life (HRQoL) in individuals with HIV/AIDS receiving antiretroviral therapy was presented in Chapter 4. The HIV/AIDS targeted quality of life (HAT-QoL) and EuroQoL-Five Dimensions – Three-Level (EQ-5D-3L) instruments were used in the assessment. The patients’ self-reported HRQoL was generally satisfactory in all the HAT-QoL dimensions as well as the two components on the EQ-5D-3L instrument. The median scores for the HAT-QoL dimensions ranged from 33.3 (financial worries) to 100 (HIV mastery). The median of the EQ-5D-3L index and visual analogue scale (VAS)
was 0.81 and 79.0, respectively. The two instruments demonstrated good internal consistency and convergent validity.

In Chapter 5, the costs and cost structures of providing antiretroviral therapy to adult outpatients living with HIV/AIDS were presented. The average cost per patient initiated on ART per year was US$268 (SD=79). The average resource utilization was high for medications, ranging from 9.3 months for Stavudine/Lamivudine/Nevirapine (D4T/3TC/NVP) to 11.8 months for Tenofovir/Lamivudine/Efavirenz (TDF/3TC/EFV). It was therefore not unexpected that drug costs (ARVs and non-ARVs) accounted for the largest share of the total costs (45.5%) followed by laboratory investigations (32.0%). Fixed costs accounted for 16.8% of the total costs whilst outpatient visits contributed 5.7%. The average cost per patient remaining in care at 12 months was US$276 (SD=75), with a similar distribution of costs components. The costs per patient initiated on ART divided by the proportion retained in care, interpreted as average cost to produce a patient in care, for this cohort was US$287.

The costs associated with producing blood and blood components were described in Chapter 6. The costs were presented for all the direct blood production activities from donor recruitment, blood collection, donation testing (screening for TTIs and blood grouping), and storage plus distribution. Indirect costs were categorized as follows: finance and administration; coordination; safety, health, environment, and quality (SHEQ); planning, information, and research (PIR); and general overheads. The activity unit costs for producing red blood cells (RBCs) were US$15.94 for donor recruitment, US$34.62 for blood collection, US$17.88 for donation testing, US$11.49 for blood processing, and US$3.06 for storage plus distribution. The overall cost of production for one unit of whole blood was US$118.42 and RBCs was US$130.94 constituting 12.4 and 13.7% of the country’s annual GDP per capita.

Chapter 7 collated information and parameters reported in the preceding chapters into an economic model assessing the cost-effectiveness of introducing individual-donor nucleic acid testing (ID-NAT), in addition to serologic tests, compared with only using serologic tests for the identification of hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) among blood donors in Zimbabwe. The model estimated the residual risk of transmission, following post-donation serological screening at 83.1, 6.8 and 8.4 per 100,000 donations for HBV, HCV and HIV, respectively. The introduction of multiplex ID-NAT in addition to serologic tests would lower HBV, HCV and HIV transmission risks to 47, 0.3 and 2.7 per 100,000 donations, respectively; and prevent additional 25, 7 and 9 HBV, HCV and HIV transfusion transmitted infections (TTIs) in Zimbabwe, respectively. The introduction of this screening strategy would save an estimated 2,174 quality-adjusted life years (QALYs). The incremental cost-effectiveness ratio was estimated at US$12,252/QALY, a value substantially higher than three times the GNI per capita for Zimbabwe.
Lastly, Chapter 8 described a systematic approach adopted and used to review the research capacity within Zimbabwe’s national blood service. The review demonstrated that the NBSZ had the basic foundations for performing and participating in high quality research activities. Several interviews with a wide range of stakeholders highlighted key areas of NBSZ’s research capacity for improvement, in particular, better dissemination of NBSZ’s research priorities and closer ties with academics and their institutions for preparing research proposals and jointly undertaking research projects. With minor adaptations, the systematic process, although adapted framework used to assess universities’ research systems, was found to be applicable for assessing research capacity within blood services.

GENERAL DISCUSSION

Implementing advanced blood safety interventions and technologies in order to meet international standards for a safe blood supply is a desire for every blood service. However, these interventions and technologies come with significant financial investments and they put immense pressure on already constrained health care budgets. In addition, the blood transfusion chain is fairly complex making it difficult to estimate the impact of blood safety measures. However, the chain is largely mechanistic, well understood and the entire process can easily be described using mathematical models, thus enabling risk assessments and health economic analyses to be performed when the appropriate data is available. Under these circumstances, cost–effectiveness analyses (CEA) can be used as a tool to inform decision makers on how and where to allocate the limited healthcare resources\(^9,10\). These analyses quantify the costs and benefits of specific public health choices or interventions compared to current practice, thus informing decisions on the responsible use of scarce health care resources. The application of health economic evaluations to in blood safety has been growing over the past 10 years\(^11-21\). However, it is appalling to note that in SSA, where there is a greater need for improvements in blood safety amid severe resource constraints, only a handful of studies have been published during the same period\(^20,21\). Health economic analyses are generally regarded as data intensive exercises, requiring appropriate setting or country specific data\(^22\). The main data elements required to inform health economic models concerning blood safety include donor epidemiology, blood bank interventions (costs and effectiveness) and the costs and outcomes associated with adverse events in patients. The unavailability of accurate and complete data on most of the components of the blood transfusion chain limits the use of risk assessments and health economic analyses in blood safety decision-making. The main focus of this thesis was to evaluate the cost-effectiveness of introducing ID-NAT in addition to the current serological tests for the screening of blood donations in a resource-limited setting. The preceding chapters described the various approaches undertaken, challenges faced, suggestions to resolve these challenges and limitations faced in collecting empiric data and/or parameters and their application in a health economic model to aid decision making on
blood safety in Zimbabwe. This section further summarizes these issues, particularly those with a bearing on economic evaluations, and provides some insights for the future.

**Blood donation and screening**

The NBSZ has a long history of strong commitment to ensuring that safe blood is distributed in Zimbabwe. This has been largely achieved by responding to emerging threat, technological advancements and meeting international standards for blood safety. As such, the Service began routine screening for antibody to human immuno-deficiency virus (HIV) on all blood donations in July 1985. Currently, all the donated units of blood at the NBSZ are tested for hepatitis B surface antigen (HBsAg), HCV antibody, HIV I & II antibody, and HIV p24 antigen (HIV combo) using Abbott Architect analyzers, which utilize a chemiluminescent immunoassay technique. The Service also maintains an up-to-date computerised database for recording and tracking blood donors hence data on blood donations and subsequent processing into components.

Serological screening costs were accurately estimated since data on costs and tests performed was readily available from the NBSZ Departments of Finance and Laboratory (Chapter 4). The test cost for NAT has not been accurately estimated, as the technology has not implemented in Zimbabwe and can only be estimated from projected costs derived from supplier quotations and experiences from other countries in the region, raising potential uncertainties. The current cost (used in the model) only included reagents and freight costs. Other implementation costs, including labour, training, utility costs, equipment and other setup costs were not available for the analysis. Inclusion of all the costs will result in an increase in the total test cost and subsequently the estimated ICER, further rendering the additional NAT testing even less cost-effective. Although, sensitivity analyses on the NAT costs were performed, a more thorough cost analyses will be required in future due to several reasons. Firstly, quoted prices are largely based on price negotiations with the supplier and therefore tend to be variable. Secondly, improvements in other activities such as donor recruitment and automation will improve efficiency and may influence the test costs. Therefore, NAT test costs are likely to fall in future due to efficient donor recruitment, negotiating the price of reagents, and the efficient use of technology. The impact of potential offset of some of the costs of NAT through the use of excess plasma for fractionation into plasma derivatives need to be investigated in future studies. Accurate and precise estimation of these costs is important since they will add on to the already high cost of producing a unit of blood in Zimbabwe as reported in Chapter 6.

**Residual risk of HBV, HCV, and HIV transmission**

The residual risk of viral transmission was estimated using the classical incidence-window period model for repeat donors and an adapted version of the model for first time donors. This was made fairly possibly because the NBSZ maintains an up-to-date computerised database for tracking blood donors. The model was chosen for its simplicity, however it may be associated
with some limitations which warrants some discussion. As with any model, the accuracy of the estimates derived from the incidence-window period model are largely dependent on how well the assumptions of the model are fulfilled and how accurate the data is. The central assumption of the model states that the frequency of donation by all donors, including seroconverting donors, is random. Any deviations from this assumption is likely to result in biased estimates of the residual risk. Some studies reported a deliberate delay in donating by donors engaging in risk behavior likely to lead to infection which may subsequently lead to the model overestimating the risk of viral transmission. Test-seeking behavior, defined as the donation of blood soon after exposure specifically to receive infection testing has been reported, and may lead to underestimation of the residual risk of viral infection. A recent analysis of inter-donation intervals using NBSZ data (unpublished) failed to detect changes in donation behavior among sero-convertors suggesting that the data complied with the key assumption of the model. Although not statistically significant, the analysis showed that on average sero-convertors tend to return early for all the three markers, possibly increasing the risk of WP donations. This finding, suggestive of test-seeking behavior, requires further studying since it has potentially huge implications on blood safety in Zimbabwe.

The structured risk management strategy active at NBSZ which classifies donors into risk categories may be another area which may result in potentially biased estimates of the residual risk. The risk classification categorizes repeat donors with at least one previous donation within 12 months and first time donors aged 16 to 20 years donating at a school venue as low risk donors. Blood collected from these low risk donors is considered usable as long as it’s not reactive for any of the markers on screening. All lapsed donors, previous donation not within 12 months and the rest of the first time donors are categorized as high risk donors and their blood is not used regardless of the test result. Inclusion of the high risk donor category (they are not going to be used anyway) in the estimation of incidence of viral infection in first time donors may lead to overestimation of residual risk.

It is common practice to incorporates a correction factor for the incidence of HBV into the model to compensate for the potential underestimation caused by the transient nature of HBsAg. The correction factor was applied by multiplying the HBV incidence by a factor found in literature to derive an adjusted incidence. This maybe a potential limitation since the literature values were derived based on epidemiological data derived from the USA and may not necessarily be valid for the Zimbabwean donors. Future attempts to deriving the correction factor based on local epidemiological data may further refine the estimate.

The incidence-window period model assumes that most of the risk per unit is due to the probability of window period donations and other sources of transfusion risk are insignificant (such as human or technical errors). This may underestimate the residual risk as well as the value of the
technology, since testing errors may be reduced by the introduction of a more sensitive technology\textsuperscript{20,21}. Quantification and qualification of the human and technical errors will ensure derivation more reliable estimates of the residual risk. More so, the model assumes that any donation during the window period of an infection with HBV, HCV, or HIV always results in an infected recipient. This is despite the fact that viral infectivity increases with time after infection of the donor. In reality the infectivity period may or may not be the same as the length of the window period commonly used to estimate residual risk. This uncertainty may lead to overestimation of residual risk and as new data becomes available, the model needs to be updated.

The accuracy of the estimates derived from the incidence-window period model could not be validated and this might be an important limitation to consider for future studies. Validation of estimates can be done by comparing them to the actual number of infections transmitted through blood transfusion or the actual yield data of NAT screening. Currently there is no data on the number of documented HBV, HCV and HIV infections transmitted through blood transfusions and NAT has not yet been implemented, so validation of the estimates was not possible. The introduction of donor lookback and recipient trackback studies may help generate data which may be useful for validating these model estimates. Furthermore, when NAT is finally introduced, there is need for comparing observed risk with expected outcomes predicted by the models in order to validate the accuracy of the model based estimates.

**Patient population and disease modelling**

The costs and outcomes of HBV, HCV and HIV infection were modelled using simplified Markov models described previously. The age distribution of patients receiving blood transfusions were obtained from a study conducted in Zimbabwe during the period from January 1, 2012 to December 31, 2012\textsuperscript{37} and are presented in Chapter 2. The costs and outcomes of transfusion-acquired diseases were modelled for the mean age (35 years) in the base model and the influence of different ages at the time of transfusion was explored in a sensitivity analyses. Despite the availability of other subgroups such as gender, diagnosis (disease), and number of units transfused, the current analysis did not attempt to identify patient subgroups where the introduction of the new technology would be considered cost-effective. Even if the analysis shows that introducing the technology in one group is shown to be more cost-effective, restricting the technology in that group would present with political, ethical and legal challenges. Such an analysis would therefore only prove useful following the establishment of a framework which includes political, practical, ethical, legal and economic aspects of blood safety\textsuperscript{38,39}. A potential limitation of the patient study is the limited number of hospitals included. The study included only four urban hospitals which may not be representative of the whole country. Although these hospitals were chosen because they consume more blood than any other facility, future studies need to be more inclusive since patient profiles and utilization patterns may vary from one facility to the other.
Estimates of the clinical outcomes (life expectancy, quality-adjusted life expectancy) and treatment costs for HIV infection (Chapter 5) were obtained from patient studies carried out in the Zimbabwe population. The healthy utility weights derived from the patient study reported in Chapter 4 were not responsive to clinical AIDS-defining events, hence further studies incorporating more patients should be carried out. Several limitations may have led to the underestimation of the treatment costs for HIV/AIDS. Cost analysis was performed for outpatient care only. This excluded any potential hospitalizations or management of adverse reactions or any other conditions/complications which may arise during antiretroviral therapy. The cost analysis was also performed from a provider’s perspective thus excluding any costs borne by the patients or the society at large. It is generally recommended that health economics and outcomes assessments of blood safety decisions must take a societal perspective and encompass all costs and effects incurred by all stakeholders, because donated blood is a societal good that involves costs, risks and benefits that accrue to different groups\textsuperscript{40}. Estimates of the clinical outcomes and treatment costs for HBV and HCV infection were obtained from literature since these were not readily available. The health care impact of the disease specific costs for HBV and HCV are not available for Zimbabwe, hence the use of estimates from Ethiopia\textsuperscript{41}. The use of data inputs derived from other countries potentially limits the accuracy of the findings. The cost analyses study used for these costs was based on the use of newer, more expensive drugs that are not yet widely used in Zimbabwe. This may have led to overestimation of the actual costs. Although sensitivity analysis demonstrated that changes in these cost estimates did not substantially affect the ICER, there is need for estimation of the costs for the treatment of HBV and HCV in Zimbabwe in order to improve the accuracy of CEA estimates. Studies to evaluate the HRQoL in specific patient groups can easily be crafted and executed in a resource limed setting. Disease progression and outcomes for HBV and HCV may require extensive literature searches in order to improve the accuracy of results of a CEA. Although the transfusion adverse events in Zimbabwe were described in Chapter 3, these were not incorporated into the CEA model because the economic burden of these adverse events was not evaluated due to lack of information on their management. A further evaluation of outcomes following blood transfusion is required in order to fully understand the costs and consequences of introducing blood safety interventions. Survival of patients following blood transfusion was limited to in-hospital mortality. Long-term excess mortality of blood transfusion recipients was not included in the model, because those data are currently not available for Zimbabwe. Estimation of long term survival should be prioritized in any future studies as this will help refine the projection of costs and consequences of new blood safety measures.

**Cost-effectiveness analysis**

Despite further reducing the risk of viral transmission through blood transfusion, the ICER for the introduction of ID-NAT in addition to the current serological screening, given the variables and underlying assumptions used, was more than three times the GNI per capita threshold
for Zimbabwe. Therefore, the implementation of this additional screening strategy, cannot, at the present time, be considered as cost-effective in Zimbabwe. Our results were comparable with ICERs reported from other blood safety interventions in Ghana of $8,306/DALY (not cost-effective) for multiplex ID-NAT compared to minipool (pool of 6 donors) NAT\textsuperscript{20}. However, these additional screening tests would represent far greater value when compared with improvements in screening blood donations in developed countries\textsuperscript{12-14,17,20,42}. These differences can be largely explained by the fact that the cost-effectiveness of infectious disease screening varies according to the underlying epidemiology (incidence/prevalence) of disease in the donor population as well as the order of adoption of screening technology when multiple strategies are in place for a defined pathogen\textsuperscript{10,43}. The risk of TTIs is higher in SSA compared to developed countries hence the introduction of additional screening strategies would identify much more additional infections leading to a cascade of beneficial effects representing greater efficiency. Many infected donations are interdicted, preventing transmissible transmitted infections thus avoiding future treatment costs\textsuperscript{10}. On the contrary, the ICERs are not favourable in developed countries because the risk of TTIs is lower hence the number of additional infections identified by additional screening strategies is very small despite the huge costs involved. Results from our sensitivity analysis demonstrated that incidence of viral markers in blood donors has the most profound impact on the cost-effectiveness of introducing NAT. Transfusion recipient age is another important variable that explains the differences in the cost-effectiveness ratios\textsuperscript{12,13,20,44}. Transfusion recipients in SSA are young (lower average age at the time of transfusion)\textsuperscript{37,45-50}, resulting in more gains in QALYs due to avoiding infections by additional screening strategies, thus making such strategies more favourable. These two fundamental differences underscore the need for using setting or country specific epidemiological data when performing economic evaluations for blood safety interventions.

As previously highlighted, improvements in screening blood donations do not compare favourably with other healthcare interventions in Sub-Saharan Africa\textsuperscript{20,21}. The base case ICER estimated in this study does not compare favourably with most healthcare interventions in Zimbabwe\textsuperscript{51}, where most interventions appear to be cost-effective. ICERs for HIV related interventions ranged from $129/DALY for prevention through access to treatment for STIs to $12,473/DALY for providing prophylaxis to prevent opportunistic diseases\textsuperscript{51}. A study that evaluated the cost-effectiveness of monitoring of antiretroviral therapy in Uganda and Zimbabwe reported an ICER of $7,793 per QALY\textsuperscript{52}. An ICER of $2,113/DALY was reported in another study, which assessed the cost-effectiveness of HIV drug resistance testing, as a tool for decision making to switch to second line antiretroviral therapy\textsuperscript{53}. Previous reports\textsuperscript{10,43} argued that larger ICERs are generally considered acceptable in blood safety and other areas of public health due to several reasons. These reports rightly indicated that it is normal for decision-makers to allocate resources to prevent outcomes such as adverse events or diseases caused by contaminated blood and blood components. They also highlighted the fact that society places high value on the prevention of
low-probability risks that may result in serious consequences hence the society will be willing to support interventions that target identifiable individuals (blood recipients)\(^{43}\). Overall, the society and regulators demand blood to be as safe as possible, and as such a lot of interventions with seemingly unfavourable cost-effectiveness have been implemented in developed countries\(^{43}\).

In the recent past, the local media has been awash with headlines on the resumption of open-heart surgery at one of the tertiary hospitals in Zimbabwe\(^{54-56}\). The procedure was last performed in the country some 13 years ago due to the economic meltdown which led to the near total collapse of the health system. The Heart Foundation of Zimbabwe estimates the cost of each procedure at over US$ 10,000 for an adult and around US$ 15,000 for a paediatric patient\(^ {57}\). Despite being expensive, the government, practitioners and the public seem to have embraced the resuscitation of open-heart surgery despite the uncertainty surrounding patient outcomes. Using these arguments, one can consider an ICER of $12,085/QALY, for introducing NAT in addition to current serological screening for blood donations, acceptable for Zimbabwe, especially considering the political and societal perceptions on the possibility of transmission of a ‘dreaded’ infection such as HIV.

It is also important to note that a cost-effectiveness analysis is simply one of several methods used to formally compare the relative value of any new intervention/technology based on the mix of interventions/technologies to which the intervention/technology is judged against. A CEA therefore does not determine if an intervention is cost-effective and one would require both the results of a CEA and the decision-maker’s context of safety, liability, politics and public opinion\(^ {10,22,43,58}\). Determining whether an intervention is cost-effective or not requires a certain threshold value, representing the society’s willingness to pay for that particular intervention. The most commonly used approaches include thresholds based on per capita GNI, benchmark interventions and league tables\(^ {58}\). The use of thresholds based on benchmark interventions and league tables is largely restricted to the developed countries due to unavailability of such values in most resource-limited settings. The threshold based on per capita GNI was used in this thesis despite the known criticisms. One such limitation is the potential for the GNI to be underestimated in lower-income economies that have more informal, subsistence activities\(^ {59}\). In addition, the current methods used to estimate GNI do not include remittances and foreign aid, despite their contribution to the country’s disposable income\(^ {60}\). This can be quite compelling for countries like Zimbabwe largely characterized by a growing informal economy with approximately more than 80% of workers employed in the informal sector\(^ {61,62}\). As a result, the use of the three times per capita GNI criteria will always result in very low corresponding threshold ratios for cost-effectiveness for countries with low development indices in SSA. These countries rely on imports for equipment and consumables resulting in significantly high costs of screening relative to the per capita GNI. The cost-effectiveness ratios of blood safety interventions, as in this study, will therefore appear unfavourable relative to the low per capita GNI derived threshold ratios. The use of the three times per capita GNI will only indicate whether an intervention is
cost-effective or not, thus obscuring important comparisons that will determine whether implementing that particular intervention will represent best use for resources. Ideally, the decision on whether to introduce ID-NAT should be made after considering other interventions that may need to be implemented to improve blood safety (assuming a blood service’s perspective). Such interventions may include setting up of haemovigilance and look-back systems, prevention of non-infectious risks such as transfusion of wrong blood, reducing bacterial contamination and reducing inappropriate or unnecessary transfusions. Currently it is challenging to consider these other measures because the risks and costs are poorly quantified in SSA.

Since determining whether the introduction of ID-NAT in Zimbabwe is favourable or not is rather arbitrary, the following could be some ‘real’ questions to be asked. Is there available budget to support the new intervention? The Ministry of Health, the blood service and development partners need to determine if they have the capacity to increase the blood service’s annual budget in order to meet the NAT requirements. This assessment may set a platform for resource mobilisation, if required. If the required budget can be met, then the question on sustainability should be considered since this technology comes with a significant budget impact. The cascade of effects that follow on the introduction of NAT also need to be assessed carefully. The introduction of NAT will almost certainly result in an increase in the cost of blood and blood components. How is this increase going to affect consumption and the cost-recovery system currently in place? Sustainability will be threatened if the increase in costs results in a decrease in utilisation, increase in debts at both public and private sectors due to failure to keep up with the high costs. Identification of funding sources to fill these gaps will be required. Most costs associated with technological advances are passed along to the consumers of the products. The introduction of NAT will increase the unit cost of blood by about US$30, further making the commodity, currently considered expensive, unaffordable. It is therefore also very important to consider the impact to society of introducing NAT, particularly on affordability and accessibility of blood and blood components. Blood and blood components are generally considered expensive and not affordable in Zimbabwe. In this low-income setting, at least 90% of the population does not have health insurance and therefore have to pay out of pocket for health care services. Consequently, with a high acquisition cost, patients may fail to procure blood components and forego transfusions or they may become impoverished following the purchase. With the majority of blood transfusions in resource limited settings being required for women with pregnant related emergencies and children with life threatening anaemia, failure to access blood and blood products will result in increased morbidity and mortality. The resulting reduced accessibility will threaten the country’s progress towards achievement of the sustainable development goals. The identification funding mechanisms and developmental partners to subsidise the cost of blood remain pivotal. The Health Transition Fund (HTF), a multi-donor pooled fund, managed by UNICEF, to support the Ministry of Health and Child Care (MoHCC) in Zimbabwe to achieve planned progress towards achieving the highest possible level of health and quality of life for all
Zimbabweans, is a good example of such cooperation. Through the Health Transition Fund, all pregnant women in Zimbabwe are able to access blood and blood components when in need. Expansion of such developmental arrangements would help increase access to blood and blood components.

Making decisions about blood safety is increasingly becoming a complex activity due to the multiplicity of factors that have to be taken into account. Some of these factors include risks, benefits, costs, ethics, political and legal issues, and stakeholder perspectives. Due to this complexity, a carefully laid out framework and set of tools is required to facilitate decision-making on the adoption of new technologies. A risk-based decision-making framework for blood safety, developed by the Alliance for Blood Operators, is available for adoption or adaptation by blood services in order to streamline blood safety decision-making. The framework is based on diverse considerations including scientific, medical, ethical, legal, political, regulatory, economic and public policy perspectives. This framework identifies health economic analysis as one of several specialist assessments that may be undertaken in the blood safety decision-making process. Therefore, despite the fact that our analysis showed that the introduction of ID-NAT in addition to serological testing cannot be considered cost-effective, the blood service may still decide to adopt the technology. This is largely because other assessments and/or priorities may override health economic considerations. It is therefore necessary to perform additional assessments on contextual issues such as social or ethical concerns about the risk of TTI or their management, legal, political and stakeholders’ considerations as these will have an impact on the decision on whether or not ID-NAT should be introduced. The blood service may perform these contextual assessments through risk communication and stakeholder engagement. These considerations have, in the past, led to the adoption of blood safety interventions that were not considered cost-effective (ICERS > $1 million per QALY), and if done in the Zimbabwean context, may result in the adoption of ID-NAT despite the lack of demonstrable cost-effectiveness.

Research capacity – towards evidence based practices
Driven by the limited availability of locally generated evidence, most sub-Saharan African countries have for long relied on evidence almost exclusively generated in high income countries in order to guide blood transfusion practices. This led to the ‘blanket’ adoption of principles of transfusion services practiced in high-income countries, which may not be suitable for the conditions that exist in these low resource settings. These challenges have largely been driven by availability of limited and uncoordinated research activities within the sub-Saharan African region. This subsequently resulted in the total unavailability, or availability of poor quality evidence. It is under this background that we undertook a systematic review, assessing the National Blood Service Zimbabwe’s research capacity as a way of guiding its research strategy. This review successfully adopted a framework which had been used to review research capacity in African universities and this paves a way for a similar application in other blood services.
in SSA. Key strengths within NBSZ, which are relevant for conducting international quality research, included experience in non-research funding applications, project management skills and sophisticated training programmes with effectiveness monitoring. The review also noted limited formal linkages with local academic institutions and with national policy-makers. Such linkages could be very useful in enhancing quality research outputs which would in turn help inform decision-making and transfusion practices. In summary a framework for carrying out research activities at NBSZ was available. However, there was need for further strengthening linkages with individuals outside the service for example academic researchers in order to further enhance this capacity. This may go a long way in easing some of the data challenges highlighted in the preceding chapters and hence lead to better blood safety decision making.

CONCLUSIONS AND FUTURE PERSPECTIVES

Blood services in sub Saharan Africa remain confronted with multi-factorial and often unique challenges, however, accessing safe and adequate quantities of blood and blood components remains the biggest challenge. Some of the issues that compromise blood safety in most countries of the region include chronic blood shortages, high prevalence of TTIs, recruitment and retention of VNRD, family and commercial blood donation, inadequate use of pharmacologic and non-pharmacologic alternatives to allogeneic blood and potential misuse of blood transfusions. In order to address the majority of these challenges, blood services require a great deal of locally driven evidence to support decisions surrounding transfusion policies and practices. Most blood services are confronted with a dearth of locally derived information and evidence to support these decisions. As efforts to resolve these challenges increase, choices between interventions are expanding while budgets remain constrained, therefore health economic evaluations may have an important contribution towards blood safety decision-making. However, economic evaluations and their use in blood safety decision-making remains limited particularly in SSA (where they are probably needed the most). Data availability, accessibility and quality are major limitations to evidence-based decision making in SSA. In most countries, manual records are still being maintained thereby making data abstraction expensive and time consuming, thus further limiting availability and accessibility. The quality of the data that is available and can be accessed also leaves a lot to be desired. Poor record keeping with issues ranging from incomplete records, missing records/files to poor (incorrect) coding; often compromises the quality and subsequently usefulness of any data collected. This thesis described the activities undertaken to gather information that was later used in a health economic model that will assist in decision making. This section provides concluding remarks and some future perspectives.

The study described in Chapter 2 provides an insight into the characteristics of blood transfusion recipients and form the basis for planning more comprehensive blood utilisation studies in
Zimbabwe. The study highlights the probable differences in utilisation patterns and practices in different settings. Similar to other SSA settings, blood transfusion recipients in Zimbabwe were relatively young, which may result in prolonging of the long-term impact of blood transfusion in these recipients and affect results of economic evaluations. A higher proportion of women received blood transfusion for conditions related to pregnancy and childbirth. Whole blood is separated into components and transfusion of red blood cells was predominant. Since the data was collected from a limited number of urban hospitals which may not accurately represent overall transfusion practices in Zimbabwe, future prospective national studies, which incorporates hospitals in all provinces at different levels of the health care system, are required in order to provide a better representation of the patterns of blood utilisation throughout the country. In order to reduce the time required for, and costs of, data extraction, investments in electronic data systems are required. There is also a great need for a wider collaboration between the blood service and the hospital in terms of information and data sharing. The blood service of course should lead these initiatives since they may have a better understanding of the need for such data in blood safety decision making.

The reported incidence of suspected transfusion adverse events reported in Chapter 3 is generally lower in Zimbabwe compared to countries with well-established haemovigilance systems, and maybe a signal indicative of underreporting. The patterns of the transfusion adverse events reported here highlights the probable differences in practice between different settings. Poor quality reports limited the accurate quantification and characterisation of transfusion-related events. There is urgent need for a more organised, standardised and systematic surveillance system in order to accurately quantify and characterize transfusion adverse events in Zimbabwe. Education and awareness campaigns for health care professionals may also be required in order to improve both the quality and quantity of reports. This further stresses the need for strengthening collaborations between the blood service and hospitals, particularly through the hospital transfusion committees. Future studies may also look into the costs associated with the management of adverse events as these will help to inform health economic models.

The patients’ self-reported HRQoL in people living with HIV/AIDS on ART was generally satisfactory. The failure of the measures used to detect differences in HRQoL across clinical AIDS-defining events limited the use of the derived health utility weights in the HIV Markov model used in the health economic model. Future studies will have to consider a much larger sample size drawn from different treatment facilities in order to increase the power of detecting any possible differences in HRQoL across subgroups. Following up the participants over time would also help provide valuable data on the relationship of the change in clinical biomarkers and changes in HRQoL scores. With the wide availability of safe and efficacious antiretroviral drugs, the HRQoL scores reported in literature may now be too low and this could have an
impact on the results of economic evaluations. Further studies seeking to update these values are warranted.

The continuous evolution of guidelines for antiretroviral therapy and changes in the costs of medicines (general decrease) will warrant periodic costing analyses in order to obtain more reliable cost estimates that will facilitate budgeting, efficient resource allocation and serve as inputs of economic evaluations of healthcare interventions. Although relatively low compared to other countries in SSA, the costs of providing HIV/AIDS treatment in Zimbabwe are substantially high relative to the country’s per capita GNI.

The costs of producing an optimally safe unit of blood are quite substantial and represent a significant burden on the health care sector in Zimbabwe when compared to the annual per capita GNI. Although desirable, the introduction of additional safety measures such as nucleic acid amplification testing and pathogen reduction technology will further increase this burden. However, full economic evaluations are required in order to inform decisions on whether or not such strategies can be implemented in different settings. The blood service and the hospitals may need to invest efforts in identifying cost-cutting measures in order to contain the service fee for blood. It is also an opportune time to start thinking about patient blood management (PBM) and alternatives to blood transfusion especially since these have a huge bearing on both costs and safety\textsuperscript{4,74–76}.

Although the introduction of NAT could further improve the safety of the blood supply and is desirable, current evidence suggests that it cannot be considered cost-effective in Zimbabwe. The use of the WHO-CHOICE criterion for cost-effectiveness based on the per capita GNI needs further review amid the several limitations highlighted in the discussion. Establishment of country specific benchmark/threshold values is warranted if economic analyses may have a chance in blood safety decision making. The health economic model described in this thesis is dependent on the data and assumptions that were used, all of which can change with time requiring updating of the model. More complete recipient data after transfusion will be required since insufficient information may lead to incomplete and biased estimates. Data on long-term survival of transfusion recipients is important for the precise estimation of QALYs gained while treatment data for adverse events is required for the precise estimation of the economic burden averted by implementing different interventions. In addition, the costs of screening have to be updated as and when they become available. This is particularly important for the test cost for NAT which has not yet been implemented in Zimbabwe.
REFERENCES


57. The Heart Foundation of Zimbabwe. Available from: http://www.heartfoundation.co.zw/about.html


70. Dunn A. Improving blood transfusion services in Africa: the launch of T-REC. Africa Health 2011;33: 22.


73. Institutional Support | MCDC. Available from: http://www.mcdconsortium.org/what-we-do/institutional-support

