Policy Briefs

Vol-2

Health Technology Assessment in India (HTAIn)

Department of Health Research

November-2022

Contents

PREFACE

To facilitate the process of evidence informed decision making in the field of health, Government of India has set up Health Technology Assessment in India (HTAIn) entrusted to conduct Health Technology Assessment and support Central and the State Governments in evidence based-decision making and policy formulations. HTAIn consists of a Secretariat based in the headquarter that coordinated with HTAIn Resource Centers and Technical Partners established throughout India in different states. Resource Centers conduct HTA studies allocated to them by the Secretariat. Secretariat can also conduct HTA studies in addition to Resource Centers and Technical Partners.

This document contains the Policy Briefs of the completed HTA Studies conducted by Health Technology Assessment in India (HTAIn), which includes HTAIn Secretariat, the Regional Resource Centers and Technical. There is an introductory overview of Health Technology Assessment in India (HTAIn) established under Department of Health Research (DHR), Ministry of Health & Family Welfare, New Delhi followed by the policy briefs of the completed studies.

Executive summary

Health Technology Assessment in India (HTAIn) is a sub-scheme under the umbrella scheme Human Resource and Capacity Building in the 15 th Financial Commission approved for year 2021-22 to 2025-26 under the Department of Health Research (DHR), Ministry of Health & Family Welfare (MoHFW), Government of India to facilitate the process of transparent and evidence-informed decision making in the field of healthcare. HTAIn is entrusted with the responsibility to analyze health technologies viz. medicines, devices and health programmes for its cost-effectiveness, clinical-effectiveness and equity issues by means of Health Technology Assessment (HTA), and in turn help in decision making for an efficient use of the limited health budget and provide people access to the quality health care reducing their out of pocket expenditures (OOPs) on health Established in 2017, HTAIn has extended support to various verticals (e.g Maternal Health, Child Health, TB division, State Health Departments, Ayushmann Bharat Program, National Program for Blindness and NCD division etc.) of the health ministry at the center and also at state level, in evidence-based decision making.

HTAIn has Completed 43 HTA studies, Established 18 resource centers,, Nominated 26 State Nodal Officers, Costing study of healthcare system, EQ-5D Utility value set study for India and 32 HTA ongoing Studies HTAIn study evidence has supported the Health Benefit Package revisions of Ayushmann Bharat, Program for Screening of Cervical Cancer, Procurement of High throughput machines for COVID testing of Low cost Ventilator procurement, Cost effective threshold for Point of Care testing for Sickle cell Diagnosis, Procurement of Safety Engineered Syringes, Addition of intra dermal contraceptive for family planning, Screening Program for Dengue and Hepatitis in Tamilnadu and Tuberculosis monitoring and Adherence device for TB management. HTAIn has also drafted the Cabinet Note for Health Technology Assessment Board.

Union Minister of State for Health and Family Welfare, Dr Bharati Pravin Pawar addressed International Symposium on Health Technology Assessment, was organized by the Department of Health Research, Ministry of Health and Family Welfare in collaboration with International Decision Support Initiative (iDSI). Best Practices into Policy for Evidence Informed Decision making in Healthcare Sector for Universal Health Coverage".

The Minister of State, Dr Bharati Pravin Pawar also released video on "The Power of HTA" and two books – "Policy Briefs" and "Development of Health-Related Quality of Life Value Sets (EQ-5D-5L) for India". The aim of EQ5D5L study was to generate the Indian Tariff Values of all the health states that is used in the HTA studies. It is the first and the largest study of its kind in South Asia conducted by HTAIn in collaboration with its Resource Centers. The Policy Brief book contains all the policy briefs of the HTA studies conducted by HTAIn and approved by the Board till date.

Honorable Minister of Health and Family Welfare

In the process of achieving universal health coverage, Govt. of India took the initiative to establish Health Technology Assessment in India (HTAIn) under Department of Health Research, Ministry of Health & Family Welfare. With advancement of technology in Health sector, it is very crucial to take a logical and evidence based decision making to adopt the health technologies like medical devices, drugs, and treatment strategies in the health care system.

HTAIn would help in formulating rational and evidence based policy decision making to both state and central governments in the country by assessing the clinical effectiveness, cost-effectiveness, socio-cultural and equity aspects of a new health technology. HTA process also involves the systematic evaluation of health programs thereby inform the decision makers about implementation strategies of a health program and addresses the cost-effectiveness of diverting the funds into health care programs. This compiled policy briefs would be really helpful for the policy makers and international organizations how health technology assessment is being undertaken and methodologies that HTAIn is following in the country.

HTAIn with its objectives of maximizing health, minimizing out of pocket expenditure, and reducing inequality will play a key role in India to provide better quality of health care at affordable prices to all its population.

Honorable Minister of State Dr. Bharati Pravin

Health Technology Assessment in India is a sustainable model of evidence based decision making in order to achieve Universal Health Coverage. HTA is important aid which helps to bridge the gap between healthcare providers and public providers, using real world evidence. The Policy Briefs Volume 2 book contains all the HTA studies conducted by HTAIn which has been approved by Medical Technology Assessment Board. The recent study on 'Cost per test and Cost of screening for sickle cell disease' has contributed remarkably by suggesting that Hem type SC Kit and Sickle SCAN Kit can be procured below INR 100, which means the best quality diagnostic equipment for sickle cell comes with minimum cost of 100 rupees.

Through these policy briefs the HTA study recommendations can be disseminated to a wider group of stakeholders in country. As country and its decision makers are moving towards evidence based decision making, these policy brief books will be an important tool to aid in robust resource allocation. HTA recommendations helps to ensure that new and existing healthcare technology are available accessible, affordable bringing India one step closer to Universal Health Coverage. India's rapid economic growth has been accompanied by slower improvements in population health. Given the need to reconcile the ambitious goal of achieving Universal Coverage with limited resources, a robust priority-setting mechanism is required to ensure that the right trade-offs are made and the impact on health is maximized.

The effective conduct and uptake of HTA depends on a well-functioning ecosystem of stakeholders adept at commissioning and generating policy-relevant HTA research, developing and utilizing rigorous technical, transparent, and inclusive methods and processes, and a strong multispectral and transnational appetite for the use of evidence to inform policy.

Dr. Rajiv Bahl, Secretary, Department of Health Research

Government of India is committed to extend good quality healthcare services to 1.38 billion people of India. There are various challenges in this direction such as limited health resources, prioritization of health services, out of pocket expenditure on healthcare etc. Health Technology Assessment has become a valuable tool to examine health care technologies for their cost-effectiveness, clinical effectiveness, safety and accessibility etc. HTA is a promising tool to address various challenges of the health system by means of evidence-informed decision-making.

Establishing HTAIn was a key milestone in strengthening Indian healthcare system. HTAIn helps central and state government in evidence informed decision making and policy formulations.

HTAIn has successfully completed 31 studies that have gone into implementation and several studies are underway on the topics received from central and state governments. It has supported Ayushman Bharat Yojana in revising its packages and package rates. This book has compiled the policy briefs of the completed HTA studies till date which could be useful for the people, in general and policy makers, in particular to understand the methodologies of HTA and adopting the policy recommendations. It will also generate an awareness and establishing the integrity of HTAIn among people.

Establishing HTAIn is a very promising step towards providing good quality healthcare to maximum number of people and taking India a step further towards Universal Health Coverage. I am sure that healthcare sector will witness transformation in healthcare sector by the means of HTA.

Ms. Anu Nagar, Joint Secretary, Department of Health Research

In the field of healthcare, it is very important to keep pace with the latest health technologies while maintaining affordable access to healthcare for patients. The Health Technology Assessment helps in maintaining this pace and provide the patients access to cost effective health technologies.

Health Technology Assessment in India (HTAIn) was established for a systematic and evidence based decision making which is proving to be a landmark for Indian healthcare and its commitment towards Universal Health Coverage.

During a short duration of five years HTAIn has completed 43 HTA studies including several multi-centric studies such as Costing of Health Services in India and generating EQ5D tariff value for India. All these studies have supported Centre and State Governments in several evidence based decision-making. It has also supported Ayushman Bharat in revising its packages.

All the completed studies as "knowledge synthesis" have been compiled in this book in the form of policy briefs which provide a quick overview of the key finding and policy recommendations. HTA is indeed the need of the hour for providing accessible and quality healthcare system in India.

Patron

Dr Rajiv Bahl

Secretary

Department of Health Research

Smt. Anu Nagar

Joint Secretary

Department of Health Research

Members Of HTAIn Secretariat

S. No.	*Name*	*Designation*
1.	*Dr. Kavitha Rajsekar*	*Scientist E*
2.	*Dr. Oshima Sachin*	*Scientist D*
3.	*Dr. Ashish K. Mehta*	*Scientist C*
4.	*Dr. A. K. Pandey*	*Scientist C*
5.	*Dr. Shivangi Khanna*	*Scientist-B*
6.	*Dr. Vishakha Bharati*	*Junior Health Economist*
7.	*Dr. Binod Kumar Singh*	*Project Manager*
8.	*Mr. Vipin Kumar*	*Admin. Officer*

Resource Centres and their PIs.

S. No.	Resource Centre	Principal Investigator
1.	PGIMER, Chandigarh	Dr. Shankar Prinja
2.	IIT, Delhi	Dr. Vivekanand Perumal
3.	AIIMS, Jodhpur	Dr. Kuldeep Singh
4.	IIPH, Gandhinagar	Dr. Somen Saha
5.	NIV, Pune	Dr. Yogesh Gurav
6.	NIRRH, Mumbai	Dr. Beena Joshi
7.	NCDIR, Bangalore	Dr. Prashant Mathur
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15.	RMRC, Bhubaneswar	Dr. Sanghamitra Pati
16.	IIPH, Shillong	Dr. Sandra Albert
17.	State Cancer Institute and KGMU Lucknow	Dr. Ayush Lohiya
18.	AIIMS, Rishikesh	Dr. Bhanu Duggal

Editorial Team

Dr. Kavitha Rajsekar
Scientist 'E'
HTAIn Secretariat
Department of Health Research Ministry of Health & Family Welfare New Delhi

Dr. Aamir Sohail
Scientist - D
HTAIn Resource Centre,
Indian Institute of Science, Bangalore.

Dr. Vishakha Bharati
Jr. Health Economist
HTAIn Secretariat
Department of Health Research Ministry of Health & Family Welfare New Delhi

For more information, kindly visit www.htain.icmr.org.in Or, Contact

Health Technology Assessment in India Secretariat
Department of Health Research Ministry of Health & Family Welfare
1st Floor, Indian Red Cross Society Building, 1, Red Cross Road,
New Delhi - 110001.
Email ID: htain-dhr@nic.in, kavitha.rajsekar@nic.in
Phone No: +91 11- 23736906/ 23736085

Policy Briefs

Health technology assessment report on congenital heart defects

The Health Technology Assessment of pediatric cardiac surgery program (Hridyam) for congenital heart disease in Kerala

Policy Brief

Pediatric Cardiac Care Continuum

Summary

Why this disease?
Congenital heart disease (CHD) has emerged as a leading contributor to infant mortality in many low- and middle-income countries (LMICs). Why is this program a priority and an appropriate topic for HTA for the state of Kerala? The state of Kerala launched Hridyam to bring down the state's IMR to a single digit. This was a state-wide population-based neonatal congenital heart defects screening program.
How is 'Hridyam' different?
The additional component of this program titled 'Hridyam' was the use of pulse oximetry at all delivery points to screen for CHDs along with usual physical examination early detection, prompt stabilization and expedited referral to a tertiary center were the program's key components.
How many hospitals are empaneled in the Hridyam Programme?
In addition to two public hospitals, five private hospitals with advanced pediatric cardiac surgery capabilities were empaneled (public- private partnership). How did the costs and the QALY compare with the non-intervention arm? Is the intervention cost-effective?
The cost borne by the health system for the detection and management of congenital heart diseases was compared for the current and non-intervention scenarios. 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.
*What are the most sensitive parameters to the ICER value?*
The sensitivity of the pulse oximetry used for neonatal screening had the highest effect on the ICER when assessed with a variation of 10% in the base case values.
What are the results of the budget impact analysis?
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 the budget because of the Hridyam project on an annual basis is Rs 8.9 crores. This model has
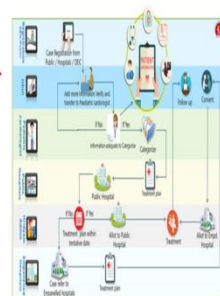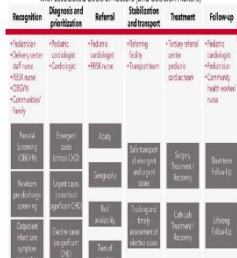
Recommendations

The package of newborn screening includes a pulse oximetry examination (sensitivity 83% (75-91)), followed by the necessary quality clinical examination. The economic evaluation shows the intervention to be cost-effective, with a budget impact of 8.9 cores for the population of Kerala.

Background

In 2012, concerned that its infant mortality rate (IMR) had been stagnant for so long, the Government of Kerala commissioned studies to evaluate the causes of IMR in the state. It showed that infant deaths from infection and malnutrition had significantly declined, birth defects were a significant cause of infant mortality (30%), and a significant reduction in IMR would require addressing this burden1. Among these, congenital heart disease (CHD) represents the world's most common class of major birth defects, affecting one in 120 newborns2. About one-fourth of all CHDs are considered critical congenital heart disease (CCHD), which requires a lifesaving procedure in the first year of life3. In 2012, the Government of India started the Rashtriya Bal Swasthya Karakorum (RBSK). 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 state Government, adequate financial resources were available for 'HRIDYAM' to address the burden of CHD in the state. This HTA aimed to conduct the economic evaluation and the budget impact analysis of the Hridyam Program.

Methods:

P opulation:

All newborn infants delivered in healthcare facilities

Intervention

CHD Patient Care Continuum under Hridyam

Comparator

Routine physical examination for screening

Outcomes

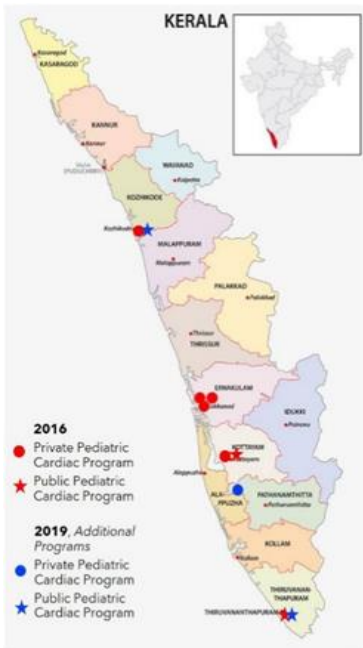ICER (Incremental cost-effectiveness ratio) (cost per QALY gained)

Budget impact of implementing *the* program in the state of Kerala.

Study Perspective

Health system

Time Horizon
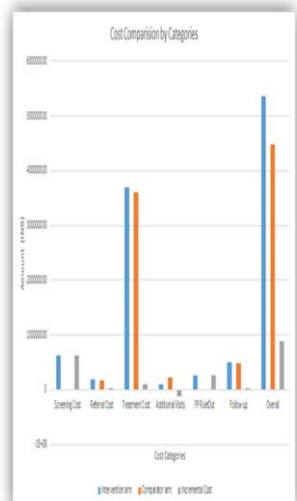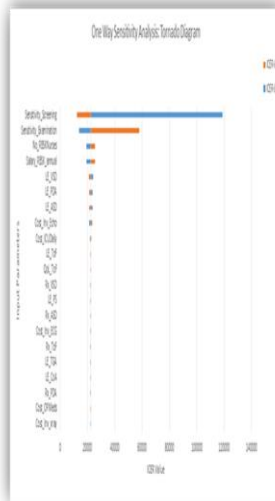
Lifetime Horizon

Study Setting

Kerala (14 administrative units, 7 existing pediatric CHD surgery centers (2 government, 5 private).

Cost-effectiveness (including sensitivity analysis) and Budget Impact Analysis:

a) ICER Calculation and BIA: The study found that compared to the usual care scenario, the Hridyam program had an incremental cost of INR 8.85 crores and generated 3947additional QALYs, resulting in an ICER of 22,145. This makes the program cost-effective at the threshold of one GDP per capita.

b) Sensitivity analysis: On one-way sensitivity analysis, 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 (Echocardiogram), and the cost of ICU admission.

c) The budget impact analysis showed that 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 the budget because of the Hridyam project on an annual basis is Rs 8.9 crores.

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYS
No-intervention	44,73,73,631	153227		
Current	53,58,46,555	157174	8,84,72,925	3947
ICER	22415			

KERALA

2016
Private Pediatric Cardiac Program
Public Pediatric Cardiac Program

2019, Additional Programs
Private Pediatric Cardiac Program
Public Pediatric Cardiac Program

One Way Sensitivity Analysis: Tornado Diagram

Cost Comparision by Categories

Policy Brief

Conclusions

Hridyam program for congenital heart diseases is cost-effective relative to the threshold of GDP per capita from a health system perspective.

To scale up the key elements of the Hridyam care continuum model to the entire state of Kerala, the burden on the exchequer will be to the tune of INR 53.6 crores.

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Health technology assessment report on Rapid UTI Diagnostic kits

COST-EFFECTIVENESS ANALYSIS OF RAPID DIAGNOSTIC KITS WITH ANTIMICROBIAL SENSITIVITY AS POINT-OF-CARE Testing UNCOMPLICATED URINARY TRACT INFECTION

Health Technology
Assessment in India (HTAIn)

Almost 50% of the women experience at least one episode of urinary tract infection (UTI) in their lifetime, among which 20-40% experience recurrent episodes[1]. The gold standard for diagnosis of UTI is urine culture followed by management based on antibiotic susceptibility test (AST) results which takes 48 to 72 hrs for final report. UTI is currently treated empirically. However, empirical treatments do not ensure appropriate stewardship which may lead to therapeutic failure and antimicrobial resistance. RightBiotic and Rapidogram are two indigenously developed rapid point-of-care antibiotic susceptibility testing devices. The lower turnaround time, i.e., 4 to 6 hours, of the devices facilitate the early administration of the appropriate antibiotics. We assessed the cost-effectiveness of RightBiotic and

Conclusions and complications

We found that both the RightBiotic and Rapidogram were cost-effective, with an ICER per QALY gain of ₹ 36 and ₹ 16, respectively. The corresponding budget implication for Tamil Nadu will be 0.75% and 0.31% of the current state health budget.
Communities having high levels of antimicrobial resistance shall be prioritized for the rollout of the analysis

Table 1: Base case result for rapid UTI diagnostic kits (N=1)

	Empirical Treatment	RightBiotic	Rapidogram
Total cost	₹ 215	₹ 224	₹ 219
Total QALYs	3.406	3.665	3.662
Incremental cost	-	₹ 9.29	₹ 3.98
Incremental QALYs	-	0.259	0.256
ICER/QALY gained	-	₹ 35.87	₹ 15.55
Net Monetary Benefits		₹ 37,715	₹ 37,281

Table 2: Budget impact analysis for implementing RightBiotic and Rapidogram at national and state level (in cores)

We adopted a decision tree with three arms (Empirical arm, RightBiotic arm, and Rapidogram arm) to model the progression and management of symptomatic uncomplicated UTI under empirical treatment and Right biotic / Radiogram-aided treatment. We simulated cohort of women aged ≥18 years with symptomatic-uncomplicated UTI over a one- month time horizon. Clinical efficacy, cost, and utility parameters were collected from secondary sources[2,3]. We estimated the incremental cost-effectiveness

Implementation cost	India (₹)	Impact on National Health Budget 22-23 (%)	Tamil Nadu (₹)	Impact on State Health Budget 22-23 (%)
Right Biotic				
1st year	2,140	2.58	134.2	0.75
2nd year	794	0.95	49.8	0.28
Rapidogram				
1st year	887	1.06	55.6	0.31
2nd year	780	0.94	48.9	0.27

What we

ICER per QALY gained with RightBiotic and Rapidogram were ₹ 35.87, and ₹ 15.55, respectively, (Table 1). The probability that RightBiotic and Rapidogram to be cost-effective is 100% at one-time GDP per capita. The net monetary benefits gained from both interventions were ₹ 37,715 and ₹ 37,281, respectively.

Introducing RightBiotic and Rapidogram at all PHCs in India will require 2.5% and 1.1% of the current national health budget respectively. Similarly, in the state of Tamil Nadu, the implementation of RightBiotic and Rapidogram requires 0.75% and 0.31% of the current state-level health budget (Table 2).

Acknowledgment

Supporting Document

HTA Report: Cost-effectiveness analysis of rapid diagnostic kits with antimicrobial sensitivity as point-of-care testing in uncomplicated urinary tract infection.

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HTA of Telemedicine Enabled Otoscope for Prevention of Ear Disease

Policy Brief
June 2022

Health Technology Assessment of Telemedicine-Enabled Otoscope (TEO) for Prevention of Ear Diseases

Health Technology Assessment in India, Regional Resource Hub, ICMR-Regional Medical Research Centre, Bhubaneswar

Department of Health Research, Ministry of Health & Family Welfare, New Delhi

Background

The World Health Organization (WHO) estimates that untreated hearing loss costs the global economy $980 billion per year. This includes healthcare costs (excluding hearing aids), support costs, lost productivity, and cost. Low-and middle-income countries (LMICs) bear roughly 57% of these costs. Untreated ear infections can lead to hearing loss, social isolation, loneliness, psychosocial distress, , and depression. The primary barriers to care are a lack of awareness and limited care in primary health care (PHCs) for ear care.

Adult-onset hearing loss was estimated to have a prevalence of 7.6 percent in India. In India, barriers to early detection and intervention for ear care include lack of infrastructure, shortage of expertise, lack of awareness on screening, and absence of advanced technology in primary health care settings.

About 20% of the population said the cost was a barrier to obtaining treatment, and 41% of screened respondents said they didn't have time for an ear checkup. Regular hearing checks were

Neglected, requiring door-step digital health services. Telemedicine services are critical in areas where the doctor-patient ratio is significantly lower than the WHO recommended ratio (1:1000). In India, there is one doctor for every 1445 Medical services, particularly doctors, are scarce in rural and remote areas, where health care services are challenging.

Rationale

Hearing loss prevention is essential throughout the life span, from prenatal and perinatal stages to middle age and beyond. It is critical to developing effective prevention strategies for hearing loss at various stages of life. Hence, community-based hearing screening using digital technology is critical for reducing the burden of hearing loss. Telemedicine was conceptualized by the Ministry of Health and Family Welfare under Ayushmann Bharat scheme during 2018. Teleconsultations in India were developed by the National Telemedicine Service of the Union Health Ministry. On April 13, 2020, the eSanjeevani out-patient-department was launched to enable patients to receive health care by a specialist at primary health care for Medicine, Obstetrics & Gynecology and Pediatric patients. However, no such tele- facilities implemented for ENT care.

Objective

To assess the cost-effectiveness and operational feasibility of implementing a telemedicine- enabled Otoscope (TEO) ear disease prevention.

Methods

This HTA study is classified into three broad areas: efficacy, economic evaluation and ethical and social implication of implementation.
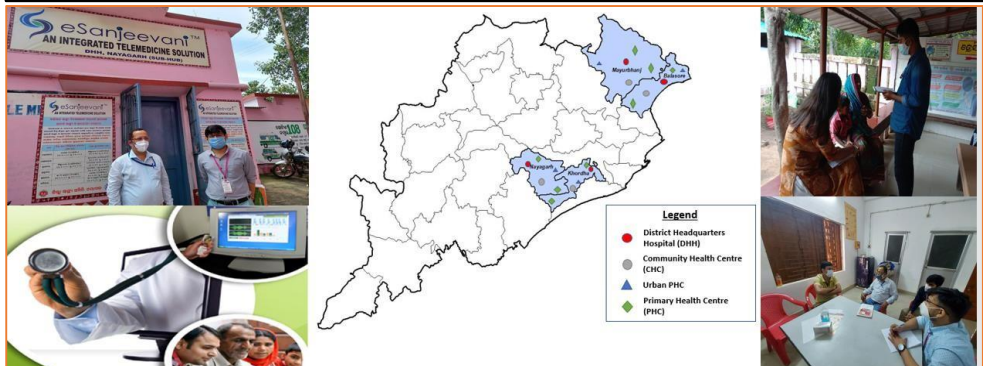
| Community | PHC/CHC | DHH/Tertiary Care Hospitals |

Traditional Ear Screening

ENT Specialist with otoscope

Advantages
- Quality of treatment/diagnosis

Disadvantages
- Increased OOP Expenditure
- Low Coverage and under-detected??
- Increased Burden

Telemedicine Enabled Otoscope at PHC

Images Sent

Treatment/Referral

Medical Officer with TEO

Diagnosis Sent

ENT Specialist

Advantages
- Ability to view External Ear by Medical Officer
- Sending the photos to ENT Specialist for diagnosis
- Increased quality of care
- Decreasing OOP Expenditure
- Increased Coverage

Disadvantages
- Need Rigors training and monitoring
- Increase health system cost

Telemedicine Enabled Otoscope at Community

Images Sent

Community Health Worker with TEO

Images Sent

Medical Officer

Diagnosis Sent

ENT Specialist

Treatment Communication/ Referred to PHC/CHC or DHH

Advantages
- Bringing Quality of Care to Community
- Sending the photos to ENT Specialist for diagnosis
- Decreasing OOP Expenditure
- Maximum Coverage (Door Step Service)

Disadvantages
- Need Rigors training and monitoring
- Increase health system cost
- Strict Follow-up for referral cases is essential

Legend
- District Headquarters Hospital (DHH)
- Community Health Centre (CHC)
- Urban PHC
- Primary Health Centre (PHC)

24

Figure 2. Population, Intervention, Comparator, and Outcome (PICO).

This project approved by the Technical Appraisal Committee, Health Technology Assessment, Department of Health Research, Ministry of Health and Family Welfare, Government of India. The ethical clearance was obtained from

Findings

The Institutional Ethical Committee of RMRC Bhubaneswar. Permission was taken from the concerned local authorities, and consent was taken from the participants.

Table 1. Pooled sensitivity and specificity of an otoscope and Telemedicine Enabled Otoscope (TEO).

Device	Sensitivity % (95% CI)	Specificity % (95% CI)
Traditional Otoscope (Overall)	89% (81– 96%)	87% (74-98%)
Telemedicine Enabled Otoscope (Overall)	82% (73-90%)	95% (91-98%)
Telemedicine Enabled Otoscope (Physician)	84% (75-92%)	91% (85-96%)
Telemedicine Enabled Otoscope (CHWs)	80% (64-94%)	97% (94-100%)

Many patients claimed that they could not travel to district hospitals due to a lack of time, distance, travel money, and the support of a companion during our initial interactions with various stakeholders. Furthermore, ENT specialists and advanced diagnostic equipment are lacking in PHCs and CHCs. Primary care physicians were optimistic about introducing TEO at Health & Wellness Centers (HWCs). The ENT doctor proposed using a cell phone or tablet to remotely observe and review the image, allowing for a faster diagnosis.

Variables	TEO by Medical Officer at each Primary health centres	TEO by Commu nity Health Workers at Community level	Screening with Traditional Otoscope by ENT specialist at tertiary health care facilities	
Annual Heath System cost per facility	₹1.46 Lakhs	₹6.49 Lakhs	₹14.5 Lakhs	
Expected no of cases per year	7280	31200	13780	
Unit cost per patient (Health System)	₹ 20.07	₹ 20.82	₹ 105.45	
Societal Cost	₹ 202.74	₹ 103.24	₹ 344.15	
Total Cost	₹ 222.81	₹ 124.06	₹ 449.60	

Table.2 Implementation cost

Average number of facilities and annual implementation cost	TEO by Medical Officer at each Primary health centres	TEO by Community Health Workers at Community level	Screening with Traditional Otoscope by ENT specialist at tertiary health care facilities
At district level (facilities)	71	71	2
At district level (Cost)	6.9 Crore	12.5 Crore	29 Lakhs
At state level (facilities)	1360	1360	62
At state level – Odisha (Cost)	132.5 Crore	239.7 Crore	9.0 Crore
At national level (facilities)	29899	29899	2258
At national level – India (Cost)	2913.5 Crore	5271.2 Crore	328.1 Crore

Table.3 Budget Implication

The annual health system cost per facility for ear screening with Otoscope by an ENT specialist at tertiary health care facilities will be 14.5 lakhs INR with per-patient cost of 105.45 INR.The annual health system cost per facility for ear screening with TEO by a Medical Officer at each Primary Health Centre will be 1.46 lakhs INR with a patient cost of 20.07 INR. The yearly health system cost per facility for ear screening with TEO by CHWs at the community level will be 6.46 lakhs INR with 20.82 INR per. The annual cost of implementing ear screening with a typical Otoscope by ENT specialists at tertiary health care facilities will be 328.1 Crore INR at the national level, coverage will be extremely low. At the national level, the yearly cost of implementing ear screening with TEO by Medical Officers in Primary Health Centers will be 436.87 Crore INR, while the CHW model with TEO will cost 1942.42 crore INR, but will provide universal coverage.
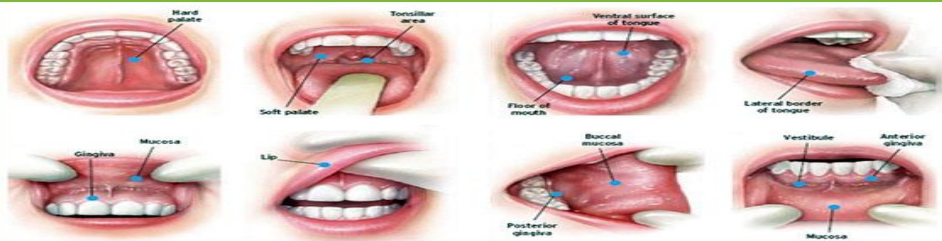
HTA on Oral
Cancer Screening

Health Technology Assessment of Strategies for Oral Cancer Screening in India

Health Technology Assessment in India (HTA In)
Kalyan Singh Super Specialty Cancer Institute (KSSSCI), Lucknow

POLICY BRIEF

Summary

In India, oral cancer is the second most common cancer in terms of incidence and is often diagnosed at an advanced stage. This health technology assessment study aims to assess the clinical and cost-effectiveness of commonly used oral cancer screening strategies. Systematic review and meta-analysis were conducted to assess pooled sensitivity and specificity of screening strategies namely conventional oral examination (COE), Toluidine blue staining (TBS), Oral cytology (OC), and Light-based detection (LBD). A Markov model approach was undertaken to derive the lifetime costs and health outcomes of various screening strategies at different intervals from a societal perspective using a discount rate of 3%. The high-risk screening strategy was cost-effective as compared to the mass-screening approach across all strategies and at various intervals. The most cost-saving approach was the conventional oral examination at an interval of 10 years for oral cancer screening in high-risk populations (tobacco &/or alcohol users) above 30 years of age.

Policy Recommendations

Conventional oral examination after training frontline health workers should be considered for screening of oral cancer and potentially malignant disorders. Oral screening of high-risk populations (tobacco &/or alcohol users) above 30 years using conventional oral examination at 10-years interval is the most cost- saving approach.

Objectives

To assess the clinical and cost-effectiveness of commonly used screening modalities for oral cancer. i.e., COE, TBS, OC, and LBD. To determine the most appropriate strategy between mass screening and high-risk screening strategy. To determine the most cost-effective interval (out of 3, 5, and 10 years) between periodic screening check-ups.

Methods and Approach

1. Assessment of clinical effectiveness

Systematic review and meta-analysis were conducted to assess pooled sensitivity and specificity of screening strategies. Population - apparently healthy individuals Intervention - COE, TBS, OC, and LBD screening by frontline health workers. Comparator - evaluation by specialist/histopathological examination (gold standard test). Outcome - sensitivity, and specificity of screening strategies. Random effects meta-analysis was performed for pooling the estimates.

2. Cost-effectiveness analysis (CEA)

Due to the high prevalence of risk factors (tobacco and alcohol) in the Indian population and its established relation with the causation of oral cancer, we identified the high-risk individuals with habits of tobacco &/or alcohol (3). Hence, two Markov models were developed. Model A adopted a mass screening strategy versus no screening, whereas Model B adopted a high-risk screening strategy versus no screening. (Figures 1 and 2). The CEA was conducted using the Markov model technique for estimating the lifetime costs and health outcomes in a hypothetical cohort of 1 lakh men and women above 30 years of age. The outcomes were measured in terms of oral cancer incident cases, oral cancer deaths averted, quality-adjusted life-years (QALYs) gained, and incremental cost -effectiveness ratio (ICER). Perspective - Societal. Discount rate - 3%. Probabilistic Sensitivity analysis (PSA) was done to address any parameter uncertainty. Software – Microsoft Excel.
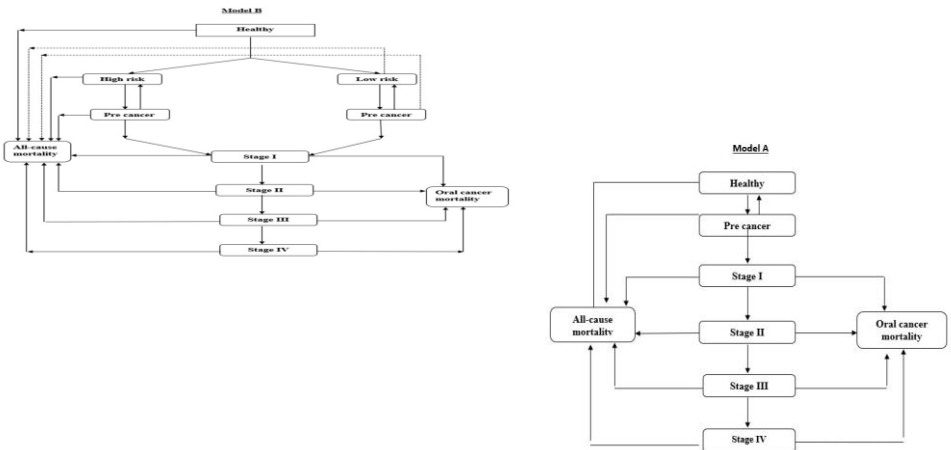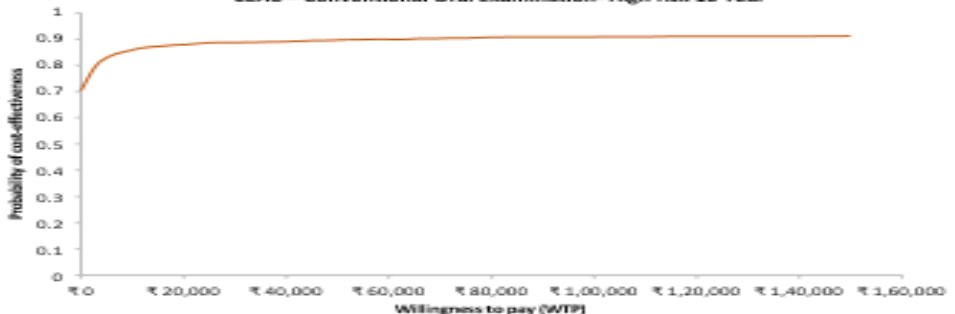

Figure 4 Cost-effectiveness acceptability curve (CEAC)

Results

1. Clinical effectiveness

There were no studies identified fitting the inclusion criteria for TBS, OC, and CLI. Five studies were identified where screening was done using COE performed by a frontline health worker. A total of 10,069 participants above the age of 20 were included. Pooled sensitivity of COE - (88.8% (95% CI: 71.6-96.1). Pooled specificity of COE - (91.9% (95% CI: 78.3-97.3).

2. Cost-effectiveness analysis

On comparing no screening vs mass screening and high-risk screening, the no-screening arm had the maximum number of new cases (5,673.59 cases). Mass-screening strategies (number of incident cases) namely LBD - 3 years (3271.68 cases) had the least number of incident cases followed by OC - 3 years (3276.92 cases), and COE - 3 years (3309.91 Cases). Mass screening/ high-risk screening averted the higher number of oral cancer deaths as compared to noscreening. Mass screening using LBD and OC at 3 years interval averted the maximum number of oral cancer deaths (459.76 each).

Screening strategy		ICER (INR/QALY)
COE	3 years HR	2,156.35
	5 years HR	-2,331.41(D)
	10 years HR	-7,213.46(D)
TBS	3 years HR	5,288.47
	5 years HR	2,376.54
	10 years HR	-4,815.80 (D)
OC	3 years HR	13,437.25
	5 years HR	10,958.36
	10 years HR	3,716.65
LBD	3 years HR	9,545.34
	5 years HR	3,867.66
	10 years HR	-1,075.17(D)

Across all the strategies, the high-risk screening was cost-saving as compared to mass screening (Figure 3). The high-risk strategies (ICER values) namely COE 5 years (-2331.41), COE 10 years (-7213.46), TBS 10 years (- 4815.80), and LBD 10 years (-1075.17) were dominant over no-screening (Table 1). PSA showed COE HR at 10-years was more than 80% cost-effective at the willingness to pay threshold of India (Figure 4) (4). The budget impact analysis showed that oral screening using COE for high- risk population at 10-year interval would cost 257 crores which is only 0.03% of annual healthcare budget of India of 86,200.65 crores

Figure 3 Base-case cost-effectiveness plane

Figure 4 Cost-effectiveness acceptability curve (CEAC)
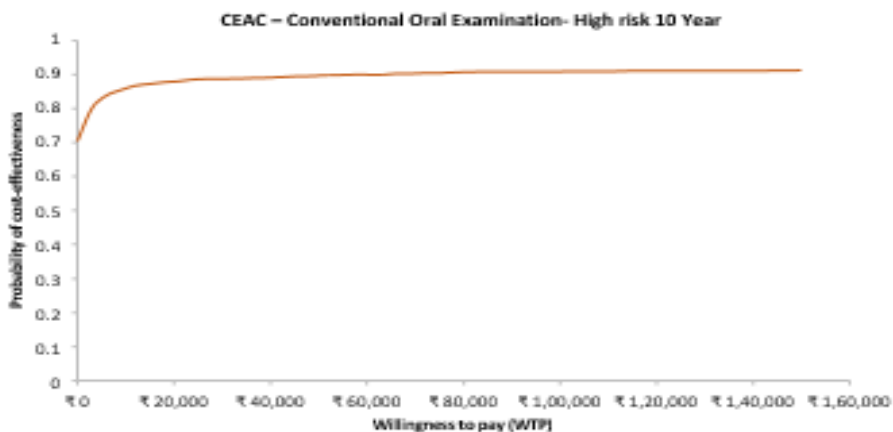
Conclusions

Conventional oral examination by trained frontline health workers had high sensitivity and specificity for oral cancer screening. High-risk oral cancer screening (tobacco &/or alcohol users) was more cost-effective than the mass-screening strategy. High-risk oral screening of population above 30 years of age using conventional oral examination at 10-years intervals was the most cost- saving strategy for the Indian population.

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alence=0

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Inj. Gentamicin in Neonatal Sepsis by ANMs before Referral

Executive Summary

Sepsis is the commonest cause of neonatal mortality, responsible for about 30-50% of the total neonatal deaths in developing countries. According to Operational guidelines on the use of gentamicin, ANMs are expected to recognize signs of suspected sepsis and provide pre-referral treatment to those neonates with suspected neonatal sepsis. But there is a paucity of the literature that assesses the ground-level scenario of this strategy and its implication. Health.

Technology Assessment (HTA) been the chosen approach to explore this question.

Cost-effectiveness was assessed using the Decision tree model utilizing data from secondary literature. ICER was calculated to be Rs.216.98 cost per QALY gained. This economic evaluation shows, it is cost- effective for ANMs to administer a pre-referral injection of Gentamicin along with oral Amoxicillin to neonates suspected of sepsis.

Operational Guidelines
Use of Gentamicin by ANMs for management of sepsis in young infants under specific situations

Policy Recommendation

The current Economic evaluation depicts the administration of a pre-referral injection of Gentamicin along with oral Amoxicillin to neonates suspected of sepsis by ANMs to be cost- effective. Further studies are needed to assess the acceptability of the program from the beneficiary perspective and ANM's perspective.

Method & Approach

Two scenarios were compared, a pre-referral dose of Gentamicin by ANM and treatment in the health facility for neonates with signs of sepsis with the current scenario where no pre-referral dose of Gentamicin is given by ANM to the infant with sign of sepsis and treatment in the health facility. ICER of pre-referral dose of gentamicin versus no-pre-referral dose and treatment at health facility was calculated to be Rs.216.98 cost per QALY gained. One-way sensitivity analysis was done to show the effect of input parameters on the ICER.
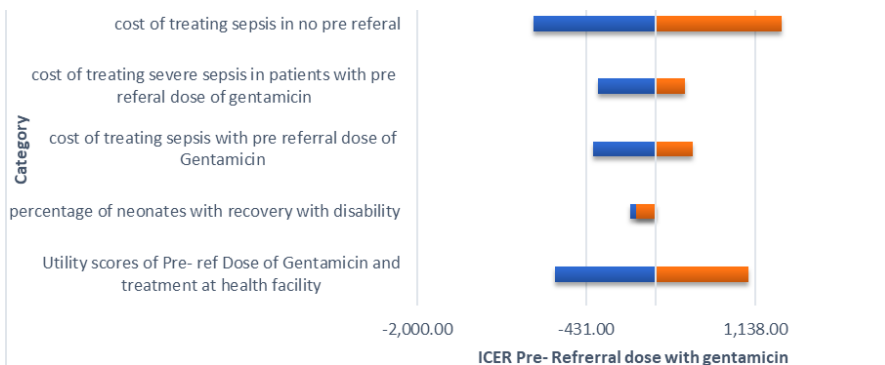
Background

Sepsis is the commonest cause of neonatal mortality; it is responsible for about 30-50% of the total neonatal deaths in developing countries. (1)(2) India has the greatest incidence of clinical sepsis (17,000/ 1, 00,000 live births) among the three million yearly neonatal sepsis cases (2202/ 1, 00,000 live births) globally. (3) Under the current health system, ANMs are responsible for the delivery of the Reproductive and Child Health Programme. According to Operational guidelines on the use of Gentamicin by ANMs for the management of sepsis in young infants (0-2 months) under specific situations in February 2014, ANMs are trained to administer appropriate antibiotic treatment for the management of cases of suspected sepsis in a new-born where referral is not feasible or refused; pre- referral or for the completion antibiotic treatment.
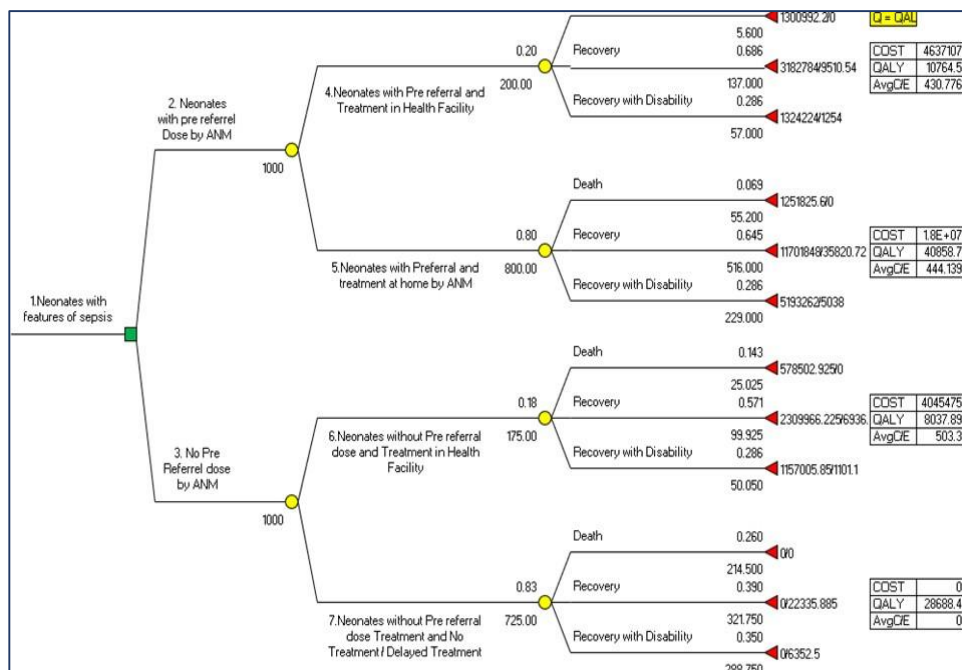
Findings

Decision tree model was used for estimating the cost and effectiveness for the neonates with the sign of sepsis administered a pre-referral dose of Inj. Gentamicin by ANM along with oral amoxicillin. The pre-referral dose of inj. Gentamicin along with oral amoxicillin was compared with current practice i.e. neonates with a sign of sepsis is directly referred to referral centre without any pre-referral dose of an antibiotic. The health outcomes were assessed in terms of Quality Adjusted Life Years (QALY) and cost-effectiveness in terms of incremental cost-effectiveness ratio (ICER) between intervention and comparator arm. Literature review was conducted to get the secondary data on effectiveness of the regime, transition probabilities and health system cost. Feasibility, accessibility, and availability of ANM was determined by consultation exercise.

Category (y-axis labels top to bottom):
- cost of treating sepsis in no pre referal
- cost of treating severe sepsis in patients with pre referal dose of gentamicin
- cost of treating sepsis with pre referral dose of Gentamicin
- percentage of neonates with recovery with disability
- Utility scores of Pre- ref Dose of Gentamicin and treatment at health facility

x-axis: -2,000.00   -431.00   1,138.00

ICER Pre- Refrerral dose with gentamicin

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HTA of Tuberculosis Monitoring Encouragement Adherence Drive (TMEAD)

Improving Adherence through Tuberculosis Medication Regimen using Tuberculosis Monitoring Encouragement Adherence Drive (TMEAD) Intervention in Nasik City of Maharashtra

Health Technology Assessment in India (HTAIn)
Indian Institute of Public Health

Policy Brief

Summary

The digital adherence technologies (DAT) may have the potential to facilitate medication adherence and monitor adherence remotely. Tuberculosis Monitoring Encouragement Adherence Drive (TMEAD) is one of such modern DATs being piloted in one of the districts (Nasik) in Maharashtra from April 2020 to December 2021. This study had enrolled 400 DSTB patients, 200 each in the intervention and control arm. The study reported overall treatment adherence at 94% among those who completed treatment. Patient reported high levels of treatment adherence in the intervention group (99%) as compared to the Control group (90%). Adherence assessed through analysing trace of Rifampicin in urine sample for intervention arm was 84% compared to control arm (80%). Per beneficiary (discounted) cost for TMEAD was INR 6,573. Incremental cost effectiveness ratio of the intervention is INR 11,599 which shows the intervention is highly cost-effective. This study concludes that, TMEAD could be an opportunistic DATs considering the above adherence, cost factors and could complement the national strategy of TB elimination by improving adherence to the treatment regimen in India.

Policy Implications and Novelty

Evaluation of patient and health worker behaviours and beliefs following implementation of TMEAD will be essential in optimising its acceptability and clinical impact. This study shows innovative approaches to adherence, promotion by creating interventions to enhance treatment adherence can improve treatment outcomes. TMEAD can complement the national strategy of TB elimination by improving adherence to the treatment regimen.

About TMEAD

TMEAD was designed and developed by SenseDose Technologies, a start-up venture supported through India Health Fund, an initiative of TATA Trust. TMEAD helps monitor and ensure patient compliance. It also creates a detailed, automated adherence dashboard of all patients for health workers and policymakers to prioritize their resources towards patient adherence.

Introduction

As per WHO report 2018, Tuberculosis (TB) is amongst the top 10 leading causes of mortality globally. India has a huge burden of TB accounting for roughly a quarter of the total global burden. Medication adherence is one of the critical challenges to TB elimination in India. Poor medication adherence is associated with an increased risk of death, disease relapse, and the development of drug resistance. Digital adherence technologies holds promise in treatment adherence. With an understanding of existing challenges of DATs, a Tuberculosis Monitoring Encouragement Adherence Drive (TMEAD) was piloted by a start-up in Maharashtra

Aim of the Study

The study aims to assess the adherence (self-reported/digital/clinical) and cost effectiveness of the new DATs i.e. TMEAD, compared to the standard of care for the drug-sensitive tuberculosis (DSTB) patients residing in the urban geography of Nasik City in Maharashtra, India.

Objectives of the Study

Primary objective of the study is to measure treatment adherence (self-reported/digital) of the TMEAD as compared to the standard of care.

Secondary objectives: To validate the adherence (clinical) through urine rifampicin levels. To estimate the cost-effectiveness of the TMEAD as compared to the standard of care for the DSTB patients.

Method

The study was undertaken prospectively at Nasik districts of Maharashtra during 2020-21. The target population for the study were newly diagnosed TB patients at selected TU as per the NTEP protocols. For Intervention 3TU and control 2TU.Based on an assumption of an increase in the adherence to TB treatment from 80% (as cited from available literature to 95% (as desired under NTEP guideline) with 95% CI and 80% power and 20% of Drop Out / Non-response / Attrition, the sample size in each of the arm was 200. During the study period, TMEAD was use as a reminder for adherence to treatment in intervention arm and standard of care was followed for control arm.

The study was mixed-method which involved Quantitative Method for longitudinal follow up of the patients assigned in each arms and Qualitative Methods by interviews with key informant and In-depth interview of the family members and DOTS supporters to document the acceptance of technology and challenges if any. Adherence was also assessed by analysing trace of rifampicin in urine among 20% of patients enrolled from both arms. Health-related quality of life (HRQoL) was assessed using the EQ-5D-5L tool at baseline and follow-up. Transition probabilities were derived from primary as well as secondary literature. Time horizon of the study was one year and 3% discounting was applied. One-way sensitivity analysis was carried out by varying model parameters to estimate uncertainty in all parameters.

Conceptual framework for Decision tree model
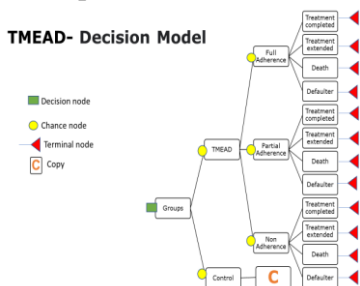
Results

Overall adherence was 94% among those who completed treatment. Adherence in the

The tornado diagram of one-way sensitivity analysis shows that ICER value is slightly changed when the input parameters were changed in multiple indicators. The cost of control arm, the cost for full adherence in the treatment completed group, QALYs among the full adherent patients in both intervention and control arm, the cost for defaulters among partial adherent to control arm were key parameters that influence the model.Budget impact analysis shows that in-order to scale up the TMEAD intervention for DSTB to the entire state of Maharashtra, the burden on the exchequer will be to the tune of 55 crores. This is just 0.02% of Maharashtra's annual health budget of 3232 crores. Further, it is important to remember that the intervention was found to be cost-effective from a health system perspective.

Outcomes	Intervention	Control
Cost (in INR) per patient treated as per modelling	6573	4764
Difference in Cost (in INR)	2042.17	
Difference in QALYs	0.176	
ICER	11,599.46	

Table 1: Incremental Cost-Effectiveness Ratio (ICER)

Conclusion

This study revealed that patient-reported treatment adherence was high in TMEAD as compared to standard therapy of care for the DSTB patients and the intervention is cost-effective. This study shows innovative approaches to adherence, promotion by creating interventions to enhance treatment adherence can improve treatment outcomes. TMEAD can complement the national strategy of TB elimination by improving adherence to the treatment regimens.

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Cost-effectiveness of Parenteral Iron Therapy for First-line Management of Iron Deficiency Anemia among Pregnant Women in a Natural Programme Setting in Gujarat

Cost-effectiveness of Parenteral Iron Therapy for First-line Management of Iron Deficiency Anemia among Pregnant Women in a Natural Programme Setting in Gujarat

Health Technology Assessment in India (HTAIn) Indian Institute of Public Health Gandhinagar

INDIAN INSTITUTE of PUBLIC HEALTH GANDHINAGAR

ESTABLISHED BY GOVT OF GUJARAT AND PFI

Policy Brief

Summary

Parenteral iron therapy is recommended to manage moderate and severe grades of anaemia. This brief explains findings from a health technology assessment study to assess the cost-effectiveness of Intravenous Iron Sucrose (IVIS) in management of moderate and severe anaemia in two districts of Gujarat
-Banaskantha and Devbhumi, Dwarka. An incremental mean change in Hb was noted in the IVIS (11.45 g/dl from 8.2 g/dl) at the time of the fourth follow-up. The mean Hb was reduced from the baseline (9.55 g/dl from 9.99 g/dl) in control arm. Per beneficiary (undiscounted) cost for IVIS was INR 7,260 and INR 4,038 for 01 group. IV iron sucrose was found to be costly but more effective than the oral therapy for the treatment of moderate and severe anemia. The ICER was calculated at INR 783.11 which is 0.049% of the country's per capita GDP (INR 1, 61,458). Further, IVIS was well tolerated as side effects are less compared to that of oral iron.

Policy implications and Novelty

•IVIS is indicated in the national guideline (1-NIPI)S for the treatment of moderate and severe anaemia. However, there is no evidence on cost-effectiveness of IVIS in local context.

•Present study aligns with 1-NIPI guideline and generates evidence on IVIS for treatment of maternal anaemia in natural program setting.

•The study outcomes has potential in contribution to the Anaemia Mukt Bharat (Anaemia Free India) strategy to achieve the ambitious target of 50% reduction of anaemia among women of reproductive age by 2025.

Recommendations

Study findings on clinical efficacy remains inconclusive due to multifactorial clinical outcomes. Considering the limited sample size and lack of blinding, larger studies are needed to validate the results findings. Future studies on clinical efficacy would be critical m establishing effect of rise in hemoglobin level on maternal and birth outcomes.

Introduction

Maternal anaerrua is a major public health issue in India. Specifically, iron-deficiency anemia (IDA) during pregnancy is a significant public health concern because of its association with perinatal mortality, preterm birth, neonatal low-birth-weight, and maternal mortality and morbidity. 1 Through intravenous iron sucrose (IVIS) administration, parenteral therapy has emerged as an effective alternative to oral treatments in pregnant women.2 Apart from its quick absorption, intravenous s (IV) mode is also known to impart a lesser incidence of hypersensitive reactions.3 A systematic review conducted by Radhika et al (2019)4 showed IVIS to be highly effective than 01 therapy.

Aim of the Study

The study aims to compare clinical efficacy and cost-effectiveness of the IVIS therapy with oral iron therapy among pregnant women with IDA in a programmatic setting at Banaskantha and Devbhoomi Dwarka district of Gujarat, India

Objectives of the Study

Primary objective of the study is to measure change in mean hemoglobin level post treatment from baseline.

Secondary objectives:

•To measure incidence of morbidity and mortality associated with iron deficiency anemia

•To measure treatment compliance to MS therapy

•To measure health-related quality of life (HRQoL) using EQ-SD tool.

Methods

The observational study was undertaken prospectively at Banaskantha and Devbhoomi Dwarka districts of Gujarat during 2020-21. Cost-effectiveness analysis was done using decision-analytic modelling with a societal perspective on healthcare costs and benefits. The target population for the study were registered pregnant women between 14- 18 weeks' gestation period who were enrolled from both districts. During the study period, patients with moderate and severe anemia were recruited. The study followed a natural Programme setting without manipulating the study environment. Classification and treatment of IDA among pregnant women was as per national guidelines. Intervention scenario (IVIS intervention) was compared with routine care scenario (where 01 therapy   was provided).   A sample of   a minimum of 32 patients in each arm in two districts or 188 patients were enrolled and 144 patients were followed-up   until   post-partum phase. Both the Programme cost i.e. the cost borne by the health system as well as the cost incurred by the patients were taken into consideration. Transition probabilities were derived from primary data for clinical indicators for both the intervention and control arms. The transition probabilities in the intervention and control arm were derived from primary study. Time horizon of the study was one year and 3% discounting was applied. One-way sensitivity analysis was carried out by varying model parameters to estimate uncertainty in all parameters.

Results

Cost-effective analysis was done based using the decision tree model. From societal perspective, IVIS incurs an incremental cost of INR 783.11 per QALY gained which is 0.49% of the per capita GDP of India. Thus, NIS intervention can be concluded to be very cost- effective.

Table 1: Results of cost-effectiveness analysis between IVIS and 01therapy

Findings

Tele-screening for DR using fundus photography is cost-saving (ICER -71'7) from a health system perspective and cost-effective from a societal perspective. (Fig.2b) However, the study pointed to considerable amounts of out-of-pocket expenditure and loss of labour associated with screening. On doing one-way sensitivity analysis, ICER in health system perspective was highly influenced by treatment uptake and cost of screening; and societal perspective ICER by utility values of late stages of DR. The budget impact analysis showed that scaling up the program to all Family Health Centers (FHCs) in Kerala will increase the burden by 16 crore rupees on the exchequer. (Table 4) However, the net impact will be saving around eight crore rupees by reducing the number of patients requiring expensive management in the late stages.

Conclusions

- The tele-screening model for diabetic retinopathy by fundus photography is a cost-effective and cost-saving tool compared to the current scenario from a health system perspective.
- It is cost-effective relative to the threshold of Indian GDP per capita, even from a societal perspective.
- The indirect expenses such as travel and wage loss cost more than the expenses of screening, hence streamlining of screening and reimbursement of travel expenses of patients need to be considered.
- As per the current model, the effectiveness of screening is dependent on the proportion of patients in the PDR stage receiving PRP/Vitreoretinal surgery. Hence, ensuring that district/subdistrict level referral hospitals can absorb the additional caseload is vital to its success.

Table 1: Treatment UDtClkP. and Budget mpact

Treatment Uptake	Screening Cost	Treatment Cost	Total Cost/FHC(Rs	Annual Cost/FHC(R	Annual Cost for
20%	12,42,1	27,72,09	40,14,264	8,02,852	13,64,84,976
30%	12,42,16	41,58,14	54,00,314	10,80,062	18,36,10,67
40%	12,42,16	55,44,19	67,86,364	13,57,272	23,07,36,376
50%	12,42,16	69,30,24	81,72,413	16,34,482	27.78,62,042
60%	12,42,16 5	83,16,29 8	95,58,463	19,11,692	32,49,87,742

Cost per test and cost of screening of rapid diagnostic tests for Sickle cell disease

To determine Cost-effectiveness of Rapid Diagnostic Tests (Hemo-Type-Sc, Sickle Scan and Gazelle) in comparison to solubility test followed by HPLC for Sickle Cell Disease/Trait diagnosis among high-risk population in India

Policy Brief

Recommendations

ICER per case detected for Hemotype SC is 3,46,437 and 3,47,466 for 2-30 years and 0-30 years, respectively.

ICER per case detected for Sickle Scan is 3,04,090 and 3,04,284 for 2-30 years and 0-30 years, respectively.

ICER per case detected suggests that if Hemotype SC Kit and Sickle SCAN Kit can be procured below INR 100, it will become cost-effective.

POC tests may be considered for adoption in Sickle cell screening programmme of neonates and children 0-2 years as existing solubility test cannot be used

POC tests are useful in identifying the SCTs and its health benefits will be reflected in next generation along with its economic benefits

Screening may be rolled out in a phased manner; Phase 1: 0-2 years; Phase 2: 2-18 years (traits), and antenatal population as well

Summary

Sickle Cell Disease (SCD) is a common genetic disorder prevalent in Sub-Saharan Africa, the Mediterranean, the Middle East, and the Indian subcontinent. Three nations, including India, bear over half of the world's SCD burden. SCD has a large impact on childhood morbidity and mortality. In India, where 1.5 lakh children are affected, 20% of infants die before the age of two. The high SCD prevalence is also reflected in the high proportion of individuals who are carriers of the sickle cell gene, also known as sickle cell trait (SCT). The overall prevalence of SCD among tribal population of India varies from 1-34%. Madhya Pradesh, has the highest load of prevalence that varies from 10%-33 % followed by Maharashtra with 0-35%, Kerala (18.2%-34.1%), Gujarat (6.3%-22.7%). With more than 5200 affected new-born with SCD each year, it is a serious public health issue in India.

The Guidelines from Ministry recommend screening and early diagnosis of SCD. Solubility test followed by confirmation with HPLC is the standard screening modality currently available in public health program. However, newborn screening cannot be performed using this method due to presence of fetal hemoglobin.

Recently, many Point of Care diagnostic tests are commercially available (not manufactured in India) for screening SCD. An HTA analysis was recommended to be carried out to assess the most cost-effective point of care test that could be used for mass scale screening of SCD.

Research Question: Which is the age group and method of population-based screening/ high-risk screening for Sickle Cell disease/traits?

Objectives:

To collate evidence on clinical-effectiveness of rapid tests (Hemo Type Sc, Sickle Scan and Gazelle) vs HPLC and solubility test to diagnose sickle cell trait/disease

To estimate cost per test of detection with rapid tests (Hemo Type Sc, Sickle Scan and Gazelle)

To assess the budget impact of using rapid test/s (Hemo Type Sc, Sickle Scan and Gazella) for universal screening vs targeted screening in the national health program

Tests for Sickle

Introduction

Sickle cell disease (SCD), an autosomal recessive disorder of the red blood cell, is the most common monogenic disease with more than 300 000 affected births annually worldwide, mostly in low- and middle-income countries. An estimated 7% of the world population carry an abnormal hemoglobin gene, while about 300,000 -500,000 are born annually with significant hemoglobin disorders. They consist of two major groups –Thalassemia and Sickle cell syndromes. Sickle cell syndromes are more frequent and constitute 70% of affected births world-wide, the rest are due to Thalassemia. Sickle cell syndromes include Sickle Cell Disease (SCD, HbSS), also called Sickle Cell Anemia (SCA), as well as disorders due to sickle cell gene combined with another hemoglobinopathy such as Hb C, E, or β thalassemia. Persons carrying only one of these genes are called 'carriers' as they do not suffer from any disease but carry the abnormal gene and transmit it to the next generation. Carriers cannot be recognized clinically but only by performing special blood tests. Where both mother and father are 'carriers', there is a chance that their children may inherit the abnormal gene from both parents and thus suffer from a severe thalassemia syndrome or a Sickle Cell syndrome or may be normal without any abnormal gene or carriers like their parents. Screening prior to conception or during pregnancy can help controlling hemoglobinopathies by preventing birth of affected children by – avoiding marriage between two carriers or by Prenatal diagnosis in pregnancies of couples where both partners are carriers, with the option of termination of pregnancy in case of an affected fetus. Newborn screening can detect abnormal hemoglobin variants like HbS, both carriers as well as those with disease (HbSS) states. SCD requires lifelong management and contributes to infant and childhood morbidity and mortality. Cost effective population screening programs are possible for detection of

HemotypeSc:
Manufactured by Silverlake Corporation USA, is a rapid diagnostic test that utilizes the competitive lateral flow immunoassay incorporating monoclonal antibodies for detection of Hb A, HbS and HbC. The kit includes, single-use test strips, single-use blood sampling devices and three reusable dropper pipette and does not need a separate buffer solution. However, it would require test vials and test tube racks for the conduct of test. It can remain viable at 15°C- 40°C for up to five years and for 30 days once opened. The time taken for carrying out the test ranges from 8 - 15 mins and requires around 1.5 microliters of blood. The limitation of the test include the inability to detect hemoglobin variants like HbD, HbE and HbF. It also cannot differentiate between HbSS and sickle-

Sickle Scan

Manufactured by Biomedomics Inc is yet another point of care for detection of sickle cell disease and works on the principle of sandwich-type lateral flow immunoassay utilizing polyclonal antibodies. It identifies HbA, HbS & HbC. The Sickle Scan test kit includes, Sickle SCAN cartridges, capillary sampler and pretreatment modules (buffer) and package insert. The time taken for carrying out the test is reported to be less than other POC tests and ranges between 5 mins to 8 mins. However, the amount of blood sample required for carrying out the test is around 5 microliters. The storage temperature is reported to be between 2 °C and 30 °C. Its ease of performance and interpretation makes it suitable to be used by non-skilled personnel. Similar to Hemotype SC, Sickle Scan cannot detect Hemoglobin variants like HbD,

Gazelle

Manufactured by Hemex health is a HemeChip cellulose acetate paper-based microchip electrophoresis system consists of Gazelle reader and Cartridge. The reader is a touch-screen tablet computer with an integrated imaging system and has a rechargeable battery. The cartridge consists of a single strip of cellulose acetate paper, a pair of blotting pads and integrated stainless-steel electrodes. Apart from HbA, HbS and HbC detected by other POCs it also detects HbA, HbF, HbA2,and HbE, thereby making it capable of differentiating between HbSS and sickle- β0-thalassemia.The time required for completion of one test by Gazelle is reported to be 13 mins and the blood volume utilized per test is approx. 0.2 microliter. It is however expected to require a skilled

Methods & Approach:

The HTA is structured to answer the policy question put forward by the Ministry about which rapid diagnostic tests (Hemo-type-Sc test, Gazelle, Sickle Scan and solubility test) is more cost effective than current standard of care in population level screening for sickle cell disease/trait. Mathematical modelling, one way and probabilistic sensitivity analysis and budget impact analysis was conducted. It was assumed that screening will be predominantly performed at primary level (70%) and rest of the screening at secondary and tertiary level. Review of literature was conducted to assess clinical effectiveness of all POCs. Robust published studies on Sickle Scan were not available in Indian settings. Gazelle was not considered a POC test due to its operational feasibility issues regarding high cost of machine, need for electric charging and expertise needed to interpret the results. The same was vetted by an experts working in the area of SCD screening.

Results:

The population to be screened was considered in a Decision Tree analytical model and analysed in three different age groups. The cohort size for age group 0 to 2 years, 2 to 30 years and 0 to 30 years was 1.37 crores, 3,07 crores and 3,41 crores, respectively. These populations were selected from the tribal districts of the 6 highest burden states (Hockham *etal.,* 2018) i.e Tamil Nadu, Chhattisgarh, Maharashtra, Odisha, Gujarat and MP (Census 2011) for sickle cell disease. According to the model, cost per individual screened using the POC tests Hemotype SC and Sickle Scan is INR 250.17 and for solubility test followed by HPLC as a confirmatory test is INR 53.32.

Screening through Hemotype SC could detect 56,180 cases, 4.97 lakh and 5.52 lakh in age group 0 to 2 years, 2 to 30 years and 0 to 30 years, respectively. Screening through Sickle Scan could detect 56,465, 5 lakh and 5.55 lakh cases in age group 0 to 2 years, 2 to 30 years and 0 to 30 years, respectively. If solubility followed by HPLC is used for screening, then 4.79 lakh and 5.32 lakh cases could be detected in age group 2 to 30 years and 0 to 30 years, respectively. Table 1 (with 95% CI values) describes all model parameters, such as, cost of rolling out screening programme in target population using the two POC tests and solubility test followed by HPLC.

## One way sensitivity Analysis (OWSA) for Price Threshold:

ICER per case detected suggests that if Hemotype SC Kit can be procured below INR 100 it will become cost effective. Similarly, if Sickle SCAN Kit can be procured below INR **110,** it will become cost-effective.

Probabilistic Sensitivity Analysis PSA:

To check the robustness of the model and address uncertainty, probabilistic sensitivity analysis (PSA) was also conducted. Using monte carlo simulation method, we ran 1000 simulations for various parameters, such as, prevalence, cost etc. Median of 999 values and lower and upper limits of 95% CI intervals were ascertained corresponding to 2.6 percentile and 97.5 percentile values.
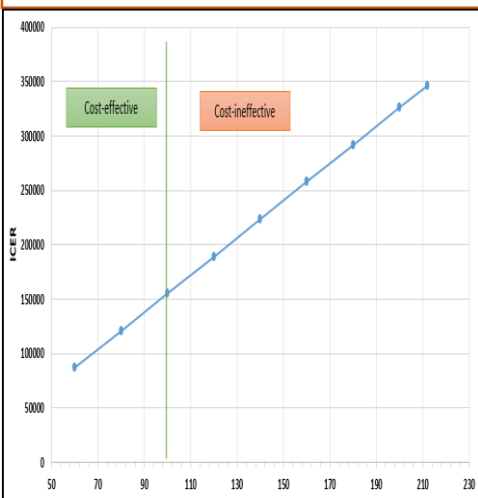
Price of Hemotype SC Kit in INR
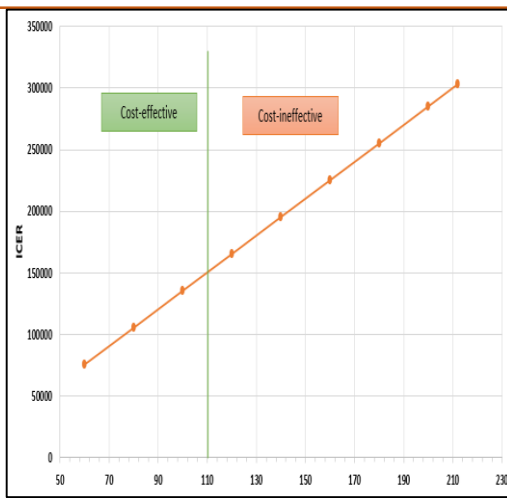
Price of Sickle Scan Kit in INR

Policy Brief

Budget impact analysis showing Total health system Cost of rolling out screening populations residing in tribal districts of 6 high prevalence states in different age groups using Hemotype SC, Sickle Scan and solubility + HPLC.

Strategy	In 0-2 years Population (95% CI) 34,56,509 Population	In 2-30 years, Population (95% CI) 3,06,75,481 Population	In 0-30 years, Population (95% CI) 3,41,31,990 Population
Cost of rolling out screening program with Hemotype SC	89.58 (84.11 – 94.91) Crores	797.71 (746.38 – 841.86) Crores	885.53 (834.18 – 942.87) Crores
Cost of rolling out			

A budget impact analysis was conducted to find the total health system costs of rolling out screening program with Hemotype SC, Sickle Scan and solubility + HPLC.

Conclusion

To summarize, both the Hemotype Sc and Sickle Scan POC tests to diagnose Sickle Cell Disease/Trait will be cost-effective for screening. The screening strategy could be rolled out in the six states of Tamil Nadu, Chhattisgarh, Maharashtra, Odisha, Gujarat and MP (Top 6 are states with high prevalence of Sickle Cell Disease among newborns. Screening may be rolled out in a phased manner, with phase one being 0-2 years and phase 2 being 2-30 years, including antenatal population as well. HPLC is only required for tertiary care.

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Cost effectiveness of IV trenexamic acid for treatment of PPH

Aims and Objective:

This study aimed to address the policy question of whether India should consider adding IV trenexamic acid for all primary PPH case management in the Indian public health system. To estimate cost-effectiveness of addition of IV Trenexamic acid to standard care treatment in the Indian public health facilities. To assess budget impact of introducing trenexamic acid in the Indian public health

Decision analytic modelling approach was adopted to answer the given policy question. A decision tree model was designed based on Indian guidelines specific to public healthcare levels/facility accessed by women for childbirth.

Perspective: Disaggregated Societal {includes health system plus out-of-pocket expenses for patients) **Population:** Hypothetical cohort of 21 year old women accessing public facilities for PPH management **Intervention:** IV TXA (1oomg/ml/ min) addition to standard care within 3 hours of birth **Comparator:** Uterotonics, supportive care **Outcome:** Cost per QALY gained, number of maternal deaths, surgeries and ICU admissions associated

Analysis:
Analysis was undertaken using HTAin reference case manual. (3) A life-time horizon was considered for analysis to account for associated health outcomes**.** Clinical and epidemiological input parameters were obtained from WOMAN trial study and literature relevant to the Indian context.C4l**.** Health system cost data was obtained from a primary bottom-up micro-economic costing exercise undertaken across public healthcare levels in India. Sensitivity analysis was undertake: Budget impact was analyzed for a 5 year period using phased bottom-up uptake of intervention from primary to tertiary care level

Diagrammatic representation of the model
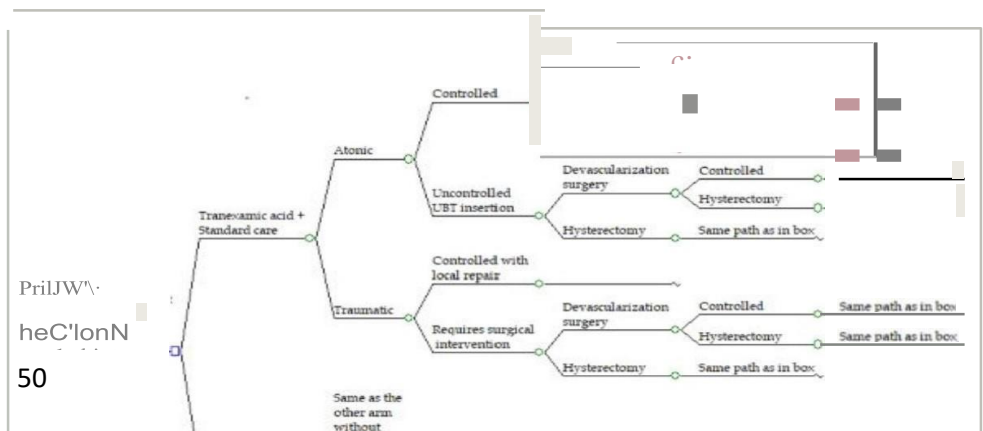
Results:

For an estimated annual cohort of 5,10,915 women who experience primary PPH in Indian public health facilities, a disaggregated societal cost of INR 6,607 is incurred per patient for PPH management with an associated gain of 20.25 discounted QALYs. Similarly, management without TXA i.e. current standard of care treatment results in a societal cost of INR 6,486 per patient with a gain of 20.16 QALYs. Addition of TXA results in a marginally higher cost incurred but is also associated with marginally better health outcomes and thus at an ICUR value of INR 1,470 per QALY gain is cost-effective. For the above cohort, this intervention is

10,000 Monte Carlo simulations for ICUR QALY
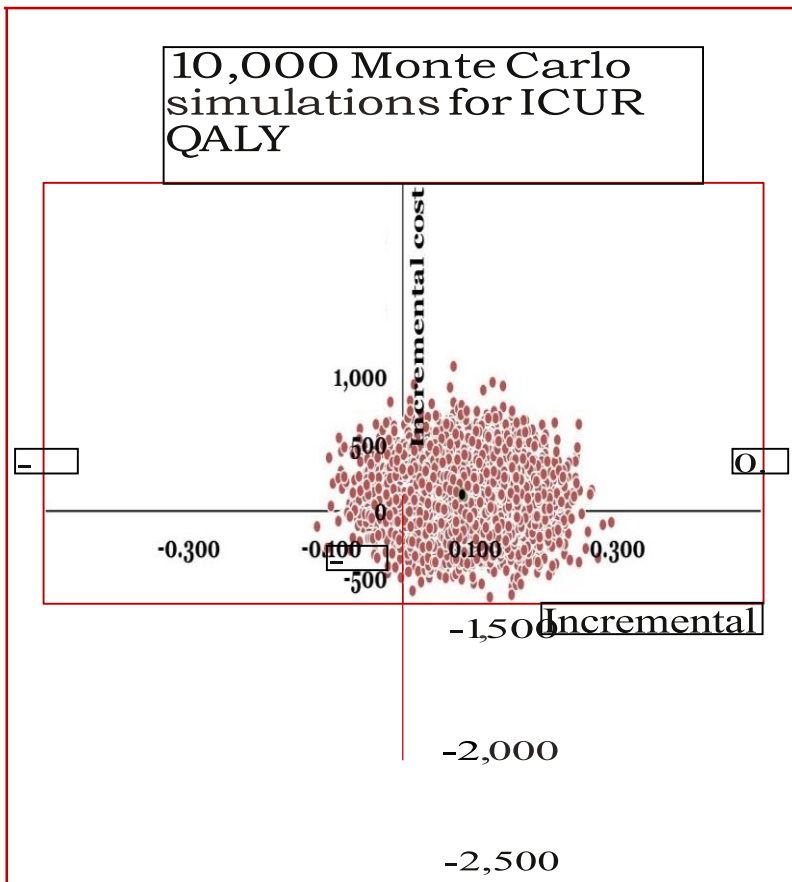
Budget Impact Analysis

This analysis aimed to assist policy makers in predicting the financial consequence of adoption and diffusion of this intervention at the national level. Uptake of TXA intervention was considered to be bottom-up in nature with implementation assumed! to take place from primary level care in the first year to addition of secondary and tertiary levels in subsequent years respectively. Budget impact analysis suggested an incremental cumulative increase in financial allocation by 2.3% over a five-year period to that currently allocated for management of primary PPH in Indian public health settings.

Conclusion:

Addition of intravenous Trenexamic Acid for primary PPH management within three hours of birth with an additional dose if required after 30 minutes or within 24 hours if bleeding restarts can be considered in the Indian public health settings from a cost-effectiveness perspective Indian policy guidance, training manuals and facility checklists on PPH management have to be updated to reflect this recommendation if accepted.

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Dengue screening strategy at PHC level for reducing the Dengue disease burden in Tamil Nadu

Decentralized dengue screening strategy at primary health care level for reducing the dengue disease burden in Tamil Nadu

HTAin Secretariat, Department of Health Research, Ministry of Health & Family Welfare, New Delhi
Regional Resource Centre for HTAin, ICMR-National Institute for Research in Tuberculosis, Chennai
April 2021

Policy Brief

Summary

Lack of effective early screening is the major obstacle for reducing the fatality rate and disease burden in dengue. Considering which the Government of Tamil Nadu has adopted decentralized dengue screening strategy at Primary health care settings using blood platelet counter. This policy brief focusses on the cost-effectiveness of this proposed strategy, so as to inform the policy makers and assist in evidence based scaling up of this strategy. A model based study was conducted to find out the cost-effectiveness of this proposed strategy in comparison to the current practice at tertiary healthcare centers. The study found that the decentralized dengue screening strategy was cost saving and more effective than the current practice. However, it is recommended to consider economic human resource cost and collateral benefits of the equipment for implementation

Problem Statement:

Dengue is the most common vector borne infection globally, with an estimated 100 to 400 million infections occurring every year.1 There is no effective vaccine or medicine available to prevent or cure dengue and it leads to around 20,000 deaths per year.2 High dengue disease burden and frequent outbreaks result in an adverse impact on country's economy and strain the health system. Lack of effective early screening is the major obstacle for reducing the fatality rate and disease burden in dengue. India contributes around 34% of the global burden of dengue. Although dengue is notifiable disease in India studies and modelling estimate suggests that the disease is grossly under reported due to the existing gaps in the public health surveillance system. Tamil Nadu is a one of the largest state in India which reported high burden of dengue infection.

Recommendations:

Decentralized dengue screening strategy at primary health care (PHC) level for dengue fever suspects helps in early diagnosis. This enables the patient to receive appropriate early treatment and timely care which will subsequently reduce the dengue severe and death cases. Thereby reducing the morbidity and mortality due to dengue. The dengue screening at PHC level for fever suspects in Tamil Nadu is cost saving when compared to the current practice at tertiary health care (THC) level. Considering implementation cost the proposed decentralized screening strategy is found to be cost at 80% coverage in the PHC over a period of five years. The high implementation cost will gradually decrease over years as majority of which is attributed to the one time proposed strategy global burden of dengue. Although capital investment of the equipment. The implementation of dengue screening strategy may effectively address the dengue disease burden in the state with cost saving to the NVBDCP in Tamil Nadu. However, it is recommended to take economic cost of human resource and collateral benefits of the equipment into consideration before scaling up of this screening strategy.

Background:

Although dengue is a notifiable disease in India, studies and modelling estimate suggests that the disease is grossly under reported due to the existing gaps in the public health surveillance system. Dengue surveillance in India is conducted through a network of more than 600 sentinel hospitals under the national vector-borne disease control programme (NVBDCP), Integrated Disease Surveillance Program (IDSP) and a network of 52 Virus Research and Diagnostic Laboratories (VRDL).4 High dengue disease burden and frequent outbreaks result in an adverse impact on country's economy and strain the health system. Tamil Nadu is a one of the largest state in India which reported high burden of dengue infection. Lack of effective early screening is the major obstacle in the timely detection of dengue in the state which could reduce the fatality rate of dengue. The diagnosis of dengue is usually made clinically. Diagnosis of dengue hemorrhage fever (DHF) can mask end stage liver disease and vice versa. The clinical diagnosis of dengue is complex due to non- specific symptoms and symptoms similar to other infections. One of the major hindrance in the control and management of dengue infection is the lack of timely and point-of-care diagnosis. The complex clinical presentation of dengue symptoms and lack of rapid screening and diagnostic tests results in delay in diagnosis and leads to rapid disease progression and mortality

Key Messages

The burden of dengue in India is high due to its high prevalence and high mortality rate. Lack of effective early screening is the major obstacle for reducing the fatality rate of dengue. At present dengue control in Tamil Nadu is being prioritized to strengthen diagnostic services and surveillance. One of the strategy adopted by the Government of Tamil Nadu is to implement blood platelet counter for screening of dengue at primary health care settings in Tamil Nadu. Under this strategy the present delay in diagnosing dengue at an earlier stage is prioritized, which could help in reduction of dengue morbidity and mortality, The proposed screening strategy for dengue at PHC level was found to be less costly and more effective than the current strategy. This was mainly due to the reduction in the number of deaths and severe dengue cases as a result of early detection and management in proposed strategy.

Decentralized dengue screening strategy

Screening and diagnosis are done at Tertiary Health Care (THC) facilities in Tamil Nadu. The Government of Tamil Nadu has recently proposed a decentralized dengue screening strategy at Primary Health Care (PHC) settings using blood platelet counter using hematology analyzer. Platelet count is assessed and those with less than 1OOOOO/mm3 platelet count will be referred to the THC facility for further management. In dengue suspects with more than 100000/mm3 platelet count will be re-assessed at two days interval. A maximum of two times repeat platelet count will be undertaken to rule out dengue (Figure- I). Under this strategy the present delay in diagnosing dengue at an earlier stage is prioritized which could help in reduction of dengue morbidity and mortality.

Summary of Evidence:

Implementation of hematology analyzer at PHC is cost saving. The ICER was estimated to be -41197 for proposed strategy over current strategy. Average incremental net monetary benefit (INMB) for the proposed strategy over control strategy was estimated to be 6105504 Sensitivity analysis showed the parameter utility of dengue hemorrhage fever and dengue shock syndrome, indirect cost of fatal cases, life expectancy of the cohort, non- medical cost of non-fatal cases, hospitalization cost and ambulatory cost of non-fatal cases had higher influence on ICER value.

Probabilistic sensitivity analysis found that 84% of the resulting ICER value was less costly and more effective. Budget Impact analysis showed additional budget requirement of 57 million for government in the base year for implementation of the proposed screening strategy

Total cost
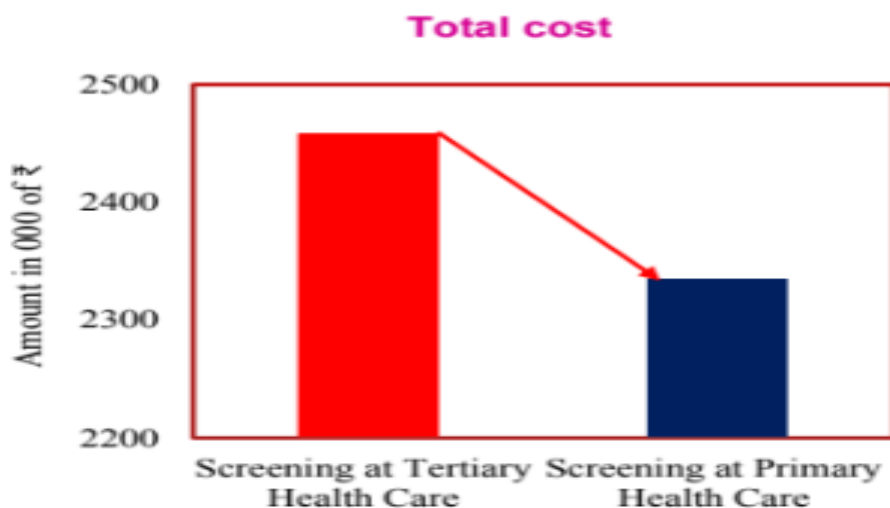
Conclusion:

The decentralised nature of our proposed diagnostic strategy was identified as a cost-saving intervention for both health system and patients. The out-of-pocket expenditure experienced by patient was found to be decreased due to the proposed intervention. The cost saving strategy could be due to early diagnosis followed by early treatment resulting in prevention of acute and prolonged illness due to delayed diagnosis.

Reduction of out-of-pocket expenditure

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HTA of TeCHO+
Programme in Gujarat

Health Technology Assessment of TeCHO+ Programme in Gujarat

INDIAN INSTITUTE OF PUBLIC HEALTH GANDHINAGAR

Policy Brief

Summary

Gujarat has been implementing mHealth Programme known as TeCHO+ (Technology for Community Health Operations). A TeCHO+ enabled mobile phone was provided to all Female Health Workers of the State in 2019. This brief addressed the cost-effectiveness of TeCHO+ as compared to E-Mamta in Gujarat.

The study participants were surveyed from 48 sub-centers across 24 Primary Health Centers from 6 Talukas of Gujarat's three selected districts. A total of 385 postpartum women and mothers of 230 children were assessed at baseline and 357 postpartum women and mothers of 157 children after one year of Programme intervention in 2020.

Key Findings

The annualized cost incurred for the TeCHO+ Programme was estimated to be INR 376, 08,26,815. With this investment, the calculated cost per beneficiary amounted to (INR) 2424. The cost-effectiveness analysis indicated that TeCHO+ incurs an incremental cost of INR 1802.84 per DALY averted, which is below the GDP per capita of India.

Recommendations

Cost-effectiveness analysis clearly shows that TeCHO+ is cost-effective for Mother and Child Care. It incurs an incremental cost of INR 1802.84 per DALY averted, which is below the GDP per capita of India. Further, TeCHO+ Programme has significantly improved health service delivery through increased accuracy of data management, high risk identification, quality and accessibility of care. The study findings indicate that the TeCHO+ Programme can be considered for replication.

Introduction

The Health & Family Welfare Department, Gujarat introduced TeCHO+ (Technology for Community Health Operations) since 2019, replacing e-Mamta - the mother and child tracking system. TeCHO+ is a mobile & web-based application that essentially enables data entry by the person providing service at the time and place of service delivery to improve the coverage and data quality. The Programme encompasses unique features such as real-time data entry, generates alerts for high-risk cases, tracks beneficiaries as well as health workers, a web-based dashboard that enables health officials at different levels to access progress reports, and extends supportive supervision to health workers. These unique features are expected to enhance Gujarat's performance in eleven priority areas.

Policy Implications and Novelty

•The study outcomes has pontial in contributing to the increased access to quality antenatal care in pregnancy, as well as post-natal care.

•TeCHO+ Programme attempt to overcome gaps in MCH data and link data with facility and services.

•No cost-effectiveness evidence available of the TeCHO+.

Aim of the study

The study aims to compare cost-effectiveness of the TeCHO+ and eMamta in Gujarat, India

METHODS

The study compared key Programme outcome indicators before and after the launch of TeCHO+ Programme. Cost-effectiveness analysis was done using decision-analytic modelling with health system perspective.

Sample size

The study participants were surveyed from 48 sub- centers spread across the three selected districts of Gujarat. The selection of the district was done based on the category of HDI ranking of Gujarat and maturity of TeCHO+ Programme. The selection of Talukas was done purposively based on their distance to their respective headquarters. However, a simple random sampli ng method was adopted to select the PHC and Sub-Centre using a table of random numbers.

We have two scenarios I) Cost analysis without software development cost and 2) cost analysis with software cost derived from pilot project ImTeCHO. TeCHO+ is based on success of ImTeCHO pilot. ImTeCHO software development cost was INR 46, 00,000 at 2016-17 price. Annual maintenance cost was INR 36, 74, 375/-.The project was piloted in 11 PHCs. Thus for 1100 PHCs, one-time cost of software development was calculated as INR 46,00,00,000 at 2016- 17. The annualized cost for software development is calculated as INR 36, 74, 37,500 and INR 53, 22, 35,151 for software maintenance at 2019-20 price. Total software cost (including maintenance cost) calculated its INR 95, 73, 72,441.

Quality of data

Quality of data reporting m follow-up survey improved as compared to baseline for all the indicators except for full ANC and reporting of delivery in trust hospitals. Improvements are noted in the case of consumption of iron-folic acid (JFA) tablets, delivery reported in government hospitals, medical termination of pregnancy and early initiation of breastfeeding. The concordance rate for routine maternal health indicators (a measure of data accuracy) improved from 69.1% to 80.5%. There is marked improvement specifically of the consumption of 180 JFA tablets (I6.3 % increase in coverage) and initiation of breast feeding within an hour of birth (18.5% increase in coverage).Improvement in coverage of important health indicators such as full ANC examination (80. l% vs 77.9%, p-value=<0.0001), consumption of at least 180 iron-folic acid tablets (93.5 % vs 77.2 %, p- value<0.000 I), and early initiation of breast feeding (42.7% vs 24.2%, p-value<0.001) were found to be statistically significant at 5% level of significant and 95% Confidence Interval. Improvement in quality of data reporting were observed for almost all the child health indicators during the follow-up survey. However, a marginal decline of quality of reporting was found for BCG vaccination at birth (change in concordance from 96.7 to 95.2 at follow-up) and full immunization (change in concordance from 89.6 to 87.5 at follow-up). The concordance rate for routine child health indicators improved from 86.6% to 92.1%. Improvement in coverage of HBVO vaccination (67.2% vs 35.3%, p-value<0.0001) and Pentavalent 2 (100% vs 95.1%, p-value=0.015) were found to be statistically significant at 5% level of significance and 95% Confidence Interval.

Matched case analysis

Since the eMamta data is considered as control, it could have resulted in bias in the analysis. To minimize this, propensity score method (PSM) was used to control demand side characteristics among women in intervention and control groups which could influence utilization of various MCH services. Thus, each woman in the intervention arm was matched on the basis of socio-demographic characteristics (such as religion, caste, region, socio-economic status). After matching, the women from intervention and control arms (n=250 each) were similar in terms of all socio-demographic characteristics, except the distribution of religion. However, the difference was very small - 41.5% and 38.5% were Muslims in both intervention and control arm. We found a statistically significant change in ANC/PNC visits, IFA consumption, high risk identification, referral, and breastfeeding within an hour between intervention and control arm. However, there was statistically insignificant change in institutional delivery, 2 TT received, and child immunization.

Cost-effectiveness

Cost-effective analysis for the TeCHO+ was done based using the decision tree model. From health system perspective, TeCHO+ incurs an incremental cost of INR 1802.84 per DALY averted of pregnant women and children which is 1.19% of the GDP per capita of India. Sensitivity analysis shows that ICER remains largely unchanged even if the input parameter is changed in multiple indicators.

Budget Impact Analysis (BIA)

Budget Impact Analysis (BIA) has been performed to estimate the cost for the roll-out of IVIS intervention at the State level. State-wide scale-up for other states would cost INR 283, 21, 74,314 for the first year, with lower costs in subsequent years. This cost is exclusive of software cost as software cost is highly variable. The nationwide scale cost covering 1, 52,326 sub- centers in the country is projected. The budget for 1st year is INR 7804, 66, 95,803/-. The budget of subsequent years is on the lower side except for the fifth-year budget, which 1s higher (INR 8608, 94, 49,343) considering 90% of service coverage, mobile replacement and the need for training.

Conclusion

Cost-effectiveness analysis clearly shows that TeCHO+ is cost-effective for Mother and Child Care. It incurs an incremental cost of INR 1802.84 per DALY averted, which is below the GDP per capita of India.

Recommendations

The TeCHO+ Programme is cost-effective and can be considered for replicating in other states or nationwide scale-up.

Feasibility and effectiveness of Community – based screening for Chronic Kidney Diseases

Health Technology Assessment in India
Department of Health Research, MoHFW

Cost effectiveness of population-based screening for Chronic Kidney Disease among adults aged 40 years and above with Type 2 DiabetesMellitus in Kerala and Puducherry

SUMMARY

Chronic Kidney Disease (CKD) is a major public health problem with increasing incidenceand prevalence, associated with a high risk of kidney failure, cardiovascular disease and premature mortality. Patients with type 2 diabetes are more than twice likely to develop CKD as compared to those with type 1 diabetes. Early detection (screening) and treatment of CKD halts the progression to end-stage renal disease (ESRD). But, currently there is no population-based screening for CKD in India. Therefore, we have undertaken a Health Technology Assessment (HTA) study to evaluate the cost-effectiveness of population-based screening for CKD in Kerala and Puducherry among the normotensive type 2 diabetic mellitus patients aged 40 years and above as compared to the current no screeening scenario. We found that population-based screening using spot urine dipstick-microalbuminuria followed by albumin creatinine ratio (ACR) test and serum creatinine, was cost-effective at one time GDP per capita of India. Compared to the current scenario, implementing Scenario 1 would prevent 179 ESRD cases per lakh population over the nextten years.

Introduction

CKD is a condition of structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR) for three months or longer. In India, the prevalence of CKD ranges between <1% and 17% (1). Patients with type 2 diabetes (T2DM) are more than twice likely to develop CKD as compared to those with type 1 diabetes (2). In India, CKD is the leading cause of kidney failure or end-stage renal disease (ESRD). About 2.2 Lakh people are diagnosed with ESRD every year (3) and over 90% of patients of them are unable to pay for renal replacement therapy (RRT) who eventually die due to lack of care (4). Currently, there is no population-based screening for CKD in India. But, studies from Asian countries showed population-based screening for CKD using micro-albuminuria as cost- effective. Therefore, we evaluated the cost-effectiveness of two population-based screening scenarios for CKD in Kerala and Puducherry among the normotensive type 2 diabetic mellitus patients aged 40 years and above, as compared to the current scenario. The two scenarios considered in the study are as follows:

Scenario 1: Spot urine dipstick-albuminuria was done twice with the interval of three months followed by spot urine ACR test and serum creatinine.

Scenario 2: Spot urine ACR test and serum creatinine were done in a parallel manner. In both scenarios, community healthcare workers (CHW) reach out to the households and measure blood pressure using digital sphygmomanometer in household members who are aged ≥40 years, followed by screening those normotensive members for type 2 diabetes using glucometer. Those normotensive T2DM patients were screened for CKD by either of the two screening scenarios.

Methodology

A decision tree combined with the Markov model was developed to analyze the screening process and changes in the natural progression of CKD under two population-based screening strategies, relative to the current scenario. A mathematical cohort (n=1) of diabetic patients was simulated over a lifetime horizon with an annual cycle. We adopted a societal perspective, taking into account direct and indirect medical expenditure along with income lost due to illness. The input parameters for the model were derived from a WHO STEPS survey, national sample survey, National Health System Cost Database for India and other relevant literature. The incremental cost-effectiveness ratio (ICER) and Net Monetary Benefit (NMB) estimates were generated for both the scenarios along with sensitivity analyses and budget impact analysis.

Results

The ICER per QALY gained for the CKD screening scenario 1 and scenario 2 were ₹ 13,916 and ₹ 14,751, respectively. (Table 1) Both the ICER values were cost-effective at the threshold of the one-time per capita GDP of India. Comparatively, screening scenario 1 was more cost- effective than scenario 2. The NMB for scenario 1 and scenario 2 were ₹ 8.4 crores and ₹ 4.9 crores, respectively. The budget impact analysis showed that the current no screening scenario resulted in a societal cost of ₹ 385 crores in Puducherry and ₹ 9,303© crores in Kerala. Scenario 1 was found to be a low-cost option than the scenario 2 for both the states. If the scenario 1 is implemented, the treatment costs associated with ESRD are expected to go down by ₹ 2.15 crore over of the next ten years, with reduction in the incidence of ESRD cases by 179 per lakh population over ten years. (Table 2)

Table 1: Base case results of CKD screening scenarios

	Non-screening	Screening scenario 1	Screening scenario 2
Total cost	₹ 45,407	₹ 98,741	₹ 100,096
Total QALY	7.6	15.2	15.3
Total life years	10.2	19.6	19.4
Incremental cost		₹ 53,334	₹ 54,689
Incremental QALY		7.6	7.7
Incremental life years		9.4	9.2
ICER/QALY gained		**₹ 7,039**	**₹ 7,136**
ICER/Life year saved		**₹ 5,685**	**₹ 5,961**
Discounted Estimates			
Total cost	₹ 40,927	₹ 119,139	₹ 89,132
Total QALY	6.1	11.7	9.4
Total life years	-	-	-
Incremental cost		₹ 78,212	₹ 48,205
Incremental QALY		5.6	3.3
Incremental life years		-	-
ICER/QALY gained		**₹ 13,916**	**₹ 14,751**
ICER/Life year saved		**₹ 5,138**	**₹ 5,254**

Conclusion

The screening scenario 1 is more cost-effecive than the scenario 2 for population-based screening for CKD. Given the current health spending of Kerala and Puducherry, both the screening scenarios were not financially feasible for implementation.

Policy implications:

If implemented, early detection of CKD through the population-based screening could reduce the incidence of ESRD cases over time. Population based CKD screening could reduce the expenditure incurred under the Pradhan Mantri National Dialysis Programme.

Table 2: Impact of population-based screening for CKD on the number of ESRD cases and the associated treatment cost over the ten years

Year	Number of ESRD cases			Number of cases prevented		Treatment cost saved (₹ in Lakhs)
	No screening	Screening scenario 1	Screening scenario 2	Scenario 1 vs 2	Scenario 1 vs No screening	Scenario 1 vs No screening
1	1142	1142	1142	0	0	0
2	1083	1083	1083	0	0	0
3	897	894	894	0	3	18.2
4	658	649	648	-1	9	64.8
5	465	447	446	-2	18	121.0
6	328	303	301	-2	25	170.0
7	236	207	204	-2	30	203.8
8	175	143	141	-3	32	220.3
9	135	102	100	-3	32	221.7
10	107	76	74	-2	31	212.5

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Clinical Effectiveness and Cost-Effectiveness of Cholecystectomy Compared with Conservative Management in People Presenting with Uncomplicated Symptomatic Gallstones (Biliary Pain) Or Cholecystitis in India

Cholecystectomy or conservative management for uncomplicated symptomatic gallstones (biliary pain) or cholecystitis ?
A Health Technology Assessment in India

## Health Technology Assessment in India (HTAin) ICMR-National Institute of Epidemiology

Recommendations:

Laparoscopic cholecystectomy to be preferred over open cholecystectomy unless deemed necessary in cases of the complicated gallbladder Early LC (within 72 hours of admission or 7 days from symptom onset) to be a preferred treatment option for uncomplicated cholelithiasis and acute Cholecystitis Evidence should be generated on long-term effectiveness of conservative management and health-related quality of life for gallstone disease in Indian context

Background:

Gallstone disease impose a significant economic burden on the healthcare systems. With the advent of laparoscopic cholecystectomy, it has become the most preferred treatment for cholelithiasis/Cholecystitis, proven clinical effectiveness yet seems costly. Conservative management, which involves pain and symptom management, has also shown effectiveness towards cholelithiasis and Cholecystitis and carries a low risk of complications and is considered an alternative to surgery in the clinical practice6. Therefore, determining cost-effective management options for gallstones for implementation into the Indian health care system is critical. This substantiates the importance of conducting health technology assessment to determine the cost-effectiveness of cholecystectomy compared with conservative management in people presenting with uncomplicated symptomatic gallstones (biliary Pain) or Cholecystitis.

Summary

Gallstone disease is the sixth commonest problem requiring surgery and emergency hospitalization in India thus imposing a significant economic burden in Indian healthcare system1. The policy question of whether cholecystectomy or conservative management (CM) should be recommended for gallstone treatment is addressed in this brief. Health Technology Assessment (HTA) been the chosen approach to explore this question. Clinical effectiveness was assessed through systematic review and met analysis (SRMA) of randomized control trials investigating the effectiveness of early cholecystectomy compared to CM/delayed cholecystectomy2. SRMA findings showed that Early cholecystectomy is effective than CM as it result in a fewer biliary complications and a reduction in reported abdominal pain. Cost-effectiveness was assessed using decision analytic Markova model utilizing data from secondary literature. The results showed that Early laparoscopic cholecystectomy (ELC), compared to Delayed laparoscopic cholecystectomy (DLC), incurred an incremental cost of -'12,001 (-$161) for 0.0002 QALYs gained, resulting in an ICER of -'6, 43, 89,441 ($8, 66,755) and is cost-saving. ELC and DLC, compared to CM, incurred an incremental cost of -'10,948 ($147) and, 1,054 ($14) for 0.032 QALYs gained. The ICER was -'3, 42,758 ($4,609) for ELC compared to CM, suggesting ELC is cost-saving and 33,183 ($446) for DLC compared to CM, suggesting DLC is cost-effective compared to CM. Further, sensitivity & Scenario

North
2-3 times higher

Prevalence 6 to 20 %[3,4,5]

South
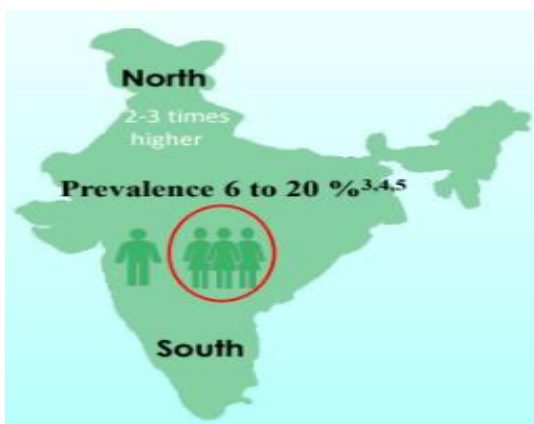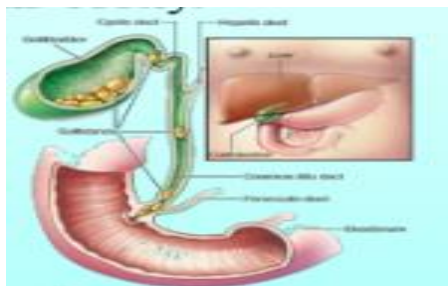
Assessment of clinical and cost- effectiveness

We systematically searched randomized control trials investigating the effectiveness of early cholecystectomy compared to conservative management/delayed cholecystectomy. We pooled the risk ratios with a 95% confidence interval, also estimated adjusted number needed to treat to harm. We conducted a cost-utility analysis using the decision-analytic Markov model to calculate and compare the costs and QALY of Early laparoscopic cholecystectomy vs. Delayed laparoscopic cholecystectomy, early laparoscopic cholecystectomy vs. Conservative management and Delayed laparoscopic cholecystectomy vs. Conservative management in patients with symptomatic uncomplicated gallstone/Cholecystitis. We adopted a lifetime time horizon with one-year cycle length from an Indian health system perspective. Clinical, cost and utility data were obtained possibly through systematic review and met analysis or from secondary literature. Both costs and outcomes were discounted at a 3% annual discount rate. Incremental cost-effectiveness ratio was calculated, and the cost-effectiveness was determined with India's 2020 GDP/capita as the willingness to pay threshold. The cost values are reported in INR and USD (1USD=74.37 INR). One-way and probabilistic sensitivity analyses were performed to test parameter uncertainties.

Key Findings

Cost-saving, Clinically effective, Requires clinical decision regarding the timing of surgery, whether early or delayed surgery?, Costs '38,883 ($520) including management of surgical complications and lifetime costs of managing recurrence symptoms, Gains 17.14 QALYs/person over a lifetime horizon

Cholecystectomy (open or laparoscopic) is cost-effective than conservative management for symptomatic uncomplicated gallstone disease (biliary colic) and acute Cholecystitis. Early cholecystectomy is cost-effective than conservative management for symptomatic uncomplicated gallstone disease. Early cholecystectomy is cost-effective for acute Cholecystitis than conservative management/delayed cholecystectomy. However, it may require a clinical decision regarding the timing of surgery, whether early or delayed surgery with initial symptomatic management followed by cholecystectomy (6-12 weeks later), considering the possible intraoperative complications in early surgery. More evidences are needed on Conservative management's effectiveness for symptomatic uncomplicated gallstone disease and acute Cholecystitis.

Budget Impact for Tamilnadu

The estimated budget for early cholecystectomy was ₹1,488 corers ($200 million) in 2021 considering 25% treatment coverage. This represents 7.9% of Tamil Nadu's 2021 health budget (₹18,632 corers ($2505 million) and will reach 21.23% of the projected health budget with full (100%) coverage by 2024. However, the budget requirement reduces in the subsequent years as the number of eligible patient's decreases with the increase in yearly coverage, and only the annual new cases would necessitate treatment.

Conclusion:

Cholecystectomy results in fewer biliary complications and a reduction in reported abdominal pain than conservative management. Early Laparoscopic Cholecystectomy is cost saving compared to other treatment options, hence should be the preferable option of gallstone disease management.

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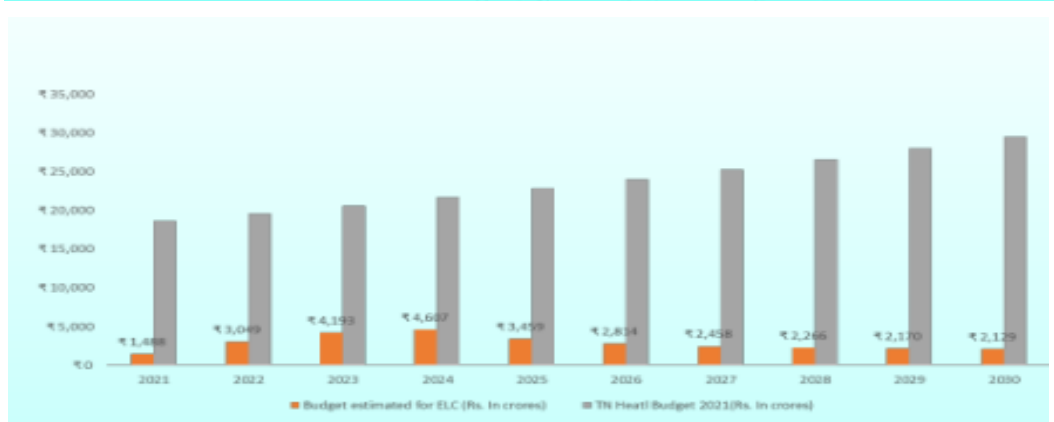
treatment.

State-wise estimated additional budget (in percentage) for offering Early LC

Available technologies for detection of diabetic retinopathy from color fundus photographs to prevent blindness in India

Available technologies for detection of diabetic retinopathy from colour fundus photographs to prevent blindness in India

Regional Technical Resource Centre for Health Technology Assessment, AMCHSS, SCTIMST, Trivandrum

Summary

A Health Technology Assessment was conducted to establish the cost-effectiveness of diabetic retinopathy screening of people with diabetes using tele-screening (retinal images/ color fundus photographs) compared to non-screening strategies. A budget impact analysis was also conducted to evaluate the overall costs of implementing systematic teleophthalmology-based screening for diabetic retinopathy to the whole state.

Tele-screening for diabetic retinopathy using fundus photography was found to be cost-saving from the health system perspective and cost-effective from the societal perspective. However, considerable out-of-pocket expenditure and loss of labour associated with screening were pointed out by the study.

The incremental cost-effectiveness ratio in the health system perspective was highly influenced by treatment uptake and the cost of screening. The budget impact analysis showed that scaling up the program to all Family Health Centers (FHCs) in Kerala will increase the burden by 16 Crore rupees on the exchequer although the net impact will be saving around 8 Crore rupees by reducing the number of patients requiring expensive management in late stages.

Recommendations

In states like Kerala, which has a robust primary healthcare infrastructure with functioning NCO clinics, the inclusion of the tele-screening model into the diabetic retinopathy care pathway is recommended as it is beneficial to the patient and the health system. However, ensuring that district-level hospitals have the capacity to absorb the patient yield from screening who require specialized ophthalmic care is important.

Background

The state government of Kerala is pressing forward to achieve universal health coverage and address the SDG on health access. The state has a high prevalence of diabetes. A recent report from Kerala suggests that one in five of the Kerala adult population has diabetes. The prevalence of diabetes mellitus in India vary from 18-34%, and Diabetic Retinopathy {DA) is a common micro vascular complication of diabetes mellitus. Diagnosis of diabetic retinopathy in the early stages can have a significant effect on its prognosis. Therefore, there is an urgent need to tackle the complications of diabetes.

The state government launched the Aardram Mission in 2017 to transform the public healthcare system to achieve the SDGs in phases with short-term goals on building infrastructure and quality care services. Evidence from across the world has shown that systematic DA screening has been effective in reducing blindness. In Kerala, the transformation of primary care through the Aardram Mission with a focus on NCDs provides the backdrop to implementing a DA care pathway attached to the established NCO clinics.{Fig.1) A Markov and decision tree model was used to simulate and analyse the screening process.
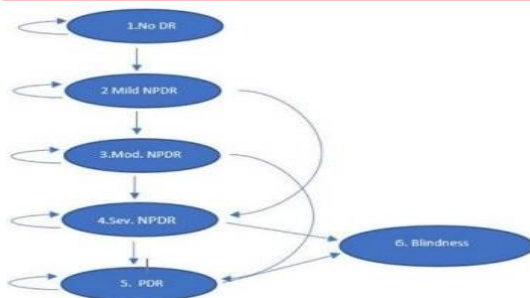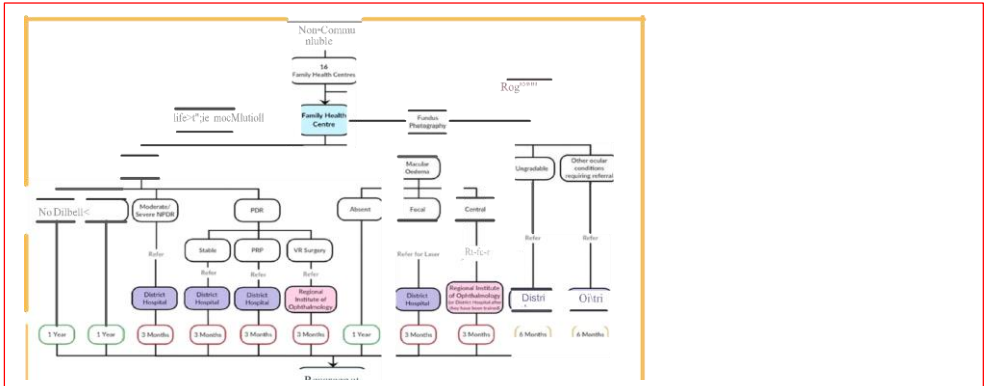

Figure 2a:Transition stagesin a Markov Model

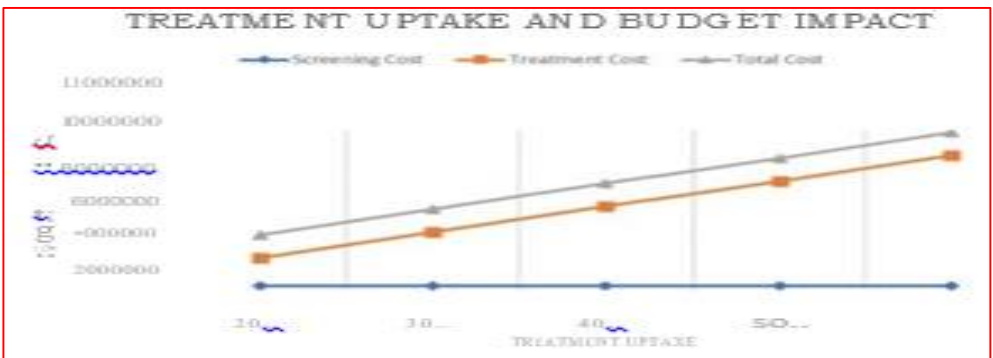Figure 1: Diabetic retinopathy screening Programme in Kerala

Figure 2b: Treatment uptake and budget impact

Findings

Tele-screening for DR using fundus photography is cost-saving (ICER -71'7) from a health system perspective and cost-effective from a societal perspective. (Fig.2b) However, the study pointed to considerable amounts of out-of-pocket expenditure and loss of labor associated with screening. On doing one-way sensitivity analysis, ICER in health system perspective was highly influenced by treatment uptake and cost of screening; and societal perspective ICER by utility values of late stages of DR. The budget impact analysis showed that scaling up the program to all Family Health Centers (FHCs) in Kerala will increase the burden by 16 Crore rupees on the exchequer. (Table 4) However, the net impact will be saving around eight Crore rupees by reducing the number of patients requiring expensive management in the late stages.

Conclusion

The tele-screening model for diabetic retinopathy by fundus photography is a cost-effective and cost-saving tool compared to the current scenario from a health system perspective.It is cost-effective relative to the threshold of Indian GDP per capita, even from a societal perspective.The indirect expenses such as travel and wage loss cost more than the expenses of screening, hence streamlining of screening and reimbursement of travel expenses of patients need to be considered.As per the current model, the effectiveness of screening is dependent on the proportion of patients in the PDR stage receiving PRP/Vitreoretinal surgery. Hence, ensuring that district/subdistrict level referral hospitals can absorb the additional caseload is vital to its success.

Estimation of recurrent cost for institutional delivery at different levels of facilities under JSSK

POLICY BRIEF

ESTIMATION OF RECURRENT COST FOR INSTITUTIONAL DELIVERY AT DIFFERENT LEVELS OFFACILITIES UNDER JSSK SCHEME

Health Technology Assessment in India – Secretariat Department of Health Research, Ministry of Health and FamilyWelfare

Government of India, New Delhi (110001)

Summary

Ministry of Health and Family Welfare launched JSSK in 2011 to ensure cashless services for all pregnant women including pre- natal, intra-natal and post-natal services including high-risk deliveries and caesarean in government healthcare facilities in both rural as well as urban areas. This study was undertaken at the request of the Maternal Health Division of DoH&FW for revision of estimates to allocate budget to various healthcare facilities according to their patient. The recurrent cost of providing comprehensive Ante-natal, Intra-natal, Post-natal maternal and childcare was estimated through normative costing methodology, using guidelines of JSSK, STWs, and NHM etc. In the public sector, the average recurrent drugs and consumables cost of providing one full antenatal care to a pregnant woman was estimated to be INR 99. Likewise, the average recurrent consumables cost per PNC was INR 87. Cost of drugs and consumables institutional delivery was INR 1964 in normal delivery and INR 2524 in cesarean delivery. The cost of providing food during hospitalization was estimated to be INR 65 per diet.

Methods:

The recurrent cost of providing comprehensive Ante-natal, Intra-natal, Post-natal maternal, and childcare was estimated through normative costing methodology, using various guidelines of JSSK, STWs, and NHM etc. Recurrent resources required to deliver these services were also confirmed from subject experts (Gynaecologists) and healthcare providers (ASHA, ANM, MO, etc.) Average of procurement prices of drugs, consumables, and diagnostics from various sources like CGHS, Rajasthan Medical Service Corporation, and Tamil Nadu Health Service Corporation.

This analysis was carried out by:

Rates of diagnostics were taken from the CGHS list or from published literature.
Expert consultations were taken to vet the resource gaps in data from public healthcare. Facilities and adding their cost in overall. Vetting was done to review any additional diagnostics, drugs, consumables required in providing comprehensive ANC, INC, PNC services. 3. Cost of diet and delivery cost (recurrent cost on drugs and consumables) was taken up from CHSI study which is carried out by DHR-PGIMER across 13 sites.

Recommendation

• Budget allocation under jssk to districts and states (especially drug cost for anc, pnc, diet and drugs & consumables cost for inc) can be updated based on results of this evaluation.
• Monetary allocation for referral cost of the patient can be guided by actual contract rates of the respective state.

Result

The cost of consumables for ANC and PNC care at SHC, PHC, and CHC level was estimated using data collected from literature and PHCs of Gujarat State. Average of procurement prices of drugs, consumables, and diagnostics from various sources like CGHS, Rajasthan Medical Service Corporation and Tamil Nadu Health Service Corporation were included in the analysis.

Estimation of resources:

In first, **Targeted Literature Review** was undertaken to collect the existing evidence regarding the **list and volume** of drugs, consumables and diagnostics using available guidelines.

Extracted data was used to develop a **Template Checklist** of drugs, consumables and diagnostics for ANC/PNC to collect **pragmatic data** on consumption from **Five Primary Health Care** (PHC) centers of Gujrat .

The updated list was then sent to a **Gynaecologist (from Maharashtra)** for vetting, based on their expert opinion.

Assigning cost to Resource:

Drugs: Tamil Nadu NHM Drug Rate List

Drugs: Rajasthan Medical Corporation Rate List

Drugs: Online Cost Databases (Amrit Pharmacy)

Diagnostics: CGHS Rate List

Food Cost: CHSI

Health Services	Cost (INR)	Source
Drugs Cost - ANC	99 (1042)*	Primary Data Collection
Drugs Cost - PNC	87 (987)*	Primary Data Collection
Cost of Diagnostics for Pregnant Woman	1254	Primary Data Collection
Drugs & Consumables Cost Normal Delivery	1964	CHSI
Drugs & Consumables Cost Cesarian Delivery	2524	CHSI
Cost of food per day During Hospitalization	195	CHSI

Particulars	Current Reimbursement	Proposed Reimbursement
Drugs for ANC	INR 200	INR 99
Drugs for PNC	-	INR 87
Diagnostics for Pregnant Woman	INR 200	INR 1254
Drugs and consumables for Normal Delivery	INR 350	INR 1964
Drugs and consumables for C-Section	INR 1600	INR 2524
Budget require for Diet/ Day	INR 100	INR 195
Referral Transport	INR 250 (Plains)/500 (Hills)	As per State Contract

74

Meghalaya mega health insurance scheme (MHIS)

Policy Brief

Background:

The Megha Health Insurance Scheme (MHIS) of the Government of Meghalaya is a universal health insurance scheme launched in December 2012 with a primary objective to reduce household out of pocket expenditure on health and provide high quality essential health care. The scheme began with the financial coverage of < 1, 60,000 per family for an enrolment fee of < 31in 2012 under MHIS-1. After various revisions, in 2017 the total insurance coverage was increased to < 2, 80,000, accompanied by an increase in the number of services included in the MHIS-III benefit package. The scheme currently in place is MHIS-IV which was launched in Dec-2018, with further increase in financial provision and expansion of eligibility criteria. Despite substantial expansion of the MHIS since the scheme's inception, there is a lack of comprehensive documentation and evaluation of the scheme's performance against its UHC objectives. No formal analysis has ever been carried out on the claims data to assess trends in service provision and how this potentially reflects the general health of the population in the state of Meghalaya.

Analysis

An analysis of the enrolment and claims data of the Meghan Health Insurance Scheme (MHIS) was initiated by the Regional Resource Hub (RRH-Than) at the Indian Institute of Public Health-Shillong in collaboration with the Directorate of Health Service, Government of Meghalaya, India. Six years of medical insurance enrolment and claims data (2013 - 2018) covering three iterations of the MHIS scheme were analyzed to assess patterns of enrolment and care provision under the scheme during the period of interest. De-identified data files included age, sex, district of residence, the district of the hospital providing care, type of hospital, date of enrolment, status at discharge, procedure categories, package codes and names, cost of package, and amount claimed. The state's budget spending on health was reviewed to understand the s: pending position in comparison to the National average and that of other selected States, and the fiscal space for expansion and sustainability of the MHIS.

Summary of Key Findings

•From MHIS-1through MHIS-III, there was a consistent increase in enrolment and this remained stable across districts, gender, age group and occupation categories. Enrolment was equal amongst both males and females in all three phases of MHIS. Enrolment data disaggregated by age showed that highest enrolment was in the age group 19-45 years in all three phases, followed by 6-18years.

•The highest volume of claims both in terms of number claimed and amount, were for services availed in private hospitals in the state (57%), with non-private sector service providers empanelled under MHIS-III providing the remaining 43% of all care claims.

•The top packages as indicated by volume of claims in MHIS-III included:
a) Packages listed under 'general ward unspecified' (GWU, 42%),
b) Maternal packages (20.2%),
c) cat/dog bite (11%), d) cataract care (1%), d) ICU care (1%),
e) Renal dialysis (0.9%), among others.

Recommendations:

The benefit package of services offered under MHIS could be consolidated in order to remove duplicate, redundant, and low value care packages and streamline what is offered into a more cost effective package of services. The use of "General Ward Unspecified" package should be placed under scrutiny and its use further investigated in order to reassess its appropriateness, and consider whether it could be disbanded, or its use discouraged except in exceptional circumstances. The extremely high rate of claims for dog and cat bites warrants a thorough investigation. It should also be noted that there is an anti-Rabies control Programme funded by the public health scheme, indicating potential. Periodic assessment of the scheme through analysis of claims data, alongside monitoring of State spending on health, is strongly encouraged in order to continually assess the performance of the MHIS against its objective to provide Universal Health Coverage to the population of Meghalaya. A detailed review of the state health budget, including Central grants, would help the State in allocating the budget more strategically and efficiently as the Govt Meghalaya looks to expand the scheme in further iterations to move closer towards the achievement of Universal Health Coverage.

In comparison, for MHIS-II – GWU (59%), normal deliveries and peritoneum repair (maternal packages, 10%) and malaria (3%) were the top volume claims categories. In MHIS-I, GWU' accrued to 65% of total number of claims, followed by maternal care packages (16.9%) and 'ICU care' (4%).

The raw number of claims for GWU doubled from MHIS I (26,892) to MHIS III (57,337), however, the number of these claims as a proportion of the total number of claims reduced from 65% to 2 42%. Age group 19-45 years and females were the highest claimants under this category in MHIS-III.

Analysis of claims data revealed that health care towards cat/dog bites contributed second highest volume of claims (11%) in MHIS-III. This included five doses of injections (INR 777 per injection) plus expenses towards dressing. Majority of claimants for cat/dog bite care availed these services from the public sector, PHC/CHCs (42%) or district hospitals (32%).

Proportion of Gross Domestic Product (GDP/GSDP) spent on health by the State in Meghalaya has been two times higher than the national average in 2017-18 (2.4 % versus 1.0%). It has also been higher than more 'developed' states such as Punjab (0.6%), Gujarat (0.6%) and Tamil Nadu (0.7%). Share of total revenue budget spent on health in Meghalaya is also two times higher than the national figure, as in 2017-18 (7.9% versus 3.4%).

The per-capita public health expenditure increased from Rs 1513 in 2014-15 to Rs 2989 in 2020-21. It is important to note that the cost of service delivery is likely to be higher in the State on account of low density of population and difficult geographical conditions, similar to other north-eastern states,
More than 50% of the total health budget was spent on facility-based curative medical care services under the MHIS

Acknowledgement:

Author s: Eliza Dutta1, Laura Downey2, Selvara ju V, Sand ra Albert1

Economic Evaluation for Transcatheter Aortic Valve Replacement (TAVR) to replace heart valves for severe aortic valve stenosis.

Economic Evaluation for Trans catheter Aortic Valve Replacement (TAVR) to replace heart valves for severe aortic valve stenosis.

Health Technology Assessment in India (HTAIn)

Policy Brief

Background

Aortic stenosis (AS) is one of the most common and serious heart defect characterized by an obstruction of flow from the left ventricle to the aorta, at the level of the aortic valve.. The aortic valve is one of four heart valves in the heart. Possible treatments may include medications, Balloon Valvuloplasty (BAV), Surgical Aortic Valve Replacement (SAVR), valve repair or valve replacement and transcatheter aortic valve replacement (TAVR). Over the last decades, transcatheter aortic valve replacement (TAVR), the nonsurgical option, has rapidly emerged as an alternative treatment. It is performed by way of a catheter inserted into the leg, which then allows the replacement valve to be guided up to the aortic valve without opening the chest or heart. Patients might be candidates for TAVR if they have AS symptoms and are at intermediate or high risk of having open-chest surgery, meaning they are more vulnerable to complications and a longer, potentially more difficult recovery from the surgical approach. The Placement of Aortic Transcatheter Valves (PARTNER) trial reported that in a cohort of patients who were unsuitable for surgical valve replacement, transcatheter aortic valve replacement (TAVR), compared with standard nonsurgical care, resulted in a 20% reduction in mortality at 12 months, as well as improved functional status and a reduction in hospital admissions for aortic stenosis.

Research Question:

Which is the most cost effective treatment modality for the management of high risk patients with severe aortic stenosis?

Aims:

To conduct a full economic evaluation to see which treatment modality is the best alternative for managing patients with severe aortic stenosis.

Specific objectives:

1. To conduct a primary survey at hospital settings to generate evidences on TAVR in India.
2. To estimate incremental cost per LYs/QALY gained by
TAVR compared to medical therapy
TAVR compared to SAVR.

Methods:

Objective 1: To conduct a primary survey at hospital settings to generate evidences on TAVR in India.

A multi- centered prospective cohort study for data collection is planned at centeres performing at least 30 TAVRs and 30 SAVRs in a year. a follow up on a standardized quality of life questionnaire at 6 months and 12 months and will be followed up at quarterly interval for 12 months using a combination of mailed questionnaire and telephonic interviews. Data on survival, quality of life, healthcare resource use, and hospital charges will be collected through the first 12 months of follow-up (the minimum follow-up duration for the trial) for all patients and will be used to calculate survival, quality-adjusted survival, and costs for the trial period.

Estimation of life-expectancy:

To estimate life expectancy for each surviving patient, we will use parametric survival models to extrapolate survival probabilities beyond the follow-up time of the trial. Survival curves will be fitted separately for the TAVR and control groups by use of exponential, Weibull, log-normal, log-logistic, logistic, and normal models. Covariates included age, sex, and medical history such as diabetes mellitus, coronary artery disease, peripheral vein disease, myocardial infarction, stroke/transient ischemic attack, prior percutaneous coronary intervention, and prior coronary artery bypass graft. To improve the model fit for the TAVR group and to optimize the resulting survival projections, the model will be conditioned on survival at 3 months to reduce the influence of periprocedural events not expected to affect long-term survival.

Objective 2: Cost-effectiveness analysis

Population of interest	High Risk Patients	Intermediate risk patients
Intervention	TAVR	TAVR
Comparator	Medical therapy	SAVR
Outcome	Cost per QALY/LY gained	Cost per QALY/LY gained
Time horizon	Lifetime	Lifetime

Fig 1: Decision tree model for ICER of TAVR compared to medical treatment
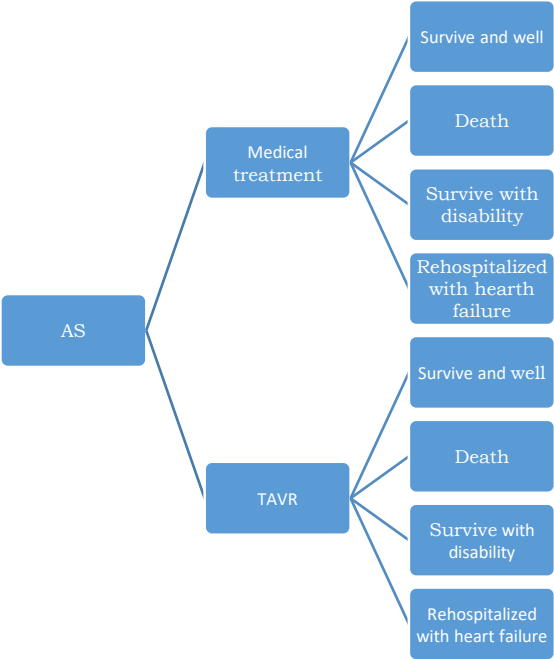
Fig 1: Decision tree model for ICER of TAVR compared to medical treatment
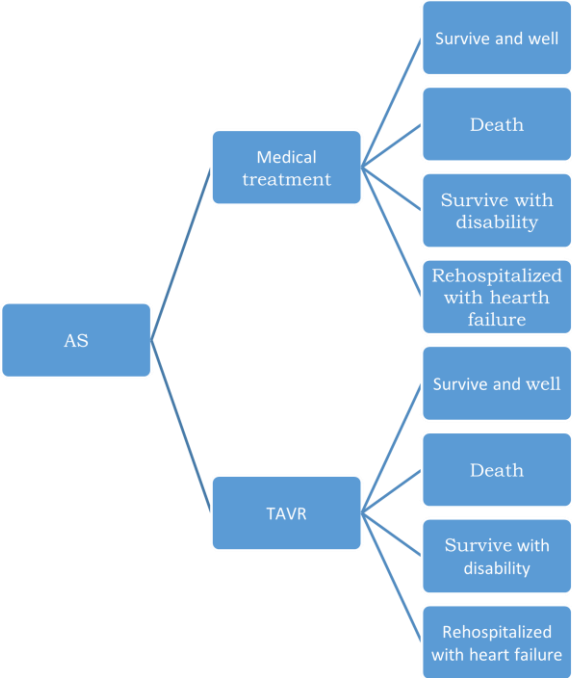
Sensitivity Analysis

During the process of this evaluation, certain assumptions are to be made and also uncertainties may arise in the parameters (in cost and effect estimates or due to discounting). For this purpose sensitivity analyses - one way and probabilistic – will be conducted to check for parameter variability and its effect on the results.

Anti-cancer drugs Cost-effectiveness Analysis studies

Cost-effectiveness of novel agent regimens for Transplant – Eligible newly diagnosed multiple Myeloma patients in India

Cost-effectiveness of Novel agent regimens for Transplant-Eligible Newly Diagnosed Multiple Myeloma patients in India

Health Technology Assessment in India (HTAIn)

Postgraduate Institute of Medical Education &

Research, Chandigarh

Executive Summary

Multiple myeloma is a second most frequent haematological malignancy accounting for 20% of haematological cancer related deaths. The therapeutic landscape of MM has changed significantly over the past few years with the introduction of novel agents like bortezomib, lenalidomide and thalidomide. Due to these advanced therapeutic combinations and standard use of AHSCT, the cost of care of MM has increased significantly in the last two decades. Since the number of treatment options for NDMM have increased substantially, it is vital to compare the costs and consequences of different induction regimens.

In this analysis, we aimed to evaluate the cost-effectiveness of novel agent regimes with and without autologous haematopoietic stem cell transplantation (AHSCT). Using a Markov model, the clinical effectiveness and cost of bortezomib-based triplets or quadruplet drug regimens in isolation and followed by AHSCT for the treatment of newly diagnosed multiple myeloma (NDMM) in the Indian context were estimated. Incremental cost per QALY gained with a given treatment option was compared against the next best alternative, and assessed for cost-effectiveness. At the current WTP threshold, VRd plus AHSCT and VTd plus AHSCT has 6.9% and 3.7% probability to be cost-effective, respectively. Reduction in current reimbursement rates of novel drugs namely VRd lenalidomide, pomalidomide plus dexamethasone under national insurance program and societal cost of transplant by 50%, would make VRd plus AHSCT and VTd plus AHSCT cost-effective at an incremental cost of ₹ 40,671 (US$ 534) and ₹ 97,639 (US$ 1,281) per QALY gained respectively.

Policy Recommendations

From the societal perspective, we recommend a 50% reduction in the reimbursement rate of VRd, pomalidomide plus dexamethasone, lenalidomide and transplant to make it a cost-effective treatment option for Indian MM patients. We would further recommend the inclusion of carfilzomib drug regimen in the HBP 2.0 for the treatment of MM patients in India. Drugs like daratumumab may also be considered for inclusion under schemes in order to further improve the survival as well as quality of life of MM patients in India. There is an urgent need to place certain price regulations in place so as to make these drugs more accessible and affordable to MM patients.

Background and Gap in Literature:

As per GLOBOCAN data from the International Agency for Research on Cancer (IARC), there were an estimated 114,000 new cases of Multiple myeloma globally in 2012 [4]. More recent estimates suggested 159,985 newly diagnosed MM worldwide (i.e. about 0.9% of all cancers and 1.1% of all cancer deaths) in 2018 [5]. Survival outcomes for multiple myeloma have improved dramatically since the introduction of novel therapeutic agents. While these drugs are highly effective in improving survival outcomes and quality of life in patients with multiple myeloma, they come at a significant cost. The therapeutic landscape of MM has changed significantly over the past few years with the introduction of novel agents like bortezomib, lenalidomide and thalidomide and are used in combinations to improve the outcomes among newly diagnosed multiple myeloma (NDMM) patients [6-7]. The improvements were marked when using the novel agents as induction therapy followed by autologous hematopoietic cell transplantation (AHSCT) [6, 8-9]. The initial therapy for transplant-eligible NDMM patients consists of 3–6 cycles of induction therapy followed by AHSCT and maintenance therapy [8-9]. Due to these advanced therapeutic combinations and standard use of AHSCT, the cost of care of MM has increased significantly in the last two decades. Since the number of treatment options for NDMM have increased substantially. So, it is vital to compare the costs and consequences of different induction regimens. According to a systematic review, few studies have evaluated the cost-effectiveness of regimens based

Aims and Objective:

This policy brief addressed the policy question of cost-effectiveness of bortezomib-based triplets or quadruplet drug regimens in isolation and followed by AHSCT for the treatment of NDMM in the Indian context. It summarizes the results of an Economic evaluation study on various NDMM treatment regimens, conducted by the HTA Resource Hub, PGIMER, Chandigarh.

Treatment arms:

Bortezomib, lenalidomide, dexamethasone (VRd) alone
Bortezomib, thalidomide, dexamethasone (VTd) alone
Bortezomib, cyclophosphamide, dexamethasone (VCd) alone
VRd followed by AHSCT
VTd followed by AHSCT
VCd followed by AHSCT
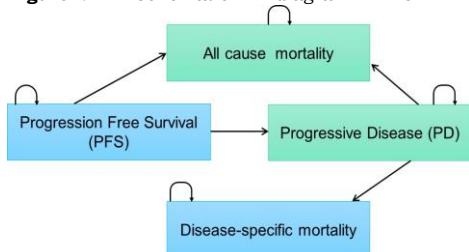Daratumumab plus VRd (DVRd) followed by AHSCT

Methods and Approach:

We undertook this cost-effectiveness analysis (CEA) using a societal perspective, which accounted for both health system and patients' costs and not indirect costs. We compared the bortezomib-based triplets or quadruplet drug regimens in isolation and followed by autologous hematopoietic stem cell transplantation (AHSCT) for the treatment of newly diagnosed multiple myeloma (NDMM). Our methodological principles are consistent with the Indian reference case for conducting economic evaluations used by the agency for Health Technology Assessment in India (HTAIn).

The analysis was performed under the following components:

Markov model was developed in Microsoft Excel to estimate health and economic outcomes (in terms of Quality Adjusted Life-years (QALYs)* and Life-years). The model consisted of three mutually exclusive health states: Progression-free survival (PFS), Progressive disease (PD) and death. (Figure 1). Reimbursement rates under publicly financed national insurance program were used to estimate the treatment cost in each health stage. However, for drugs not included under insurance scheme, their market price was used from published literature. In order to obtain the Out-of-Pocket Expenditure (OOPE), the primary data collected based on the CADCQoL database was analysed [14].

Transition probabilities for treatment arms-VRd plus AHSCT, VTd plus AHSCT and VCd plus AHSCT were obtained from survival functions calculated from data obtained from published literature. However, for patients who did not undergo transplant stratified by the induction regimen, a gradient was calculated and used to derive the probability. For DVRd plus AHSCT arm, estimates reported in the GRIFFIN trial was used. Stage wise utility scores were estimated from the CADCQoL primary data collected from 320 MM patients to measure the HRQoL. The Indian tariff values were used to calculate the index utility score.

Figure1: Schematic diagram for the Markov state transition model.

*Quality Adjusted Life-years:

QALY is a generic measure of health and is used to compare the health gains across different diseases and hence provide a uniform platform to compare effectiveness across all the different areas of healthcare. EQ5D is the most utilised tool worldwide to measure QoL.

Results:

Among the seven treatment sequences, VCd alone arm has lowest cost and health benefits as compared to four treatment sequences namely VTd alone, VRd alone,VRd plus AHSCT and DVRd plus AHSCT VTd plus AHSCT and VCd plus AHSCT arm are extendedly dominated (ED) by combination of two alternative treatments. The ICER of DVRd plus AHSCT arm [₹ 824,969 (US$ 10,826)] is 5.6 times the per-capita GDP of India and hence not cost-effective at the currently recommended willingness to pay (WTP) threshold of per capita GDP. Among the five non-dominated strategies, VRd has an incremental cost of ₹ 2,20,093 (US$ 2,888) per QALY gained compared to VTd alone followed by VRd plus AHSCT, with an incremental cost of ₹ 3,14,530 (US$ 4,128) per QALY gained.

Price Threshold Analysis:

At the current WTP threshold of one-time per capita GDP (₹ 146,890) of India, VRd alone and VRd plus AHSCT has 38.1% and 6.9% probability to be cost-effective, respectively. On reducing the current reimbursement rates under national insurance program by 50% i.e. from ₹ 17,800 to ₹ 8,900 for VRd, ₹ 7200 to ₹ 3600 for pomalidomide plus dexamethasone, ₹4800 to ₹ 2400 for lenalidomide and societal cost of transplant from ₹3,53,027 to ₹1,76,513, VRd plus AHSCT (against VTd plus AHSCT) becomes cost-effective at an ICER value of ₹ 40,671 (US$ 534) followed by VTd plus AHSCT treatment at an incremental cost of 97,639 (US$ 1281) per QALY gained (against VCd plus AHSCT) which is much below current WTP threshold of India.

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Cost – effectiveness of first line treatment options of metastatic renal cell carcinoma

HTAIn

A model-based analysis for first-line treatment of metastatic Renal cell carcinoma: Implications from the perspective of AB PM-JAY

Health Technology Assessment in India (HTAIn)
Postgraduate Institute of Medical Education & Research, Chandigarh

Policy Brief

Executive Summary:

Renal cell carcinoma (RCC) accounts for 3% of all adult cancers and 85% of all kidney tumours (1). The incidence of RCC has been reported to be about 2 per 100,000 and 1 per 100,000 among males and females respectively in India (2). It is more common among the elderly with median age of presentation ranging from 50-60 years with clear cell carcinoma being the commonest histological type accounting for 70-80% of RCC (3).

In this analysis, we aimed to determine the most cost-effective treatment option for newly diagnosed metastatic RCC (mRCC) patients in India. Using a Markov model, the clinical effectiveness and costs of monotherapies (either Sunitinib, or Pazopanib) and combination therapies (either Pembrolizumab/Lenvatinib, or Nivolumab/Ipilimumab) were estimated. Incremental cost per QALY gained with a given treatment option was compared against the next best alternative, and assessed for cost-effectiveness. We found that sunitinib is a non-dominated treatment option with an average cost of ₹ 116,971 per QALY lived. Moreover, Pazopanib incurs an incremental cost of ₹ 1.1 million per QALY gained as compared to sunitinib and nivolumab/ipilimumab incurs an incremental cost of ₹ 16.4 million per QALY gained as compared to pazopanib which is not cost-effective at the current WTP threshold of 1-time per

Policy Recommendations:

From the perspective of current reimbursement rates, sunitinib is the most cost-effective treatment for newly diagnosed mRCC patients in India. Pazopanib offers better health outcomes than sunitinib, and should therefore be added in the health benefit package at a reduction of 59% from the current market price. The use of combination therapies are currently not value for money in the Indian context.

Background and Gap in Literature:

National Cancer Grid (NCG) and Evidence-based Management (EBM) guidelines recommend the use of Tyrosine-kinase Inhibitors (TKIs) such as Sunitinib and Pazopanib as the first-line therapy for favourable-risk metastatic RCC patients. The high price of these agents in the Indian context made it unaffordable for majority cancer patients. However, the introduction of low-cost generics in the Indian market has provided some relief to the Indian mRCC patients. Moreover, India's government funded health insurance program – the Ayushman Bharat Pradhan Mantri Jan Aarogya Yojana (PM-JAY) has recently included various targeted therapies (such as sunitinib, cabozantinib and sorafenib) for the treatment of mRCC in its health benefit package (HBP). This has helped in reducing the financial hardship currently being faced by many Indian patients. The CHECKMATE-214 and CLEAR clinical trial paved the way for the use of Immune checkpoint inhibitors (ICIs) such as pembrolizumab and nivolumab in combination with TKIs (4,5). This combination has shown significant improvement in both progression free survival (PFS) and overall survival (OS), with less toxicities as compared to the conventional sunitinib monotherapy. However, the newer ICIs are presently expensive both in the Indian and global markets. Therefore, the cost-effectiveness analysis has an important role, especially in the low-middle income countries such as India, in helping the physicians and payers in choosing appropriate therapy which represents value for money.

Aims and Objective

This policy brief addressed the policy question of the most cost-effective treatment option for newly diagnosed RCC patients from the point of view of reimbursement rates set under AB PM-JAY scheme. It summarizes the results of a Economic evaluation study on various RCC treatment regimens, conducted by the HTA Resource Hub, PGIMER, Chandigarh.

Methods and Approach

We undertook this cost-effectiveness analysis (CEA) using a societal perspective, which accounted for both health system and patients' costs. We compared the costs and consequences associated with sunitinib, pazopanib, combination of pembrolizumab/Lenvatinib and nivolumab/ipilimumab . Our methodological principles are consistent with the Indian reference case for conducting economic evaluations used by the agency for Health Technology Assessment in India (HTAIn).

Treatment arms:

Sunitinib (50 mg orally once daily for 4 weeks of treatment followed by 2 weeks with no treatment); Pazopanib (800 mg orally once daily); Pembrolizumab (200 mg intravenously 3-weekly) plus Lenvatinib (20 mg orally once daily); Nivolumab (240 mg intravenously 2-weekly) plus Ipilimumab 50 mg (4 doses intravenously once every 6 weeks)
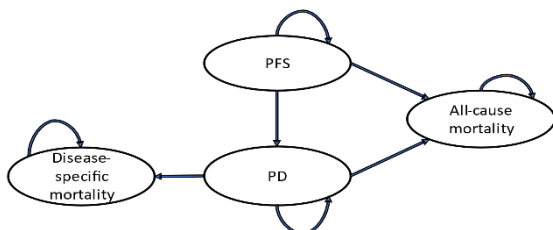
The analysis was performed under the following components:

1. **Markov model** was developed in Microsoft Excel to estimate the lifetime costs and consequences (in terms of Quality Adjusted Life-years (QALYs)* and Life-years). The model consisted of three mutually exclusive health states: Progression-free survival (PFS), Progressive disease (PD) and death. A 6-weekly cycle length based on the treatment schedule of the sunitinib treatment arm was considered (Figure 1).
2. Reimbursement rates (for sunitinib, cabozantinib and sorafenib) and market prices (pazopanib, pembrolizumab, lenvatinib, nivolumab, ipilumumab and axitinib) were used to estimate the treatment cost in each health state.
3. In order to obtain the Out-of-Pocket Expenditure (OOPE) incurred on out-patient consultations, the primary data was analysed as a part **CADCQoL database** (7).
4. Transition probabilities and effectiveness parameters were obtained from the pivotal clinical trials for each of the drugs – COMPARZ, CLEAR and CHECKMATE-214 (4,5,6).
5. The Quality of Life (QoL) scores were estimated from the published studies (8).
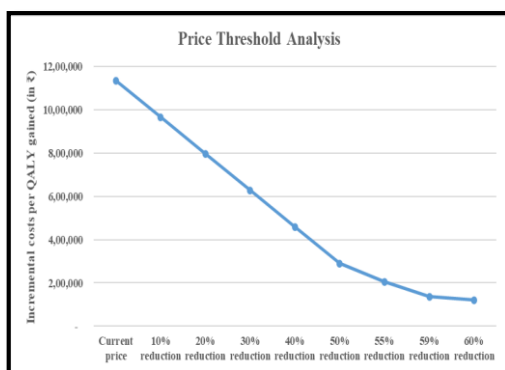
Price Threshold Analysis

At the current WTP threshold of one-time per capita GDP (₹ 141,225) of India, sunitinib and pazopanib has 71.1% and 43.2% probability of being cost-effective respectively.

Pazopanib offers slightly better health outcomes than sunitinib.

A 59% reduction in the market of pazopanib will make it a cost-effective treatment option in the Indian context.

Results:

- Sunitinib is the most cost-effective treatment option and incurs an average cost of ₹ 116,971 per QALY lived in the Indian context.
- Pazopanib offers better health outcomes at an incremental cost of ₹ 1.1 million per QALY gained as compared to sunitinib.
- None of the combination therapies are cost-effective at the current WTP threshold of 1-time per capita GDP of India.

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Value of New Drug Therapies for the Treatment of Chronic Leukemia (CLL)

Value of new drug therapies for the treatment of chronic lymphocytic leukaemia

Health Technology Assessment in India (HTAIn)

Policy Brief

Executive Summary

Chronic Lymphocytic Luekemia (CLL) though less common in India than the west, has high morbidity burden. The cost- effectiveness of treatment therapies with the following three drug regimes, i.e., chlorambucil plus prednisolone (CP), bendamustine plus rituximab (BR), and ibrutinib for the treatment of CLL in India is assessed here. Ibrutinib is proven to be more effective than BR which has shown better effectiveness than CP. However, CP is cheapest while Ibrutinib is the costliest amongst these three regimes in India. Being a chronic disease, a patient of CLL requires around 2 lines of therapies in a lifetime. Here we evaluate which combination therapy of the above drugs provides best value for the treatment of CLL in Indian context. The incremental costs of a treatment line and its potential health gains are compared conducting a Health Technology Assessment (HTA). Literature review, primary data collection, and economics evaluation via Markov model was done for the HTA.

Recommendations

Treatment of CLL with 1st line CP and 2nd line BR is the most cost-effective option at current prices of drugs in India.We recommend reimbursement of this cost-effective strategy for all public funded insurance schemes. However, if the prices of both BR and ibrutinib are reduced by 80%, treatment with strategy of BR as 1st line and ibrutinib as 2nd line therapy becomes cost- effective for India.Hence, we recommend reducing the prices accordingly to consider it for reimbursement schemes.

Context:

Chronic lymphocytic leukaemia (CLL) in India accounts for around 7673 new cases and approximately 6195 deaths annually. The CLL patients are generally diagnosed at younger age with poor performance status and have high morbidity burden. While patients in stage 0, I and II are mostly kept on observation and treatment is initiated when there is progression, those in stage III and IV are immediately put on radical treatment. Chlorambucil, a drug no longer in practice in developed nations, is still commonly prescribed in India mainly for financial reasons. Newer drugs like Bendamustine and ibrutinib have shown greater effectiveness than chlorambucil based therapies.

Though these newer drug regimens lead to improved survival, they are also associated with higher cost as well as high incidence of side effects. Regarding anti-CLL drugs, no economic evaluations are reported from India or even the South-East Asia Region (SEAR). All the existing literature on cost-effectiveness of these drugs has been reported from the context of developed countries. However, none of the economic evaluation has directly compared the three drugs in question, i.e., chlorambucil, bendamustine and ibrutinib.
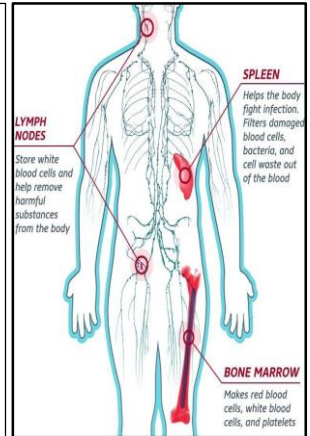

Treatment of CLL through BR as 1st line therapy and Ibrutinib as 2nd line therapy costs INR 3,44,852 to gain 1QALY when compared to treatment arm of 1st line CP and 2nd line BR.

Treatment arms compared in the study

Arm A: 1st Line Chlorambucil +Prednisolone (CP) followed by 2nd line Bendamustine +Rituximab (BR) Arm B: 1st line CP followed by 2nd line Ibrutinib Arm C: 1st line BR followed by 2nd line Ibrutinib Arm D: 1st line Ibrutinib followed by 2nd line BR Scenario Analysis: Done to compare single line therapies of CP, BR, and

Methods and Approach:

HTA was done using Markov modelling technique (Fig. 1) to estimate the lifetime costs and health consequences for patients of chronic lymphocytic leukaemia. Treatment done with different combination in (arm B, C, D) was compared with the treatment with 1st line CP and 2nd line BR (arm A). The health outcomes were evaluated in terms of life years (LY) and quality adjusted life years (QALY) lived. The cost effectiveness was assessed in terms of incost effectiveness ratio (ICER) between the intervention and control arm. Literature review was done, and clinical effectiveness data was taken from studies by Hillmen et al and Woyach et al for-1st line drugs and Ghia et al and Xiaojun et al for-2nd line drugs. Trial data was extrapolated using standard methods and extrapolated data was used for analysis. Data was collected on OOPE and quality of life values (CADCQoL database) while the health system costs were derived from the previously undertaken costing studies from India.
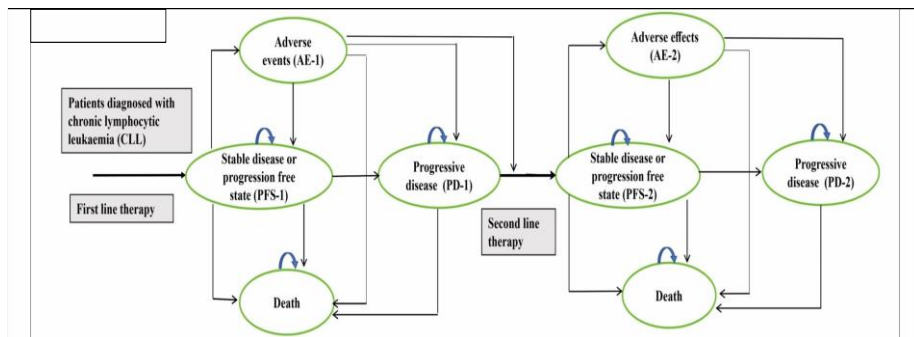
Dosages:

Chlorambucil and prednisolone was taken as 10 mg/m^2 and of 60mg/m^2 respectively for five days in a 28-day cycle, for 6 cycles. Bendamustine was estimated as 90 mg/m^2 on day 1 and 2, by with rituximab (375 mg/m^2 on day 1) in a 28-day cycle, for 6 cycles. Ibrutinib was administered at a dose of 420 mg daily.

Results and Discussion

Life Years and QALYs gained by a patient following treatment for CLL varied from 5·63 (Arm A) to 12·57 (Arm D) and 3·8 (Arm A) to 9·71 (Arm D), respectively, among the treatment arms. Similarly, lifetime costs ranged from INR 3, 22,910 (Arm A) to INR 36,25,031 (Arm D) incurred on the treatment of CLL. This resulted in incremental cost effectiveness ratio of: INR 1,043,083 per QALY gained for Arm B; INR 3,44,852 per QALY gained for Arm C; INR 5,68,502 per QALY gained for Arm D, when compared to arm A. The analysis suggests that treatment of CLL with 1st line CP and 2nd line BR (Arm A) is the most cost-effective option at current prices of drugs in India. However, if the prices of both BR and ibrutinib are reduced by 80%, treatment with strategy of BR as 1st line and ibrutinib as 2nd line therapy (Arm C) becomes cost-effective. The threshold analysis (Fig.2) showed that the results could vary highly on varying the costs of BR and Ibrutinib.
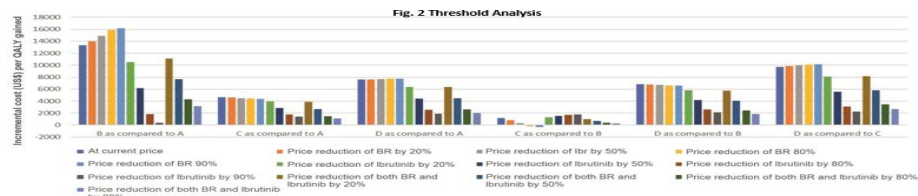
Use of CDK4/6 Inhibitors in the Treatment of Metastatic Breast Cancer

Use of CDK4/6 inhibitors in the treatment of Metastatic Breast Cancer: "Is the cost worth it?"

Health Technology Assessment in India (HTAIn)
Postgraduate Institute of Medical Education & Research, Chandigarh

Policy Brief

Executive Summary:

Breast cancer is the most prevalent cancer among women all over the world. Nearly, 13.3 out of per 1 lakh women die of the metastatic breast cancer (MBC) every year (1). Endocrine Therapy is the mainstay of treatment for the Hormone Receptor-positive (HR+), Human Epidermal growth factor Receptor 2-negative (HER2-) MBC.

In this analysis, we aimed to determine the most cost-effectiveness second-line treatment option for HR+, HER2- MBC among postmenopausal Indian women. We compared Ribociclib/Palbociclib combination therapy, Fulvestrant monotherapy, single-agent Paclitaxel and single-agent Capecitabine in the Indian context from two different point of views: Scenario I – as per the prevailing market prices of the drugs; and Scenario II – as per the reimbursement rates set up by the publicly financed national-level health insurance scheme.

We found that CDK4/6 inhibitors are not cost-effective in the Indian scenario even if the

Aims and Objective

This policy brief addressed the policy question of cost-effectiveness of Ribociclib and Palbociclib as well as other second-line options for the treatment of MBC in the Indian context. It summarizes the results of a Economic evaluation study on various MBC treatment regimens, conducted by the HTA

Background and Gap in Literature:

The introduction of targeted agents like CDK 4/6i (**Ribociclib and Palbociclib**) have added a new option in the management of HR+ HER2- MBC. Various trials have shown that use of CDK4/6i along with ET improves disease-free survival (DFS) and overall survival (OS) (2,3). However, in countries like India, it is important to determine whether the cost of treatment using CDK4/6i plus Fulvestrant is justified given the extent of treatment success, as compared to Fulvestrant alone, or the conventional chemotherapy which is currently offered to majority of the patients. Majority of the studies have either evaluated the first line therapy only, or did not include the comparison between CDK4/6i and chemotherapy. In view of the limitation of existing evidence, we undertook this study to determine the cost-effectiveness of CDK4/6i (Ribociclib and Palbociclib) as compared to **Fulvestrant monotherapy** as well as **single-agent chemotherapeutic regimens**

Policy Recommendations:

From the societal perspective, we recommend a 72% reduction in the reimbursement rate of Fulvestrant to make it a cost-effective treatment option for Indian MBC patients.

We also recommend a 78% reduction in the prevailing market price of Fulvestrant to make it a cost-effective treatment option.

The use of CDK4/6 inhibitors – Ribociclib and Palbociclib is not cost-effective as per current prices.

Use of these drugs for certain specific subgroups and subtypes should be explored and evaluated further.

Treatment arms:

Tab. Ribociclib 600mg OD daily + Inj. Fulvestrant 500mg monthly
Tab. Palbociclib 125mg OD daily + Inj. Fulvestrant 500mg monthly
Inj. Fulvestrant 500mg monthly

Inj. Paclitaxel 175mg/m^2 three weekly

Tab. Capecitabine 1250mg/m^2 OD daily for two weeks

Quality Adjusted Life-years:

QALY is a generic measure of health and is used to compare the health gains across different diseases and hence provide a uniform platform to compare effectiveness across all the different areas of healthcare.

EQ5D is the most utilized tool worldwide to measure QoL.

Methods and Approach

We undertook this cost-effectiveness analysis (CEA) using a societal perspective, which accounted for both health system and patients' costs and not indirect costs. We compared the combination of CDK4/6i (both Ribociclib and Palbociclib) and Fulvestrant with single-agent Fulvestrant as well as with chemotherapy (Paclitaxel and Capecitabine) respectively. Our methodological principles are consistent with the Indian reference case for conducting economic evaluations used by the agency for Health Technology Assessment in India (HTAIn).

The analysis was performed under the following components:

- **Markov model** was developed in Microsoft Excel to estimate the lifetime costs and consequences (in terms of Quality Adjusted Life-years (QALYs)* and Life-years). The model consisted of three mutually exclusive health states: Progression-free survival (PFS), Progressive disease (PD2) and death. A monthly cycle length based on the treatment schedules in the MONALEESA-3 trial was considered (Figure 1).
- Costs related to the treatment and the adverse effects were estimated for all the health states for both the scenarios using secondary sources. In order to obtain the Out-of-Pocket Expenditure (OOPE), the primary data was analysed from 843 MBC patients as a part **CADCQoL database** (4).
- Transition probabilities and effectiveness parameters were obtained from the Ribociclib pivotal trial – **MONALEESA-3** and published systematic review and network meta-analysis by **Wilson et al.**
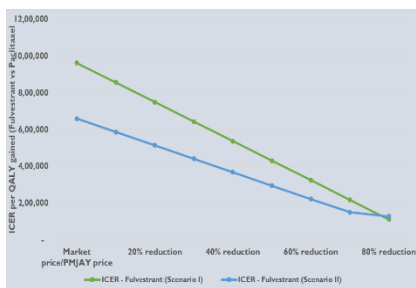
Results and Price Threshold analysis:

None of the treatment strategies are cost-effective at the current WTP threshold of 1-time per capita GDP of India.

Fulvestrant incurs an incremental cost of ₹ 963,208 and ₹ 660,797 per QALY gained as compared to single-agent paclitaxel for Scenario I and II respectively.

A 72% and 78% reduction is required in the current reimbursement rates and the market prices to make Fulvestrant monotherapy a cost-effective treatment option in the Indian context (Figure 2).

Figure 1: Schematics of the Markov state transition model. PFS: Progression-free state; PD: Progressive Disease

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Figure 2: Price Threshold **Analysis (Fulvestrant)**

Cost effectiveness of Temozolamide for Treatment of Glioblastoma Multiforme in India

Cost-Effectiveness of Temozolamide for Treatment of Glioblastoma Multiforme in India
Health Technology Assessment in India (HTAIn)
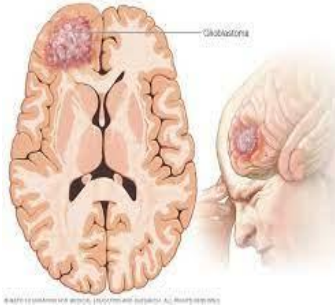### Postgraduate Institute of Medical Education & Research, Chandigarh

Policy Brief

Executive Summary:

Glioblastoma multiforme (GBM) is the most common and the most aggressive brain tumor in adults (1). The standard of care for patients with newly diagnosed GBM includes maximum possible safe resection followed by adjuvant radiotherapy (2). Temozolamide has shown positive outcomes in patients with newly diagnosed GBM (3), however it is an expensive in drug in resource-limited countries like India. Therefore, its assessment for value for money is important.

We undertook this study to estimate the incremental cost per QALY gained in patients with newly diagnosed GBM in India, who received temozolamide in addition to adjuvant radiotherapy as compared with radiotherapy alone. Incremental cost per QALY gained with a given treatment option was compared against the next best alternative, and assessed for cost-effectiveness. The use of temozolamide incurs an incremental cost of ₹212,020 INR (138,127-401,466) per QALY gained, which has a 4.7% probability to be cost-effective at 1-time per capita Gross Domestic Product (GDP) threshold. In case the current price of temozolamide could be decreased by 90%, the probability of its use for GBM being cost-effective increases to 80%.

Policy Recommendations

At current prices, temozolamide is not cost-effective for treatment of patients with GBM in India.

The use of temozolamide incurs an incremental cost of Indian national rupee 212,020 (138,127-401,466) per QALY gained.

Temozolamide can only be cost-effective with a 90% reduction in drug price.

Aims and Objective

This policy brief addressed the policy question of the cost-effectiveness of concomitant temozolamide with radiation and maintenance temozolamide for 6 months of treatment for GBM in India. The study was conducted by the HTAIn Resource center at PGIMER, Chandigarh

Background and Gap in Literature

The addition of concomitant temozolamide to radiation followed by 6 months of maintenance temozolamide in patients with newly diagnosed GBM has been reported to improve the median overall survival (OS) by 2.5 months and the progression-free survival (PFS) by 1.9 months (3). Temozolamide has been shown to be cost-effective in developed countries like United States, the United Kingdom, Mexico, and Canada, but at the same time, the drug has been shown to be cost-ineffective in China. This is due to the fact that the high-income countries have a higher willingness to pay (WTP) threshold as compared to the developing countries. There have been several methodological limitations in the above cost-effectiveness studies. For example, Lamers et al (4) and Uyl-de Groot et al (5) reported outcomes in terms of life years (LYs) and not quality-adjusted LYs (QALYs) gained. In the study by Wu et al, (6) discounted rates were not applied in view of short survival associated with patients with GBM. Several cost-effectiveness analyses (6) have estimated outcomes up to what has been reported in trials—either until 2 years or 5 years of onset of disease. Life-term consequences have not been assessed robustly. Therefore, we aimed to assess the cost-effectiveness of temozolamide in the context of low- and middle-income country such as India.

Intervention and control arms

Temozolamide at 75 mg/m2 once daily concomitant with radiation for a period of 6 weeks, followed by 4-weekly six cycles of maintenance temozolamide Adjuvant radiation without concomitant or maintenance temozolamide.

Methods and Approach

We undertook this cost-effectiveness analysis (CEA) using a societal perspective, which accounted for both health system and patients' costs. We compared the costs and consequences associated with patients who received temozolamide in addition to adjuvant radiotherapy as compared to radiotherapy alone. Our methodological principles are consistent with the Indian reference case for conducting economic evaluations used by the agency for Health Technology Assessment in India (HTAIn).

The analysis was performed under the following components:

1. A Markov model with three health states—PFS, progressive disease (PD), and death—was developed. Patients with newly diagnosed GBM entered the model at the age of 50 years.
2. A cycle length of 1 month was considered appropriate based on the maintenance treatment cycles. Lifetime horizon was considered in the model.
3. Market prices were obtained to estimate the per cycle cost of temozolamide drug (7).
4. Cost of treatment and management of complications were estimated using the data from the National Health System Cost Database and Indian studies (8,9).
5. The data of OS and PFS as reported in the European Organisation for Research and Treatment of Cancer (EORTC)-NCIC trial at a 5-year follow-up were used for our analysis (10).
6. Utility values for the GBM health states reported by Garside et al (11) were used in our analysis.

Results:

The incremental cost per QALY gained was ₹212,020 INR (138,347-401,466) ($2,963; 95% CI, 1,927 to 5,602).There is a 4.7% probability for temozolamide to be cost-effective at the willingness-to-pay threshold equally to the per capita GDP (Fig 1). However, decreasing the price of temozolamide by 90% increases the probability of temozolamide to be cost-effective to 80% (Fig 2).

Parameters	Temozolamide	No Temozolamide
Lifetime costs per patients (in ₹)	181,235 (156,274-210,458)	105,502 (88,762-122,978)
LYs	1.85 (1.67-2.08)	1.26 (1.15-1.42)
QALYs	1.45 (1.21-1.73)	1.12 (0.92-1.33)
Incremental cost per QALY gained (in ₹)	212,020 (138,127-401,466)	-

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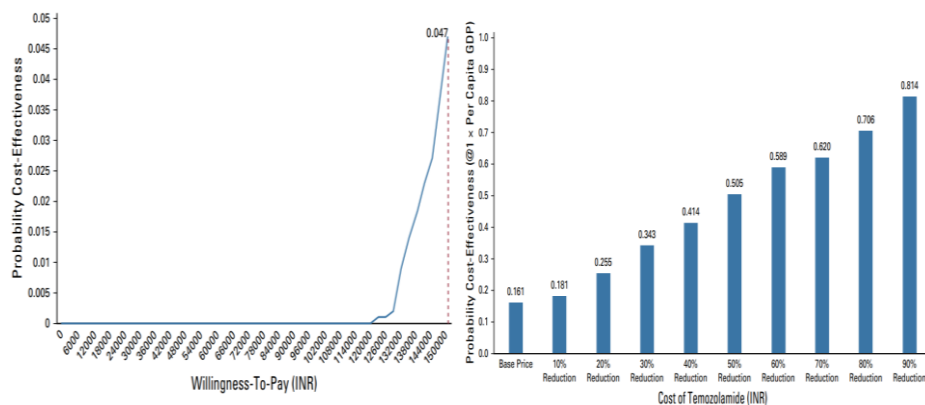
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Cost effectiveness of Trastuzumab for Management of Breast Cancer in India

Policy Brief

Executive Summary:

Breast cancer is the most common cancer among women in India and accounts for 27% of all cancers in that country. Addition of the HER2-targeted mono-clonal antibody trastuzumab to chemotherapy in adjuvant treatment has shown to improve disease-free survival (DFS) by 50% and overall survival (OS) by 30% among human epidermal growth factor receptor (HER)-2 positive early and advanced breast cancers. However, trastuzumab is an expensive drug. It was reported to have been used in only 8.6% of eligible patients, half of whom were enrolled in a clinical trial. The low rate of trastuzumab demands evidence on whether public resources should be used to make this treatment routinely accessible in India. We used a Markov model to estimate the incremental cost and benefits of using trastuzumab (for 1 year, 6 months, or 9 weeks) as compared to with chemo-therapy alone using a societal perspective. Use of trastuzumab for 1 year is not cost effective in India at the current price. At the current price, 1-year trasutuzumab use has just a 4% to 57% probability of being cost-effective. However, trastuzumab use for 9 weeks is cost effective and should be included in clinical guidelines and reimbursement policies. A price reduction of 15% to 35% increases the probability of 1-year trastuzumab use being cost effective, to 90%.

Aims and Objective

This policy brief addressed the policy question of the cost-effectiveness of adjuvant trastuzumab in combination with standard chemotherapy compared with chemotherapy alone in the Indian context. The study was conducted by the HTAIn Resource center at PGIMER, Chandigarh.
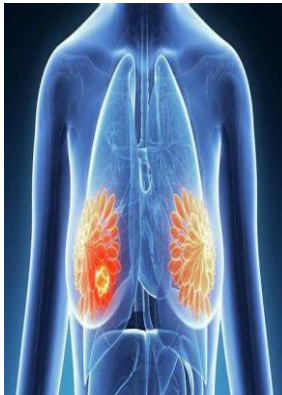
Policy Recommendations:

One-year use of trastuzumab is not cost effective, or there is significant uncertainty around its cost effectiveness. Reducing the price of the drug by 35% would make 1-year trastuzumab use cost effective. In the current scenario, use of trastu-zumab for 9 weeks is the most efficient option. The clinical guidelines and provider payments for cancer treatment under health insurance schemes should be accordingly revised.

Background and Gap in Literature:

Addition of the HER2-targeted mono-clonal antibody trastuzumab to chemotherapy in ad-juvant treatment has been shown to improve disease-free survival (DFS) by 50% and overall survival (OS) by30% [1-3]. However, trastuzumab is an expensive drug. It was reported to have been used in only 8.6% of eligiblepatients, half of whom were enrolled in a clinical trial [4]. Many cost-effectiveness analyses of trastuzumab have been reported, with variable results [5-13]. A major limitation of the existing literature is thata majority of these model-based cost-effectiveness analyses have based their outcome valuation on the interim results of clinical trials with relatively shortfollow-up. No cost-effectiveness analysis has yet been published taking into account the long-term clinicalbenefits based on the Herceptin Adjuvant (HERA) trial (ClinicalTrials.gov identifier: NCT00045032) [3]. More-over, although a majority of previous economic evaluations have used effectiveness estimates from the HERA trial, the HERA trial protocol is not commonly followed in routine clinical practice by oncologists in India [14].

We undertook this cost-effectiveness analysis of adjuvanttrastuzumab in combination with standard chemotherapy compared with chemotherapy alone in the Indian context. The base case presents the analysis for 1-year use of trastuzumab, which is standard practice. Detailed subgroup analyses were also undertaken, and we present cost-effectiveness findings for 6-month and 9-week trastuzumab use.

Policy Brief

Methods and Approach

We undertook this cost-effectiveness analysis (CEA) using a societal perspective, which accounted for both health system and patients' costs. We developed a Markov model and compared the costs and consequences of treating a cohort of patients with surgically resected HER2-positive breast cancer at age ≥ 50 years with adjuvant chemotherapy or adjuvant chemotherapy plus trastuzumab. Our methodological principles are consistent with the Indian reference case for conducting economic evaluations used by the agency for Health Technology Assessment in India (HTAIn).

Intervention and control arms:

Trastuzumab infusion at 8 mg/kg for the first cycle and 6 mg/kg for the remaining 16 cycles was considered for all patients in the first year. Adjuvant chemo- therapy (comprising anthracycline and taxane-based drugs).
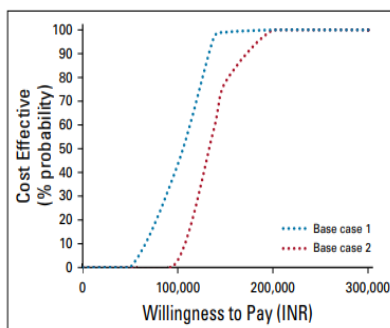
Figure 2: Probability of 1-year trastuzumab use being cost effective at varying willingness-to-pay thresholds. INR, Indian national rupees
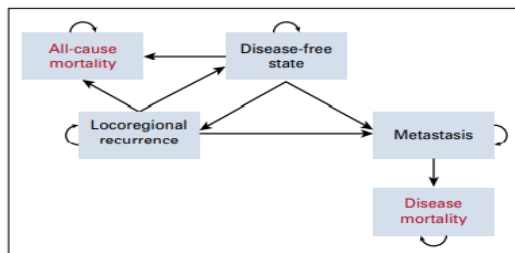
The analysis was performed under the following components:

A Markov model with 5 health states–disease-free state, locoregional recurrence (LR), metastasis, death resulting from breast cancer, and all- cause mortality—was developed. Patients with surgically resected HER-2-positive breast cancer entered the model at the age of 50 years. A cycle length of 1 year was considered appropriate based on the available literature. Lifetime horizon was considered in the model. The base case analysis is presented in 2 scenarios. In base case 1, we used the effectiveness evidence from the HERA trial, whereas in base case 2, the effect size of the joint analysis was used; everything else remained constant. The cost of treatment was estimated by using rates of use of various treatment options among patients in different health states, as reported in the pooled data from Indian cancer registries [15] To elicit the unit costs of various diagnostic and therapeutic services provided to these patients, locally published studies [16,17] and provider payment rates under the national social insurance scheme for central government employees [18] were used. Medicine process were obtained from procurement rates of the medical service corporation in Tamil Nadu state [19].

Results:

The incremental cost per QALY gained was INR 178,877 (HERA trial) and INR 1,34,413 (Joint Analysis of NSABP B-31 and NCCTG N9831 Trials) Use of trastuzumab for 1 year is not cost effective in India at the current price. At the current price, 1-year trasutuzumab use has just a 4% to 57% probability of being cost-effective. However, trastuzumab use for 9 weeks is cost effective and should be included in clinical guidelines and reimbursement policies. A price reduction of 15% to 35% increases the probability of 1-year trastuzumab use being cost effective, to 90%.

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Price and trade margin regulation of Anti-Cancer medicines

Impact of price and trade margin regulation on cancer medicine in India? An interrupted time series analysis

Public Health Foundation of India

Policy Brief

Executive Summary:

In 2016, cancers accounted for 5% of the total Disability Adjusted Life Years (DALYs) and over 8% of total deaths in India. Besides the humongous disease burden, cancer also places significant socio-economic burden on patients and their families. The National Pharmaceutical Pricing Policy, 2012 was notified in order to control prices of medicines including cancer medicines listed on the National List of Essential Medicines using a market based formula. National. In addition, in February, 2019, 42 anti-cancer drugs were brought under 30% trade margin cap.

The objective of the present study was to ascertain the impact of price and trade margin regulation on the sales of anti-cancer medicines in the private retail market in India with the help of Interrupted time series analysis, a quasi-experimental research design. A reference market outside regulation was used as control group to further

Background and Literature:

The average out of pocket expenditure for cancer patients is in fact 2.5 times that for other diseases. Borrowings, sales of existing assets and contributions from friends and relatives have been found to be sources of financing cancer treatment of some 40% of hospitalised cases. Impoverishment of households as a result of out of pocket expenditure on medicines in India has been reported in previous studies. Medicine price regulation is therefore imperative.

Literature suggests that while policies involving direct price control are effective in reducing prices and controlling expenditures, they may not lead to a reduction in medicine expenditures in the long run since manufacturers find ways to increase sales of formulations outside regulation. A recent study found that despite the attempts to regulate prices as well as trade margins of some anti-cancer medicines in India, their prices have remained high and that there is considerable variation in the prices of the same medicines marketed by different manufacturers. The study also observed that anti-cancer medicines priced lower are not necessarily purchased more. Some pharmaceutical companies are known to have left certain product categories after the implementation of price regulation.

These observations raise questions on the effectiveness of policies aimed at reducing medicines prices and expenditure in increasing consumption as was reported in previous studies

Policy Recommendations:

The coverage of price regulation policy must be expanded to include all strengths and dosage forms of medicines under the NLEM including therapeutically equivalent drugs so as to avoid the switch from price regulated to unregulated medicines.

Similarly, trade margin regulation should be expanded to other cancer drugs and also therapeutic areas leaving out over the counter drugs.

A system of effective monitoring of availability and sales of regulated medicines must be implemented to ensure that regulated medicines are not gradually phased out of the market.

Aims and Objective

This policy brief addresses the policy question of the impact of policies of price and trade margin regulation of select cancer medicines the sales of anti-cancer medicines in the private retail market in India. It summarizes the results of a the impact evaluation study, carried out by the Public Health Foundation of India.

Methods and Approach

Interrupted time series, a quasi-experimental research design, capture the impact of price and trade margin regulation on anti-ca in India. A reference market outside regulation was used as c further strengthen our research design.

Interventions under study:

1. The most recent policy in the country, the National Pharmaceutical Pricing Policy (NPPP), 2012 was notified by the National Pharmaceutical Pricing Authority (NPPA) in order to control prices of 'essential medicines' defined as medicines listed on the National List of Essential Medicines (NLEM) using a market based formula. The market based formula, uses a simple average of prices to retailers (PTR) of brands of a formulation with market share greater than or equal to 1% and allowing 16% retail margin. The Drug Price Control Order (DPCO), 2013 was subsequently notified to implement the provisions of NPPP, 2012 for drugs including those used for cancer treatment on the NLEM, 2011. The NLEM is a dynamic list and was revised in 2015.

2. In February, 2019, the NPPA invoked para 19 of DPCO, 2013 and notified another 42 anti-cancer drugs for 30% trade margin cap through a 'Trade Margin Rationalization Approach'

The preferences of prescribers could have either shifted in the interest of the patient as they would have chosen to prescribe the drugs under regulation instead of equally effective alternatives as they were made available at lower

Equation:

$$Y_t = \alpha + \beta1 \text{ time t} + \beta2 \text{ intervention t} + \beta3 \text{ time after intervention t} + \epsilon_t$$

- The dependent variable (Y_t) appeared as 'logarithm of sales volume' of anti-cancer medicines.
- 'Time' appeared as an independent variable.
- Two binary variables were introduced to estimate the immediate level change (variable name: intervention) as well as trend change (variable name: time after intervention) after the intervention in the outcome variable (see equation 1 below).
- The variable 'intervention' was assigned as a binary variable taking the value '0' for the pre-intervention period and the value '1' for the post-intervention period, whereas time after intervention was a continuous variable for the post-intervention period.

Our analysis suggests that post intervention (notification of ceiling prices), of total 17 cancer medicines under study, 7 medicines witnessed both an immediate and sustained increase in sales in the post-intervention period, 3 medicines witnessed an immediate increase in sales followed by a sustained decline, 6 medicines witnessed an immediate and sustained decline in sales and 1 medicine witnessed an immediate decline followed by a sustained increase in sales. Our analysis also suggests that post intervention (notification on trade margin cap), of total 26 cancer medicines 2 medicines witnessed both an immediate and sustained increase in sales in the post intervention period, 10 medicines witnessed an immediate increase in sales followed by sustained decline, 5 medicines witnessed an immediate and sustained decline in sales and 9 medicine witnessed an immediate decline followed by a sustained increase in the

Health Technology Assessment on the use of PET for cancer care in India

Evidence Summary

Limited evidence to suggest that PBT is a clinically effective technology in comparison to current clinical practice. Less than half of published clinical trials of PBT are prospective. Only 10% of prospective studies of PBT are randomized. Most of the studies reporting clinical effectiveness of PBT are single armed observational studies. Current indication for proton therapy in a few international clinical guidelines for PBT is only for a small number of cancers such as skull, spine, ocular soft tissue cancers and few pediatric cancers. No international agency has strongly appraised the effectiveness of PBT in comparison to IMRT, CRT, and SBRT. Indian literature suggests that even IMRT and 3D- CRT are not cost-effective at current threshold. Proton beam therapy in comparison to existing current clinical practices including CRT, SBRT, IMRT, Carbon-ion therapy, photon radiotherapy, enucleation and plaque brachytherapy is recommended as cost-ineffective technology.

Policy Recommendations

Limited evidence to suggest that PBT is clinically effective technology in comparison to current clinical practice. Less than half of published clinical trials of PBT are prospective. Only 10% of prospective studies of PBT are randomized. Current indication for proton therapy in a few international clinical guidelines for PBT is only for a small number of cancers such as skull, spine, ocular soft tissue cancers and few paediatric cancers. No international agency has strongly appraised the effectiveness of PBT in comparison to IMRT, CRT, and SBRT. Indian literature suggests that even IMRT and 3D-CRT are not cost- effective at current threshold.

Background and gap in literature

Radiation therapy is a vital speciality in cancer management as it is effective in treating malignancies as radical or palliative treatment. It is based on high energy beams/radioactive substances to halt the growth and division of tumour cells. Nearly two-third of cancer patients require radiation therapy as a unique treatment or as part of more complex therapeutic protocol. Earliest form of radiation was based on single large exposure. Various modalities were established in order to minimize the side effects and maximize the tumour dose. The establishment of cobalt units was a notable discovery. There is growing interest in the use of proton beam therapy (PBT) for the treatment of cancer. Proton therapy is a form of radiation treatment used to destroy tumour cells. Unlike x-rays (regular radiation treatment), it uses protons to sends beams of high energy that can target tumours more precisely than X-ray radiation. However, given the limited capacity and higher costs, decisions on which radiation therapy should be used to treat cancer patients should be based on comparisons of proton therapy against current best practice.

Research question

Is establishing Proton Technology Equipment for cancer treatment cost-effective For India?

Population

Adult or paediatric population suffering from any type of cancer irrespective of stage

Intervention

Proton Beam Therapy (PBT)

Comparators

Conventional radiotherapy (CRT) Stereotactic body therapy (SBRT) Intensity Modulated Radiation therapy (IMRT) Carbon ion therapy Photon radiotherapy Enucleation and plaque brachytherapy

Outcome Interest

Local recurrence-free survival, overall survival, toxicity, relapse-free survival including local recurrence, loco-regional recurrence, distant metastasis and death, quality of life and economic costs.

Methods and approach

We have attempted a review of existing literature on clinical effectiveness of PBT relative to other available modalities for radiation therapy. Furthermore, existing literature on health economic evidence and recommendations of various international guidelines was being reviewed using methods for rapid health technology assessment.

Health Economic Evidence

Study and year	Country	Cancer type	Interventions assessed	Stated Perspective	Reported main result
Grutters et al 2010	The Netherlands	Inoperable stage I nonsmall cell lung cancer	PBT, carbonion therapy, CRT, and SBRT	Dutch health Care perspective	PBT and CRT dominated by carbon-ion therapy and SBRT
Parthan et al 2012	USA	Localized prostate cancer	PBT, IMRT, and SBRT	Health care payer and societal	PBT and IMRT dominated by SBRT in both perspectives
Ramaekers et al 2013 Dutch	The Netherlands	Locally advanced (stage 3–4) head and neck cancer	PBT for all patient, IMRT for all patients, and PBT if efficient	health Care perspective	ICER for PBT if efficient versus IMRT for all: €60,278 ICER for PBT for all versus IMPT if efficient: €127,946
Moriaty et al 2015	USA	Intraocular melanoma	PBT, enucleation, and plaque brachytherapy	Provider perspective	ICER for PBT versus enucleation: $106,100 ICER for plaque brachytherapy versus enucleation: $77,500 ICER for PBT versus plaque brachytherapy not reported
Mailhot Vega et al 2016.	USA	Breast cancer	PBT and photon radiotherapy	Societal perspective	In base case analysis with $50,000 threshold: Women with no CRFs: PBT not cost-effective for all ages and for all photon MHD tested (up to 10 Gy).
Leung et al 2017	Taiwan	Inoperable advanced hepatocellular carcinoma (large tumours)	PBT and SBRT	Single payer healthcare system	ICER for PBT versus SBRT: NT$ 213,354 (equivalent to US $14,180 in 2016 prices)
Sher et al 2018	USA	Oropharyngeal squamous cell carcinoma	PBT and IMRT	Payer perspective and societal perspective	HPV-positive patients: ICERs for PBT versus IMRT: $288,000 and $390,000 in the payer and societal perspectives respectively. HPV-negative patients: ICERs for PBT versus IMRT: $516,000 and $695,000 in the payer and societal perspectives respectively

Clinical Guidelines on PBT:

NICE	PBT for the treatment of malignant brain tumors and prostate cancer is currently being monitored
ILROG	Adults with mediastinal lymphomas and for young women. Heavily pretreated patients who are at elevated risk for radiation-related toxicity to the heart, lungs, and/or bone marrow.
National Comprehensive Cancer Network	Chondosarcomas of the skull base and axial skeleton, cancer of the nasopharynx, nasal cavity, or paranasal sinuses, cranio-spinal irradiation. No clear evidence supports a benefit or decrement to proton therapy over IMRT for either treatment efficacy or long-term toxicity.
ASTRO	• Ocular tumors, including intraocular melanomas, Tumors that approach or are located at the base of skull, including but not limited to Chordoma, Chondrosarcomas • Primary or metastatic tumors of the spine where the spinal cord tolerance may be exceeded with convention treatment or where the spinal cord has previously been irradiated. Hepatocellular cancer • Primary or benign solid tumors in children treated with curative intent and occasional palliative treatment of childhood tumors when at least one of the four criteria noted above apply
ESMO	No recommendation on PBT due to lack of clear evidence on benefits associated with PBT

Results

Particle therapy results in higher survival rates than CRT in stage I inoperable NSCLC patients. No firm conclusions can be drawn on the reduction of side effects after particle therapy. Particle therapy may be more beneficial in stage III NSCLC, where survival is only 26–36% with concurrent chemo-radiation with photons, and severe adverse events. Occur more frequently. However, more evidence is needed on whether particle therapy is actually beneficial in advanced stage NSCLC.

Health Technology Assessment in India (HTAIn)

Department of Health Research

Ministry of Health & Family Welfare

Government of India