

**ECONOMIC IMPACT OF NUCLEIC ACID TESTING
IN THE BLOOD TRANSFUSION SERVICES
IN A DEVELOPING COUNTRY:
AN ECONOMIC MODELLING STUDY**

Dr. Angel Mary Sam

PDCC THESIS

2024



**SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES
AND TECHNOLOGY, TRIVANDRUM**

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A THESIS SUBMITTED BY

Dr. Angel Mary Sam

TO

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND
TECHNOLOGY, TRIVANDRUM.

IN FULFILMENT OF THE REQUIREMENTS

FOR THE AWARD OF

Post Doctoral Certificate Course (PDCC) in Transfusion Transmitted

Disease Testing, Department of Transfusion Medicine

2024

DECLARATION BY THE STUDENT

I, Dr. Angel Mary Sam hereby certify that I had personally carried out the work depicted in the thesis titled, **“ECONOMIC IMPACT OF NUCLEIC ACID TESTING IN THE BLOOD TRANSFUSION SERVICES IN A DEVELOPING COUNTRY: AN ECONOMIC MODELLING STUDY”**.

No part of this thesis has been submitted for the award of any other degree or diploma prior to this date.



Dr. Angel Mary Sam

Date: 30th November 2024



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Clearance was obtained from the Institutional Ethics Committee for carrying out the study.

Date: 19.12.2024

Signature

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30th November, 2024



Dr. Angel Mary Sam

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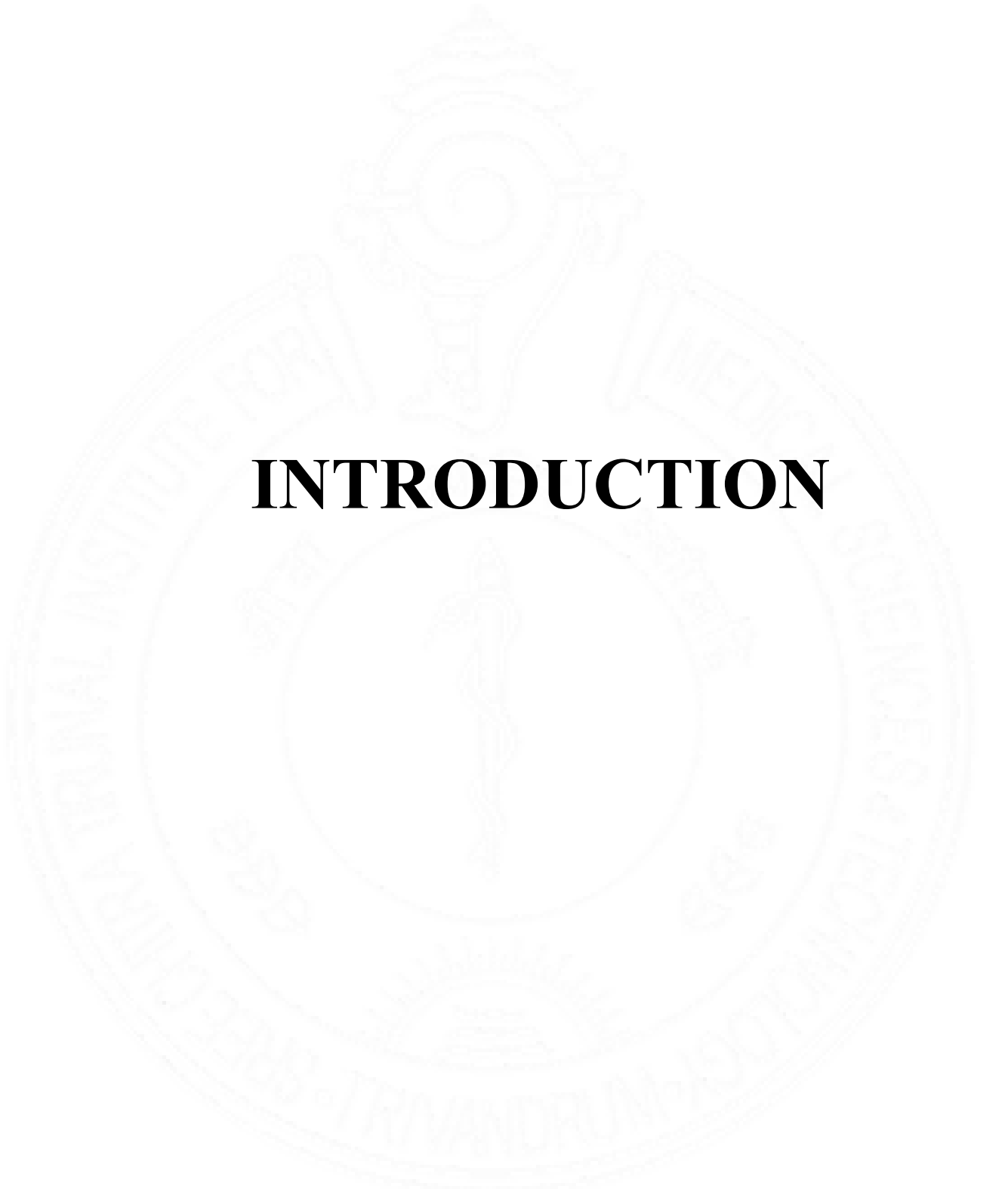
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LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
ART	Anti-retroviral Therapy
CLIA	Chemiluminescence Immunoassay
CPP	Cryo-poor Plasma
ELISA	Enzyme Linked Immuno-Sorbent Assay
FFP	Fresh Frozen Plasma
GDP	Gross Domestic Product
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
ICER	Incremental Cost Effectiveness Ratio
ID-NAT	Individual Donation Nucleic Acid Testing
IHME	Institute for Health Metrics and Evaluation
NACP	National AIDS and STD Control Programme
NAT	Nucleic Acid Testing
NBTC	National Blood Transfusion Council
NVHCP	National Viral Hepatitis Control Program
OOP	Out-of-pocket
PC	Platelet Concentrate
PRC	Packed Red Cells
QALY	Quality-Adjusted Life Year
TTI	Transfusion Transmissible Infection
TTV	Transfusion Transmissible Virus



INTRODUCTION

1. INTRODUCTION

The main transfusion transmissible viruses (TTVs) include hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). The likelihood of transmitting these viruses through the transfusion of infected blood remains significantly elevated, irrespective of the viral load, compared to other transmission routes.[1]

The key blood safety strategies are: [2]

- Acquiring comprehensive blood supplies from altruistic, non-compensated, and consistent blood donors without high-risk behaviours or practices,
- implementing efficient strategies for the selection of blood donors., and
- screening all donated blood for TTV markers utilizing highly sensitive and specific assays.

The interval between a donor's exposure to a virus and its subsequent detection by any testing method is referred to as the "window period." During this critical timeframe, the risk of undetected infection in donated blood may be overlooked by existing immunoassays utilized in blood transfusion services in India.[3] In India, the mandatory screening of donated blood includes tests for malaria, syphilis, HIV-1 and HIV-2, hepatitis B virus (HBV), and hepatitis C virus (HCV) through serological methods such as Rapid Card Tests, ELISA, or Chemiluminescence Immunoassay (CLIA). Nucleic Acid Testing (NAT), a more recent advancement in testing technology, is currently conducted at the discretion of individual Blood Centres, as it is not yet mandated by national regulations. [4, 5]

Globally, it is estimated that about 85 million red blood cell units are transfused each year, and more than 60 million donations per year are NAT tested worldwide.[6, 7] Recent data from the World Health Organization indicates that 55 countries worldwide implement universal nucleic acid testing (NAT) for screening donated blood units.[8]

Transfusion-transmitted hepatitis B has the potential to result in chronic Hepatitis B infection. The primary concern associated with chronic HBV infection lies in its long-term complications, which include an elevated risk of progression to primary liver cancer, recognized as the sixth most prevalent cancer globally. Furthermore, HBV-related fatalities rank as the tenth leading cause of death worldwide. Throughout their

lifetimes, approximately 15% to 40% of individuals with chronic HBV infection may experience complications, which can range from hepatocellular carcinoma (HCC) to HBV-related mortality.[9, 10] In a study conducted in India regarding Hepatitis B, it was found that 13.9% of participants reported a history of receiving blood transfusions.[11]

Hepatitis C transmitted via transfusion can also lead to its chronic infection. Chronic hepatitis C can have a profound effect on the health-related quality of life of the patient.[12] It is an important cause of liver-related morbidity and mortality. HCV infection has been associated with more than 30 extrahepatic manifestations, some of which are a consequence of the proliferation of B lymphocytes with consequent monoclonal and polyclonal production of antibodies showing the activity of the rheumatoid factor or cryoglobulins. [13] Moreover, chronic hepatitis B and C continue to pose significant challenges in healthcare, with associated costs escalating in correlation with the progression of liver disease.[14]

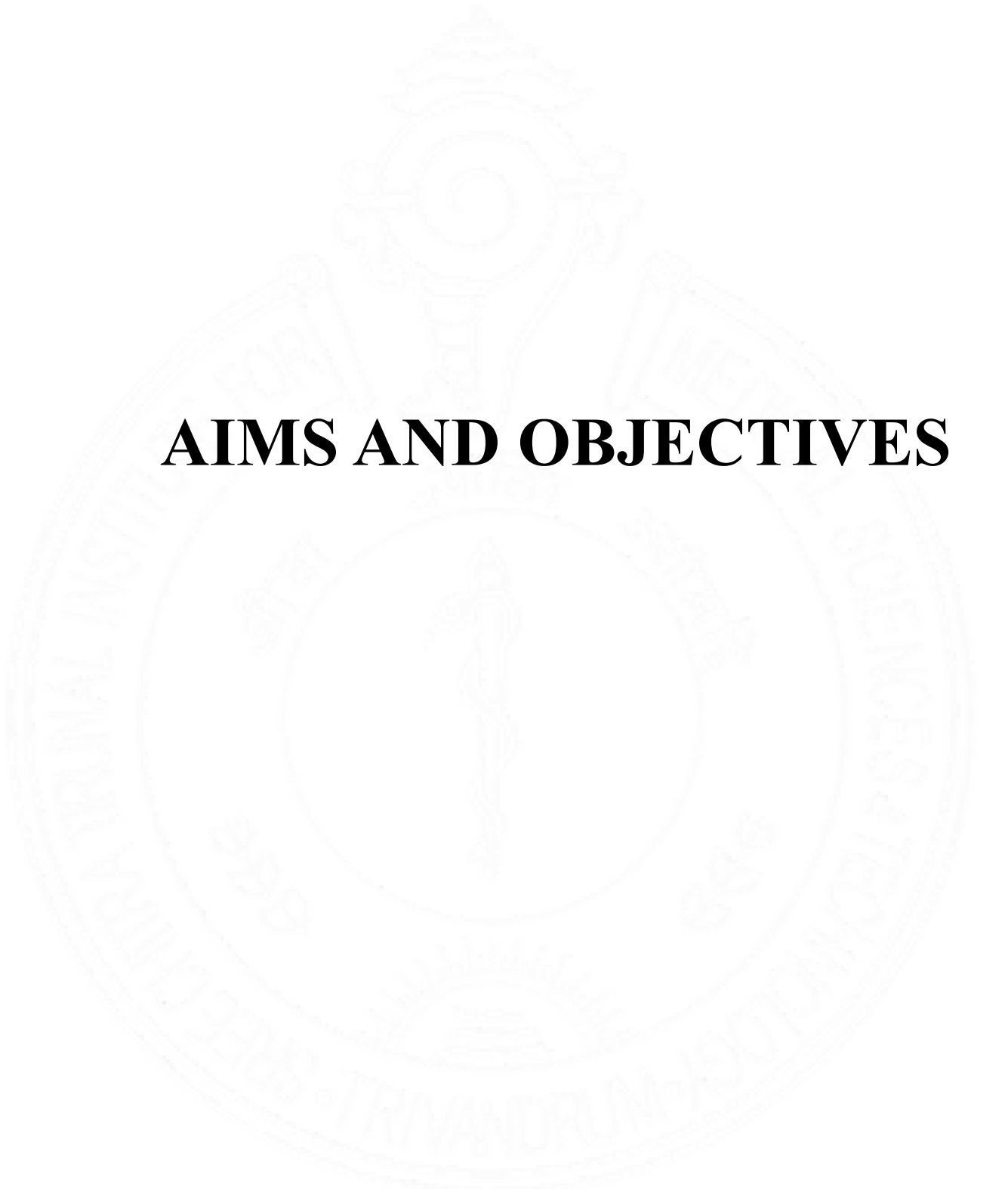
Acquired Immune Deficiency Syndrome (AIDS) can be transmitted through the transfusion of blood or blood products infected with the HIV. Approximately 60% of acute HIV infections manifest as a non-specific flu-like illness, with an incubation period ranging from 2 to 4 weeks. The acute phase of the infection typically resolves within weeks to a few months, leading to an asymptomatic period that may extend for several years. During this asymptomatic phase, HIV viremia persists, and there is a gradual decline in the number of CD4⁺ lymphocytes, which are the primary target of HIV. The depletion of CD4⁺ lymphocytes predispose individuals to opportunistic infections, while the virus also exerts direct effects on multiple organ systems. Collectively, these factors contribute to mortality, with an average life expectancy post-infection of approximately 8 to 10 years. [15] Transfusion transmitted HIV infection contributes to 2%–4% of all cases of HIV worldwide.[16]

Advancements in molecular screening for TTIs through the implementation of NAT in transfusion medicine have markedly diminished the risk of infection transmission associated with blood transfusions. NAT can be categorized into Mini-pool NAT (MP-NAT) and Individual Donation NAT (ID-NAT). MP-NAT is conducted on a diverse range of donor samples, whereas ID-NAT is executed on each sample individually. The advantages of NAT encompass the ability to directly identify viral genomes (DNA or

RNA) with exceptional specificity. Furthermore, its sensitivity surpasses that of traditional antigen and/or antibody immunological assays by several orders of magnitude.[3, 17]

NAT has significantly decreased the window period associated with transfusion-transmitted viral infections.[18, 19] NAT testing of collected blood started in India around late 2000s with first multicentric study on NAT evaluation published in 2008.[5] NAT testing was subsequently implemented by only a few centres across India. The main barriers to implementation of NAT testing in India remain the de-centralised blood collection system, inadequate technical manpower and cost implications of implementing the technology.[20]

The significance of clinical outcomes and the economic implications of utilizing NAT-based screening for blood units warrant thorough investigation. This research is essential to support informed decision-making regarding the potential implementation of universal NAT testing in India. To our knowledge, an economic evaluation of nucleic acid testing of donated blood units has not been done in the Indian scenario. I propose using the data generated from SCTIMST Blood Bank, which has been using NAT universally since January 2019, to build an economic model to explore the cost-effectiveness of universal screening with NAT. As mentioned earlier, such a study will go a long way in providing evidence-based support for policy regarding the introduction of this protocol universally as part of the national guidelines.



AIMS AND OBJECTIVES

2. AIMS AND OBJECTIVES

- i. To map out the economic impacts of transfusion transmissible viral infections (HIV, HBV and HCV).
- ii. To perform a costing of outcome pathways with and without NAT
- iii. To project the long-term cost-effectiveness by implementing NAT



REVIEW OF LITERATURE

3. REVIEW OF LITERATURE

Nucleic Acid Testing (NAT) for blood donations originated in the late 1980s with the use of PCR to assess the transmission rates of Hepatitis C Virus (HCV) and Human Immunodeficiency Virus-1 (HIV-1) through transfusions. German blood centers pioneered the implementation of NAT for HCV, HBV, and HIV-1, and were also the first to adopt NAT for HIV-2, hepatitis A virus, and Parvovirus B19. As commercial manufacturers developed test kits and instruments tailored to the needs of blood banks, many other countries began to adopt NAT testing.[7]

Blood transfusions have been known to transmit infections since before 1941, when transfusion-transmitted syphilis was first identified. This understanding led to the early implementation of syphilis screening in blood donors, even before the widespread establishment of blood banks. In 1943, Paul Beeson provided a seminal account of transfusion-transmitted hepatitis. Additionally, the malarial parasite was recognized as the first microbe to be transmitted through transfusion.[6]

The global distribution of blood products contaminated with HCV and HIV-1 led to widespread impact. In France, haemophiliacs were knowingly given HIV-contaminated blood, resulting in 4,000 infections. The USA saw 10,000 infections, while Italy, the UK, and Spain each reported approximately 1,300 infections.[7]

The recognition of widespread HBV infection emerged in 1963 with the advent of HBsAg testing, revealing a high prevalence among patients receiving multiple transfusions. Acute HBV infection, whether contracted through transfusion, intravenous drug use, perinatal transmission, or sexual contact, can be asymptomatic or manifest as clinical viral hepatitis with nonspecific symptoms like jaundice. In rare cases, acute infections, including those from transfusion-transmitted HBV, may lead to fulminant liver failure and death. Occult HBV infections have been shown to transmit the virus through blood transfusions, although the rate of infectivity is less than 100%.[21, 22]

Early diagnosis is crucial for timely treatment of viral hepatitis B, as many infected individuals remain asymptomatic and often present with advanced disease. Challenges in managing the disease include inadequate awareness among the public and healthcare providers, the asymptomatic nature of early infection, the need for lifelong treatment,

and access to quality diagnostics. Although antiviral agents can suppress HBV replication, prevent cirrhosis, and reduce the risk of HCC and liver-related deaths, they generally do not eradicate the virus, requiring potentially lifelong treatment.[23]

HCV infection, traditionally associated with liver issues, is now recognized as a systemic condition due to its ability to infiltrate and replicate within major cellular systems. This chronic condition significantly impacts patients, with symptoms ranging from fatigue and cognitive impairment to severe ascites and delirium, all of which can diminish quality of life. Extrahepatic symptoms may overshadow or exacerbate liver-related issues, affecting cardiovascular, joint, skin, kidney, and neurological systems. Hepatic encephalopathy is a common sign of central nervous system involvement in liver cirrhosis patients. Evidence suggests that chronic HCV infection may directly cause brain dysfunction, as seen in patients without cirrhosis or cryoglobulinemia who often experience various non-specific neurological symptoms. [24, 25]

In India, approximately 40 million individuals are chronically infected with Hepatitis B Virus (HBV). Regional studies suggest that 6-12 million people are affected by Hepatitis C. Chronic HBV infection is responsible for 40-50% of hepatocellular carcinoma (HCC) cases and 20-30% of cirrhosis cases. Meanwhile, chronic HCV infection contributes to 12-32% of HCC cases and 12-20% of cirrhosis cases.[23] Liver cirrhosis ranks among the leading causes of mortality in India.[26]

The National Viral Hepatitis Control Program (NVHCP) was initiated in July 2018 to bridge existing gaps in addressing viral hepatitis in India. This program aims to integrate current initiatives to enhance awareness, prevention, and treatment of viral hepatitis types A, B, C, D, and E. The introduction of new, safe medications for Hepatitis C has facilitated its effective management, while potent and safe treatments for Hepatitis B help maintain viral suppression over extended periods, thereby mitigating the risk of cirrhosis and liver cancer.[23] The testing policy and key activities are illustrated in Figures 1 and 2.

Hepatitis B surface antigen (HBsAg) positivity in India varies from 1.1% to 12.2% among the general population, with an average prevalence of 3-4%, as reported by the National Viral Hepatitis Control Programme (NVHCP). The prevalence of anti-Hepatitis C virus (HCV) antibodies in the general population is estimated to range from

0.09% to 15%.[23] The national HIV prevalence stands at 0.2%, while in Kerala, it is notably lower at 0.07%.[27]

The budget requirement for the NVHCP is projected at Rs 907 crore over three years, approved under the Government of India's National Health Mission (NHM) domestic funds. Activities through existing programs and schemes, such as UIP, IEC, NACP, and Swachh Bharat, which also address viral hepatitis, are mandated under their respective frameworks.[23]

Figure 1: Testing of Hepatitis under the National Viral Hepatitis Control Program (NVHCP). Source - NVHCP Technical Guidelines Document[28]

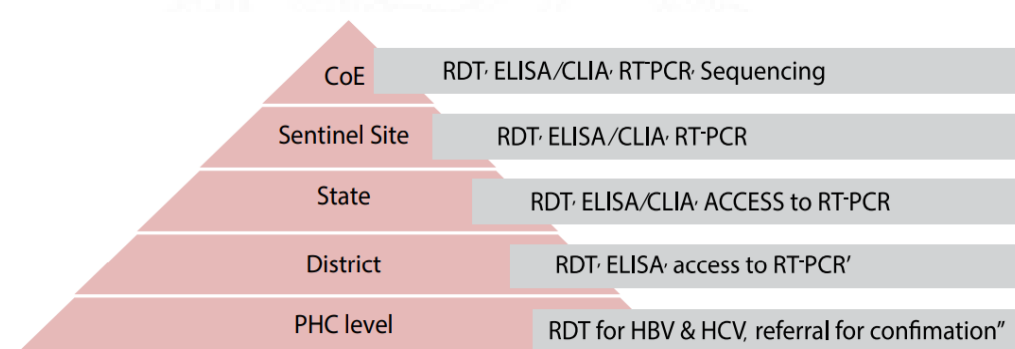


Figure 2: Key activities under NVHCP (Source [28])

Visit Number	Key activity (but not limited to)	Responsible person
First visit and baseline, after confirmation of Chronic HBV infection	Ascertain Diagnosis of Chronic HBV infection	Attending doctor
	Enter patient details in Hepatitis B Enrollment Register and demographic details in treatment card	Peer Supporter
	Take a detailed history and examination	Attending Doctor
	Categorize presence/Absence of Cirrhosis and fill relevant section in Treatment card	Attending Doctor
	Select Regimen and start treatment	Attending Doctor
	Explain patient on adherence and follow up date	Peer supporter and pharmacist
	Dispense prescribed medicines	Pharmacist
	Get the baseline investigations done and (furnish report to center (treatment site	Lab technician, Doctor
Follow up visit	Educate on treatment adherence and regular follow up	Doctor ,Peer supporter and pharmacist
	Dispense prescribed medicines	Pharmacist
	Check for any side effects	Attending Doctor, pharmacist
	Get any investigations needed as per technical guidelines, prescribe the medicines	Attending Doctor
	Update investigations in treatment card	Lab technician, Doctor
	Recheck the contact details including phone number and pincode / post office	Peer supporter / data entry operator
For all visits	Update the record from the register and card to the excel based sheet	Data entry operator

The medication will initially be dispensed for 30 days over a period of 6-12 months. The first follow-up should occur after 25 days, followed by subsequent visits every 30 days. This schedule ensures a 5-day buffer stock, preventing missed doses if appointments are delayed. Once the doctor confirms the patient's stability, the dispensation period can extend to 3 months. Patients must bring their medication bottles to each visit for pill counting, exchanging the old bottle for a new one. As this treatment is lifelong, all staff must counsel patients on the importance of adherence to the regimen.

Non-invasive techniques are increasingly replacing liver biopsy as the preferred method for evaluating liver disease stages, primarily due to the limited availability and accessibility of liver biopsies. These methods have been validated in adults with chronic hepatitis B (CHB). Blood and serum markers, such as APRI and FIB-4, along with transient elastography (FibroScan), are utilized to exclude advanced fibrosis.

Hepatitis B virus (HBV) can lead to both temporary and long-lasting liver infections. Temporary infections might result in severe illness, with about 0.5% ending in fatal, fulminant hepatitis. Chronic infections can also be severe, with nearly 25% resulting in untreatable liver cancer.[29] Newborns have a 90% chance of developing chronic hepatitis if infected, whereas the likelihood is 29–40% for children and 5–10% for adults.[30]

HIV transmission through intravenous administration of infected blood products is highly efficient. In the early 1980s, 50% of haemophiliacs treated with Factor VIII were infected, and all who received more than 500,000 units were infected. In 1982, the risk of HIV in the San Francisco area was approximately 1 in 100 for transfused products. [15] Five cases of HIV transmission have been reported in the United States, Germany, and France, involving donations that tested negative by NAT mini-pool testing. Detailed investigations revealed several common findings: the viral load was too low for detection by pooled testing, which typically requires more than 90 copies/ml. Retrospective analysis showed that seroconversion in these donors was recent, accounting for the low viral load. Crucially, further questioning of the donors uncovered risk factors, particularly recent male-to-male sexual contact, which had been denied during the initial screening interview. Retesting stored donor samples with ID NAT was reactive in the cases where it was conducted.[31–34]

India's approach to the HIV/AIDS epidemic began with sero-surveillance in 1985. Initially, efforts (1985-1991) concentrated on identifying HIV in various populations and locations, ensuring blood screening before transfusions, and raising awareness. The National AIDS and STD Control Programme (NACP) was launched in 1992, marking the start of a comprehensive response to the epidemic. Over 35 years, NACP has become one of the world's largest programs, evolving through five distinct phases.

The first phase (1992-1999) emphasized awareness and blood safety. The second phase introduced direct interventions across prevention, detection, and treatment, along with state capacity building in program management. The third phase (2007-2012) focused on scaling up and decentralizing program management to the district level. The fourth phase (2012-2017) was characterized by consolidation and increased government funding. NACP Phase-IV (Extension) was initially approved for 2017-2020 and extended to 2020-21, introducing several groundbreaking initiatives.

This phase began with the HIV and AIDS (Prevention and Control) Bill, 2017, and the 'Test and Treat' policy for HIV patients in April 2017. The Bill guaranteed equal treatment rights for those with HIV and AIDS and aimed to prevent discrimination. The Act was enforced in September 2018. As the 'Test and Treat' policy expanded, "Mission Sampark" was launched in 2017 to reconnect People Living with HIV (PLHIV) who had discontinued treatment after starting ART. This was complemented by the introduction of universal viral load testing for on-ART PLHIV in February 2018.

NACP Phase-V is a Central Sector Scheme, fully funded by the Government of India, with a budget of Rs 15471.94 crore. It aims to reduce new HIV infections and AIDS-related deaths by 80% by 2025-26, compared to the 2010 baseline.[35]

NAT testing of clotting factor batches, immunoglobulins, and production pools showed significant HCV contamination, especially in non-inactivated samples. This led to the recommendation of using NAT to test donor blood, alongside antibody and antigen testing, prior to the start of the manufacturing process.[36–38]

To enhance blood safety, U.S. blood banks started using nucleic acid testing (NAT) in the late 1990s to complement serology testing, initially targeting HIV and HCV, and subsequently HBV and West Nile Virus (WNV). Currently, NAT is used to screen the entire U.S. blood supply for HIV, HCV, WNV, and HBV. Since 2016, NAT has also been a mandatory requirement for blood services in China.[39]

The initial ELISA tests for detecting anti-HIV were effective in identifying most asymptomatic HIV carriers, but newly infected individuals experienced a window period of about 56 days before seroconversion. Advances in second and third-generation anti-HIV tests shortened this window to 33 and 22 days, respectively. In March 1996, the HIV P-24 antigen test was introduced to further decrease the window period.[22]

Biswas and colleagues demonstrated that mini-pool (MP) NAT and individual donor (ID) NAT assays significantly shortened the HBV window period (WP) by 9–11 days and 25–36 days, respectively, when compared to the currently licensed HBsAg tests. This comparison involved seven HBsAg assays and seven NAT assays, including three ID NAT and four MP NAT tests on acute-phase seroconversion panels.[40]

NAT is recommended to be used alongside serological testing to detect low-level infections and those at the limits of detection windows. There is no agreement on whether single-donor NAT or a specific pool size is best, and this may vary based on the country's HBV prevalence.[22]

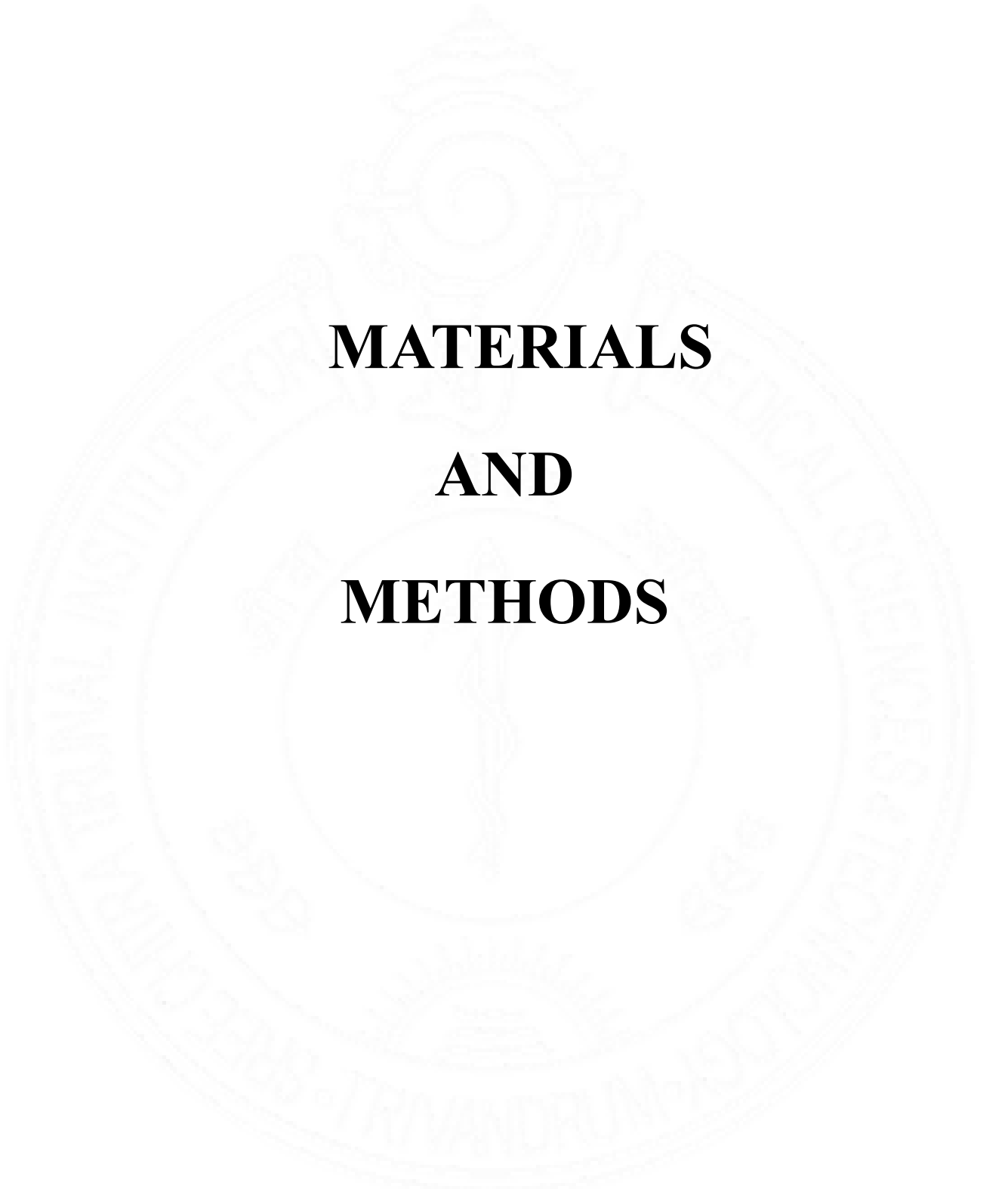
In India, the NAT yield rate reported by centers that implemented NAT varied between 1:476 and 1:17,753, with an average of 1:1,361. Different centers across the country utilized both MP-NAT and ID-NAT methods.[20]

The research by Heyns et al in South Africa found that implementing NAT significantly enhanced blood supply safety. For HIV, it reduced the risk during the incidence-window period, and within six months, NAT identified nine additional viraemic donations that were antibody-negative.[41]

In a German study, there was one confirmed transmission case each for HCV and HIV-1. These incidents were not detected by NAT due to low-level viremia and/or suboptimal amplification efficiency. Additionally, evidence was found for a case where a red blood cell unit with low-level HIV-1 contamination did not result in transmission.[42]

Cost-effectiveness for NAT, as found by Jackson et al. in 2003, is suboptimal when compared to numerous accepted medical interventions. Enhancing cost-effectiveness could be achieved by reducing NAT costs and/or removing certain redundant tests on blood donations.[43]

In a study on Indonesia's health economy, it was concluded that ID-NAT incurs extra costs for blood safety. However, when comparing the incremental costs of serology combined with ID-NAT to serology testing alone, there was an estimated minimum savings of USD \$27 million.[44]



MATERIALS AND METHODS

4. MATERIALS AND METHODS

4.1. Study Setting:

An economic modelling study was conducted in the Department of Transfusion Medicine, Sree Chitra Tirunal Institute for Medical Sciences and Technology from July 2024 to November 2024.

4.2. Data source:

Data of all blood donations like age, gender, type of donation (voluntary or replacement), number of donations yearly and donors deferred from blood donation from January 2021 to July 2024 was collected from various registers and software in the Blood Centre.

Data pertaining to TTI screening results was also obtained from these registers and software.

NAT yield was calculated by finding out the number of blood units which were non-reactive for HIV, HBV and HCV by CLIA but were found to be reactive by ID-NAT.

All personal identifiers were removed from the data set.

4.3. Donor Deferral:

Deferral of registered donors was performed either by the counsellor or by the medical officer based on the criteria laid down by the National Blood Transfusion Council (NBTC).

Donors found to have behaviours, practices or exposure to TTIs, prone for high-risk of transmission of infections like HIV, HCV, HBV and syphilis were strictly deferred from donating blood.

4.4. Donation Procedure:

Donors were selected by following the Indian Guidelines for Blood Donor Selection developed by the National Blood Transfusion Council (NBTC).[45] Whole blood, either 350mL or 450mL was collected from the eligible donors.

All units were separated into components – Packed Red Cells (PRC), Fresh Frozen Plasma (FFP) and Platelet Concentrate (PC) or Cryo-poor Plasma (CPP) and Cryoprecipitate.

4.5. Testing of Donated Blood:

According to the Indian national guidelines, all blood units in the blood centre are to be tested using an immunoassay prior to release. NAT is not a mandatory test.[4]

However, in our centre, all units are routinely tested by chemiluminescence immunoassay (CLIA) on Roche Cobas e 411 as well as individual donor nucleic acid testing (ID-NAT) on Grifols Procleix Panther ID-NAT system for HIV, HBV and HCV.

4.6. Cost related data:

Data about various expenditures involved in NAT was obtained from the purchase department, finance department as well as from the National Blood Transfusion Council (NBTC) guidelines for costing of blood processing and testing.

Cost incurred for serological testing in our Centre is ₹ 70 per HBsAg test, ₹ 80 per HIV Test and ₹ 150 per HCV test.

The imputed costs regarding lifetime expenses occurring if a patient contracts a TTI via transfusion was obtained from Indian literature.[46]

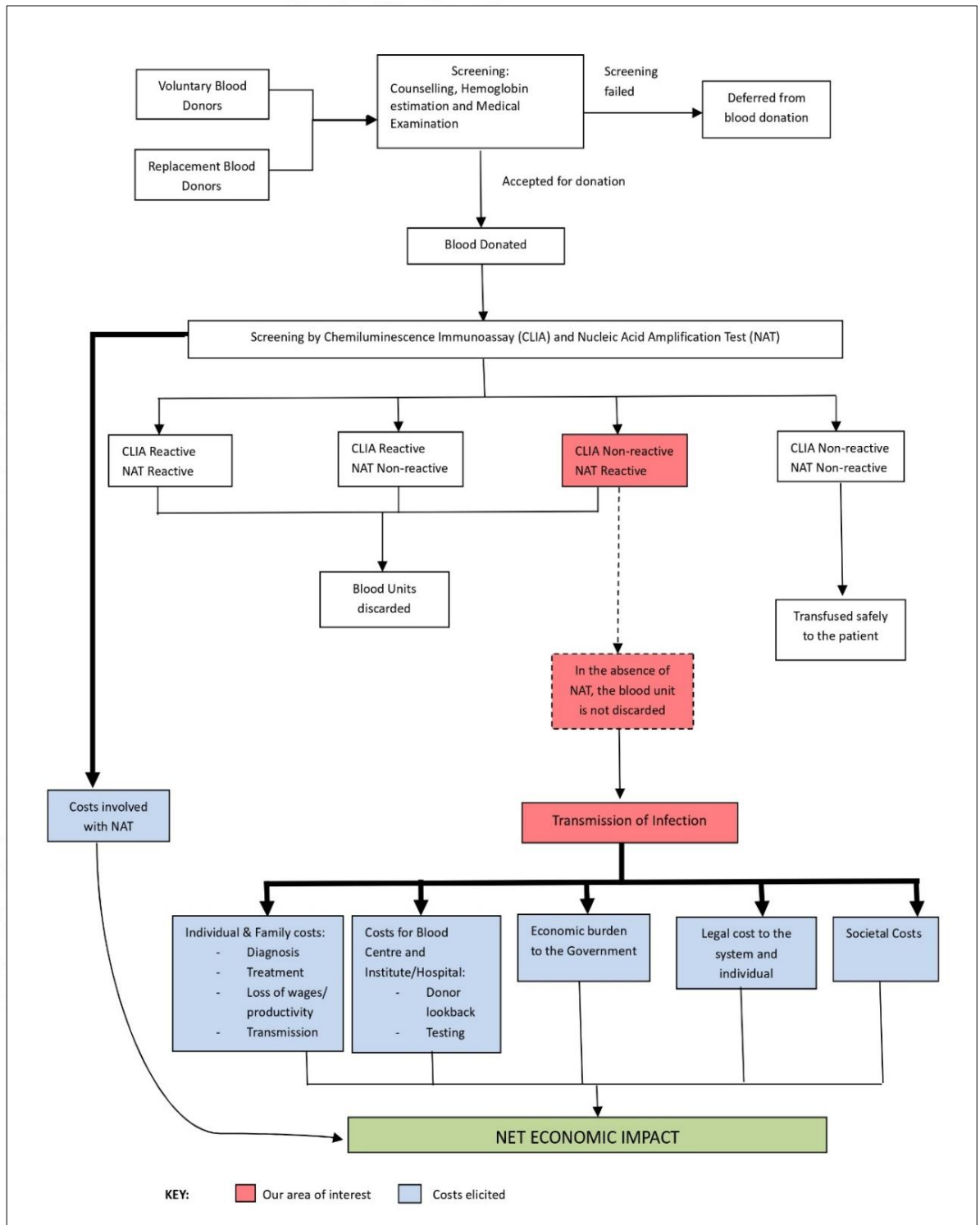
Costs are depicted in Indian Rupee (INR).

<i>Sl No</i>	<i>Cost</i>	<i>Source</i>	<i>Comments</i>
1.	Nucleic Acid Testing costs	Purchase Department, Finance Department, SCTIMST Revised Guidelines-2022 for Recovery of Processing Charges for Blood and Blood Components [47]	
2.	Diagnosis and Treatment costs for Hepatitis B	Muniyandi M <i>et. al.</i> , 2021 [46] Balasundaram P <i>et.al.</i> , 2020 [11]	Drug cost obtained by calculating annual expenditure based on treatment regimen as per NVHCP[23] and applying market costs of the drug as per November 2024 rates.
3.	Donor Look-back and Patient trace-back	Testing cost – obtained from the designated cost per test in the institute. Out of pocket expenses for donor	Transportation (to and fro average autorickshaw charge)
4.	Legal costs	Compensation costs – Supreme court verdicts [48] Out-of-pocket expenses to carry out a legal case	Personal Communication with a Supreme Court lawyer
5.	Societal/Indirect costs	Singapore based literature source[49]	No Indian data available in literature

4.7.Methodology:

Step 1: A protocol map showing the blood donor pathway in various scenarios was developed. (Figure 3)

Figure 3: Our Economic Model Map



Step 2:

- a) Imputed costs from Indian literature was applied to the protocol as relevant.

Imputed costs were calculated by:

1. Obtaining data regarding life-cycles and complications of each of these diseases

Data regarding the stage-wise distribution of Hepatitis B infected patients was adopted from the National Viral Hepatitis Control Programme. [23] (Table 1)

Table 1: Stage-wise distribution of HBV patients as per NVHCP [23]			
Stage	Base case	Lower	Upper
Delayed clearance	0.55	0.275	0.825
Chronic hepatitis	0.195	0.0975	0.2925
Compensated cirrhosis	0.14	0.07	0.21
Decompensated cirrhosis	0.045	0.0225	0.0675
Hepatocellular carcinoma	0.07	0.035	0.105

Longitudinal studies of untreated persons with CHB show an 8–20% cumulative risk of developing cirrhosis over five years. In those with cirrhosis, there is an approximately 20% annual risk of hepatic decompensation. [28]

4.7.1. Data pertaining to the life expectancy:

Data regarding normal life expectancy of Indian population was collected from the Institute for Health Metrics and Evaluation (IHME) database. The average life expectancy of an Indian is about 74 years (Male – 70.9 years and Female – 76.8 years).[26]

Life expectancy decreases with the disease condition. The following life expectancies were derived from the 5-year survival rate values obtained from literature. [50, 51] (Table 2)

Table 2: Imputed life expectancies	
<i>Disease State</i>	<i>Years of survival after the modal age of 50 years</i>
No TTI	25
Chronic HBV	22
Compensated cirrhosis	20
Decompensated cirrhosis	16
Hepatocellular Carcinoma (HCC)	13
Post-transplantation - HCC	16

2. Costs were obtained from available Indian Literature from publications by Muniyandi et al [46], Balasundaram et al [11], and publicly available databases of the Government of India centre for health economics developed by PGI Chandigarh[52]. (Table 3)

- b) Costs for provision for NAT testing in this institute was calculated

Step 3:

The experience from our blood centre was applied to the above to create an economic model.

Table 3: Costs for HBV Diagnosis and Treatment[46]				
	Parameter	Base Case	Lower	Upper
Diagnostic costs	Diagnosis cost of rapid test	85.00	42.5	127.5
	Diagnosis cost of ELISA	1157.00	587.5	1735.5
	Diagnostic cost pre-treatment RNA, LFT, Fibro-scan	8000	4000	12000
	Diagnostic cost post-treatment	6000	3000	9000
Treatment costs	Drug cost*			
	- Acute case	25500	21600	29400
	- Chronic case	42000	33000	51000
	Treatment cost intensive care (Chronic cases)	73228.00	36614	109842
	Out-of-pocket (OOP) cost	64321.00	32160.5	96481.5

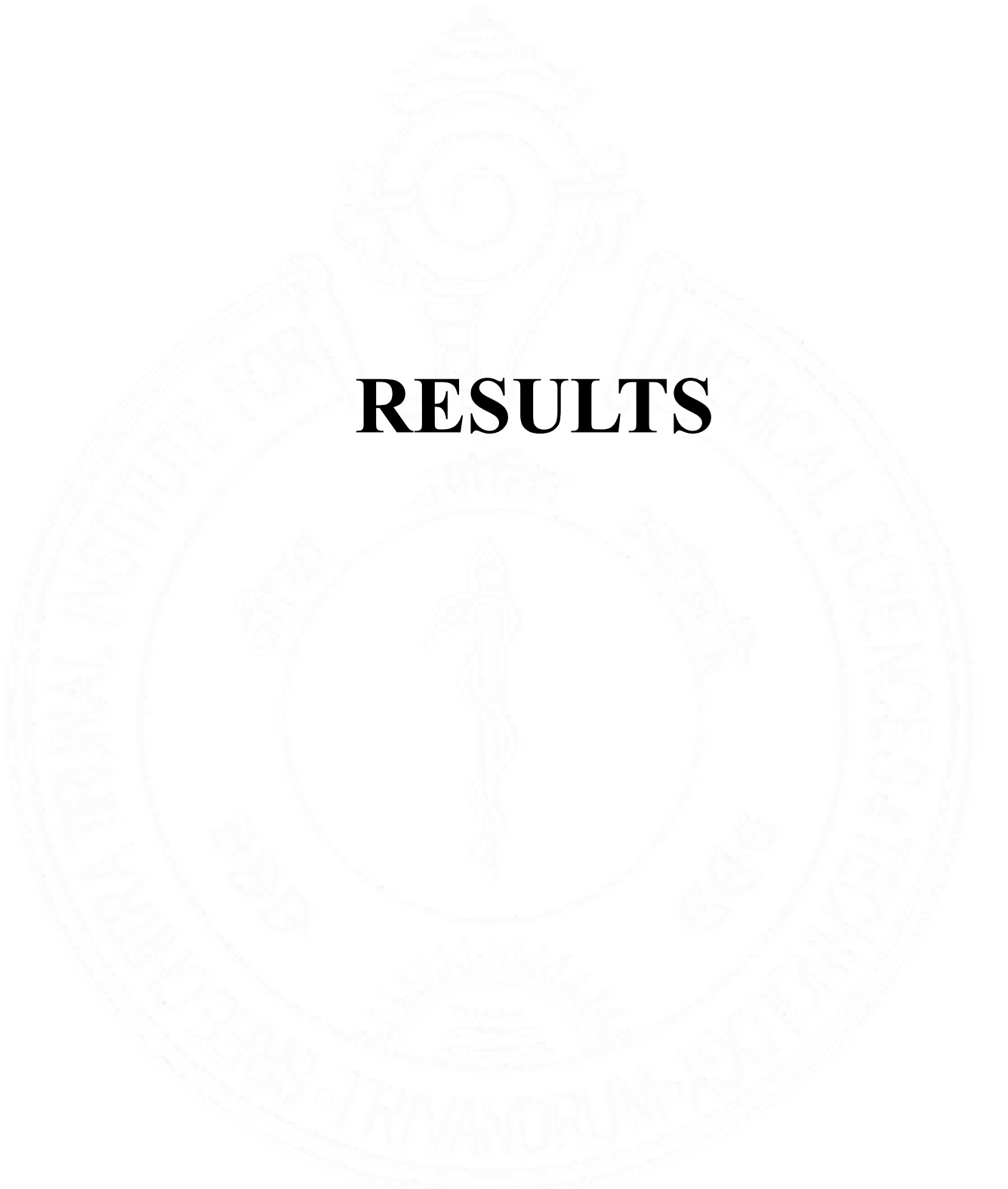
*Drug cost obtained by calculating annual expenditure based on treatment regimen as per NVHCP and applying market costs of the drug as per November 2024 rates.

4.8. Analysis:

1. Descriptive analysis was done using Microsoft Excel and IBM SPSS Statistics Version 29.
2. The cost of implementing NAT in our institute was computed.
3. The lifetime expenses involved in the event of transmissible Hepatitis B was analyzed using data obtained from literature.
4. The data obtained was applied to the economic model – A decision tree model was created to compare CLIA alone and NAT+ CLIA in screening for transfusion transmitted infections. A cohort size of 10,000 was used, and yield of NAT was incorporated in the model as additional infections occurring in the CLIA only arm. A scenario analysis was done with best reported yield in available Indian studies. Costs and QALYs associated with both arms were estimated. An Incremental Cost Effectiveness Ratio (ICER) which is the difference in costs in both arms divided by the difference in QALYs, was derived.

$$\text{Incremental Cost-Effectiveness Ratio (ICER)} = \frac{(\text{Cost}_{\text{CLIA+NAT}} - \text{Cost}_{\text{CLIA alone}})}{(\text{QALY}_{\text{CLIA+NAT}} - \text{QALY}_{\text{CLIA alone}})}$$

5. Cost effectiveness was analysed by comparing ICER to the cost-effectiveness threshold of GDP per capita of India for the year 2024, which is ₹ 2.24 Lakhs.



RESULTS

5. RESULTS

A total of 50,731 donors registered for blood donation at our Centre from January 1st 2019 to July 31st 2024. After medical examination and pre-donation counselling, 33.8% (n=17,153) of the registered donors were deferred from blood donation. Total collection was 33,578 units of blood.

Prior to the COVID-19 pandemic, 100% of the registrations and collections were sourced exclusively from voluntary donors, predominantly through outdoor blood donation camps. Throughout the years, the percentage of voluntary donors consistently exceeded that of replacement donors. (Tables 4-6)

Table 4: Year-wise Distribution of donors registered for blood donation							
Registrations							
Year	Total	Male	Female	In Blood Centre	Outdoor Camps	Voluntary Donors	Replacement Donors
2019	10383	7717	2666	1542	8841	10383	0
2020	6605	5691	914	4289	2316	4132	2473
2021	9742	7942	1800	6535	3207	5352	4390
2022	9501	7575	1926	5480	4021	5628	3873
2023	9431	6984	2447	2281	7150	8300	1131
2024*	5069	3823	1246	1450	3619	4433	636
TOTAL	50731	39732	10999	21577	29154	38228	12503
* till July 31 st 2024							

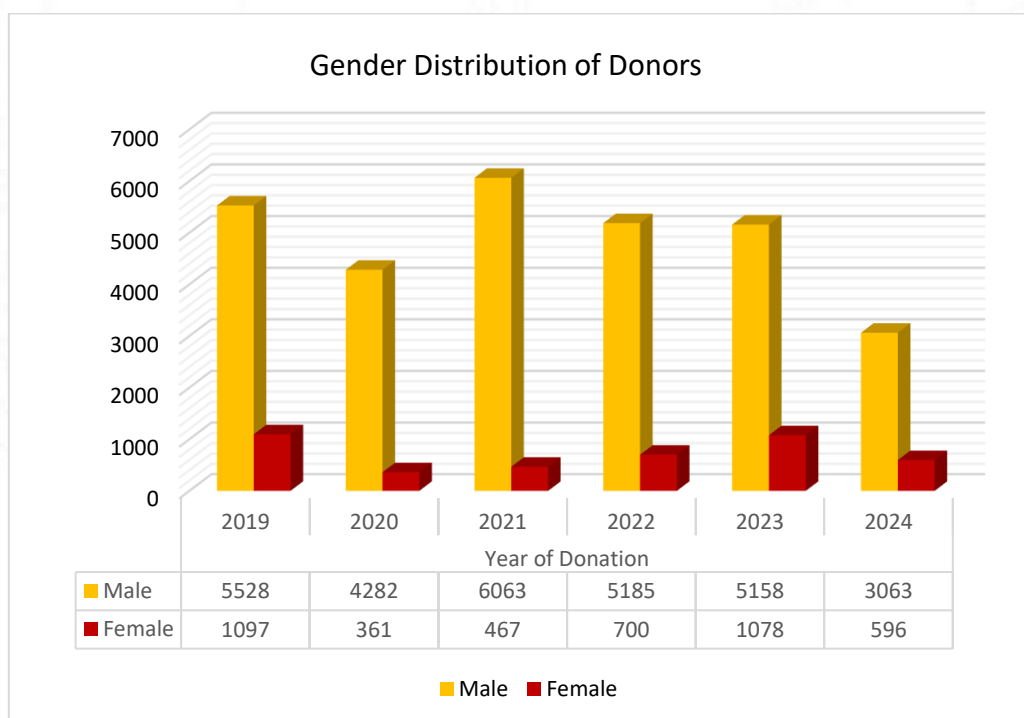
Table 5: Year-wise Distribution of donors deferred from blood donation							
Deferrals (33.8%)							
Year	Total	Male	Female	In Blood Centre	Outdoor Camps	Voluntary Donors	Replacement Donors
2019	3758	2189	1569	367	3391	3758	0
2020	1962	1409	553	1046	916	1185	777
2021	3212	2441	771	1879	1333	2501	711
2022	3616	2390	1226	1337	2279	2228	1388
2023	3195	1826	1369	504	2691	2954	241
2024*	1410	760	650	274	1136	1307	103
TOTAL	17153	11015	6138	5407	11746	13933	3220
* till July 31 st 2024							

Table 6: Year-wise Distribution of donors who donated blood							
Donations							
Year	Total	Male	Female	In Blood Centre	Outdoor Camps	Voluntary Donors	Replacement Donors
2019	6625	5528	1097	1175	5450	6625	0
2020	4643	4282	361	3243	1400	2947	1696
2021	6530	6063	467	4656	1874	2851	3679
2022	5885	5185	700	4143	1742	3400	2485
2023	6236	5158	1078	1777	4459	5346	890
2024*	3659	3063	596	1176	2483	3126	533
TOTAL	33578	29279	4299	16170	17408	24295	9283
* till July 31 st 2024							

5.1. Age and Gender Distribution

87.2% (n=29279) of total number blood donors were male and 12.8% (n=4299) were female. (Figure 4)

Figure 4: Gender Distribution of Blood Donors



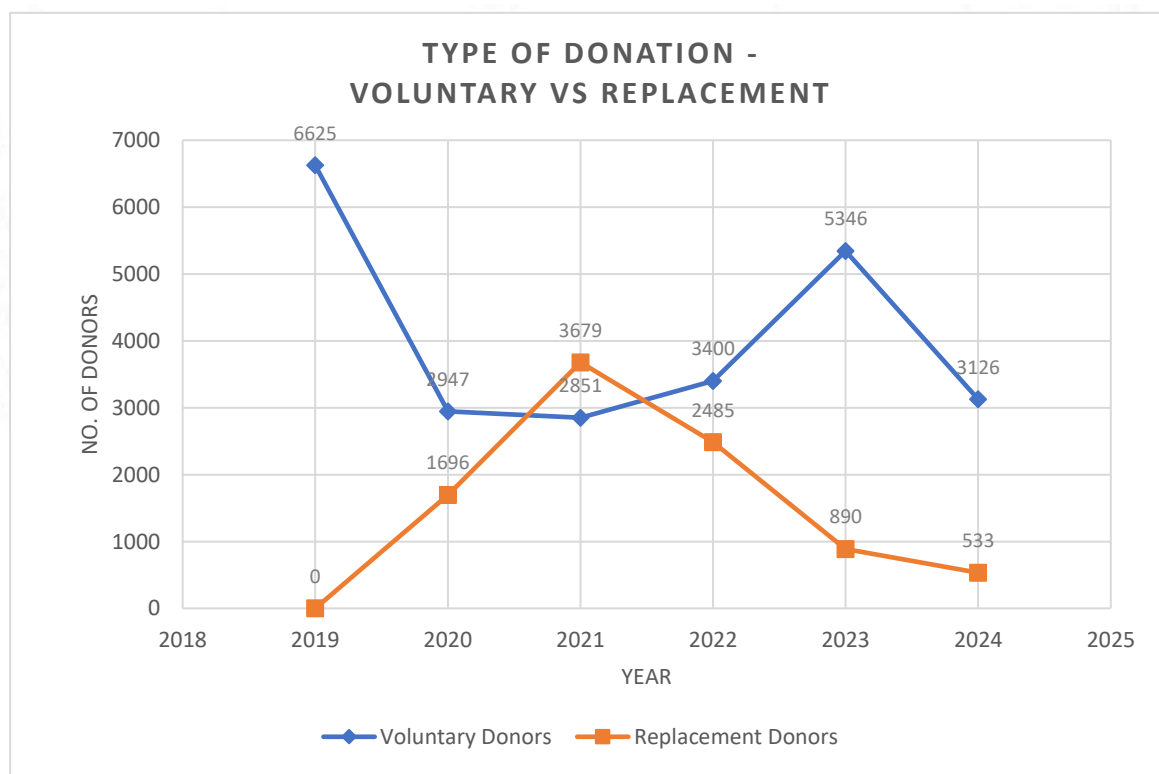
The mean age of donors was 29 ± 9 years. Table 7 depicts the age distribution of the donors who donated blood in this Centre. 61.4% of the donors were within the age range of 18 to 30 years. The proportion of donors decreased with increase in age.

Table 7: Distribution of Age of Blood Donors		
	<i>Frequency(n)</i>	<i>Percent (%)</i>
18 - 30 years	20616	61.4
31 - 45 years	10516	31.3
46 - 60 years	2417	7.2
60 - 65 years	29	0.1
Total	33578	100

5.2. Type of Donation

72.4% (n=24295) were voluntary donations and 27.6% (n=9283) were replacement donations, the year-wise distribution being depicted in Figure 5.

Figure 5: Donor distribution based on the type of blood donation – year wise



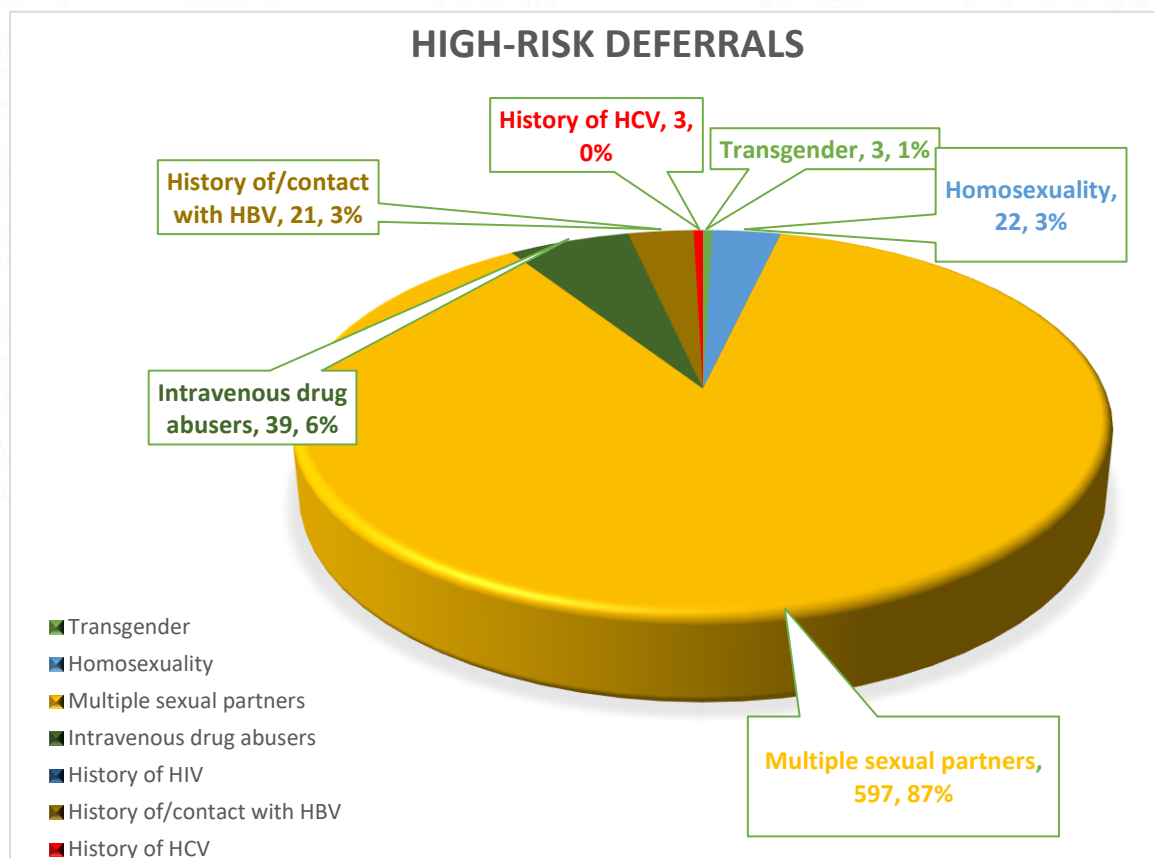
5.3. Donor Deferral

33.8% (n=17153) donors were deferred over this time period (Tables 5 and 8), out of which, 4% (n=685) were deferred in view of high risk for transfusion transmissible infections (TTI). The most common cause of deferral among those with high risk for TTI was history of multiple sexual partners (87.2%, n=597) (Figure 6)

Table 8: Year wise tabulation of Donor Deferrals

Year	Registrations (n)	Deferrals (n %)
2019	10383	3758 (36.2%)
2020	6605	1962 (29.7%)
2021	9742	3212 (33%)
2022	9501	3616 (38.1%)
2023	9431	3195 (33.9%)
2024*	5069	1410 (27.8%)
TOTAL	50731	17153 (33.8%)
* till 31st July		

Figure 6: Distribution of donors deferred in view of high risk for transfusion transmissible infections (n=685)



5.4. TTI reactive donations

All of the collected units were subjected to testing by serological assay as well as by Individual Donor – Nucleic Acid Testing (ID-NAT).

Among the total, 0.5% (n=171) of the donations were positive for either HBV, HCV or HIV (out of which 2 units were reactive for both HIV and HBV).

Sero-reactivity rate was 0.49%. The sero-prevalence of Hepatitis B, Hepatitis C and HIV in this study is 0.24%, 0.13% and 0.12% respectively.

Tables 9 and 10 represent the distribution of TTI reactive donations.

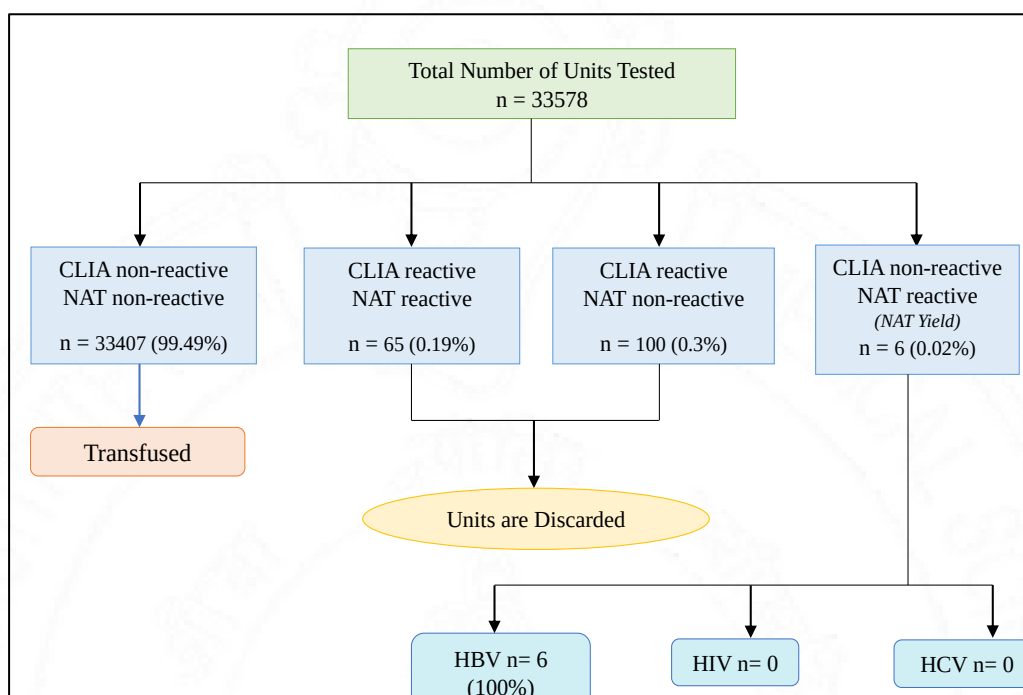
Table 9 : Distribution of TTI reactive donations based on Gender, Age and Type of donation		
Donor Characteristic		TTI Reactive Donations n=171 (n %)
Gender	Male	158 (0.54%)
	Female	13 (0.30%)
Age	18 to 30 years	99 (0.48%)
	31 to 45 years	61 (0.58%)
	46 to 60 years	11 (0.46%)
	above 60 years	0
Donor type	Voluntary	105 (0.43%)
	a. In house donation	22 (0.32%)
	b. Outdoor Camps	83 (0.48%)
	Replacement	66 (0.71%)

Table 10: Distribution of Test Reactive Donations – HBV, HCV and HIV							
Donor Characteristic	Serology Reactive for			NAT Reactive for			
	HBV (n=81 49.1%)	HCV (n=44 26.7%)	HIV (n=40 24.2%)	HBV (n=59 83.1%)	HCV (n=2 2.8%)	HIV (n=10 14.1%)	
Gender (including 2 donations which were HBV + HIV reactive)							
	Male	76	38	40	55	2	10
	Female	6	6	1	4	0	0
Age Group							
	18 to 30 years	38	28	30	23	1	5
	31 to 45 years	40	11	8	33	1	4
	46 to 60 years	3	5	2	3	0	1
	above 60 years	0	0	0	0	0	0
Donor Type							
	Voluntary	45	33	23	36	2	8
	a. In house donation	11	6	4	6	0	0
	b. Outdoor Camps	34	27	19	30	2	8
	Replacement	36	11	17	23	0	2
Donation Year							
	2019	4	12	0	4	0	0
	2020	10	2	0	11	0	0
	2021	32	8	14	18	1	3
	2022	15	7	13	12	0	3
	2023	14	13	8	10	0	2
	2024*	6	2	5	4	1	2
	*till July 31st						

5.4.1. NAT Yield

3.64% (n=6 units) which were non-reactive by serological testing were found reactive by NAT. Hence, our NAT yield is 1 in 5596. Hepatitis B Virus nucleic acid was detected in all 6 NAT yields. No NAT yield was detected for HCV and HIV. (Figure 7)

Figure 7: TTI Screening Test for HBV, HCV and HIV (n=33578)



5.5.COSTING

5.5.1. Costs involved with NAT

Over the study period, costs incurred with NAT was ₹ 5,12,63,500. (Table 11)

Table 11: Costs involved with NAT in our Centre from January 2019 to July 2024		
Sl no	Costs of	Amount in INR
1	Equipment - Reagent Rental basis	0
2	Consumables - Kits and Reagents	₹ 5,05,57,500
3	Electricity Charges	₹ 6,40,000
4	Other contingent expenses	₹ 66,000
	TOTAL	₹ 5,12,63,500

5.5.2. Costs involved if infection occurs, in the absence of NAT

If NAT was not performed, according to this study, potentially 18 patients would have been transfused with the infected blood components.

Based on the natural history of HBV infection, 80-90% (n=15) of adults would have an acute infection whereas 10-20% (n=3) will have a chronic phase. [30] (Figure 8,9)

Figure 8: Potential Infection transmission in the absence NAT

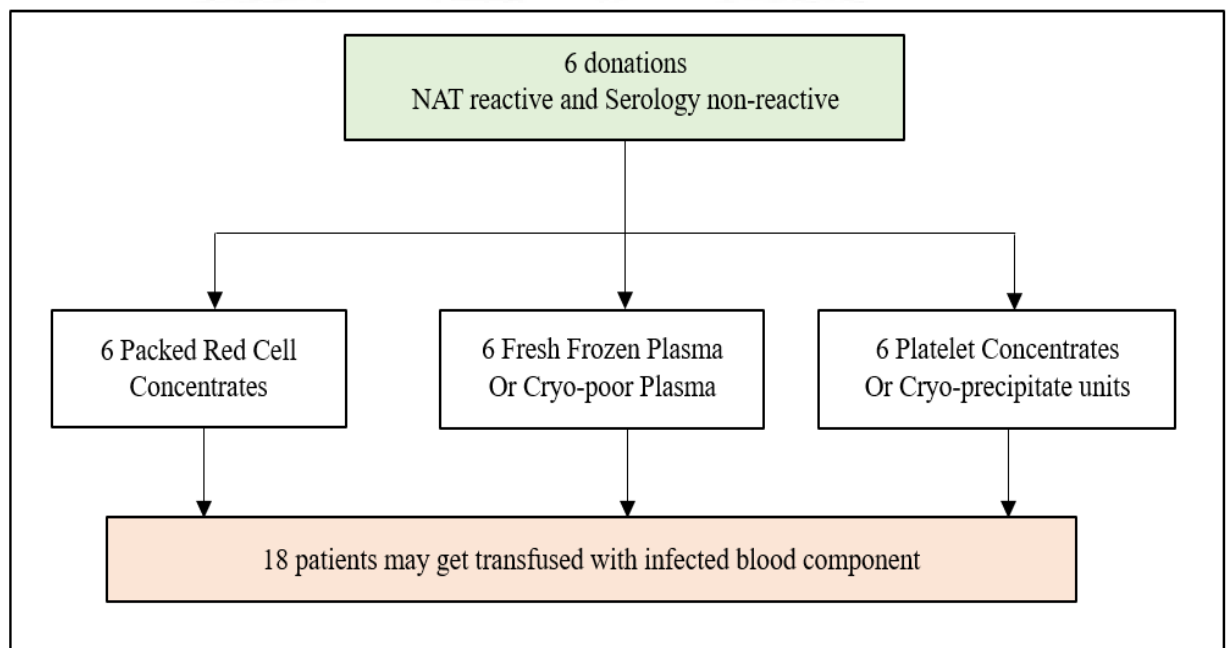
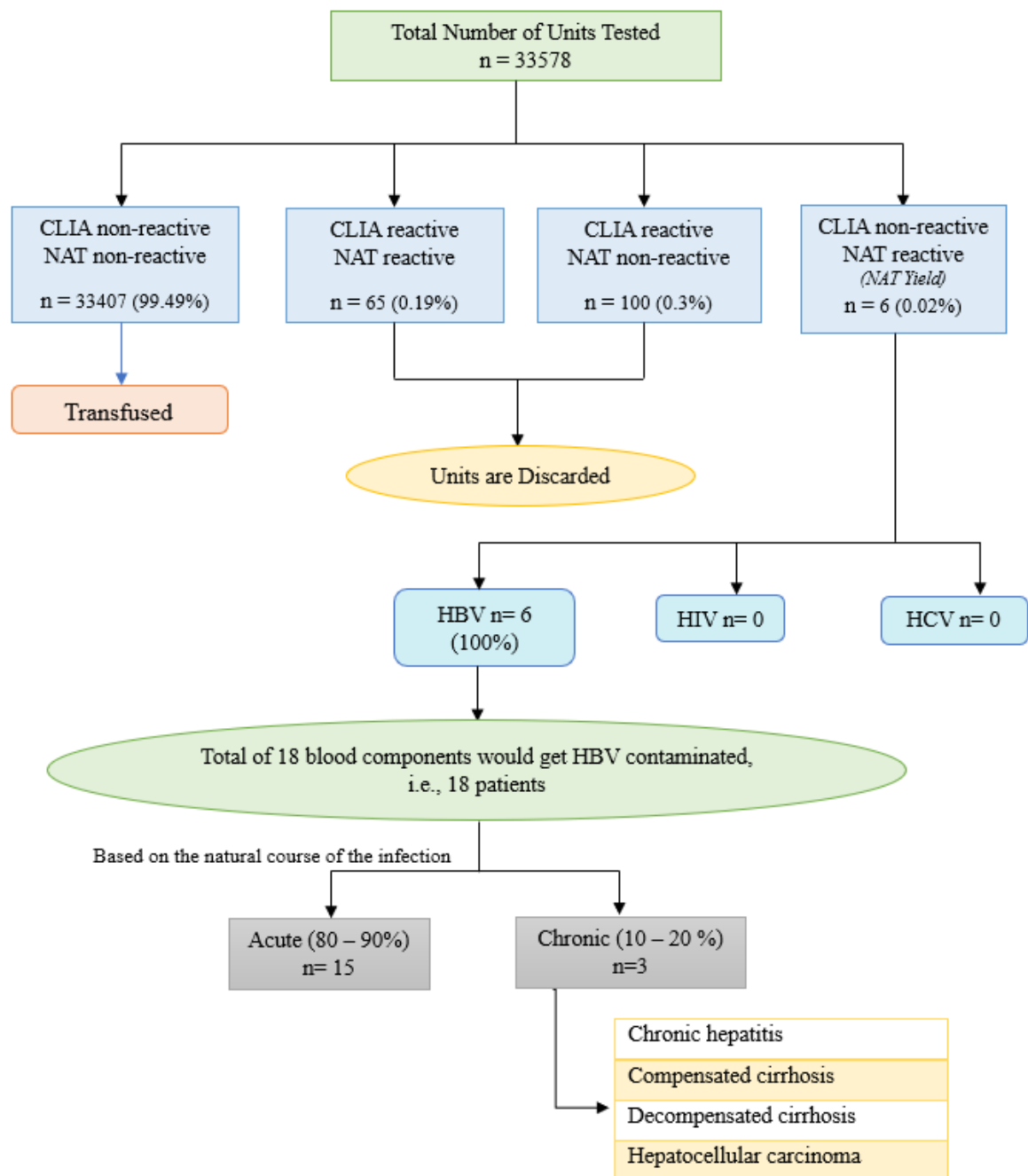


Figure 9: Overview of Testing and Potential Disease Transmission



NOTE: This flowchart illustrates a hypothetical scenario where there is a potential risk of Hepatitis B transmission if units that are CLIA non-reactive but NAT reactive are not properly discarded. In our center, we ensure that these units are also discarded to maintain safety and compliance.

5.5.3. Individual and Family Costs

- Costs incurred by patient (Table 12)

Table 12: Costs incurred by the patients for HBV Diagnosis and Treatment per annum				
	Parameter	Base Case	Lower	Upper
Diagnostic costs	Diagnosis cost of rapid test	85.00	42.5	127.5
	Diagnosis cost of ELISA	1157.00	587.5	1735.5
	Diagnostic cost pre-treatment RNA, LFT, Fibro-scan	8000	4000	12000
	Diagnostic cost post-treatment	6000	3000	9000
Treatment costs	Drug cost			
	- Acute case	25500	21600	29400
	- Chronic case	42000	33000	51000
	Treatment cost intensive care (Chronic cases)	73228.00	36614	109842
	Out-of-pocket (OOP) cost	64321.00	32160.5	96481.5
TOTAL (INR) costs incurred per annum per case	For Acute Cases	1,05,063	61390.5	148744.5
	For Chronic Cases	1,94,791	1,09,404.5	2,80,186.5

Assuming the mean age of the population receiving transfusion is 50 years, and considering the average life expectancy as denoted in Table 2 and applying the proportion of cases in various stages of chronic Hepatitis B as mentioned in Table 1, the total average cost incurred is found to be ₹ 1,38,18,559 (Table 13)

Table 13: Approximate costing in our model			
	Cost incurred		
Type of Infection	Base Case	Lower	Upper
Acute Infection (n=15)	₹ 15,75,945.00	₹ 9,20,857.50	₹ 22,31,167.50
Chronic Infection (n=3) calculated based on life expectancy	₹ 1,22,42,614	₹ 68,76,073	₹ 1,76,09,722
Total cost	₹ 1,38,18,559	₹ 77,96,930	₹ 1,98,40,889

5.5.4. Costs for Blood Centre and Institute/Hospital

- **Costs involved with Donor Look-back**

When a TTI is suspected, the individuals identified as potential donors are contacted to confirm the suspicion. Table 14 portrays the minimum costs involved.

Table 14: Costs involved with Donor Look-back per donor	
Parameter	Cost in INR
Out-of-pocket expenses for the donor	₹ 150
Repeat Testing cost	₹ 70
Total cost	₹ 220
Thus, total cost for 6 donors	₹ 1320

- ***Costs involved with patient Trace-back***

When a transfusion transmissible infection is identified, all the patients who received transfusion from that particular donor has to be traced back, tested and treated if

Table 15: Costs involved with Patient Trace-back	
Parameter	Cost in INR
Out-of-pocket expenses for the patients (Travel, etc.)	₹ 150
Testing cost (per test)	₹ 70
Total cost	₹ 220
Thus, total cost for 18 patients	₹ 3960

infected. Table 15 depicts the costs involved for the same.

5.5.5. Economic burden to the Government

With the advent of the National Viral Hepatitis Control Programme (NVHCP), the government of India provides free treatment to all patients diagnosed to have Hepatitis B and/or Hepatitis C. [23] This causes an economic burden to the Government. The costs incurred on individual basis, which is on an average between ₹ 77,96,930 and ₹1,98,40,889 (Table 13) is now borne by the Government.

5.5.6. Legal Costs (Table 16)

a. To the System

- ***Compensation to be paid by the Hospital Administration to the patients who received infected blood***

As a result of transfusion transmitted Hepatitis, the Supreme Court of India directed to pay compensation of Rs.5,00,000/- to the complainant in 2020 within 45 days from the date of receipt of certified copy of the order.[48]

b. To the Individual

- Out-of-pocket expenses to carry out a legal case = ₹25,000 – ₹ 50,000. Thus an average of ₹ 37,500.

Table 16: Implicated Legal Costs	
Compensation to be paid by the Hospital Administration to the patients who received infected blood	₹ 90,00,000
Out-of-pocket expenses of the individual	₹ 37,500
Total	₹ 90,37,500

5.5.7. Societal / Indirect costs

Since no Indian data regarding the indirect costs could be obtained from Indian literature, costing data was adopted from a Singapore based literature source. Considering parameters like medical leave, time-off claimed and reduced productivity, the annual indirect cost depicted by them was US\$ 7635.27, which is equivalent to ₹ 6,44,187.73. [49]

Table 17: Approximate indirect costing in our model	
Type of Infection	Average costs incurred
Acute Infection (n=15)	₹ 96,62,816
Chronic Infection (n=3) for 24 years	₹ 4,63,81,517
Total cost	₹ 5,60,44,333

5.5.8. Total Cost that could have been involved in the absence of NAT:

Total Cost that could have been involved in the absence of NAT based on our model is ₹7,09,16,303.9. (Table 18)

Table 18: Total Cost that could have been involved in the absence of NAT	
Costs involved	
1. Direct Costs	₹ 1,38,18,559
2. Indirect Costs	₹ 5,60,44,333
3. Costs for Blood Centre and Institute/Hospital	₹ 5,820
4. Legal Costs	₹ 90,37,500
TOTAL	₹ 7,89,06,212

5.5.9. Net monetary Gain by introduction of NAT

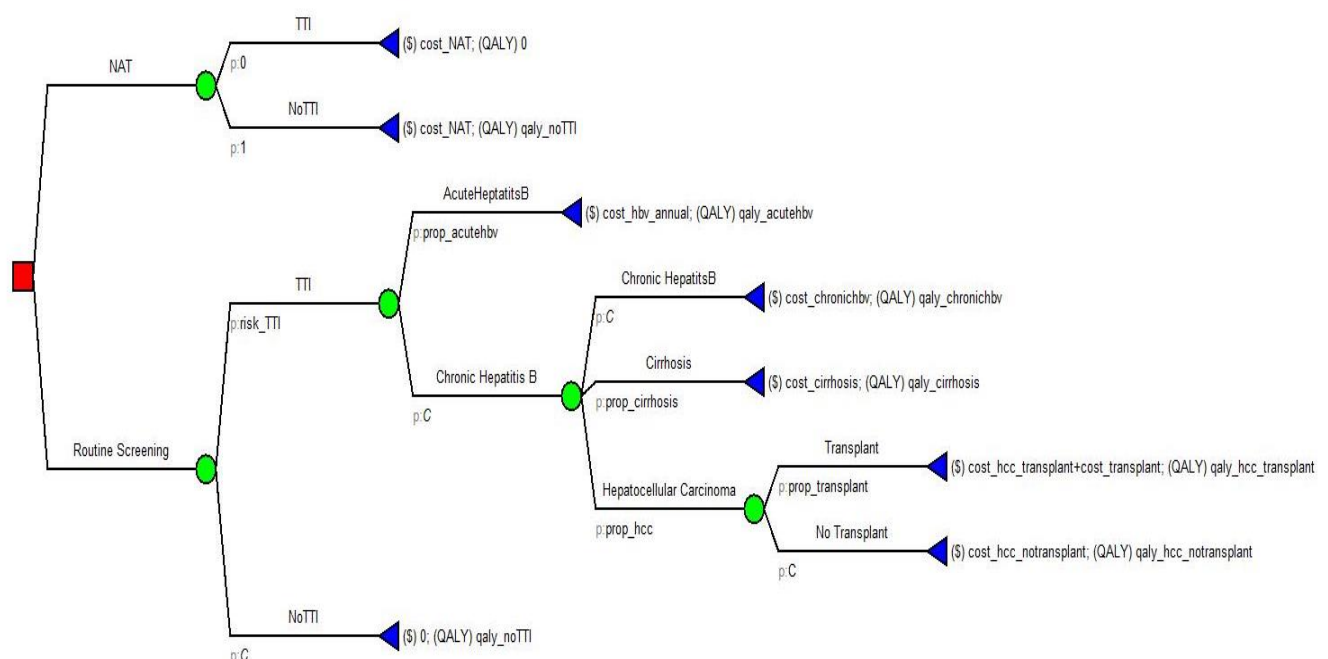
There is a net monetary gain of ₹ 2,76,42,712. (Table 19)

Table 19: Net monetary Gain by introduction of NAT	
Total Cost that could have been involved in the absence of NAT	₹ 7,89,06,212
Costs involved with NAT in our Centre	₹ 5,12,63,500
Net Gain due to introduction of NAT in our Centre	₹ 2,76,42,712

5.6.COST-EFFECTIVENESS ANALYSIS

The cost-effectiveness analysis was conducted utilizing a decision tree methodology at this phase. (Figure 10) Analysis was done from a health system perspective.

Figure 10: Decision Tree used to analyse our NAT yield of 1:5596. Red Square - Decision Node, Green circles - Chance node, Blue triangles - Terminal Node



In our analysis, we evaluated two branches within the decision tree: the routine screening arm, utilizing CLIA, and the nucleic acid testing arm.

In the NAT arm, we assume that TTI will be prevented when NAT is performed with CLIA in a cohort of 10,000 patients. Hence, we assume that their utility value will be equal to that of general population which is 0.99 [46] . So, if their life expectancy is for another 30 more years, the QALY generated will be 29.7 years.

In the routine screening arm, without NAT, the probability of acquiring a TTI is 1 in 5596, which is the NAT yield. This represents the TTI division. Here, in a cohort of 10,000 patients, less than 2 patients constitute this group.

The remaining patients in the cohort are assumed to have no risk for a TTI and hence their QALY generated will be 29.7 years.

Considering the natural history of Hepatitis B infection, 80% of those infected will experience an acute form of the disease. For this group, the applied cost represents the annual cost utilized. The QALY calculation involved an initial reduction in utility value for the first year, after which the standard utility value was applied for the subsequent 29 years.

For the 20% of individuals with chronic Hepatitis B, further analysis was conducted based on their disease status, which includes long-standing chronic Hepatitis B, liver cirrhosis, and hepatocellular carcinoma. The cohort anticipated to develop hepatocellular carcinoma was further categorized into two groups: those undergoing liver transplantation and those not undergoing transplantation. The calculation of QALY was derived from the individual's projected life expectancy and associated utility value. The cost was determined by multiplying the anticipated lifespan with the annual expenses incurred.

By decision tree analysis method, the Incremental Cost-Effectiveness Ratio (ICER) calculated by applying our NAT yield of 1:5596 was ₹19,35,063.80. In other words, to avert a single infection, an expenditure of ₹19,35,063.80 would be required. This ICER exceeds the commonly considered threshold which is ₹2.24 lakh per Quality-Adjusted Life Year (QALY) per capita GDP.

An analysis of various components in our protocol revealed that our deferral rate of 33.8 % was much higher than the national average of about 11%. Similarly, the prevalence of Hepatitis B, Hepatitis C and HIV will vary in the catchment populations of different Blood centres. These may contribute to altering the ICER values.

Hence, we performed a sensitivity analysis with different NAT yields.

Sensitivity Analysis

The designated cost for each NAT test is currently set at ₹1200, as determined by the Ministry of Health and Family Welfare.

Sensitivity analysis reveals that any NAT yield greater than 1:1000 will be cost-effective at the current GDP threshold. (Table 20)

Table 20: Sensitivity Analysis			
NAT yield	Cost per test (INR)	ICER (INR)	Interpretation
1:500	1200	6043	Cost-effective
1:1000	1200	117361	Cost-effective
1:1361 (national average[20])	1200	226462	At par with per capita GDP threshold
1:2000	1200	419580	Not cost-effective
1:5596 (our yield)	300 (reduced cost)	196433	Cost-effective

To achieve cost-effectiveness in our study, we determined that the cost of NAT should be limited to ₹300 or less, given a NAT yield of 1:5596.



DISCUSSION

6. DISCUSSION

In India, prevalence of HBV, HCV and HIV among blood donors ranges from 1 to 1.2%, 0.2 to 0.4 % and 0.3 to 0.4 % respectively. [53, 54] But, in our study we observed a sero-prevalence of 0.2%, 0.1% and 0.1% respectively, which is lesser than the national prevalence. This is probably due to stringent donor deferral policy adapted in our Blood Centre. [45] We deferred 33.8% of our blood donors, which is much higher than other centres in India. (Table 21)

Table 21: Deferral percentage in other centres in India		
Study	Deferral percent	Reference
<i>Shrivastava M et al</i> , Bhopal Memorial Hospital and Research Centre, Bhopal, Madhya Pradesh, 2016	11.5%	[55]
<i>Bahadur S et al</i> , Lady Hardinge Medical College, New Delhi, 2009	9 %	[56]
<i>Kandasamy D et al</i> , Kasturba Medical College, Manipal, 2020	10.6 %	[57]
<i>Malhotra S et al</i> , PGIMER, Chandigarh, 2023	16%	[58]

Those donors who are found to have a history of high-risk behaviours or practices, which can lead to contracting a TTI are deferred from donating blood. They are also referred for testing and further management.

From the 1st of October 2016, our Centre switched over to 100% blood collection through voluntary blood donation, which continued till February 2020. With the advent of COVID-19 pandemic from March 2020 onwards, the voluntary blood donation came

to a halt due to the nation-wide lock-down for which we had no other option but resort to autologous blood transfusion and collection from replacement donors also. It is important to highlight that, despite facing a challenging situation, a significant 72.3% of our inventory was comprised of voluntary blood donations. The COVID-19 pandemic resulted in a rise in replacement donations; however, our centre successfully boosted voluntary donations. This achievement was made possible by organizing a greater number of outdoor blood donation camps, which were designed to accommodate a limited number of donors while strategically avoiding high-risk areas. This proactive approach not only ensured the safety of donors but also contributed to the overall increase in voluntary contributions during a time of crisis.

Our proportion of voluntary donations over the years is higher than other centres in India where 46.2% was stated by Malhotra et al. Agnihotri N et al depicted that only 59.6% were voluntary donations. This could also be a reason as to why we observed a lower prevalence of TTI compared to the national prevalence.

The observed reactivity of CLIA in reactivity with the non-reactivity of NAT may be ascribed to either being carriers, false positives or the yield of serological testing. The yield of serology is noted when antibody titres are sufficiently elevated to neutralize the pathogen, thereby preventing active replication.

The findings indicate that the yield of NAT for Hepatitis B is significantly greater compared to that of Hepatitis C or HIV, as evidenced by our study and corroborated by other research. (Table 22)

The primary concern arises from occult Hepatitis B infections, where individuals test negative for Hepatitis B surface antigen (HBsAg). Such individuals pose a significant risk to blood safety. Furthermore, advancements in ELISA and CLIA technologies have significantly reduced the window period associated with these infections.

The NAT yield in our study was lower than what was observed in other Indian studies. (Table 22) This could be attributed to our higher deferral rate, higher proportion of voluntary blood donors as well as the prevalence of these infections among our donors.

Table 22: Comparison of NAT yield in other Indian studies with our study								
Study	No. of units tested	NAT yield	Prevalence	HIV	Hepatitis B	Hepatitis C	Co-infection	Reference
<i>This study</i>	33578	6	1:5596	0	6	0	0	NA
All India Institute of Medical Sciences, New Delhi. 2013	73898	121	1:610	1	73	37	10 (HBV-HCV)	[59]
GSL Medical College, Andhra Pradesh, 2015	15000	4	1:2000	0	4	0	0	[60]
Armed Forces Transfusion Centre, Delhi, 2020	54895	71	1:773	3	46	12	10 (HBV-HCV)	[61]
Apollo Hospitals and Health City, Hyderabad, Telangana, 2021	79938	20	1:3997	0	20	0	0	[62]
Dayanand Medical College and Hospital, Ludhiana, Punjab, 2024	149304	82	1:1831	0	45	37	0	[63]

In a review article by Ghosh et al, NAT results from 11 publications and one personal communication showed that 389387 blood units have been NAT tested from various parts of the country. NAT yield varied from 1:476 to 1:4403 in various studies, which is still higher than what was observed by our Centre.[20]

From this analysis it is clear that the cost-effectiveness of an intervention like NAT depends not only on the performance of an individual test but also depends on the deferral rate, proportion of voluntary donors, prevalence of TTIs and the cost of NAT. A preliminary sensitivity analysis indicated that, for instance, if the NAT yield exceeds 1:1000, the ICER will fall below the threshold of one per capita GDP, making universal NAT testing cost = effective at that threshold.

Deferral rate

The deferral rate at our center exceeds that of other centers in India, where deferral rates range from 3% to 17%.[64, 65] The observed trend is largely due to comprehensive pre-donation counselling and thorough medical examinations. A lower deferral rate at our center might have resulted in a higher NAT yield. Despite the ICER derived from our data not demonstrating cost-effectiveness, centers in India with a higher NAT yield could potentially benefit from NAT implementation.

Moreover, the donor pool could potentially be expanded if NAT is mandated, as it may detect occult TTIs.

Voluntary donors

Our proportion of voluntary blood donors outdoes the national average, primarily due to the rise in outdoor blood donation camps. Consequently, the number of altruistic donors has increased, leading to a reduction in the NAT yield. In a nation such as India, even individuals who voluntarily donate may conceal their high-risk behaviors and practices due to societal concerns. Hence, even if a near 100% voluntary donation is attained, it would still mandate NAT in donated blood units.

Prevalence

The National Viral Hepatitis Control Programme (NVHCP) in India reports that the prevalence of Hepatitis B surface antigen (HBsAg) positivity in the general population varies between 1.1% and 12.2%, with an average prevalence rate of 3% to 4%.[23] Research conducted in Kerala indicates that the prevalence rate is lower compared to

the typical rate across the country. [66] The lower NAT yield observed in our Centre, as compared to the national average, may also be attributed to this factor. Thus, the elevated ICER obtained in our study necessitates careful consideration as it cannot be compared to the rest of the country.

Nucleic Acid Testing Costs

To ensure cost-effectiveness in our study with a NAT yield of 1:5596, we found that the NAT cost should be capped at ₹300 or less.

Also, to make it cost-effective at the current rate of ₹1200 for NAT testing prescribed by the Government of India, the [47] NAT yield should be greater than 1:1000, which gives an ICER of ₹117361, which is lesser than the current threshold GDP per capita in India (₹2,24,000 per QALY).

In India, the average reported NAT yield rate from centers that implemented NAT is 1:1361.[20] The calculated Incremental Cost-Effectiveness Ratio (ICER) stands at ₹2,26,462, derived from the specified rates for nucleic acid tested blood units as per the Government of India. This figure aligns closely with the projected GDP per capita threshold in India for 2024, estimated at ₹2,24,000 per Quality-Adjusted Life Year (QALY). Details are mentioned in Table 20.

Developing an indigenous NAT platform could potentially reduce the financial burden and lower the cost per test.

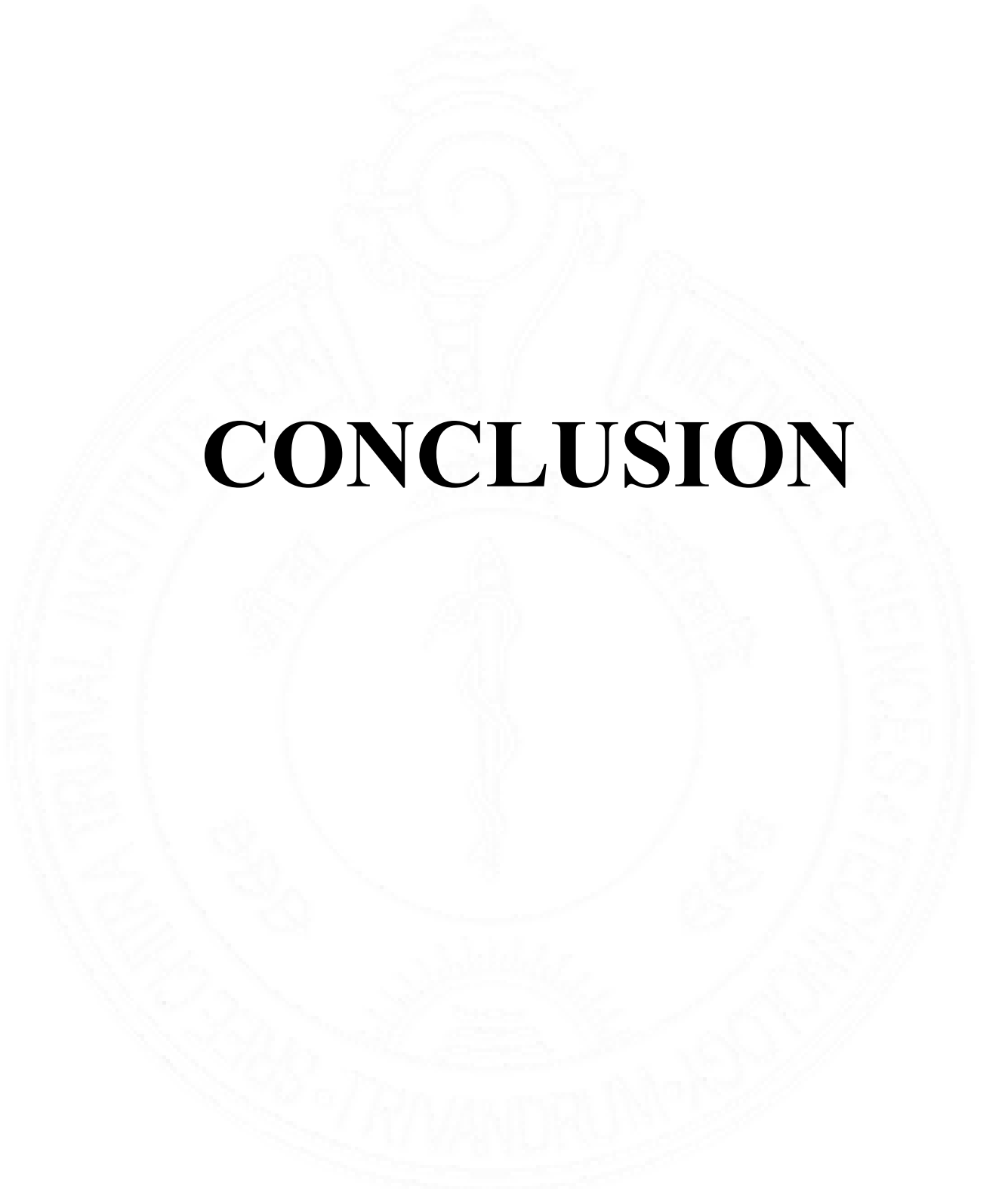
In India, the annual demand for blood is approximately 14.6 million units, with a shortfall of around 1 million units.[67] There are a total of 4153 licensed Blood Centres in the country, as on November 2023 data. [68] The average annual collection of blood in India is about 12 million units. [69] Out of these, only about 7% of all collected blood units undergo NAT. [20] Given the average national NAT yield of 1:1361, it can be inferred that approximately 8,200 donations among the 93% of donor units that are not subjected to NAT testing may potentially evade detection for transfusion-transmissible infections (TTIs) through serological tests. Assuming a minimum of 3 components prepared per whole blood unit, about 24,600 patients can get infected. An estimated annual expenditure of approximately ₹ 4.18 million may be necessary for the treatment of these patients, presenting a significant challenge to the country's economic burden.

The study by Balasundaram et al. highlights that the annual cost of treating HBV ranges from ₹ 16,600 to ₹ 1,709,000, with a median expenditure of ₹ 193,500. Treatment costs escalate with disease severity. Approximately 80% of patients experienced financial strain, with only 23% utilizing insurance coverage. Around 40% resorted to selling or mortgaging assets. Common financial repercussions included mortgaging assets (21.3%), selling assets (19.3%), reducing food expenses (15.2%), job loss (6.2%), halting children's education (3.1%), and delaying family marriages (2.8%). Overall, 57.8% of respondents reported experiencing family impoverishment due to treatment expenses.[11]

With regard to the compensation to be paid, individuals registered with a UK Infected Blood Support Scheme, who have been affected by contaminated blood and blood products, are eligible for additional interim compensation. These payments, amounting to £210,000, were disbursed in June 2024.[70] This is equivalent to ₹2,25,78,024 (exchange rates as on November 13th 2024).

With reference to a case of transfusion transmitted HIV, the Supreme Court of India put forward an order to pay ₹ 1,50,00,000 as compensation to the petitioner.[71]

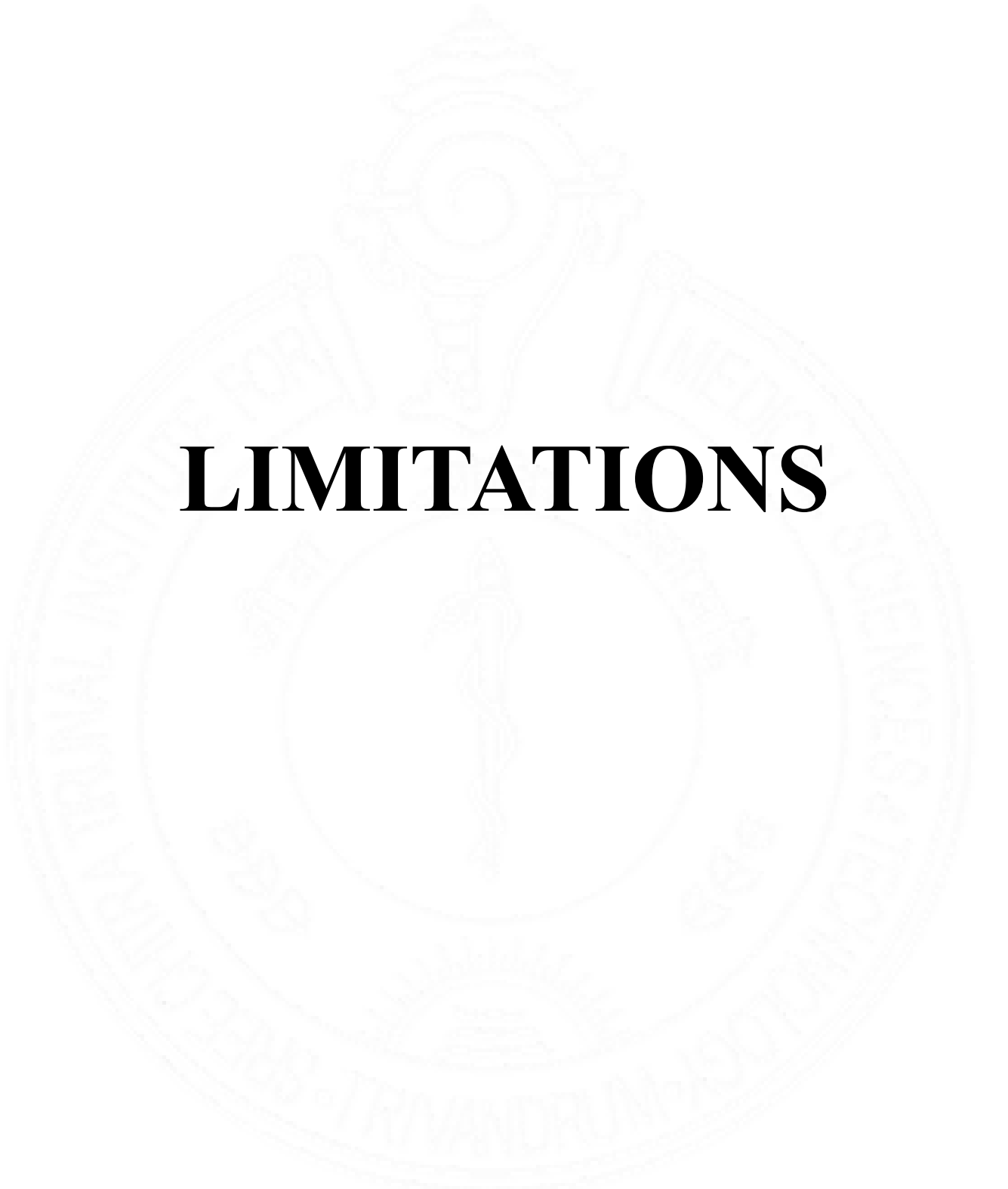
In addition to the financial implications, there is also a significant psychological burden placed on the administrators and staff of the Blood Centre, as well as on the patients and their families which are called intangible costs that are very difficult to quantify.



CONCLUSION

7. CONCLUSION

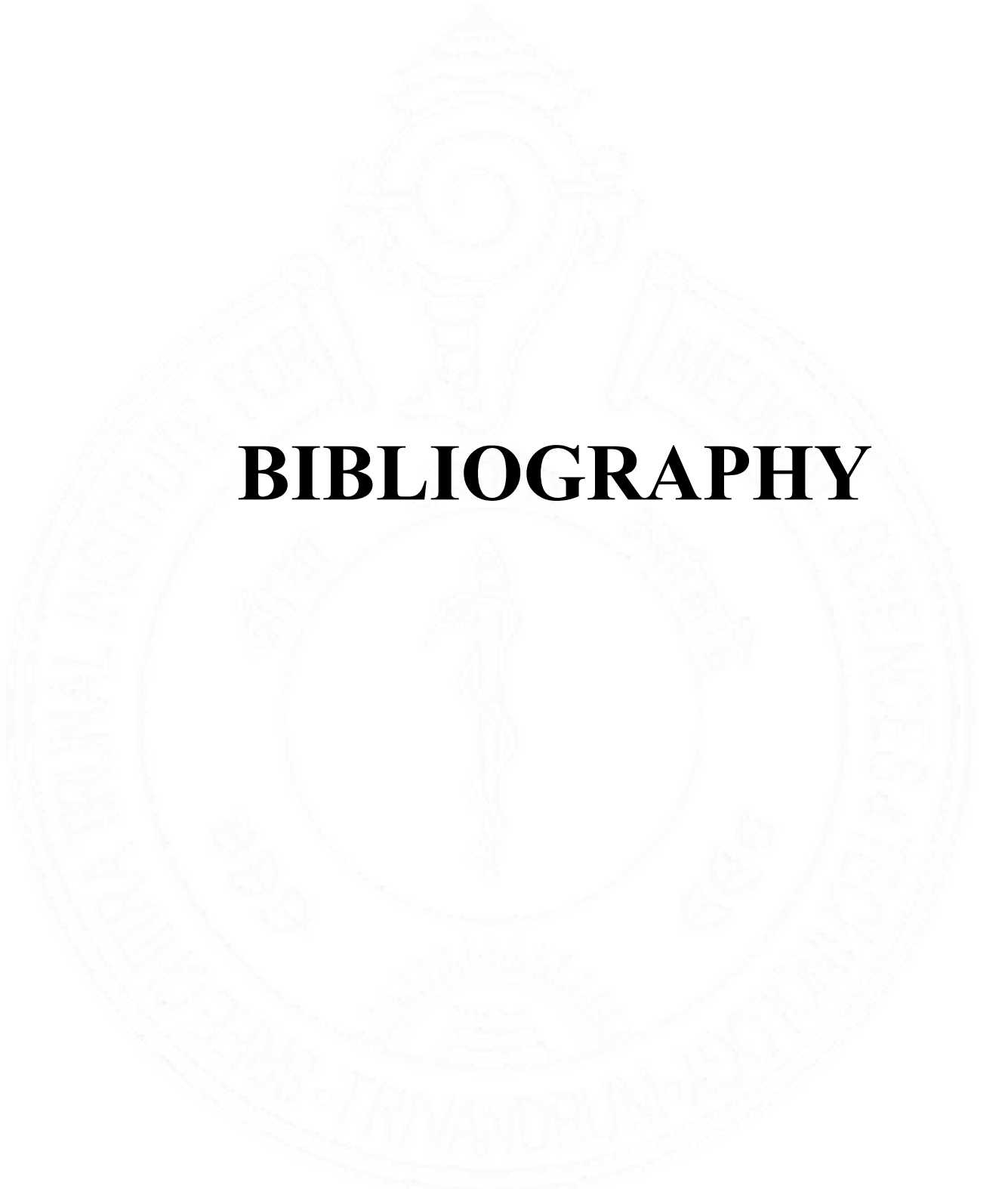
- When evaluating both direct and indirect costs, our Centre has achieved a net monetary gain of ₹ 2,76,42,712.
- A cost-effectiveness analysis conducted from a health system perspective indicated that the Incremental Cost-Effectiveness Ratio (ICER) exceeded the per capita GDP threshold in India, highlighting the Centre's lack of cost-effectiveness.
- However, upon integrating the national average NAT yield rates into our model, we determined that it proved to be cost-effective.
- Reducing the cost per test will render NAT cost-effective, even in scenarios with low NAT yield due to elevated deferral rates and a higher proportion of voluntary donations.
- Nucleic Acid Testing (NAT) enhances the efficiency of identifying reactive cases, facilitating timely notifications to blood donors for appropriate management and disease prevention. This proactive approach significantly mitigates the economic burden on the country.



LIMITATIONS

8. LIMITATIONS

1. Markov modeling, a valuable tool for elucidating the natural progression of a disease, was not implemented in this study.
2. This study primarily focuses on adult recipients, and the results or depictions are not directly applicable to pediatric populations.
3. In the Indian setting, reliable and comprehensive data on indirect costs, such as lost productivity, caregiver burden, or transportation expenses, was unavailable. These costs, however, form a significant component of the total economic burden of diseases or interventions. To address this gap, data from a Singaporean study has been adopted as a proxy for estimating indirect costs.
4. The calculated costs may not represent the precise figures, as the costing data was sourced from various literary references and utilized in this study.
5. In this study, inflation adjustments were not applied when calculating the costs. While accounting for inflation is standard in economic evaluations to ensure that costs reflect the current value of money, its exclusion in this case was due to the reason that the data sources used for cost estimation were derived from studies conducted in specific timeframes without sufficient granularity to apply inflation adjustments accurately.



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9. BIBLIOGRAPHY

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श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
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Institutional Ethics Committee

CDSCO Registration No: ECR/189/Inst/KL/2013/RR-21
DHR Registration No: EC/NEW/INST/2022/2775

SCT/IEC/2237/JUNE/2024

15.07.2024

Dr. Angel Mary Sam
Senior Resident
Department of Transfusion Medicine
SCTIMST, Thiruvananthapuram

Dear Dr. Angel Mary Sam,

The Institutional Ethics Committee held on 15th June, 2024, reviewed and discussed your application to conduct the study titled **"ECONOMIC IMPACT OF NUCLEIC ACID TESTING IN THE BLOOD TRANSFUSION SERVICES IN A DEVELOPING COUNTRY: AN ECONOMIC MODELLING STUDY (IEC /2237) "**.

Principal Investigator	Dr. Angel Mary Sam, PDCC, Department of Transfusion Medicine, SCTIMST
Co-Principal Investigator(s)	Dr. Debasish Gupta, Professor and Head, Department of Transfusion Medicine, SCTIMST Dr. Rakhal Gaitonde, Professor, Achutha Menon Centre for Health Science Studies, SCTIMST
Duration of the study	6 months

The following members of the Ethics Committee were present at the meeting held on 15th June, 2024

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. Kusuma Kumary P	M D in Paediatrics	Female	Clinician (Chairperson)	No
2.	Dr. Pradeep S	MBBS, MD	Male	Basic Medical Scientist	No
3.	Dr. Annapurna.Y	MD	Female	Basic Medical Scientist	No
4.	Dr. Indu PV	MBBS, DPM, MPhil, PhD	Female	Clinician	No
5.	Dr. Rejnish Kumar	MBBS, MD, DNB	Male	Clinician	No
6.	Adv. N Anand	BAL, L.LB	Male	Legal Expert	No
7.	Smt. Rekha Radhakrishnan	M.A (Eng.); B.Ed	Female	Lay person	No
8.	Dr. Harikrishna Varma PR	Ph.D (Materials Science)	Male	Medical Technology	Yes
9.	Dr. Manikandan.S	MBBS, MD, PDCC	Male	Clinician	Yes
10.	Dr. Narayanan Namboodiri. K K	MBBS, MD, DM	Male	Clinician	Yes
11.	Dr. Syam K	MBBS, MD, DM	Male	Clinician	Yes
12.	Dr. Srinivas G	PhD	Male	Basic Medical Scientist (Member Secretary)	Yes

The following documents were reviewed:

1. Checklist Form
2. Covering letter addressed to the Chairman, IEC, SCTIMST dated 26.03.2024
3. IEC Application Form
4. Declaration Form
5. Study Proposal
6. CV of PI and Co-PIs
7. Proforma
8. Responses/Amendments made based on the Reviewer's comments
9. SRC Recommendation Letter

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Dr. Syam. K

Alternate Member Secretary, IEC



ECONOMIC IMPACT OF NUCLEIC ACID TESTING IN THE ...

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1. INTRODUCTION The main transfusion transmissible viruses (TTVs) include hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). The likelihood of transmitting these viruses through the transfusion of infected blood remains significantly elevated, irrespective of the viral load, compared to other transmission routes.[1] The key blood safety strategies are: [2] ? Acquiring comprehensive blood supplies from altruistic, non-compensated, and consistent blood donors without high-risk behaviours or practices, ? implementing efficient strategies for the selection of blood donors., and ? screening all donated blood for TTV markers utilizing highly sensitive and specific assays. The interval between a donor's exposure to a virus and its subsequent detection by any testing method is referred to as the "window period." During this critical timeframe, the risk of undetected infection in donated blood may be overlooked by existing immunoassays utilized in blood transfusion services in India.[3] In India, the mandatory screening of donated blood includes tests for malaria, syphilis, HIV-1 and HIV-2, hepatitis B virus (HBV), and hepatitis C virus (HCV) through serological methods such as Rapid Card Tests, ELISA, or Chemiluminescence Immunoassay (CLIA). Nucleic Acid Testing (NAT), a more recent advancement in testing technology, is currently conducted at the discretion of individual Blood Centres, as it is not yet mandated by national regulations.[4, 5] Globally, it is estimated that about 85 million red blood cell units are transfused each year, and

more than 60 million donations per year are NAT tested worldwide

4

.[6, 7] Recent data from the World Health Organization indicates that 55 countries worldwide implement universal nucleic acid testing (NAT) for screening donated blood units.[8] Transfusion-transmitted hepatitis B has the potential to result in chronic Hepatitis B infection. The primary concern associated with chronic HBV infection lies in its long- term complications, which include an elevated risk of progression to primary liver cancer, recognized as the sixth most prevalent cancer globally. Furthermore, HBV- related fatalities rank as the tenth leading cause of death worldwide. Throughout their lifetimes, approximately 15% to 40% of individuals with chronic HBV infection may experience complications, which can range from hepatocellular carcinoma (HCC) to HBV-related mortality.[9, 10] Hepatitis C transmitted via transfusion can also lead to its chronic infection. Chronic hepatitis C can have a profound effect on

the health-related quality of life of

11

the patient.[11] HCV infection significantly contributes to liver-related morbidity and mortality. It has been linked to over 30 extrahepatic manifestations, many of which arise from the proliferation of B lymphocytes, leading to both monoclonal and polyclonal antibody production. This activity is indicative of the presence of rheumatoid factor or cryoglobulins.[12] Moreover, chronic hepatitis B and C continue to pose significant challenges in healthcare, with associated costs escalating in correlation with the progression of liver disease.[13] Acquired Immune Deficiency Syndrome (AIDS) can be transmitted through the transfusion of blood or blood products infected with the Human Immunodeficiency Virus (HIV).

Approximately 60% of acute HIV infections manifest as **a non-specific flu-like illness, with an incubation period** ranging from **2** to 4 **weeks. The acute** phase of the **infection** typically **resolves** within **weeks to a few months**, leading to **an asymptomatic period that may** extend **for** several **years. During this** asymptomatic phase, **HIV viremia persists, and**

1

there is a gradual decline in

the number of CD4+ lymphocytes, which are the primary target of HIV

1

. The depletion of CD4+ lymphocytes predispose individuals to

opportunistic infections, while **the virus** also exerts **direct effects on multiple** organ systems. Collectively, **these**

1

factors contribute to mortality, with an average life expectancy post-infection of approximately 8 to 10 years.[14]

Transfusion transmitted HIV infection contributes to 2%–4% of all cases of HIV

6

worldwide.[15] Advancements in molecular screening for TTIs through the implementation of NAT in transfusion medicine have markedly diminished the risk of infection transmission associated with blood transfusions. NAT can be categorized into Mini-pool NAT (MP- NAT) and Individual Donation NAT (ID-NAT). MP-NAT is conducted on a diverse range of donor samples, whereas ID-NAT is executed on each sample individually. The advantages of NAT encompass the ability to directly identify viral genomes (DNA or RNA) with exceptional specificity. Furthermore, its sensitivity surpasses that of traditional antigen and/or antibody immunological assays by several orders of magnitude.[3, 16] Nucleic Acid Testing (NAT) has significantly decreased the window period associated with transfusion-transmitted viral infections.[17, 18] NAT testing of collected blood started in India around late 2000s with first multicentric study on NAT evaluation published in 2008.[5] NAT

testing was subsequently implemented by only a few centres across India. The main barriers to implementation of NAT testing in India remain the de-centralised blood collection system, inadequate technical manpower and cost implications of implementing the technology.[19] The significance of clinical outcomes and the economic implications of utilizing NAT-based screening for blood units warrant thorough investigation. This research is essential to support informed decision-making regarding the potential implementation of universal NAT testing in India.To our knowledge, an economic evaluation of nucleic acid testing of donated blood units has not been done in the Indian scenario. I propose using the data generated from SCTIMST Blood Bank, which has been using NAT universally since January 2019, to build an economic model to explore the cost- effectiveness of universal screening with NAT. As mentioned earlier, such a study will go a long way in providing evidence-based support for policy regarding the introduction of this protocol universally as part of the national guidelines.

2. REVIEW OF LITERATURE

Nucleic Acid Testing (NAT) for blood donations originated in the late 1980s with the use of PCR to assess the transmission rates of

Hepatitis C Virus (HCV) and Human Immunodeficiency Virus -1 (HIV-14

) through transfusions. German blood centers pioneered the implementation of NAT

for HCV, HBV, and HIV -1, and were4

also the first to adopt NAT for

HIV-2, hepatitis A virus, and Parvovirus B1910

. As commercial manufacturers developed test kits and instruments tailored to the needs of blood banks, many other countries began to adopt NAT testing.[7] Blood transfusions have been known to transmit infections since before 1941, when transfusion-transmitted syphilis was first identified. This understanding led to the early implementation of syphilis screening in blood donors, even before the widespread establishment of blood banks. In 1943, Paul Beeson provided a seminal account of transfusion-transmitted hepatitis. Additionally, the malarial parasite was recognized as the first microbe to be transmitted through transfusion.[6] The global distribution of blood products contaminated with HCV and HIV-1 led to widespread impact. In France, haemophiliacs were knowingly given HIV-contaminated blood, resulting in 4,000 infections. The USA saw 10,000 infections, while Italy, the UK, and Spain each reported approximately 1,300 infections.[7] The recognition of widespread HBV infection emerged in 1963 with the advent of HBsAg testing, revealing a high prevalence among patients receiving multiple transfusions. Acute HBV infection, whether contracted through transfusion, intravenous drug use, perinatal transmission, or sexual contact, can be asymptomatic or manifest as clinical viral hepatitis with nonspecific symptoms like jaundice. In rare cases, acute infections, including those from transfusion-transmitted HBV, may

lead to fulminant liver failure and death. Occult HBV infections have been shown to transmit the virus through blood transfusions, although the rate of infectivity is less than 100%.[20, 21] The National Viral Hepatitis Control Program (NVHCP) was initiated in July 2018 to bridge existing gaps in addressing viral hepatitis in India. This program aims to integrate current initiatives to enhance awareness, prevention, and treatment of viral hepatitis types A, B, C, D, and E. The introduction of new, safe medications for Hepatitis C has facilitated its effective management, while potent and safe treatments for Hepatitis B help maintain viral suppression over extended periods, thereby mitigating the risk of cirrhosis and liver cancer.[22] The testing policy and key activities are illustrated in Figures 1 and 2.

HIV transmission

through

intravenous administration of infected blood products is highly efficient

1

. In

the

early 1980s, 50%

of

haemophiliacs treated with Factor VIII were infected, and all who received more than 500,000 units were infected. In 1982, the risk of HIV in the San Francisco area was approximately 1 in 100 for transfused products. [14] Five cases of HIV transmission have been reported in the United States, Germany, and France, involving donations that tested negative by NAT mini- pool testing. The National AIDS and STD Control Programme (NACP) was launched in 1992, marking the start of a comprehensive response to the epidemic. Over 35 years, NACP has become one of the world's largest programs, evolving through five distinct phases. NAT testing of clotting factor batches, immunoglobulins, and production pools showed significant HCV contamination, especially in non-inactivated samples. This led to the recommendation of using NAT to test donor blood, alongside antibody and antigen testing, prior to the start of the manufacturing process.[35–37] Biswas and colleagues demonstrated that mini-pool (MP) NAT and individual donor (ID)

NAT assays significantly

shortened

the HBV

window period (

WP

5

) by 9–11 days and 25–36 days, respectively, when

compared to

the

currently licensed HBsAg tests

5

. This comparison involved

seven HBsAg assays and seven NAT assays

, including

three

ID NAT

and four

5

MP NAT tests on acute-phase seroconversion panels.[39] NAT is recommended to be used alongside serological testing to detect low-level infections and those at the limits of detection windows. There is no agreement on whether single-donor NAT

or a specific pool size is best, and this may vary based on the country's HBV prevalence.[21] In India, the NAT yield rate reported by centers that implemented NAT varied between 1:476 and 1:17,753, with an average of 1:1,361. Different centers across the country utilized both MP-NAT and ID-NAT methods.[19] The research by Heyns et al in South Africa found that implementing NAT significantly enhanced blood supply safety. For HIV, it reduced the risk during the incidence-window period, and within six months, NAT identified nine additional viraemic donations that were antibody-negative.[40] 3. AIMS AND OBJECTIVES i. To map out the economic impacts of transfusion transmissible viral infections (HIV, HBV and HCV). ii. To perform a costing of outcome pathways with and without NAT iii. To project the long-term cost-effectiveness by implementing NAT 4. MATERIALS AND METHODS 4.1.Study Setting: An economic modelling study was conducted in the Department of Transfusion Medicine, Sree Chitra Tirunal Institute for Medical Sciences and Technology from July 2024 to November 2024. 4.2.Data source: Data of all blood donations like age, gender, type of donation (voluntary or replacement), number of donations yearly and donors deferred from blood donation from January 2021 to July 2024 was collected from various registers and software in the Blood Centre. Data pertaining to TTI screening results was also obtained from these registers and software. NAT yield was calculated by finding out the number of blood units which were non- reactive for HIV, HBV and HCV by CLIA but were found to be reactive by ID-NAT. All personal identifiers were removed from the data set. 4.3.Donor Deferral: Deferral of registered donors was performed either by the counsellor or by the medical officer based on the criteria laid down by the National Blood Transfusion Council (NBTC). Donors found to have behaviours, practices or exposure to TTIs, prone for high-risk of transmission of infections like HIV, HCV, HBV and syphilis were strictly deferred from donating blood. 4.4.Donation Procedure: Donors were selected by following the Indian Guidelines for Blood Donor Selection developed by the National Blood Transfusion Council (NBTC).[44] Whole blood, either 350mL or 450mL was collected from the eligible donors. All units were separated into components – Packed Red Cells (PRC), Fresh Frozen Plasma (FFP) and Platelet Concentrate (PC) or Cryo-poor Plasma (CPP) and Cryoprecipitate. 4.5.Testing of Donated Blood: According to the Indian national guidelines, all blood units in the blood centre are to be tested using an immunoassay prior to release. NAT is not a mandatory test.[4] However, in our centre, all units are routinely tested by chemiluminescence immunoassay (CLIA) on Roche Cobas e 411 as well as individual donor nucleic acid testing (ID-NAT) on Grifols Procleix Panther ID-NAT system for HIV, HBV and HCV. 4.6.Cost related data: Data about various expenditures involved in NAT was obtained from the purchase department, finance department as well as from the National Blood Transfusion Council (NBTC) guidelines for costing of blood processing and testing. Cost incurred for serological testing in our Centre is ? 70 per HBsAg test, ? 80 per HIV Test and ? 150 per HCV test. The imputed costs regarding lifetime expenses occurring if a patient contracts a TTI via transfusion was obtained from Indian literature.[45] Costs are depicted in Indian Rupee (INR). SI No Cost Source Comments 1. Nucleic Acid Testing costs Purchase Department, Finance Department, SCTIMST Revised Guidelines-2022 for

Recovery of Processing Charges for Blood and Blood Components

6

[46] 2. Diagnosis and Treatment costs for Hepatitis B Muniyandi M et. al., 2021 [45] Balasundaram P et.al., 2020 [47] Drug cost obtained by calculating annual expenditure based on treatment regimen as per NVHCP[22] and applying market costs of the drug as per November 2024 rates. 3. Donor Look- back and Patient trace-back Testing cost – obtained from the

designated cost per test in the institute. Out of pocket expenses for donor Transportation (to and fro average autorickshaw charge) 4. Legal costs Compensation costs – Supreme court verdicts [48] Out-of-pocket expenses to carry out a legal case Personal Communication with a Supreme Court lawyer 5. Societal/Indirect costs Singapore source[49] based literature No Indian data available in literature 4.7.Methodology: Step 1: A protocol map showing the blood donor pathway in various scenarios was developed. (Figure 3) Figure 3: Our Economic Model Map Step 2: a) Imputed costs from Indian literature was applied to the protocol as relevant. Imputed costs were calculated by: 1. Obtaining data regarding life-cycles and complications of each of these diseases Table 2: Imputed life expectancies Disease State Years of survival after the modal age of 50 years No TTI 25 Chronic HBV 22 Compensated cirrhosis 20 Decompensated cirrhosis 16 Hepatocellular Carcinoma (HCC) 13 Post-transplantation - HCC 16 Data regarding the stage-wise distribution of Hepatitis B infected patients was adopted from the National Viral Hepatitis Control Programme. [22] (Table 1)

Longitudinal studies of untreated persons with

8

CHB show

an 8–20% cumulative risk of developing cirrhosis over five years

8

. In those with cirrhosis, there is an approximately 20% annual risk of hepatic decompensation. [27] 4.7.1. Data pertaining to the life expectancy: Data regarding normal life expectancy of Indian population was collected from the Institute for Health Metrics and Evaluation (IHME) database. The average life expectancy of an Indian is about 74 years (Male – 70.9 years and Female – 76.8 years).[25] Life expectancy decreases with the disease condition. The following life expectancies were derived from the 5-year survival rate values obtained from literature. [50, 51] (Table 2) 2. Costs were obtained from available Indian Literature from publications by Muniyandi et al [45], Balasundaram et al [47], and publicly available databases of the Government of India centre for health economics developed by PGI Chandigarh[52]. (Table 3) b) Costs for provision for NAT testing in this institute was calculated Step 3: The experience from our blood centre was applied to the above to create an economic model. *Drug cost obtained by calculating annual expenditure based on treatment regimen as per NVHCP and applying market costs of the drug as per November 2024 rates. 4.8. Analysis: 1. Descriptive analysis was done using Microsoft Excel and IBM SPSS Statistics Version 29. 2. The cost of implementing NAT in our institute was computed. 3. The lifetime expenses involved in the event of transmissible Hepatitis B was analyzed using data obtained from literature. 4. The data obtained was applied to the economic model – A decision tree model was created to compare CLIA alone and NAT+ CLIA in screening for transfusion transmitted infections. A cohort size of 10,000 was used, and yield of NAT was incorporated in the model as additional infections occurring in the CLIA only arm. A scenario analysis was done with best reported yield in available Indian studies. Costs and QALYs associated with both arms were estimated. An Incremental Cost Effectiveness Ratio (ICER) which is the difference in costs in both arms divided by the difference in QALYs, was derived. Incremental Cost-Effectiveness Ratio (ICER) = (Cost CLIA +NAT– Cost CLIA alone) (QALY CLIA+NAT – QALY CLIA alone) 5.

Cost effectiveness was analysed by comparing ICER to the cost-effectiveness threshold of GDP per capita of India for the year 2024, which is ₹ 2.24 Lakhs. RESULTS 5. RESULTS A total of 50,731 donors registered for blood donation at our Centre from January 1st 2019 to July 31st 2024. After medical examination and pre-donation counselling, 33.8% (n=17,153) of the registered donors were deferred from blood donation. Total collection was 33,578 units of blood. Prior to the COVID-19 pandemic, 100% of the registrations and collections were sourced exclusively from voluntary donors, predominantly through outdoor blood donation camps. Throughout the years, the percentage of voluntary donors consistently exceeded that of replacement donors. (Tables 4-6) Table 4: Year-wise Distribution of donors registered for blood donation Registrations Year Total Male Female In Blood Centre Outdoor Camps Voluntary Donors Replacement Donors 2019 10383 7717 2666 1542 8841 10383 0 2020 6605 5691 914 4289 2316 4132 2473 2021 9742 7942 1800 6535 3207 5352 4390 2022 9501 7575 1926 5480 4021 5628 3873 2023 9431 6984 2447 2281 7150 8300 1131 2024* 5069 3823 1246 1450 3619 4433 636 TOTAL 50731 39732 10999 21577 29154 38228 12503 * till July 31st 2024 Table 5: Year-wise Distribution of donors deferred from blood donation Deferrals (33.8%) Year Total Male Female In Blood Centre Outdoor Camps Voluntary Donors Replacement Donors 2019 3758 2189 1569 367 3391 3758 0 2020 1962 1409 553 1046 916 1185 777 2021 3212 2441 771 1879 1333 2501 711 2022 3616 2390 1226 1337 2279 2228 1388 2023 3195 1826 1369 504 2691 2954 241 2024* 1410 760 650 274 1136 1307 103 TOTAL 17153 11015 6138 5407 11746 13933 3220 * till July 31st 2024 Table 6: Year-wise Distribution of donors who donated blood Donations Year Total Male Female In Blood Centre Outdoor Camps Voluntary Donors Replacement Donors 2019 6625 5528 1097 1175 5450 6625 0 2020 4643 4282 361 3243 1400 2947 1696 2021 6530 6063 467 4656 1874 2851 3679 2022 5885 5185 700 4143 1742 3400 2485 2023 6236 5158 1078 1777 4459 5346 890 2024* 3659 3063 596 1176 2483 3126 533 TOTAL 33578 29279 4299 16170 17408 24295 9283 * till July 31st 2024

5.1. Age and Gender Distribution 87.2% (n=29279) of total number blood donors were male and 12.8% (n=4299) were female. (Figure 4) Figure 4: Gender Distribution of Blood Donors Gender Distribution of Donors 7000 6000 5000 4000 3000 2000 1000 0 2019 2020 2021 2022 2023 2024 Year of Donation Male 5528 4282 6063 5185 5158 3063 Female 1097 361 467 700 1078 596 Male Female The mean age of donors was 29 ± 9 years. Table 7 depicts the age distribution of the donors who donated blood in this Centre. 61.4% of the donors were within the age range of 18 to 30 years. The proportion of donors decreased with increase in age. Table 7: Distribution of Age of Blood Donors Frequency(n) Percent (%) 18 - 30 years 20616 61.4 31 - 45 years 10516 31.3 46 - 60 years 2417 7.2 60 - 65 years 29 0.1 Total 33578 100 5.2. Type of Donation 72.4% (n=24295) were voluntary donations and 27.6% (n=9283) were replacement donations, the year-wise distribution being depicted in Figure 5. Figure 5: Donor distribution based on the type of blood donation – year wise TYPE OF DONATION - VOLUNTARY VS REPLACEMENT 7000 6625 6000 5346 5000 NO. OF DONORS 4000 3679 3400 2947 3126 3000 2851 2485 2000 1696 890 1000 533 0 0 2018 2019 2020 2021 2022 2023 2024 2025 YEAR Voluntary Donors Replacement Donors 5.3. Donor Deferral 33.8% (n=17153) donors were deferred over this time period (Tables 5 and 8), out of which, 4% (n=685) were deferred in view of high risk for transfusion transmissible infections (TTI). The most common cause of deferral among those with high risk for TTI was history of multiple sexual partners (87.2%, n=597) (Figure 6) Table 8: Year wise tabulation of Donor Deferrals Year Registrations (n) Deferrals (n %) 2019 10383 3758 (36.2%) 2020 6605 1962 (29.7%) 2021 9742 3212 (33%) 2022 9501 3616 (38.1%) 2023 9431 3195 (33.9%) 2024* 5069 1410 (27.8%) TOTAL 50731 17153 (33.8%) * till 31st July

Figure 6: Distribution of donors deferred in view of high risk for transfusion transmissible infections (n=685) HIGH-RISK DEFERRALS History of HCV, 3, 0% Transgender, 3, 1% History of/contact with HBV, 21, 3% Homosexuality, 22, 3% Intravenous

drug abusers, 39, 6% Transgender Homosexuality Multiple sexual partners Intravenous drug abusers History of HIV Multiple sexual partners, History of/contact with HBV 597, 87% History of HCV 5.4. TTI reactive donations All of the collected units were subjected to testing by serological assay as well as by Individual Donor – Nucleic Acid Testing (ID-NAT). Among the total, 0.5% (n=171) of the donations were positive for either HBV, HCV or HIV (out of which 2 units were reactive for both HIV and HBV). Sero-reactivity rate was 0.49%. The sero-prevalence of Hepatitis B, Hepatitis C and HIV in this study is 0.24%, 0.13% and 0.12% respectively. Tables 9 and 10 represent the distribution of TTI reactive donations. Table 9 : Distribution of TTI reactive donations based on Gender, Age and Type of donation Donor Characteristic TTI Reactive Donations n=171 (n %)

Donor Characteristic	TTI Reactive Donations n=171 (n %)
Male	158 (0.54%)
Gender Female	13 (0.30%)
18 to 30 years	99 (0.48%)
31 to 45 years	61 (0.58%)
Age 46 to 60 years	11 (0.46%)
above 60 years	0
Voluntary	105 (0.43%)
Donor type a. In house donation	22 (0.32%)
b. Outdoor Camps	83 (0.48%)
Replacement	66 (0.71%)

Table 10: Distribution of Test Reactive Donations – HBV, HCV and HIV Donor Characteristic Serology Reactive for NAT Reactive for HBV HCV HIV HBV HCV HIV (n=81 (n=44 (n=40 (n=59 (n=2 (n=10 49.1%) 26.7%) 24.2%) 83.1%) 2.8%) 14.1%) Gender (including 2 donations which were HBV + HIV reactive) Male 76 38 40 55 2 10 Female 6 6 1 4 0 0 Age Group 18 to 30 years 38 28 30 23 1 5 31 to 45 years 40 11 8 33 1 4 46 to 60 years 3 5 2 3 0 1 above 60 years 0 0 0 0 0 0 Donor Type Voluntary 45 33 23 36 2 8 a. In house donation 11 6 4 6 0 0 b. Outdoor Camps 34 27 19 30 2 8 Replacement 36 11 17 23 0 2 Donation Year 2019 4 12 0 4 0 0 2020 10 2 0 11 0 0 2021 32 8 14 18 1 3 2022 15 7 13 12 0 3 2023 14 13 8 10 0 2 2024* 6 2 5 4 1 2 *till July 31st

5.4.1. NAT Yield 3.64% (n=6 units) which were non-reactive by serological testing were found reactive by NAT. Hence, our NAT yield is 1 in 5596. Hepatitis B Virus nucleic acid was detected in all 6 NAT yields. No NAT yield was detected for HCV and HIV. (Figure 7) Figure 7: TTI Screening Test for HBV, HCV and HIV (n=33578) Total Number of Units Tested n = 33578 CLIA non-reactive CLIA reactive CLIA reactive CLIA non-reactive NAT non-reactive NAT reactive NAT non-reactive NAT reactive (NAT Yield) n = 33407 (99.49%) n = 65 (0.19%) n = 100 (0.3%) n = 6 (0.02%) Transfused Units are Discarded HBV n= 6 HIV n= 0 (100%) HCV n= 0

5.5.COSTING 5.5.1. Costs involved with NAT Over the study period, costs incurred with NAT was ₹ 5,12,63,500. (Table 11) Table 11: Costs involved with NAT in our Centre from January 2019 to July 2024 SI no Costs of Amount in INR 1 Equipment - Reagent Rental basis 0 2 Consumables - Kits and Reagents ₹ 5,05,57,500 3 Electricity Charges ₹ 6,40,000 4 Other contingent expenses ₹ 66,000 TOTAL ₹ 5,12,63,500

5.5.2. Costs involved if infection occurs, in the absence of NAT If NAT was not performed, according to this study, potentially 18 patients would have been transfused with the infected blood components. Based on the natural history of HBV infection, 80-90% (n=15) of adults would have an acute infection whereas 10-20% (n=3) will have a chronic phase. [29] (Figure 8,9) Figure 8: Potential Infection transmission in the absence NAT Figure 9: Overview NOTE: This flowchart illustrates a hypothetical scenario where there is a potential risk of Hepatitis B transmission if units that are CLIA non-reactive but NAT reactive are not properly discarded. In our center, we ensure that these units are also discarded to maintain safety and compliance.

5.5.3. Individual and Family Costs ? Costs incurred by patient (Table 12) Assuming the mean age of the population receiving transfusion is 50 years, and considering the average life expectancy of an Indian adult as 74 years [25], the total average cost incurred is found to be ₹ 1,56,00,897.00 (Table 13) Table 13: Approximate costing in our model Cost incurred Type of Infection Base Case Lower Upper Acute Infection (n=15) ₹ 15,75,945.00 ₹ 9,20,857.50 ₹ 22,31,167.50 Chronic Infection (n=3) for 24 years ₹ 1,40,24,952.00 ₹ 78,77,124.00 ₹ 2,01,73,428.00 Total cost ₹ 1,56,00,897.00 ₹ 87,97,981.50 ₹ 2,24,04,595.50

5.5.4. Costs for Blood Centre and Institute/Hospital ? Costs involved with Donor Look-back When a TTI is suspected, the individuals identified as potential donors are contacted to confirm the

suspicion. Table 14 portrays the minimum costs involved. Table 14: Costs involved with Donor Look-back per donor
 Parameter Cost in INR Out-of-pocket expenses for the donor ? 150 Repeat Testing cost ? 70 Total cost ? 220 Thus, total cost for 6 donors ? 1320 Table 15: Costs involved with Patient Trace-back Parameter Cost in INR Out-of-pocket expenses for the patients (Travel, etc.) ? 150 Testing cost (per test) ? 70 Total cost ? 220 Thus, total cost for 18 patients ? 3960 ? Costs involved with patient Trace-back When a transfusion transmissible infection is identified, all the patients who received transfusion from that particular donor has to be traced back, tested and treated if infected. Table 15 depicts the costs involved for the same. 5.5.5. Economic burden to the Government With the advent of the National Viral Hepatitis Control Programme (NVHCP), the government of India provides free treatment to all patients diagnosed to have Hepatitis B and/or Hepatitis C. [22] This causes an economic burden to the Government. The costs incurred on individual basis, which is on an average between ? 1,05,063 and ?1,94,791 (Table 12) is now borne by the Government. 5.5.6. Legal Costs (Table 16) a. To the System ? Compensation to be paid by the Hospital Administration to the patients who received infected blood As a result of transfusion transmitted Hepatitis, the Supreme Court of India

directed to pay compensation of Rs.5,00,000/- to the complainant

3

in 2020

within 45 days from the date of receipt of certified copy of the order

3

[48] b. To the Individual ? Out-of-pocket expenses to carry out a legal case = ?25,000 – ? 50,000. Thus an average of ? 37,500. Table 16: Implicated Legal Costs Compensation to be paid by the Hospital Administration to the patients who received infected blood ? 90,00,000 Out-of-pocket expenses of the individual ? 37,500 Total ? 90,37,500 5.5.7. Societal / Indirect costs Since no Indian data regarding the indirect costs could be obtained from Indian literature, costing data was adopted from a Singapore based literature source. Considering parameters like

medical leave, time-off claimed and reduced productivity , the annual indirect cost

9

depicted by them was US\$ 7635.27, which is equivalent to ? 6,44,187.73. [49] Table 17: Approximate indirect costing in our model Type of Infection Average costs incurred Acute Infection (n=15) ? 96,62,815.95 Chronic Infection (n=3) for 24 years ? 4,63,81,516.55 Total cost ? 5,60,44,332.5 5.5.8. Total Cost that could have been involved in the absence of NAT: Total Cost that could have been involved in the absence of NAT based on our model is ?7,09,16,303.9. (Table 18) Table 18: Total Cost that could have been involved in the absence of NAT Costs involved 1. Direct Costs ? 1,56,00,897.00 2. Indirect Costs ? 5,60,44,332.5 3. Costs for Blood Centre and Institute/Hospital ? 5,820 4. Legal Costs ? 90,37,500 TOTAL ? 8,06,88,549.50 5.5.9. Net monetary Gain by introduction of NAT There is a net monetary gain of ? 2,86,96,129.50 Table 19: Net monetary

Gain by introduction of NAT Total Cost that could have been involved in the absence of NAT ? 8,06,88,549.50 Costs involved with NAT in our Centre ? 5,12,63,500 Net Gain due to introduction of NAT in our Centre ? 2,94,25,049.50

5.6.COST-EFFECTIVENESS ANALYSIS

The cost-effectiveness analysis was conducted utilizing a decision tree methodology at this phase. (Figure 10) Analysis was done from a health system perspective. Figure 10: Decision Tree used to analyse our NAT yield of 1:5596. Red Square - Decision Node, Green circles - Chance node, Blue triangles - Terminal Node

In our analysis, we evaluated two branches within the decision tree: the routine screening arm, utilizing CLIA, and the nucleic acid testing arm. In the NAT arm, we assume that TTI will be prevented when NAT is performed with CLIA in a cohort of 10,000 patients. Hence, we assume that their utility value will be equal to that of general population which is 0.99 [45]. So, if their life expectancy is for another 30 more years, the QALY generated will be 29.7 years. In the routine screening arm, without NAT, the probability of acquiring a TTI is 1 in 5596, which is the NAT yield. This represents the TTI division. Here, in a cohort of 10,000 patients, less than 2 patients constitute this group. The remaining patients in the cohort are assumed to have no risk for a TTI and hence their QALY generated will be 29.7 years. Considering the natural history of Hepatitis B infection, 80% of those infected will experience an acute form of the disease. For this group, the applied cost represents the annual cost utilized. The QALY calculation involved an initial reduction in utility value for the first year, after which the standard utility value was applied for the subsequent 29 years. For the 20% of individuals with chronic Hepatitis B, further analysis was conducted based on their disease status, which includes long-standing chronic Hepatitis B, liver cirrhosis, and hepatocellular carcinoma. The cohort anticipated to develop hepatocellular carcinoma was further categorized into two groups: those undergoing liver transplantation and those not undergoing transplantation. The calculation of QALY was derived from the individual's projected life expectancy and associated utility value. The cost was determined by multiplying the anticipated lifespan with the annual expenses incurred. This unit cost was calculated as shown above in section....pg... By decision tree analysis method, the Incremental Cost-Effectiveness Ratio (ICER) calculated by applying our NAT yield of 1:5596 was ? 19,35,063.80. In other words, to avert a single infection, an expenditure of ?19,35,063.80 would be required. This ICER exceeds the commonly considered threshold which is ?2.24 lakh per Quality-Adjusted Life Year (QALY) per capita GDP. An analysis of various components in our protocol revealed that our deferral rate of 33.8 % was much higher than the national average of about 11%. Similarly, the prevalence of Hepatitis B, Hepatitis C and HIV will vary in the catchment populations of different Blood centres. These may contribute to altering the ICER values. Hence, we performed a sensitivity analysis with different NAT yields.

Sensitivity Analysis

The designated cost for each NAT test is currently set at ?1200, as determined by the Ministry of Health and Family Welfare. Sensitivity analysis reveals that any NAT yield greater than 1:1000 will be cost-effective at the current GDP threshold. (Table 20)

Table 20: Sensitivity Analysis NAT yield Cost per test (INR)	
ICER (INR)	1200
Interpretation	1:500 1200 6043 Cost-effective
	1:1000 1200 117361 Cost-effective
	1:1361 (national average[19]) 1200 226462 At par with per capita GDP threshold
	1:2000 1200 419580 Not cost-effective
	1:5596 (our yield) 300 (reduced cost) 196433 Cost-effective

To achieve cost-effectiveness in our study, we determined that the cost of NAT should be limited to ? 300 or less, given a NAT yield of 1:5596.

DISCUSSION

In India, prevalence of HBV, HCV and HIV among blood donors ranges from 1 to 1.2%, 0.2 to 0.4 % and 0.3 to 0.4 % respectively. [53, 54] But, in our study we observed a sero-prevalence of 0.2%, 0.1% and 0.1% respectively, which is lesser than the national prevalence. This is probably due to stringent donor deferral policy adapted in our Blood Centre. [44] We deferred 33.8% of our blood donors, which is much higher than other centres in India. (Table 21)

Table 21: Deferral percentage in other centres in India	
Study	Deferral percent
Reference	Shrivastava M et al,

Bhopal Memorial Hospital and Research Centre, Bhopal, Madhya Pradesh, 2016 11.5% [55] Bahadur S et al, Lady Hardinge Medical College, New Delhi, 2009 9 % [56] Kandasamy D et al, Kasturba Medical College, Manipal, 2020 10.6 % [57] Malhotra S et al, PGIMER, Chandigarh, 2023 16% [58] Those donors who are found to have a history of high-risk behaviours or practices, which can lead to contracting a TTI are deferred from donating blood. They are also referred for testing and further management. From the 1st of October 2016, our Centre switched over to 100% blood collection through voluntary blood donation, which continued till February 2020. With the advent of COVID-19 pandemic from March 2020 onwards, the voluntary blood donation came to a halt due to the nation-wide lock-down for which we had no other option but resort to autologous blood transfusion and collection from replacement donors also. Also, it is note-worthy that, despite this adverse scenario, 72.3% of our inventory was made of voluntary blood donation. Even though COVID-19 led to increased replacement donations, our centre managed to increase voluntary donations by increasing the number of outdoor blood donation camps with limited donors and avoiding hot-spot areas. Our proportion of voluntary donations over the years is higher than other centres in India where 46.2% was stated by Malhotra et al. Agnihotri N et al depicted that only 59.6% were voluntary donations. This could also be a reason as to why we observed a lower prevalence of TTI compared to the national prevalence. The observed reactivity of CLIA in reactivity with the non-reactivity of NAT may be ascribed to either being carriers, false positives or the yield of serological testing. The yield of serology is noted when antibody titres are sufficiently elevated to neutralize the pathogen, thereby preventing active replication. The findings indicate that the yield of NAT for Hepatitis B is significantly greater compared to that of Hepatitis C or HIV, as evidenced by our study and corroborated by other research. (Table) The primary concern arises from occult Hepatitis B infections, where individuals test negative for Hepatitis B surface antigen (HBsAg). Such individuals pose a significant risk to blood safety. Furthermore, advancements in ELISA and CLIA technologies have significantly reduced the window period associated with these infections. The NAT yield in our study was lower than what was observed in other Indian studies. (Table 22) This could be attributed to our higher deferral rate, higher proportion of voluntary blood donors as well as the prevalence of these infections among our donors.

Table 22: Comparison of NAT yield in other Indian studies with our study

Study No.	of units tested	NAT yield	Prevalence HIV	Hepatitis B	Hepatitis C	Co- infection	Refe- rence
This study	33578	6	1:5596	0	6	0	0 NA
All India Institute of Medical Sciences, New Delhi.	2013 73898	121	1:610	1	73	37	10 (HBV- HCV) [59]
GSL Medical College, Andhra Pradesh,	2015 15000	4	1:2000	0	4	0	0 [60]
Armed Forces Transfusion Centre, Delhi,	2020 54895	71	1:773	3	46	12	10 (HBV- HCV) [61]
Apollo Hospitals and Health City, Hyderabad, Telangana,	2021 79938	20	1:3997	0	20	0	0 [62]
Dayanand Medical College and Hospital, Ludhiana, Punjab,	14930	4	82	1:1831	0	45	37 0 [63]

In a review article by Ghosh et al,

NAT results from 11 publications and one personal communication showed that

2

389387 blood units have been NAT tested from various parts of the country. NAT yield varied from 1:476 to 1:4403 in various studies

2

, which is still higher than what was observed by our Centre.[19] From this analysis it is clear that the cost-effectiveness of an intervention like NAT depends not only on the performance of an individual test but also depends on the deferral rate, proportion of voluntary donors, prevalence of TTIs and the cost of NAT. A preliminary sensitivity analysis indicated that, for instance, if the NAT yield exceeds 1:1000, the ICER will fall below the threshold of one per capita GDP, making universal NAT testing cost = effective at that threshold. Deferral rate The deferral rate at our center exceeds that of other centers in India, where deferral rates range from 3% to 17%.[64, 65] The observed trend is largely due to comprehensive pre-donation counselling and thorough medical examinations. A lower deferral rate at our center might have resulted in a higher NAT yield. Despite the ICER derived from our data not demonstrating cost-effectiveness, centers in India with a higher NAT yield could potentially benefit from NAT implementation. Moreover, the donor pool could potentially be expanded if NAT is mandated, as it may detect occult TTIs. Voluntary donors Our proportion of voluntary blood donors outdoes the national average, primarily due to the rise in outdoor blood donation camps. Consequently, the number of altruistic donors has increased, leading to a reduction in the NAT yield. In a nation such as India, even individuals who voluntarily donate may conceal their high-risk behaviors and practices due to societal concerns. Hence, even if a near 100% voluntary donation is attained, it would still mandate NAT in donated blood units. Prevalence The National Viral Hepatitis Control Programme (NVHCP) in India reports that the prevalence of

Hepatitis B surface antigen (HBsAg) positivity in the general population varies between **1.1** % and **7**
12.2%, with an average prevalence rate **of 3**

% to 4%.[22] Research conducted in Kerala indicates that the prevalence rate is lower compared to the typical rate across the country. [66] The lower NAT yield observed in our Centre, as compared to the national average, may also be attributed to this factor. Thus, the elevated ICER obtained in our study necessitates careful consideration as it cannot be compared to the rest of the country. Nucleic Acid Testing Costs To ensure cost-effectiveness in our study with a NAT yield of 1:5596, we found that the NAT cost should be capped at ₹300 or less. Also, to make it cost-effective at the current rate of ₹1200 for NAT testing prescribed by the Government of India, the [46] NAT yield should be greater than 1:1000, which gives an ICER of ₹117361, which is lesser than the current threshold GDP per capita in India (₹2,24,000 per QALY). In India, the average reported NAT yield rate from centers that implemented NAT is 1:1361.[19] The calculated Incremental Cost-Effectiveness Ratio (ICER) stands at ₹2,26,462, derived from the specified rates for nucleic acid tested blood units as per the Government of India. This figure aligns closely with the projected GDP per capita threshold in India for 2024, estimated at ₹2,24,000 per Quality-Adjusted Life Year (QALY). Developing an indigenous NAT platform could potentially reduce the financial burden and lower the cost per test. COSTS INVOLVED In India, the annual blood requirement in India is about 14.6 million, having a shortage of about 1 million units. [67] There are a total of 4153 licensed Blood Centres in the country, as on November 2023 data. [68] The average annual collection of blood in India is about 12 million units. [69] Out of these, only about 7% of all collected blood units undergo NAT. [19] Given the average national NAT yield of 1:1361, it can be inferred that approximately 8,200 donations among the 93% of donor units that are not subjected to NAT testing may potentially evade detection for transfusion-transmissible infections (TTIs) through serological tests. Assuming a minimum of 3 components

prepared per whole blood unit, about 24,600 patients can get infected. An estimated annual expenditure of approximately ? 4,18,20,00,000 may be necessary for the treatment of these patients, presenting a significant challenge to the country's economic burden. With regard to the compensation to be paid, individuals registered with a UK Infected Blood Support Scheme, who have been affected by contaminated blood and blood products, are eligible for additional interim compensation. These payments, amounting to £210,000, were disbursed in June 2024.[70] This is equivalent to ?2,25,78,024 (exchange rates as on November 13th 2024). With reference to a case of transfusion transmitted HIV, the Supreme Court of India put forward an order to pay ? 1,50,00,000 (\$1,77,788.3) as compensation to the petitioner.[71] In addition to the financial implications, there is also a significant psychological burden placed on the administrators and staff of the Blood Centre, as well as on the patients and their families. CONCLUSION ? When evaluating both direct and indirect costs, our Centre has achieved a net monetary gain of ?2,94,25,049.50. ? A cost-effectiveness analysis conducted from a health system perspective indicated that the Incremental Cost-Effectiveness Ratio (ICER) exceeded the per capita GDP threshold in India, highlighting the Centre's lack of cost- effectiveness. ? However, upon integrating the national average NAT yield rates into our model, we determined that it proved to be cost-effective. ? Reducing the cost per test will render NAT cost-effective, even in scenarios with elevated deferral rates and a higher proportion of voluntary donations. ? Nucleic Acid Testing (NAT) enhances the efficiency of identifying reactive cases, facilitating timely notifications to blood donors for appropriate management and disease prevention. This proactive approach significantly mitigates the economic burden on the country. Limitations 1. Markov modeling, a valuable tool for elucidating the natural progression of a disease, was not implemented in this study. 2. This study primarily focuses on adult recipients, and the results or depictions are not directly applicable to pediatric populations. 3. In the Indian setting, reliable and comprehensive data on indirect costs, such as lost productivity, caregiver burden, or transportation expenses, was unavailable. These costs, however, form a significant component of the total economic burden of diseases or interventions. To address this gap, data from a Singaporean study has been adopted as a proxy for estimating indirect costs. 4. The calculated costs may not represent the precise figures, as the costing data was sourced from various literary references and utilized in this study. 5. In this study, inflation adjustments were not applied when calculating the costs. While accounting for inflation is standard in economic evaluations to ensure that costs reflect the current value of money, its exclusion in this case was due to the reason that the data sources used for cost estimation were derived from studies conducted in specific timeframes without sufficient granularity to apply inflation adjustments accurately.

sources:

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Proforma

Year-wise Data collection

Economic Impact of Nucleic Acid Testing in the Blood Transfusion Services in a Developing Country: An Economic Modelling Study

Year:

Total no. of Donations:

Donor details

Age group:

18-30 yrs	30-45 yrs	45- 55 yrs	55-65 yrs

Gender:

Male	Female

Type of Donation:

Voluntary	Replacement

Total deferrals:

Deferrals due to high-risk behaviours/practices:

Transgender	Homosexual	Multiple sexual partners	IV drug abusers

Deferrals due to History/ contact with transfusion transmissible infections

HIV	HBV	HCV

Screening results

HIV			
CLIA -ve NAT -ve	CLIA +ve NAT-ve	CLIA -ve NAT +ve	CLIA +ve NAT +ve

Hepatitis B			
CLIA -ve NAT -ve	CLIA +ve NAT-ve	CLIA -ve NAT +ve	CLIA +ve NAT +ve

Hepatitis C			
CLIA -ve NAT -ve	CLIA +ve NAT-ve	CLIA -ve NAT +ve	CLIA +ve NAT +ve

SL NO	AGE	GENDER (Male=1, Female=2)	Type of Donation		Donation Year	Place of Donation			Serology HBSAG	Serology HIV	Serology HCV	NAT general	NAT HBsAg	NAT HIV	NAT HCV
			Voluntary = 1, Replaceme nt= 2)	In house = 1/ Camp= 2		Serology Reactive General									
1	22	2	2019	1	2	1	1	0	0	0	1	0	0	0	0
2	54	1	2019	1	2	1	1	0	0	0	1	1	0	0	0
3	23	1	2019	1	2	1	1	0	0	0	1	1	0	0	0
4	32	1	2019	1	2	1	1	1	0	0	0	0	1	0	0
5	29	1	2019	1	1	1	1	1	0	0	0	0	1	0	0
6	21	2	2019	1	2	1	1	0	0	0	1	1	0	0	0
7	45	1	2019	1	1	1	1	0	0	0	1	1	0	0	0
8	22	1	2019	1	2	1	1	0	0	0	1	1	0	0	0
9	33	1	2019	1	2	1	1	0	0	0	1	1	0	0	0
10	34	1	2019	1	2	1	1	0	0	0	1	1	0	0	0
11	30	1	2019	1	1	1	1	0	0	0	1	1	0	0	0
12	22	1	2019	1	2	1	1	0	0	0	1	1	0	0	0
13	26	1	2019	1	2	1	1	0	0	0	1	1	0	0	0
14	18	1	2019	1	2	1	1	0	0	0	1	1	0	0	0
15	42	1	2019	1	2	1	1	1	1	0	0	0	1	0	0
16	20	1	2019	1	2	1	1	1	1	0	0	0	1	0	0
17	31	1	2020	1	2	1	1	1	1	0	0	0	1	0	0
18	22	1	2020	1	2	1	1	1	1	0	0	0	1	0	0
19	21	1	2020	1	2	1	1	1	1	0	0	0	1	0	0
20	31	1	2020	1	2	1	1	1	1	0	0	0	1	0	0
21	27	1	2020	1	1	1	1	0	0	0	1	1	0	0	0
22	31	1	2020	1	1	1	1	1	1	0	0	0	1	0	0
23	24	1	2020	1	1	1	1	1	1	0	0	0	1	0	0
24	19	1	2020	2	1	1	1	0	0	0	1	0	0	0	0
25	18	1	2020	1	2	1	1	1	1	0	0	0	1	0	0
26	25	1	2020	2	1	1	1	1	1	0	0	0	1	0	0
27	45	1	2020	1	2	1	1	1	1	0	0	0	1	0	0
28	29	1	2020	2	1	1	1	1	1	0	0	0	1	0	0

29	25	1	2021	2	1	1	1	1	0	0	0	0	0	0	0
30	23	1	2021	2	1	1	1	0	0	0	0	0	0	0	0
31	26	1	2021	2	1	1	1	0	0	1	1	0	0	0	0
32	43	1	2021	2	1	1	1	0	0	1	1	0	0	0	0
33	21	1	2021	1	2	1	1	0	0	0	0	0	0	0	0
34	45	1	2021	1	1	1	1	0	0	0	0	0	0	0	0
35	29	1	2021	2	1	1	1	0	0	0	0	0	0	0	0
36	35	1	2021	1	1	1	1	0	0	0	0	0	0	0	0
37	39	1	2021	2	1	1	1	0	0	1	1	0	0	0	0
38	20	1	2021	2	1	1	1	0	0	0	0	0	0	0	0
39	46	1	2021	2	1	1	0	0	1	0	0	0	0	0	0
40	21	1	2021	2	1	1	1	0	0	0	0	0	0	0	0
41	25	1	2021	2	1	1	1	0	0	0	0	0	0	0	0
42	29	1	2021	2	1	1	0	0	1	0	0	0	0	0	0
43	26	1	2021	2	1	1	1	0	0	0	0	0	0	0	0
44	21	1	2021	2	1	1	0	0	0	0	0	0	0	0	0
45	27	1	2021	1	1	1	0	0	0	0	0	0	0	0	0
46	22	2	2021	1	2	1	1	0	0	0	0	0	0	0	0
47	25	1	2021	2	1	1	1	0	0	1	1	0	0	0	0
48	43	1	2021	1	2	1	1	1	0	0	0	0	0	0	0
49	43	1	2021	1	2	1	1	0	0	1	1	0	0	0	0
50	39	1	2021	2	1	1	1	0	0	0	0	0	0	0	0
51	23	1	2021	2	1	1	1	0	1	0	0	0	0	0	0
52	31	1	2021	2	1	1	1	0	0	1	1	0	0	0	0
53	20	2	2021	1	2	1	0	0	1	0	0	0	0	0	0
54	19	1	2021	2	1	1	0	1	0	0	0	0	0	0	0
55	19	1	2021	1	2	1	0	1	0	0	0	0	0	0	0
56	40	1	2021	1	1	1	1	0	0	0	0	0	0	0	0
57	27	1	2021	2	1	1	0	1	0	0	0	0	0	0	0
58	46	1	2021	1	2	1	0	1	0	1	0	1	1	0	0
59	21	1	2021	1	2	1	0	1	0	1	0	0	1	0	0
60	44	1	2021	1	2	1	1	0	0	1	1	0	0	0	0
61	39	1	2021	1	2	1	1	0	0	1	1	0	0	0	0
62	30	1	2021	2	1	1	1	0	0	0	0	0	0	0	0

63	40	1	2021	1	1	2	2	1	0	1	0	1	1	0	1	0
64	27	1	2021	1	1	2	1	1	0	1	0	1	1	0	1	0
65	45	1	2021	1	1	1	2	1	1	1	0	1	1	0	0	0
66	27	1	2021	1	1	2	1	1	0	1	0	1	0	0	0	0
67	43	1	2021	1	1	2	1	1	1	1	0	0	0	0	0	0
68	26	1	2021	1	1	2	1	1	0	1	0	0	0	0	0	0
69	23	1	2021	1	1	2	1	1	0	1	0	0	0	0	0	0
70	27	1	2021	1	1	2	1	1	1	0	0	1	1	0	0	0
71	38	1	2021	1	1	1	2	2	0	0	1	1	0	0	1	1
72	37	1	2021	1	1	2	1	1	1	1	0	1	1	0	0	0
73	35	1	2021	1	1	2	1	1	1	1	0	1	1	0	0	0
74	47	1	2021	1	1	2	1	1	1	1	0	1	1	0	0	0
75	43	1	2021	1	1	1	2	2	0	1	1	0	0	0	0	0
76	27	1	2021	1	1	2	1	1	0	0	0	0	0	0	0	0
77	29	1	2021	1	1	2	1	1	1	1	0	1	1	0	0	0
78	32	1	2021	1	1	2	1	1	1	1	0	1	1	0	0	0
79	23	1	2021	1	1	2	1	1	0	0	1	0	0	0	0	0
80	39	1	2021	1	1	2	1	1	1	1	0	1	1	0	0	0
81	48	1	2021	1	1	2	1	1	0	0	1	0	0	0	0	0
82	31	1	2021	1	1	2	1	1	0	1	0	0	0	0	0	0
83	40	1	2021	1	1	2	1	1	0	0	1	0	0	0	0	0
84	41	1	2022	1	1	1	1	1	0	0	1	0	0	0	0	0
85	42	2	2022	2	2	1	1	1	1	1	0	0	0	0	0	0
86	37	1	2022	1	1	1	2	1	0	1	1	0	0	0	0	0
87	26	1	2022	1	1	2	1	1	0	1	0	0	0	0	0	0
88	23	1	2022	1	1	2	1	1	0	0	1	1	0	0	0	0
89	30	2	2022	2	2	2	1	1	0	1	0	0	0	0	0	0
90	29	1	2022	1	1	2	1	1	0	1	1	0	0	0	0	0
91	20	2	2022	2	2	1	1	1	1	0	0	1	1	0	0	0
92	21	2	2022	2	2	1	1	1	0	0	1	0	0	0	0	0
93	26	1	2022	1	1	2	1	1	1	1	0	0	0	0	0	0
94	37	1	2022	1	1	2	1	1	1	1	0	0	0	0	0	0
95	21	1	2022	1	1	2	1	1	0	1	0	0	0	0	0	0
96	39	1	2022	1	1	1	2	2	1	1	0	1	1	0	0	0

97	20	1	1	2022	1	1	1	1	0	0	1	0	0	0	0
98	49	1	1	2022	2	1	1	1	1	0	0	1	1	0	0
99	26	1	1	2022	2	1	1	1	0	1	0	0	0	0	0
100	19	1	1	2022	1	2	1	1	1	0	0	0	0	0	0
101	22	1	1	2022	1	1	1	1	1	0	0	0	0	0	0
102	44	1	1	2022	1	2	1	1	1	0	0	1	1	0	0
103	41	1	1	2022	1	1	1	1	0	1	0	0	0	0	0
104	33	1	1	2022	2	1	1	1	1	0	0	1	1	0	0
105	21	1	1	2022	2	1	1	1	0	1	0	0	0	0	0
106	37	1	1	2022	2	1	1	1	1	0	0	1	1	0	0
107	22	1	1	2022	2	1	1	1	1	0	0	1	1	0	0
108	34	1	1	2022	2	1	1	1	1	0	0	1	1	0	0
109	29	1	1	2022	1	2	1	1	1	0	0	1	1	0	0
110	31	1	1	2022	1	2	1	1	1	0	0	1	1	0	0
111	19	1	1	2022	2	1	1	1	0	0	1	0	0	0	0
112	27	1	1	2022	2	1	1	1	0	0	0	0	0	0	0
113	19	1	1	2022	1	2	1	1	0	0	0	0	0	0	0
114	26	1	1	2022	2	1	1	1	0	0	0	1	0	1	0
115	40	1	1	2022	1	2	1	1	0	0	1	1	0	1	0
116	27	1	1	2022	1	2	1	1	0	0	0	0	0	0	0
117	43	1	1	2022	2	1	1	1	0	0	1	0	0	0	0
118	23	1	1	2022	2	1	1	1	0	0	1	0	0	1	0
119	22	2	2	2023	1	2	1	1	0	0	1	0	0	0	0
120	34	1	1	2023	1	2	1	1	1	0	1	1	1	0	0
121	40	1	1	2023	1	2	1	1	0	0	0	0	0	0	0
122	27	1	1	2023	1	2	1	1	0	0	0	0	0	0	0
123	26	1	1	2023	1	2	1	1	1	0	1	1	1	0	0
124	25	1	1	2023	2	1	1	1	1	0	0	0	0	0	0
125	20	1	1	2023	1	2	1	1	0	0	0	0	0	0	0
126	29	1	1	2023	1	2	1	1	0	0	0	1	0	1	0
127	52	1	1	2023	1	1	1	1	0	0	1	0	0	0	0
128	29	1	1	2023	2	1	1	1	0	0	1	0	0	0	0
129	38	1	1	2023	2	1	1	1	1	0	0	0	0	0	0
130	20	1	1	2023	1	2	1	1	0	0	1	0	0	0	0

131	21	1	2023	1	2	1	0	1	0	0	0	0	0	0	0	0	0	0	0
132	22	1	2023	1	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0
133	43	2	2023	2	1	1	1	1	0	1	0	1	1	0	0	0	0	0	0
134	22	1	2023	1	2	1	0	1	1	0	0	0	0	0	0	0	0	0	0
135	53	1	2023	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0
136	30	2	2023	1	2	1	0	1	0	1	0	0	0	0	0	0	0	0	0
137	19	1	2023	1	2	1	0	1	0	1	0	0	0	0	0	0	0	0	0
138	31	1	2023	1	2	1	1	1	0	0	0	1	1	1	0	0	0	0	0
139	35	1	2023	1	2	1	1	1	0	0	0	1	1	1	0	0	0	0	0
140	25	1	2023	1	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0
141	54	1	2023	1	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0
142	44	1	2023	1	2	1	1	1	0	0	0	1	1	1	0	0	0	0	0
143	27	1	2023	1	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0
144	22	2	2023	1	2	1	1	1	0	0	0	1	1	1	0	0	0	0	0
145	29	1	2023	1	2	1	1	1	0	0	0	0	0	0	0	0	0	0	0
146	32	1	2023	1	2	1	1	1	0	0	0	0	0	1	0	0	0	0	0
147	21	1	2023	1	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0
148	20	1	2023	1	2	1	0	1	1	0	1	0	1	0	1	0	1	0	0
149	21	1	2023	1	2	1	1	1	0	1	0	0	0	0	0	0	0	0	0
150	45	1	2023	1	2	1	0	1	1	0	0	0	0	0	0	0	0	0	0
151	28	1	2023	1	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0
152	47	1	2023	1	2	1	0	1	0	1	0	0	0	0	0	0	0	0	0
153	30	1	2023	1	2	1	1	1	0	0	0	1	1	1	0	0	0	0	0
154	33	1	2024	1	1	1	1	1	0	0	0	1	1	1	0	0	0	0	0
155	45	1	2024	1	2	1	0	1	1	0	1	1	1	0	0	1	0	0	0
156	40	1	2024	1	2	1	0	1	0	1	0	0	0	0	0	0	0	0	0
157	24	1	2024	1	2	1	0	1	0	1	1	1	0	0	0	0	0	1	1
158	27	1	2024	1	2	1	0	1	1	0	0	0	0	0	0	0	0	0	0
159	36	1	2024	2	1	1	1	1	0	1	0	0	0	0	0	0	0	0	0
160	23	1	2024	1	2	1	1	1	0	0	0	0	0	0	0	0	0	0	0
161	19	1	2024	1	2	1	0	1	1	0	0	0	0	0	0	0	0	0	0
162	19	1	2024	1	2	1	1	1	1	1	0	0	0	0	0	0	0	0	0
163	31	1	2024	1	2	1	0	1	1	0	1	0	1	0	0	1	0	1	0
164	23	2	2024	1	2	1	1	1	0	0	1	1	1	1	0	1	0	0	0

165	20	1	2024	1	2	1	1	0	0	1	1	0
166	43	1	2020	1	2	0	0	0	0	1	1	0
167	28	1	2021	1	1	0	0	0	0	1	1	0
168	32	1	2022	2	1	0	0	0	0	1	1	0
169	24	1	2022	2	1	0	0	0	0	1	1	0
170	49	1	2023	1	2	0	0	0	0	1	1	0
171	34	1	2024	1	2	0	0	0	0	1	1	0