THE HEALTH TECHNOLOGY ASSESSMENT OF A PEDIATRIC CARDIAC SURGERY PROGRAM (HRIDYAM) FOR CONGENITAL HEART DISEASE IN KERALA

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PROPOSAL CONCEIVED AND STUDY CONDUCTED BY:

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TABLE OF CONTENT

EXECUTIVE SUMMARY

Congenital heart disease (CHD) has emerged as a leading contributor to infant mortality in many low-and middle-income countries (LMICs). The state of Kerala undertook a population-based neonatal congenital heart defects screening program. The primary aim of this program was to bring down the state's IMR to a single digit.

The additional component of this program titled 'Hridyam' was the use of pulse oximeters at all delivery points to screen for CHDs in addition to physical examination. Early detection, prompt stabilization and expedited referral to a tertiary center were the key components of the program. In addition to two public hospitals, five private hospitals with advanced pediatric cardiac surgery capabilities were empanelled (public-private partnership).

The cost borne by the health system for the detection and management of congenital heart diseases were compared for the current scenario and the non-intervention scenario. The total cost incurred for the birth cohort of 550,000 in the current scenario is Rs. 53,58,46,555, compared to the non-intervention arm for which the total cost is Rs. 44,73,73,631. The QALY gained was 3947, yielding an ICER of Rs. 22,415, making the intervention cost-effective compared to the comparator arm.

The sensitivity of the pulse oximeter used for neonatal screening had the highest effect on the ICER when assessed with a variation of 10% in the base case values. The Hridyam pathway costs Rs 53.6 crores compared to the comparator arm which costs the health system Rs 44.7 crores. The net increase in budget because of the Hridyam project on an annual basis is Rs 8.9 crores. This model has potential applications for other conditions, and in other jurisdictions, especially LMICs considering building CHD capacity.

1. INTRODUCTION

The Context

The sustainable development goals adopted in 2015 set ambitious targets for all its member nations to follow. The proposed goal 3.2 of Sustainable Development Goals (SDGs) aims to end preventable death of newborns and children under 5 years of age by 2030. The target is for all countries to reduce neonatal mortality rate (NMR) to at least as low as 12 per 1,000 live births and under-5 mortality (U5-MR) to at least as low as 25 per 1,000 live births. The Infant Mortality Rate (IMR) in Kerala is the lowest in India. It was hovering around 10-14 between 2014 to 2018. The last decade did not witness a significant drop in the IMR.

This prompted the state government to evolve strategies to bring down the IMR in Kerala to a single digit. It was evident that the state needed to explore all possibilities in Rashtriya Bal Swasthya Karyakram (RBSK) in their plans. From a public health perspective, congenital heart disease surfaced as one of the leading causes of IMR once the infectious and nutritional causes were addressed to a good extent. The data available within the health department showed that almost 25% of IMR in Kerala is contributed by CHD, and around 60% of children with critical CHD die before the first birthday.

The post-natal screening of newborns for CHDs using a combination of pulse oximetry and physical examination was seen as a feasible, reproducible, and low cost (and accurate) technology that could play a significant role in lowering the IMR. This was already being implemented in major delivery points in the state especially, the government medical colleges. It was seen as a viable option to replicate the newborn pre-discharge screening with minimal addition of expertise, infrastructure, and logistics.

It was also decided that the increase in the number of cases due to the improved screening, would need to be completed with the appropriate treatment (surgery) without delay. The number of cardiac surgeries would have to be increased once the screening program was in full swing because the expectation was that there would be a significant spike in the detection of CHD cases. The improvement of existing government facilities, recruitment of additional trained human resources, and the empanelling of private tertiary care facilities were considered.

Congenital Heart Defects (CHDs)

Congenital heart defects (CHD) are the commonest congenital malformations and remain a major cause of neonatal mortality and morbidity in the developed world[1]. Critical congenital heart defects (CCHD) are the most serious form of CHD, with an incidence of between two and three per 1000 live births[2]. Babies with CCHD are at risk of cardiovascular collapse, acidosis, and death in the first few days of life, usually following the closure of the ductus arteriosus. Survival of infants with CHDs depends on how severe the defect is, when it is diagnosed, and how it is treated. Therefore, early diagnosis is essential to reduce the possibility of these complications and to improve outcomes following cardiac surgery. Children with congenital heart disease often require surgical or interventional treatments and continued medical care throughout their life.

In middle-income countries, most babies are routinely screened for CCHD using antenatal ultrasound scanning and postnatal physical examination. However, both procedures have a relatively low detection rate, and up to a third of babies with CCHD may be discharged from the hospital before a diagnosis is made[3]. Newborn screening (NBS) can save lives. Launching a screening program for all or almost all newborn infants, will result in the identification of a few with the affected condition. The up-front costs and logistical challenges of establishing screening of all can deter policymakers from instituting new screening programs or adding conditions to an existing program. The economic balance between the costs and benefits of screening has long been recognized as a desirable attribute of population screening programs[4].

RBSK & Shalabham Jatak Seva

In 2012, the Government of India started the Rashtriya Bal Swasthya Karyakram (RBSK), a national child health initiative for screening and treatment of childhood diseases and disabilities, including CHD. This program, administered by the National Health Mission (within the Ministry of Health and Family Welfare), provides funding and technical assistance to individual States. With the addition of funds and commitment by the Government of Kerala, adequate financial resources were available for an innovative population health approach to address the burden of CHD in the state.

Shalabham Jaatak Seva is a comprehensive newborn screening program initiated by the Department of Health Services, Government of Kerala as a part of Rashtriya Bal Swasthya Karyakram (RBSK) of the National Health Mission. The program which aims to detect visible, functional, metabolic, and neurological defects in new-born children has a major role in the government's drive to lower Kerala's infant mortality rate. The **Hridyam Program** is a component of Shalabham, designed for early detection and management of congenital heart diseases. Under the program, all new-born infants are screened for congenital heart diseases through clinical examination and pulse oximetry at the point of delivery. The infants with a positive screen undergo specialist evaluation, and those diagnosed to have CCHDs are provided required treatment either at government facilities or empanelled private hospitals at no cost to the families.

The Hridyam Program

Under the Hridyam program, all new-borns are screened at the point of delivery by clinical examination and pulse oximetry for signs of CCHDs. Those infants who screen positive are referred for specialised evaluation, and if diagnosed with a CCHD, registered in the Hridyam online portal. Once registered, the case will get a unique Case Number and will be notified to concerned District Early Intervention Centre (DEIC) of the district where the child lives. After verification by the DEIC, case will be categorised primarily into category 1,2 or 3 and will be reflected on the table put in the dashboard.

Five Paediatric Cardiologist are identified across Kerala who will categorise cases based on the diagnosis, clinical condition, and urgency to do the case as per the predefined categories. Category 1 (a-g), Category 2 A (1-3) primary and category 2B (1-3) staged procedures and category 3 Medical Follow up, so that surgery dates may be fixed by the institutions. They will give opinion on individual cases and forward the same to SCTIMST or MCH Kottayam. These institutions will give surgery dates to individual cases as per the set protocol for each category. If the allotted dates are beyond the permitted dates, cases will be automatically referred to empanelled hospitals, who will give surgery dates based on the choice of the family.

How Pulse Oximetry Works.

Pulse oximetry (PO) measures blood oxygen saturations and is a well-established, accurate, non-invasive method of detecting low oxygen levels (hypoxaemia)[1]. The rationale for using

PO to screen for CCHD is that hypoxaemia is present in the majority of cases of CCHD, but the degree of desaturation is often comparatively mild and may be clinically undetectable, even by experienced clinicians[5]. Therefore, the addition of PO screening (POS) following delivery will detect those babies with hypoxaemia, who can then be assessed and the presence of a CCHD established before the babies develop acute collapse. Essentially, the current practice of screening for CCHD involves post-natal clinical examination by pediatricians. Currently, screening for various types of critical congenital heart disease (CCHD) can be done using pulse oximetry.

Oxygenated blood absorbs red light at a wavelength of 640 nm and deoxygenated blood absorbs light in the infrared spectrum at 940 nm. Pulse oximeters contain 2 light emitting diodes at different wavelengths and sensors that measure the amount of red and infrared light emerging from the tissue. The ratio of oxygenated to deoxygenated hemoglobin can be calculated from this, and an oxygen saturation level displayed. Because most forms of CCHD rely on the ductus arteriosus to supply blood flow to the pulmonary circulation, the systemic circulation, or, preferentially, the lower half of the body, hypoxemia or a saturation difference is often present.

Pulse oximetry has been used in its current form since the early 1980s[6,7] and has been validated by comparison with arterial blood gases[8]. During the past decade, there have been advances in the technology used in these devices to address their performance in historically challenging settings, including patient movement or poor perfusion[9]. Newer devices have been shown to have improvements with regard to patient motion[10], false or missed hypoxic or bradycardic alarms[11], and time needed to obtain a reliable reading[12]. New pulse oximeters are also extremely precise even when the anatomic location of the sensor is varied. Pulse oximeters are extremely accurate within the range of arterial saturations of 85%-100%, which is the range that would be most important in a newborn screening program for those forms of CHD that are likely to cause early morbidity and mortality.

Clinical Case Definition

Congenital heart disease, or a congenital heart defect, is a heart abnormality present at birth. The problem can affect the heart walls, the heart valves or the blood vessels. There are

numerous types of congenital heart defects. They can range from simple conditions that don't cause symptoms to complex problems that cause severe, life-threatening symptoms.

CHD malformations occur as single lesions or in combination with other heart defects. Commonly diagnosed CHD lesions isolated, or single lesions include atrial septal defects (ASD), ventricular septal defects (VSD), and pulmonary stenosis (PS). Complex or combination lesions include atrioventricular septal defects (AVSD), tetralogy of Fallot (TOF), and transposition of the great arteries (TGA). TOF and TGA are the two most common cyanotic CHD conditions that result in oxygen saturation below 90%. Majority of septal defects such as VSD, ASD and AVSD are classified as acyanotic CHD lesions with oxygen saturation normally above 95%.

Table 1: Classification of CHD

Type of lesion	Type of CHD
Acyanotic lesions	Atrial Septal Defect (ASD)
	Ventricular Septal Defect (VSD)
	Patent Ductus Arteriosus (PDA)
	Atrio-ventricular septal defect
	Pulmonary valve stenosis (PS)
	Aortic stenosis (AS)
	Coarctation of aorta
Cyanotic lesions	Tetralogy of Fallot
	Truncus arteriosus
	Ebstein's Anomaly of the Tricuspid Valve
	Transposition of great arteries
	Total anomalous pulmonary venous connection

Critical congenital heart disease (CCHD) has been defined as congenital heart defects that require surgery or catheter intervention within the first year of life[1]. Based on available estimates from recent studies, clinical case criteria for this analysis will include 12 screening-detectable CCHD conditions: aortic interruption atresia/hypoplasia, coarctation hypoplasia of the aortic arch, dextro-transposition of the great arteries, double-outlet right ventricle,

Ebstein anomaly, hypoplastic left heart syndrome, pulmonary atresia (intact septum), single ventricle, tetralogy of Fallot, total anomalous pulmonary venous connection, tricuspid atresia, and truncus arteriosus.

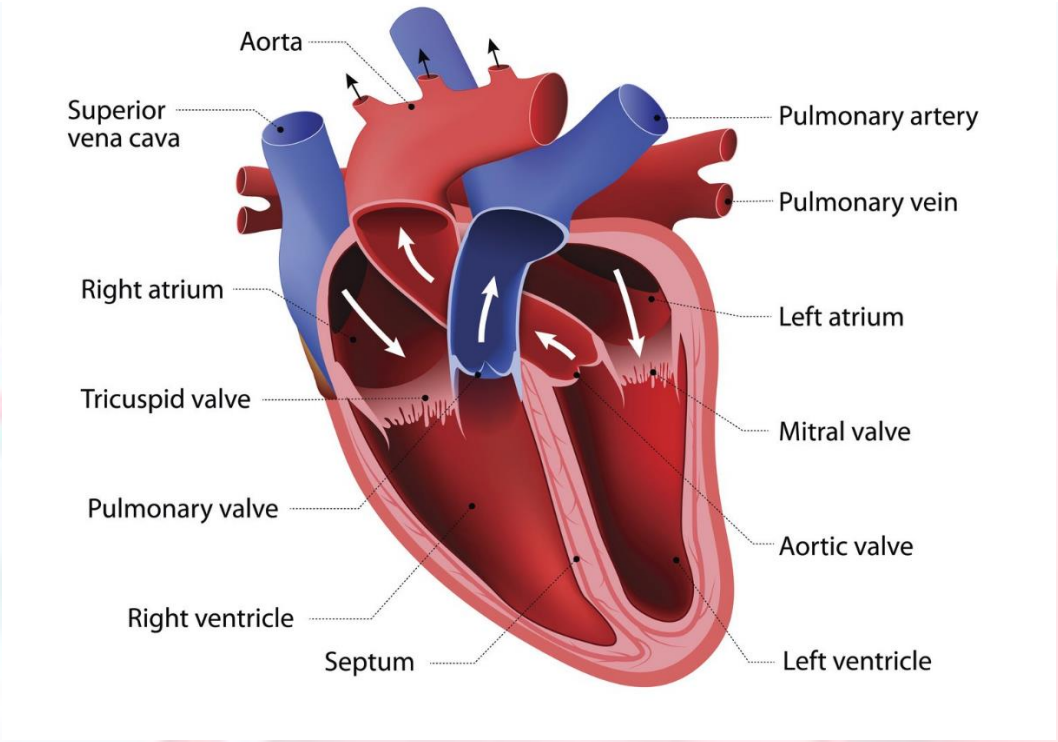


Figure 1: Diagram of the Heart

Screening strategies

The Hridyam registry website was stablished in August 2017. Steady growth in case registrations and surgical treatments is documented, as well as a trend toward newborn and infant procedures. Well before the activation of Hridyam, the Kerala government undertook several complementary initiatives to address the systemic deficiencies. These interventions, categorized by their position in the CHD Care Continuum, are given in the table below:

Table 2: Pediatric Care Continuum under 'Hridyam'

Steps of care continuum	Decision factors	Interventions undertaken

Recognition	Newborn physical examination	Pediatricians trained for early recognition
	Neonatal pulse oximetry screening	Neonatal pulse oximetry program established
	Post-natal screening	Neonatal nurses perform pre-discharge physicals
Diagnosis and prioritization	Establish precise diagnosis	Record review and patient triage by a designated panel of pediatric cardiologists
	Facilitate communication	Notify parents of consultation appointments, dates of surgery, and other patient related information
	Avoid delays in referral	Remote review and triage within 24 hours
Referral	Immediate referral	Based on diagnosis and geography
Stabilization and Transport	Transport network	Web-based transport app + transport network developed by the government
Treatment	Seven surgical centers had been identified in Kerala, with the capacity to treat ~ 50% of the estimated new cases of cCHD annually	Expansion of public sector capacity and collaboration with private sector in an effectively integrated system.

All newborn infants will undergo pulse oximetry, but we also considered the likely pathway the infant would follow in the absence of pulse oximetry, according to current practice. The recommended threshold for a positive pulse oximetry test is saturation <95% or a differential of >3% between the two.

PASS: >=95% in right hand and foot AND <=3% difference between right hand and foot.

FAIL: <95% in right hand or foot OR >3% difference between right hand and foot.

The model strategy referred to as clinical examination represents routine practice and refers to the clinical pathway followed if pulse oximetry had not been carried out (**comparator strategy**). Typically, all infants receive a routine clinical examination by a trained professional before discharge from hospital. If the clinical examination result is abnormal the infant will receive further tests depending on the abnormality or concern raised. If a CHD is suspected, the infant will usually require a diagnostic echocardiogram. The model strategy referred to as pulse oximetry as an adjunct to clinical examination is the **intervention strategy**. Infants for whom pulse oximetry is considered normal (test negative) will receive the same clinical examination and will, in the model, follow the same pathway as they would have, they not undergone pulse oximetry. If at any stage the clinical examination provides an abnormal result which is suggestive of a CHD, the infant will be sent for a diagnostic echocardiogram.

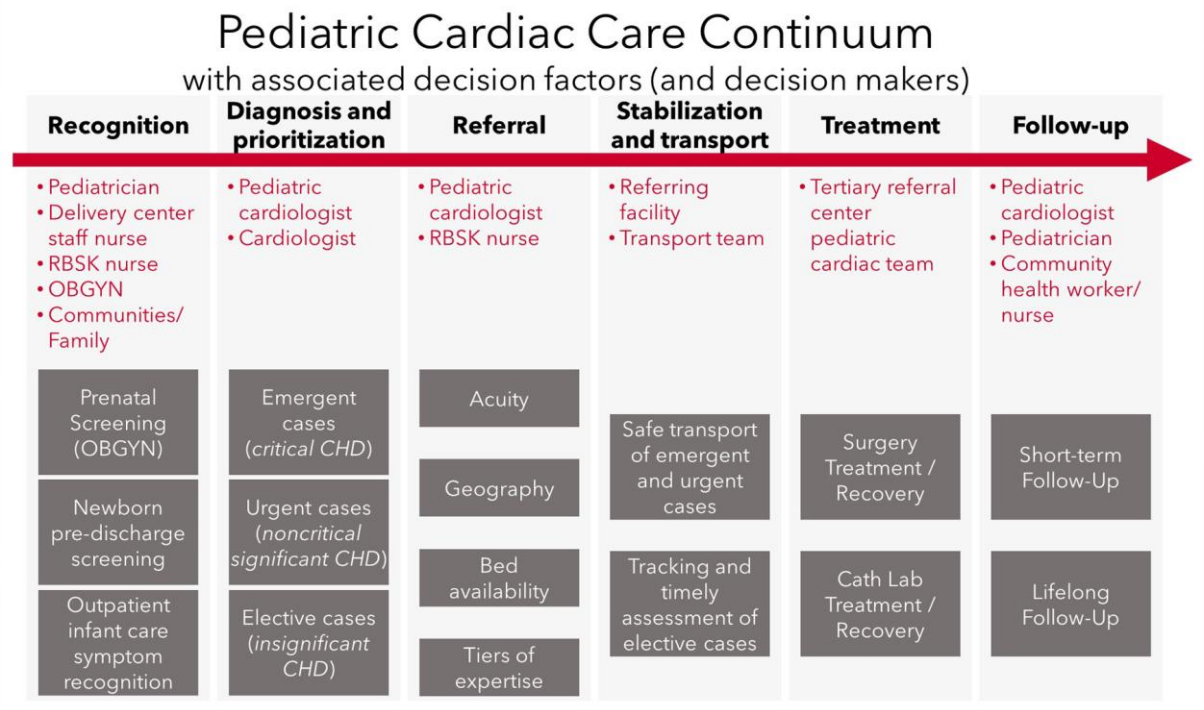


Figure 2: CHD Patient Care Continuum under Hridyam [Hridyam Website]

If a non-CHD abnormality is suspected the infant will be sent for alternative appropriate tests. All infants with an abnormal pulse oximetry test result (test positive) receive an expedited clinical examination (ECE) which is primarily checking for signs of a CHD and is usually undertaken sooner than the routine clinical examination. If the ECE shows an abnormality (test positive) the infant will undergo diagnostic echocardiogram. If the ECE suggests no CHD-related abnormality (test negative) the infant will undergo a second pulse oximetry test. If

this is still abnormal (test positive) a diagnostic echocardiogram will be performed. If the second pulse oximetry test is normal (test negative) infants receive the remaining component of the routine clinical examination that was not part of the ECE, that is, the non-cardiac aspects (such as checking the eyes, hips etc.), and continue to follow routine care as described in the comparator strategy, receiving non-CHD related interventions if appropriate. In both strategies, the diagnostic echocardiogram is confirmatory and any infant with a CHD will receive appropriate treatment.

2. AIMS AND OBJECTIVES

Broad objective of the HTA

The broad objective of the HTA is to find out if the Hridyam program - is a cost-effective intervention? The program, spans from the recognition of symptoms of CHD to diagnosis and prioritisation, to referral and transport, to the treatment. Given current gaps of knowledge, this HTA will try to do a synthesis of published quantitative and qualitative studies on the clinical effectiveness and cost effectiveness of interventions like Hridyam. In addition to the evidence synthesis and economic evaluation, we will also do the budget impact analysis. Understanding these factors, is crucial for the Government of Kerala to achieve the newly set SDG targets and set the pace for other states. The economic evaluation is essential for the decision making on the continuation and up-scaling of the Hridyam program.

Policy Question

Is early detection of congenital heart defects through newborn pre-discharge screening, and providing surgical treatment in tertiary referral facilities, for reducing the IMR to a single digit to achieve the SDG goals, a cost-effective strategy?

Objectives

(i) To conduct the economic evaluation of the CHD patient care continuum under Hridyam program by estimating the incremental cost effectiveness ratio (ICER) (cost per Quality adjusted life years (QALY) gained) compared with the current scenario.

(ii) To conduct the budget impact analysis of the Hridyam program.

3. RESEARCH METHODS

Economic Evaluation

Framework – PICO

Population (P): All newborn infants delivered in healthcare facilities

Intervention (I): CHD Patient Care Continuum under Hridyam

Comparator (C): No Hridyam, only routine physical examination for screening

Outcome (O): ICER (Incremental cost-effectiveness ratio) (cost per QALY gained)

Study perspective

The present study was conducted from a societal perspective. The costs incurred by the provider (health system) and patients (direct and indirect costs along with income loss due to illness) for alternative interventions and comparator were included in the economic evaluation.

Time Horizon

The cost and consequences associated with the intervention and the comparator were modelled using a simple decision tree with a lifetime horizon.

Study setting

The Kerala government resolved to develop a comprehensive plan to address the problem of CHD in general and CCHD. With input from stakeholders, a continuum of care model describing the lifetime path for such children were developed, rather than viewing their care as a one-time surgical event. The continuum of care identified stages of treatment, including the stage of surgical treatment, that would together contribute to a successful long-term outcome.

Currently, all 14 administrative units (district), seven existing paediatric CHD surgery centres (2 public and 5 private), 12 paediatric cardiologists and 10 paediatric cardiac surgeons are part of the program. The population of Kerala is approximately 33 million. Considering the current fertility rates the number of children born per year would be approximately 0.5 million. The IMR of the state when the program was launched in 2017 was 12/1000 live births.

The Intervention (CHD Patient Care Continuum under Hridyam)

The aim of this systems approach was to increase the number of children receiving treatment and their chances of survival. The interventions focused on improvement of the sensitivity and timeliness of CCHD recognition and referral, so that all infants could make it to a treatment center in optimal preoperative condition, enhancing the surgical outcome which is then better sustained by means of coordinated follow-up care.

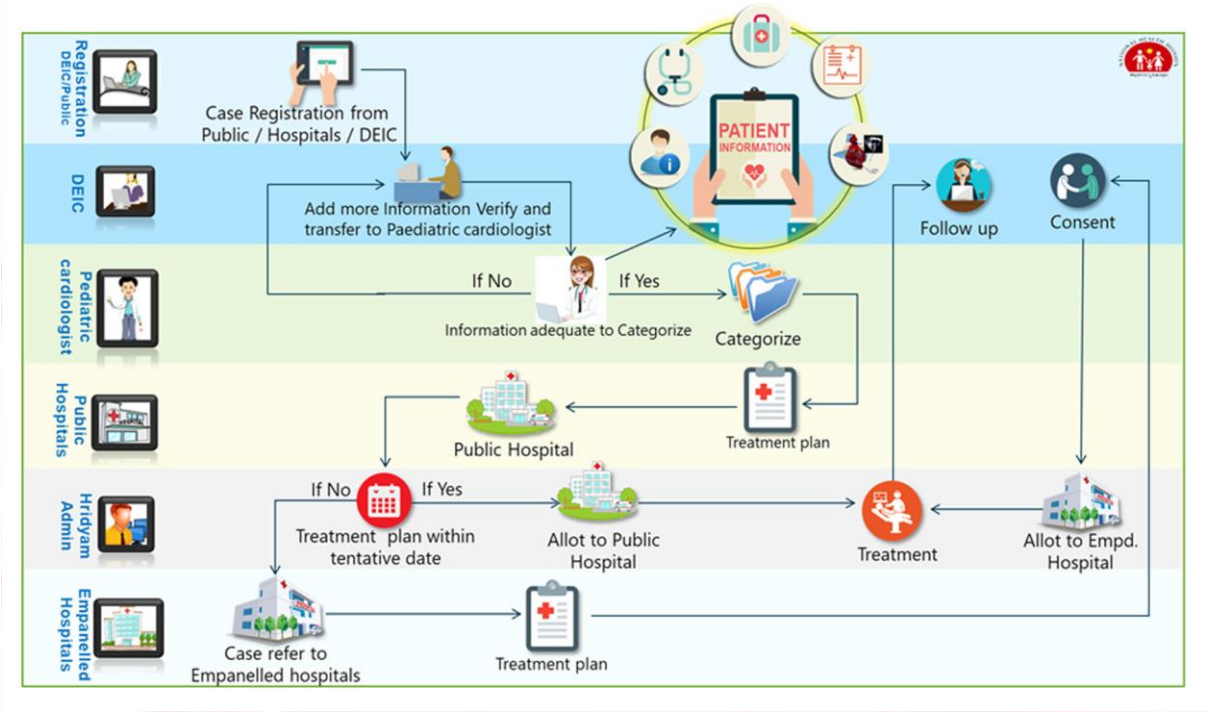


Figure __: Hridyam Process map

In 2017, the Kerala government developed and launched a comprehensive web-based application, to accelerate each infant's progression through the continuum stages, track their progress, and yield measurable outcomes. Named 'Hridyam—for little hearts,' it functions first as a registry for children 0–18 years with suspected CHD of all types. Any physician within Kerala can add a name. Once registered, each child's progress is coordinated at the local level by the District Early Intervention Center (DEIC, under the National Health Mission), but monitored centrally by the National Health Mission under Department of Health.

The incentive for universal registration is that Hridyam serves as the sole entry point for accessing government-funded treatment via the RBSK scheme. Once listed, a paediatric cardiologist is obliged to review the online record within 24 hours and classify the case

according to urgency for treatment. (In situations of insufficient information, that same cardiologist may direct the DEIC to acquire further tests.) A referral is made, based on a protocol that favors geographically proximate public institutions, but liberally acknowledges when special public or private hospital expertise favors a more distant referral within Kerala.

This act of triage and referral triggers a timeline for diagnostic fine-tuning and the development of a treatment plan. A new timeline then activates, and if treatment does not occur within an allotted interval, referral elsewhere is considered. Outcomes are tracked on the same website, and the Hridyam protocol also directs the nature and timing of follow-up care. Everything concerning each registrant's case occurs in real-time, is tracked and directed as needed by the government agency

The Comparator (Pre-Hridyam era)

Before Hridyam was launched, the care pathway for the CHD patients was fragmented. At the symptom recognition phase, there was no neonatal pulse oximetry screening program. Only the pre-discharge physical examination was present. The paediatricians in the health services were not given additional training for early recognition of symptoms. Most of the CHDs that were missed during the neonatal period via physical examination were diagnosed later when the patients returned to the outpatient with symptoms. A fraction of the missed CHD patients also returns to the hospitals with worsening of symptoms resulting in IP/ PICU admission. The efficiency of the referrals was also suboptimal. There were no remote reviewing facility or triage options. The web-based transport app was also non-existent, and patients usually resorted to personal conveyance / private ambulances.

Model overview and cost effectiveness

Decision trees were used to determine the probabilities of the occurrence of the two possible outcome states (Intervention v Comparator) in a hypothetical Kerala cohort of newborn infants. The cohort would either undergo a screening programme (Hridyam CHD Care pathway) or not undergo Hridyam CHD Care pathway.

Scenario 1 (Hridyam Pathway): In the intervention arm, the patients undergo neonatal pulse oximetry screening + pre-discharge physicals as part of symptom recognition. The possible outcomes are symptoms for CHD positive and negative. This includes the true positives, true

negatives, false positives, and false negatives. The diagnosis of CHD is confirmed by the triad of chest X-ray, electrocardiogram (ECG), and the neonatal echocardiography. The false negatives will return to the system via worsening of symptoms to the outpatient department (OPD) where the treating paediatrician will pick it up via symptom recognition and confirmation via the abovementioned tests. A minor portion of the false negative patients will develop complications and expire in the community or in the hospital due to complications of the underlying undiagnosed/ delayed diagnosed CHD. The diagnosed cases are categorised based on the severity of the diagnosed condition and referred to the most geographically proximal tertiary centre with the paediatric cardiac surgery units.

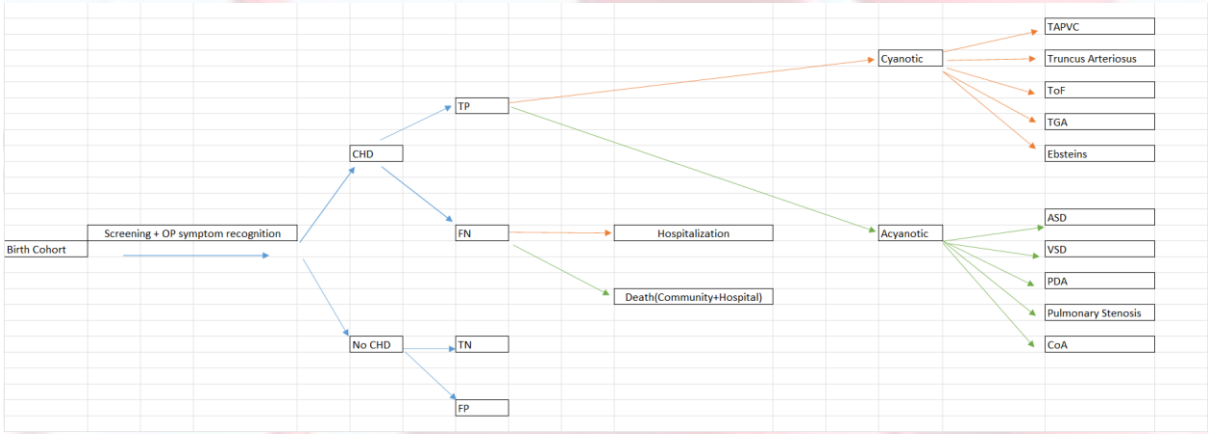


Figure __: Decision tree of scenario 1

Scenario 2 (Non-Hridyam Pathway): In the comparator arm, the patients undergo only the pre-discharge physicals as part of symptom recognition. The possible outcomes are symptoms for CHD positive and negative. The major difference is in the sensitivity of the pulse oximeter in the diagnosis of CHD, compared to physical examination alone. The number of true positives in this arm is less compared to the intervention arm. Here also, the diagnosis of CHD is confirmed by the triad of chest X-ray, electrocardiogram (ECG), and the neonatal echocardiography. The false negatives will return to the system via worsening of symptoms to the outpatient department (OPD) where the treating paediatrician will pick it up via symptom recognition and confirmation via the abovementioned tests. A minor portion of the false negative patients will develop complications and expire in the community or in the hospital due to complications of the underlying undiagnosed/ delayed diagnosed CHD. The diagnosed cases are categorised based on the severity of the diagnosed condition and

referred to the most geographically proximal tertiary centre with the paediatric cardiac surgery units.

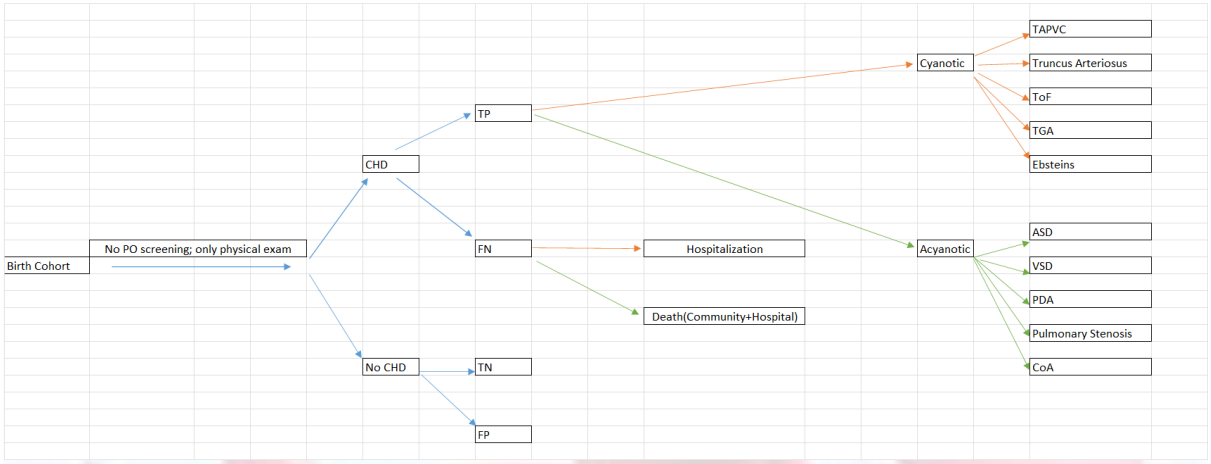


Figure ___: Decision tree of scenario 2

The most common cyanotic lesions seen in Kerala are TAPVC, Truncus arteriosus, ToF, TGA, and Ebstein's anomaly. The most common acyanotic lesions seen are ASD, VSD, PDA, pulmonary stenosis, and coarctation of aorta. The major change in the two scenarios is the addition of the pulse oximetry at all delivery points for screening of neonates before discharge. This helps in early recognition and the initiation of the remaining steps of the pediatric cardiac care continuum.

Data collection and model inputs

The source of data for different components of the model are provided as a table below. Overall, the data points for the model were derived from literature review, published government documents, expert consensus, and some were derived via computation.

Cost estimates

Cost of human resources

The cost of hiring additional trained human resource (HR) for the intervention arm (delivery centre RBSK Nurse) were taken from government sources. The cost of training the HR were calculated from previous training records. The treatment cost

The Hridyam program was empanelling hospitals which already had a functioning paediatric cardiology and paediatric cardiac surgery unit. Therefore, no additional cost was factored in for hiring the paediatric cardiologist and the surgical team.

Cost of instrument (screening)

The cost of pulse oximeter has been taken from the KMSCL device procurement list.

Cost of travel

The CHD and CCHD cases are referred to tertiary care facilities considering the severity of cases and geographical proximity of the patient's place of residence to the hospital. The rates for the transport of patients have been calculated from the tender documents of 108 ambulance services for advanced life support (ALS) with the Government of Kerala.

Cost of investigations and treatment

The cost of investigations has been taken from the Ayushman Bharat Pradhan Mantri Jan Arogya Yojana (AB-PMJAY) Health Benefit Package (HBP) rates. The cost of the treatment (surgeries) has been taken from the RBSK rates.

Clinical data

Diagnostic accuracy of screening tests

The diagnostic accuracy of pulse oximeters for screening of CHDs was identified from targeted literature review.

Clinical spectrum

The clinical spectrum of congenital heart disease, its proportion in the population, and the treatment for each defect was identified via targeted literature search and expert opinion.

The natural history of patients (life expectancy) with different types of CHD was identified through targeted literature search and expert opinion.

Utility estimates

The utility estimates (QALY) for the different types of CHDs were captured through a targeted literature search. Because these are relatively newer concepts, the historical paediatric

cardiology reference textbooks didn't have these values. Whenever utility weights were unavailable, a consensus was achieved between the clinicians interviewed.

Model Input Parameters				
Parameters	Base Case	Lower limit	Upper limit	References
Screening				
Sensitivity (PO + PE)	83.0	74.7	91.3	Targeted Literature Review
Specificity (PO + PE)	97.8	88.0	97.8	
Sensitivity (PE)	62.5	56.3	68.8	
Specificity (PE)	98.1	88.3	98.1	
Life Expectancy				
ASD	50	45	55	Targeted Literature Review
VSD	50	45	55	
ToF	10	9	11	
TGA	20	18	22	
PS	10	9	11	
Truncus Arteriosus	10	9	11	
PDA	50	45	55	
Ebstein	5	4.5	5.5	
Coarctation of aorta	45	40.5	49.5	
TAPVC	50	45	55	
Quality of life (QALY)				
ASD	0.97	0.87	0.97	Targeted Literature Review
VSD	0.97	0.87	0.97	
ToF	0.8	0.72	0.88	
TGA	0.89	0.80	0.98	
PS	0.98	0.88	0.98	
Truncus Arteriosus	0.8	0.72	0.88	
PDA	0.99	0.89	0.99	
Ebstein	0.5	0.45	0.55	

Coarctation of aorta	0.99	0.89	0.99	
TAPVC	0.97	0.87	0.97	
Case Mix				
ASD	0.20	0.18	0.22	Targeted literature review & consensus between experts
VSD	0.26	0.23	0.29	
ToF	0.14	0.13	0.15	
TGA	0.04	0.036	0.044	
PS	0.1	0.09	0.11	
Truncus Arteriosus	0.03	0.027	0.033	
PDA	0.21	0.189	0.231	
Ebstein	0.004	0.0036	0.0044	
Coarctation of aorta	0.01	0.009	0.011	
TAPVC	0.006	0.0054	0.0066	
Costs				
Training_RBSK_Nurse_Day	500	450	550	Computed
Salary_RBSK_Nurse_Month	14000	12600	15400	RBSK rates
Surgery_PDA	54000	48600	59400	
Surgery_ToF	105000	94500	115500	
Surgery_PS	40000	36000	44000	
Surgery_TGA	155000	139500	170500	
Surgery_CoA	67143	60429	73857	
Surgery_TruncusArteriosus	150000	135000	165000	
Surgery_TAPVC	150000	135000	165000	
Surgery_Ebsteins	135000	121500	148500	
Surgery_ASD	90000	81000	99000	
Surgery_VSD	96250	86625	105875	
X-Ray	100	90	110	Health Benefit package rates
ECG	170	153	187	
Echocardiogram	2000	1800	2200	
CT	2000	1800	2200	
MRI	4000	3600	4400	

Cost_OP_Consultation	200	180	220	
Cost_ICU_Day	2000	1800	2200	
Cost_Travel_ALS_Ambulance_Km	70	63	77	KANIV 108 rates

QALY estimation

Using the formula given below, the overall health gain in the form of QALY from the utilities and life-years saved at each arm and its associated health states were estimated. Other estimates such as the number of additional CHD cases detected, and the number of life-years saved in both the comparator and intervention arms were calculated.

QALY = Utility weights * Life expectancy

ICER estimation

The present economic evaluation model aimed to estimate the Incremental Cost-Effectiveness Ratio (ICER), cost per QALY gained of the Hridyam program compared to the no screening for CHD scenario.

Incremental cost = Unit cost of intervention – Unit cost of comparator

Incremental effect = QALYs gained $_{\text{(Hridyam arm)}}$ – QALYs gained $_{\text{(non-Hridyam arm)}}$

ICER = Incremental cost / Incremental effect

Sensitivity Analysis

The robustness of the model and parameters used in the model were assessed through one-way sensitivity analysis (OWSA). The analyses were carried out in MS excel. The results of OSWA are represented in the tornado graph.

Budget Impact Analysis

The budget impact analysis (BIA) model was based on the decision analytics model for the CHD screening scenario compared with the current scenario of no screening. We estimated the financial costs and budgetary implications associated with annual population-based newborn CHD screening and its treatment in Kerala.

4. RESULTS

Base-case results

The study evaluated the cost-effectiveness of population based neonatal screening of CHD (Hridyam) and compared it with the non-screening scenario. The cost incurred in the screening arm and the cost incurred in the non-screening arm are given below:

Cost Screening Arm	
Screening Cost	6,31,35,000
Referral Cost	1,81,03,008
RxCost	36,93,18,402
RxCost_FN	98,53,853
Cost_FP	2,62,56,454
Cost_FU_ScrArm	4,91,79,838
Total	**53,58,46,555**

The costs are divided into the following heads: cost of screening, cost of referral, treatment cost (cost of surgeries), costs incurred in the false negative path, costs incurred in the false positive pathway, and cost of follow-up.

Cost Non-Screening Arm	
Cost of Pre-discharge Diagnosis	0
Referral Cost	1,76,48,400
RxCost	36,00,43,971
RxCost_Undiagnosed	2,17,36,440
Cost_FU_NScrnAr	4,79,44,820
Total	**44,73,73,631**

The costs incurred in the non-screening arm includes the referral cost, the cost of treatment (cost of the surgeries), cost of treating the undiagnosed patients at a later stage, and the cost of follow-up.

The QALYs gained in the intervention and the comparator arm are given below:

Screening Arm				
	Number	QoL	LE	QALYs
TAPVC	29.52	0.97	50	1431.826
Truncus Arteriosus	141.71	0.8	10	1133.652
ToF	608.16	0.8	10	4865.257
TGA	153.52	0.89	20	2732.574
Ebsteins	17.71	0.5	5	44.28329
ASD	850.24	0.97	50	41236.6
VSD	1110.03	0.97	50	53836.67
PDA	915.19	0.99	50	45301.8
Pulmonary Stenosis	431.02	0.98	10	4224.035
CoA	53.14	0.99	45	2367.385
			Total	157174.1

Non-Screening Arm				
	Number	QoL	LE	QALYs
TAPVC	28.78082	0.97	50	1395.87
Truncus A	138.1479	0.8	10	1105.184
ToF	592.8849	0.8	10	4743.079
TGA	149.6603	0.89	20	2663.953
Ebsteins	17.26849	0.5	5	43.17123
ASD	828.8877	0.97	50	40201.05
VSD	1082.159	0.97	50	52484.71
PDA	892.2055	0.99	50	44164.17
Pulmonar	420.2	0.98	10	4117.96
CoA	51.80548	0.99	45	2307.934
			Total	153227.1

Incremental Cost: 8,84,72,925

Incremental QALYs: 3,947.01

ICER (Health System): 22,415

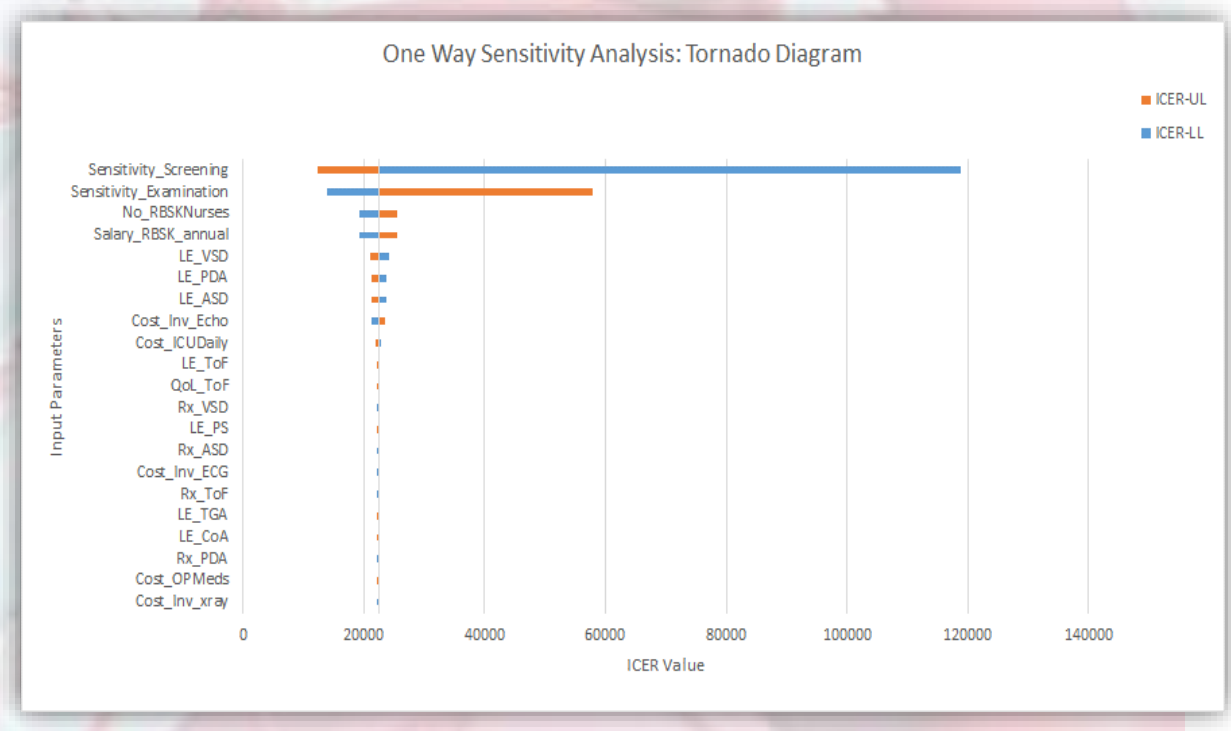
The cost borne by the health system for the detection and management of congenital heart diseases were compared for the current scenario and the non-intervention scenario. The total cost incurred for the birth cohort of 550,000 in the current scenario is Rs. 53,58,46,555, compared to the non-intervention arm for which the total cost is 44,73,73,631. The QALY gained was 3947, yielding an ICER of Rs.22,415, making the intervention cost-effective compared to the comparator arm.

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYS
Non-screening	44,73,73,631	153227		
Hridyam	53,58,46,555	157174	8,84,72,925	3947
ICER	**22415**			

Sensitivity analysis

One-way sensitivity analysis

Variations in the ICER concerning the higher and lower base case parameter values are presented in the figure below. The sensitivity of the pulse oximeter used for neonatal screening had the highest effect on the ICER when assessed with a variation of 10% in the base case values. Other parameters that influenced ICER values were the number of RBSK nurses, the salary of the RBSK nurses, the life expectancy of certain types of CHDs, the cost of the investigations (Echcardiogram), and the cost of ICU admission. The influence of other parameters on the ICER is presented in the figures.

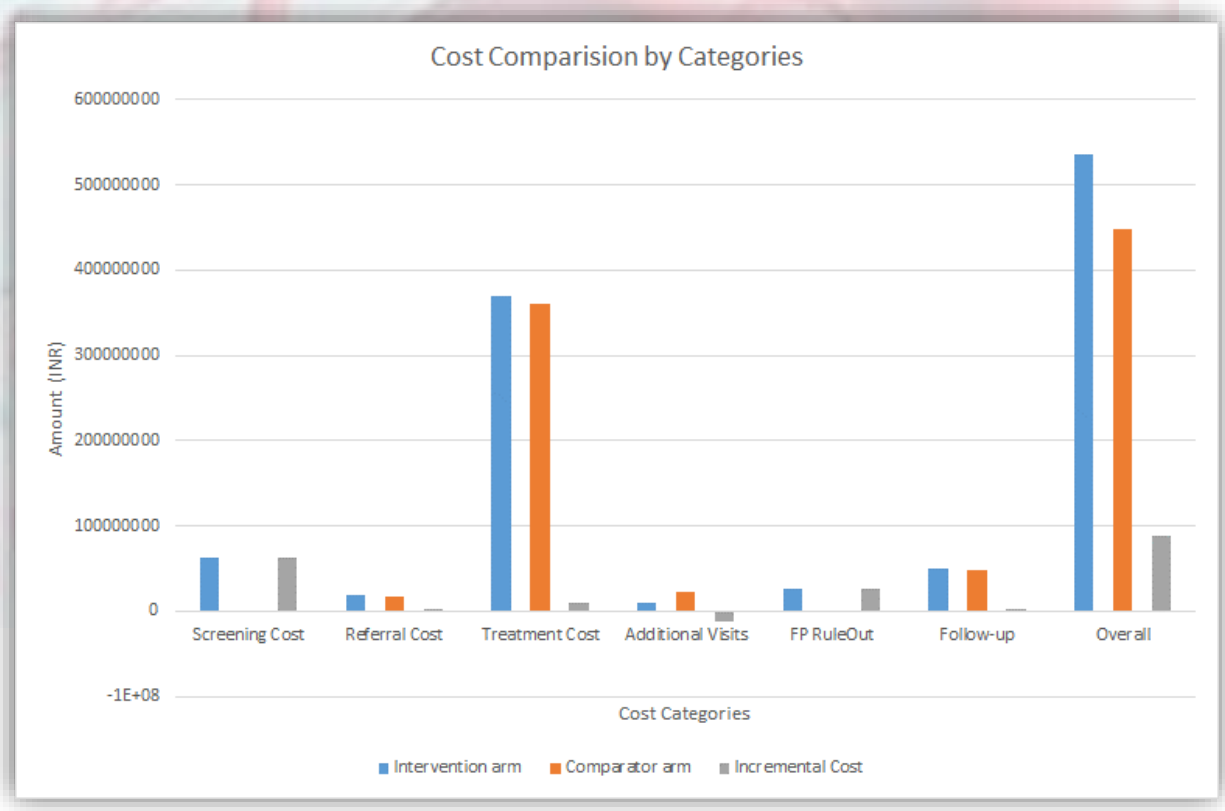


Budget Impact Analysis

The table below displays the year-wise disaggregated distribution of budget estimates for the target population over a lifetime horizon for the Hridyam Pediatric Cardiac care continuum.

The Hridyam pathway costs Rs 53.6 crores compared to the comparator arm which costs the health system Rs 44.7 crores. The net increase in budget as a result of the Hridyam project on an annual basis is Rs 8.9 crores.

	Intervention arm	Comparator arm	Incremental Cost
Screening Cost	63135000	0	63135000
Referral Cost	18103008	17648400	454608
Treatment Cost	369318401.7	360043970.6	9274431.076
Additional Visits	9853852.8	21736440	-11882587.2
FP RuleOut	26256454.4		26256454.4
Follow-up	49179838.4	47944820	1235018.4
Overall	**535846555.3**	**447373630.6**	**88472924.68**



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