Health Technology Assessment in India (HTAIn)

Policy Briefs

Vol-2

March-2023

सत्यमेव जयते

Department of Health Research
Ministry of Health & Family Welfare
Government of India

Policy Briefs

Volume 2

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PREFACE

The Government of India has established **"Health Technology Assessment in India (HTAIn)"** under the Department of Health Research Ministry of health and family Welfare to conduct Health Technology Assessment and support Central and the State Governments in evidence based-decision making and policy formulations. HTAIn prepares a detailed HTA Study Report of the completed studies which is reviewed by a Technical Appraisal Committee (TAC) and approved by the Medical Technology Assessment Board (MTAB) and handed over to the User Department for the implementation of its recommendations. HTAIn follow several consultative and deliberative process including Stakeholder meeting while conducting the study and preparing its reports.

The Policy Brief Book contains a collection of Policy Briefs of all the completed HTA Studies conducted by HTAIn and approved by TAC and MTAB. The first volume of the Policy Brief Book was released on *31st December, 2020* in an *International Symposium on Health Technology Assessment* by *Dr. Bharati Praveen Pawar. Hon'ble Minister of State, Health & Family Welfare,* contained 19 Policy Briefs of the studies completed by HTAIn till 2020 and is available on the HTAIn website - https://htain.icmr.org.in/images/pdf/ishta_Policy_Briefs.pdf. The present Policy Brief Book - Volume 2 contains 27 Policy Briefs of the studies completed by HTAIn, till date. These books are beneficial for policymakers and researchers from various health sectors to get an overview of HTAIn approach of conducting studies and understanding the usefulness of HTA and its applications in evidence-informed decision-making and policy formulation.

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सत्यमेव जयते

आज़ादी का अमृत महोत्सव

मंत्री
स्वास्थ्य एवं परिवार कल्याण
व रसायन एवं उर्वरक
भारत सरकार
Minister
Health & Family Welfare
and Chemicals & Fertilizers
Government of India

MESSAGE

It gives me immense pleasure to know that the Health Technology Assessment in India, Department of Health Research, Ministry of Health & Family Welfare is releasing the **Policy Brief Volume 2.** It is a rich, diverse & detailed compilation of the Health Technology Assessment Studies which have greatly contributed to Policy Makers' decision-making. With the advancement of technology in the health sector, it is very crucial to take logical and evidence-based decision making to adoptthe health technologies like medical devices, drugs, and treatment strategies in the healthcare system.

India is home to one of the world's largest healthcare systems. The Healthcare system is very diverse and very different from other Countries it provides healthcare to over one billion people. Health systems and policies have a critical role in determining the manner in which health services are delivered, utilized and affect health outcomes. The strengthening of the healthcare system should be based on evidence, quality, safety, clinical effectiveness, cost effectiveness and equity of health interventions.

The Government under the leadership of Hon'ble Prime Minister Narendra Modi Ji has been working relentlessly towards leveraging the power of technological advancements for the welfare of citizens and strengthening the governance, management and performance of the overall healthcare system of the country.

Health Technology Assessment in India as a sub scheme of the Department of Health Research with its objectives will play a key role in India to provide better Affordable, Accessible and Quality Healthcare technologies for achieving the country's commitment to Universal Health Coverage.

I am sure that this compilation of policy briefs will benefit all stakeholders to help undertake evidence-based decision-making for better health outcomes.

(Dr. Mansukh Mandaviya)

01 March 2023

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№ 1798

स्वास्थ्य एवं परिवार कल्याण राज्य मंत्री
भारत सरकार

MINISTER OF STATE FOR HEALTH & FAMILY WELFARE GOVERNMENT OF INDIA

डॉ. भारती प्रविण पवार
Dr. Bharati Pravin Pawar

आज़ादी का अमृत महोत्सव

PHOTO

MESSAGE

Health Technology Assessment (HTA) 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 recommendations of the HTA studies conducted by the Department of Health Research. This is an important step towards universalization of the healthcare system with the most clinically effective and cost effective technology.

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. As country and its decision makers are moving towards evidence based decision making with HTA, an important tool to aid in robust resource allocation. HTA recommendations helps to ensure that new and existing healthcare technology are available, accessible and affordable bringing India one step closer to Universal Health Coverage.

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

Government of India, under the visionary leadership of Hon'ble PM Shri Narendra Modi ji has started work on skilled manpower for future medical technology and high-end manufacturing and research. The Department of Health research is envisaged to bridge the gap between the researchers, technology developers and policy makers.

BPv

(Dr. Bharati Pravin Pawar)

"दो गज की दूरी, मास्क है जरूरी"

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सत्यमेव जयते

आज़ादी का अमृत महोत्सव

सचिव
भारत सरकार
स्वास्थ्य अनुसंधान विभाग
स्वास्थ्य एवं परिवार कल्याण मंत्रालय एवं
महानिदेशक
भारतीय आयुर्विज्ञान अनुसंधान परिषद

Secretary
Government of India
Department of Health Research
Ministry of Health & Family Welfare and
Director-General
Indian Council of Medical Research

Message

The Government of India's commitment to ensure Universal Health Coverage has laid the path for Affordable, Accessible and Available Healthcare Technologies with the establishment of Health Technology Assessment in India (HTAIn) under the department of Health Research, Ministry of Health and Family Welfare. The challenges for efficient allocation of the limited resource and provide Quality care to every individual can be supported by HTA by means of evidence-informed decision-making.

The need for a strong healthcare system to support Universal Health Coverage is to build a collaborative scientific environment which paves way for inter-sectoral coordination between academia, research institutions, start-up technology companies, Industry, and Policy makers. The main concept for UHC covers three key elements — access, quality, and financial protection. India is committed to achieving Universal Health care for all by 2030. The focus needs to be on the promise of the National Health Policy by ensuring availability, access, and utilization of high-quality primary care through government health services.

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. Effective HTA processes are able to ensure methodological rigour; and use multi-disciplinary inputs to produce and disseminate high-quality, policy-relevant evidence for decision-makers for an efficient and accountable healthcare system. The success of the Health technology assessment program will be in terms of implementation of the evidences by Central and State Health Departments. It will be our endeavour to provide such evidences for informed decision making for the health sector in the Country.

Rajiv Bahl

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अनु नागर
संयुक्त सचिव

ANU NAGAR
Joint Secretary

सत्यमेव जयते

आज़ादी का अमृत महोत्सव

भारत सरकार
स्वास्थ्य एवं परिवार कल्याण मंत्रालय
स्वास्थ्य अनुसंधान विभाग

Government of India
Ministry of Health & Family Welfare
Department of Health Research

Message

Health Technology Assessment in India (HTAIn) has been established in Department of Health Research to facilitate evidence based decision making for use of affordable and quality health interventions to achieve Universal Health Coverage. Establishment of an institutional structure for HTA is an important milestone towards synthesis of scientifically backed evidence for promoting development of standardized cost-effective interventions leading to reduction in the cost variations in patient care, decreasing in overall cost of medical treatment and reducing out of pocket expenditure of patients.

In Indian context, strengthening the Health System requires a joint effort of the Centre and the States in prioritizing healthcare, efficiently using the health resources to ensure optimal health gain for maximum number of people, adoption of quality standards, fulfilling the skill gaps, updating and complying with a standard treatment protocol, quality of health improvement programs and reducing out of pocket expenditure on health services. Hence, there is growing need for evidence-informed health policies to make the public health systems more effective and efficient.

Since its inception 5 years ago, HTAIn has completed 42 HTA studies including several multi-centric studies. All these studies have supported Centre and State Governments in evidence based decision making for implementation of various health programs.

The compilation of this second volume of Policy Briefs of the HTA studies will support the decision makers to facilitate efficient resource allocation and to provide affordable healthcare.

(Anu Nagar)

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Executive Summary

The Government of India is committed to extend healthcare services to its 1.39 billion population and is constantly making endeavours to provide affordable and quality healthcare. The National Health Policy, 2017 has envisaged an increase in public health spending on healthcare services to 2.5% of GDP. These resources can be optimally utilised with the help of Health Technology Assessment (HTA), which is a widely used methodology globally, for optimization of resource allocation and utilization in health.

HTA is a multidisciplinary process that assess health technologies i.e., drugs, devices, healthcare programmes etc. for their safety, efficacy, cost- effectiveness and equity issues. It analyzes the medical, social, ethical, and economic implications of development, diffusion, and use of health technology in a robust and transparent manner.

HTA methods are evolving and their applications are increasingly diverse such as priority setting in healthcare, efficient resource allocation across different health schemes, designing health benefit packages, strategic purchasing during procurements, informing the standard treatment guidelines etc. Altogether, HTA helps the policymakers for evidence- informed health decision-making and policy formulations in healthcare.

HTA provides systematic evaluation of properties, effects and/or impacts of health technologies or interventions. The assessment is conducted by interdisciplinary groups using explicit analytical frameworks, drawing on clinical, epidemiological, health economic and other information and methodologies. It may be applied to health interventions, public health programmes, priority setting in health care, identifying price for medicines and other technologies based on their cost–effectiveness, and for guiding clinical guidelines.

Health Technology Assessment in India (HTAIn) is a sub-scheme under the umbrella scheme Human Resource and Capacity Building in the 15th Financial Commission approved for year 2021-22 to 2025-26 under the Department of Health Research (DHR), Ministry of Health and Family Welfare (MoHFW), Government of India to facilitate the process of transparent and evidence-informed decision making in the field of healthcare. 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.

HTAIn is entrusted with the Objective to conduct Health Technology Assessment and support Central and the State Governments in evidence based-decision making and policy formulations. It evaluates health technologies viz. medicines, devices and health programmes for its cost- effectiveness, clinical-effectiveness and equity issues by means of Health Technology Assessment, and in turn helps 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.

HTAIn has Completed 43 HTA studies, established 18 resource centers, initiated a Costing study of healthcare system, Completed the EQ-5D 5L Utility value set study for India and many more studies are ongoing. 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, Low cost Ventilators, Cost-effective threshold for Point of Care testing for Sickle Cell Diagnosis, Addition of intra dermal contraceptive for family planning, Screening Program for Dengue and Hepatitis and Tuberculosis monitoring and Adherence device for TB management.

The Policy Brief Volume-1 was released in December 2021 in the 1st International Symposium by Honourable Minister of State for Health and Family Welfare Dr Bharati Pravin Pawar. The Volume 2 of the Policy Briefs contains recommendations of the completed HTA Studies by Health Technology Assessment in India (HTAIn), Department of Health Research (DHR), Ministry of Health & Family Welfare, New Delhi. This document has been compiled together to facilitate Evidence based decision making for policy makers.

Policy Briefs

Cholecystectomy or Conservative Management for Uncomplicated Symptomatic Gallstones (Biliary Pain) Or Cholecystitis?

Cholecystectomy or conservative management for uncomplicated symptomatic gallstones (biliary pain) or cholecystitis ?

A Health Technology Assessment in India

Policy Brief

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

About...

Gallstones are stones formed due to concentration of bile which precipitates as sludge and later develops into gallstones

Cholecystectomy is the surgical removal of gallbladder performed either as open cholecystectomy (OC) or laparoscopic cholecystectomy (LC). **Early Cholecystectomy** is performed within 72 hours of hospitalization whereas **Delayed Cholecystectomy** involves initial symptomatic management followed by surgery performed 6-12 weeks later

Conservative management involves symptomatic management with analgesics, antibiotics and lifestyle modifications.

Summary

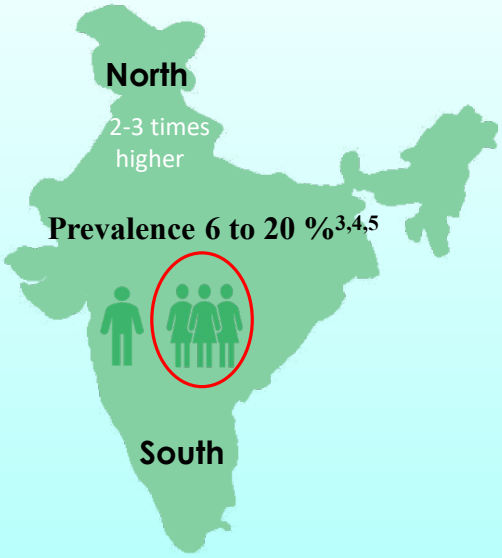
Gallstone disease is the sixth commonest problem requiring surgery and emergency hospitalization in India thus imposing a significant economic burden in Indian healthcare system[1]. The policy question of whether cholecystectomy or conservative management (CM) should be recommended for gallstone treatment 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 metanalysis (SRMA) of randomized control trials investigating the effectiveness of early cholecystectomy compared to CM/delayed cholecystectomy[2]. 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.

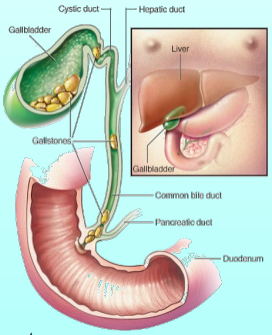
Cost-effectiveness was assessed using decision analytic markov model utilizing data from secondary literature. The results showed that Early laparoscopic cholecystectomy (ELC), compared to Delayed laparoscopic cholecystectomy (DLC), incurred an incremental cost of -₹12,001 (-$161) for 0.0002 QALYs gained, 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 analysis showed that the results were robust to the changes in the input parameters.

Background

Policy Brief



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.



Source: Mayo clinic

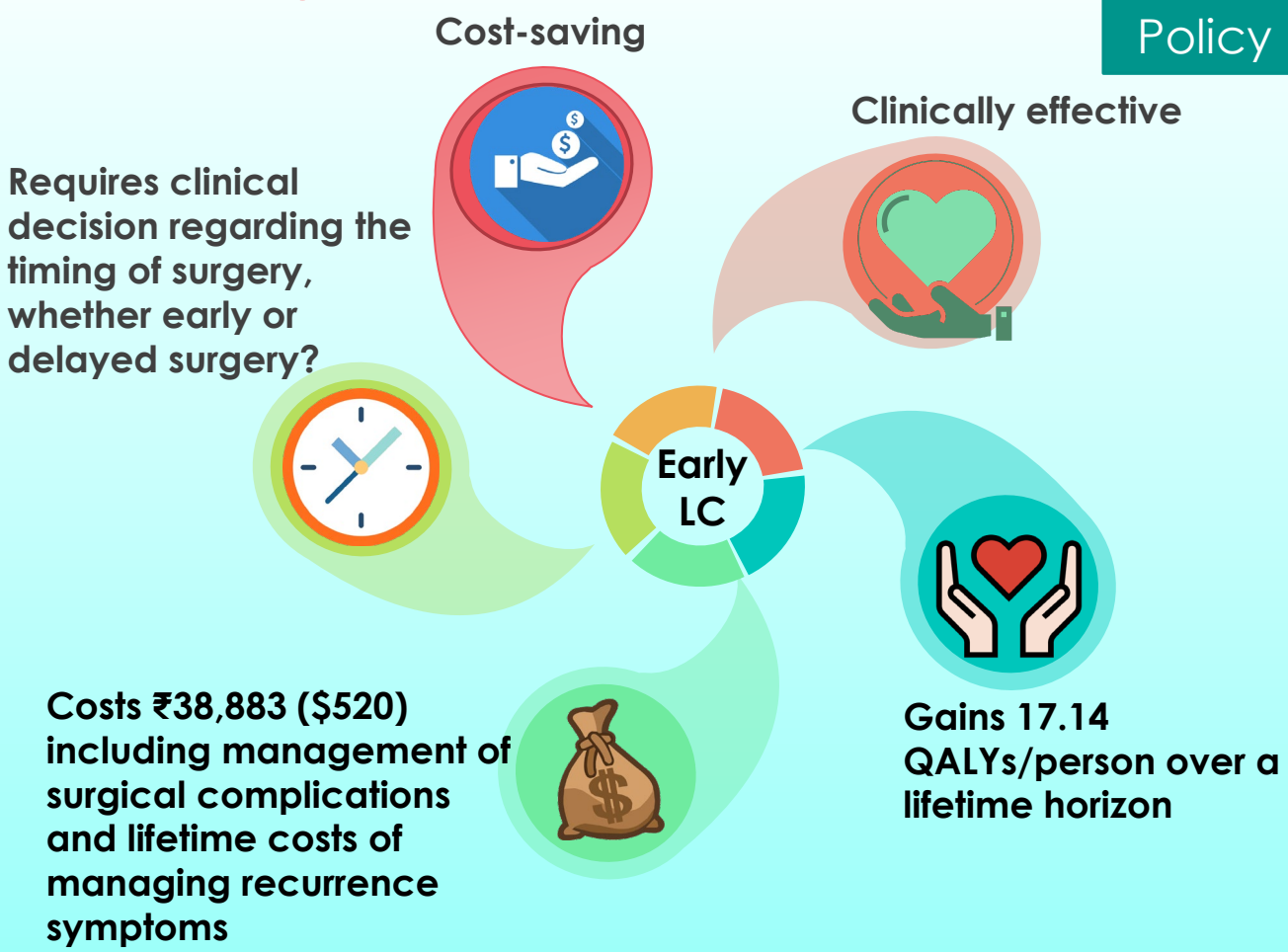
Conservative management, which involves pain and symptom management, has also shown effectiveness towards cholelithiasis and cholecystitis and carries a low risk of complications and is considered an alternative to surgery in the clinical practice[6]. Therefore, determining cost-effective management 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.

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 metanalysis 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

Policy Brief

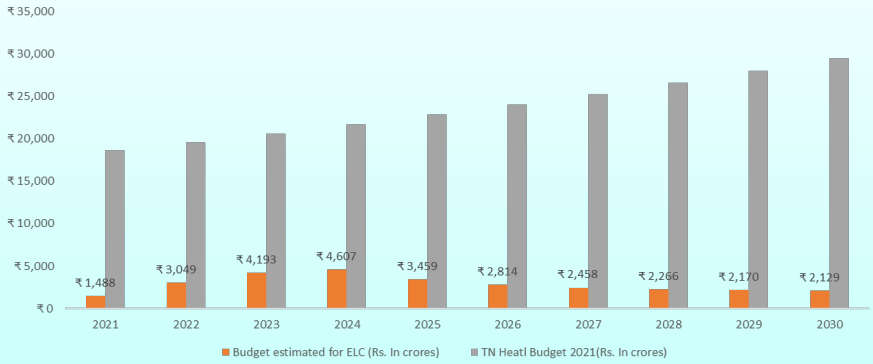


Policy Implications

- 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

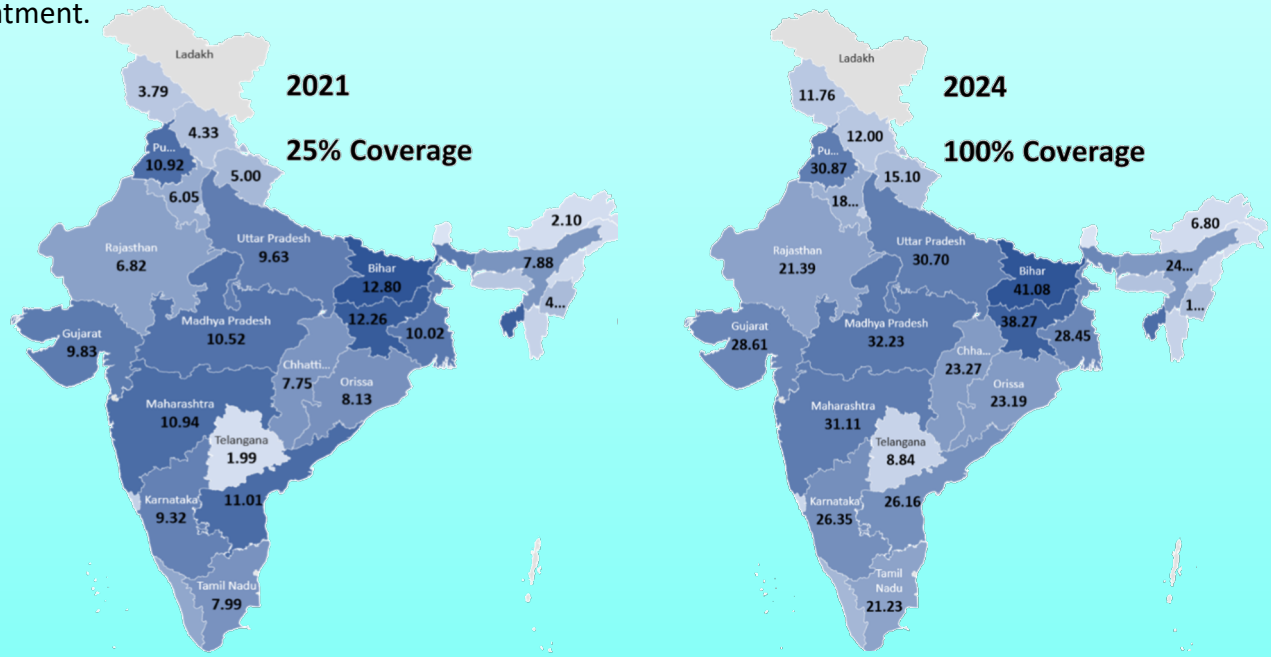
Budget Impact for Tamilnadu

Policy Brief



The estimated budget for early cholecystectomy was ₹1,488 crores ($200 million) in 2021 considering 25% treatment coverage. This represents 7.9% of Tamil Nadu's 2021 health budget (₹18,632 crores ($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 patients decreases with the increase in yearly coverage, and only the annual new cases would necessitate treatment.



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

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.

References:

1. Bhasin SK et al. Indian J Surg. 2011;73(2):131-5.
2. Bagepally BS et al. BMJ Open Gastroenterol. 2021;8(1).
3. Unisa S et al HPB (Oxford). 2011;13(2):117-25.
4. Stinton LM et al. Gut Liver. 2012;6(2):172-87.
5. Prasad A, Sinha A. Standard Treatment Guidelines-Cholecystectomy. In: Department of Surgery SH, ed.:6-13.
6. Loozen CS, Oor JE, van Ramshorst B, et al. Conservative treatment of acute cholecystitis: a systematic review and pooled analysis. *Surg Endosc* 2017;31(2):504-15. doi: 10.1007/s00464-016-5011-x [published Online First: 2016/06/19]

Available technologies for Detection of Diabetic Retinopathy from Colour Fundus Photographs to Prevent Blindness India

POLICY BRIEF

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/ colour 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 Centres (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 NCD 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 (DR) is a common microvascular 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 DR 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 DR care pathway attached to the established NCD clinics. (Fig.1) A Markov and decision tree model was used to simulate and analyze the screening process. (Fig. 2a)

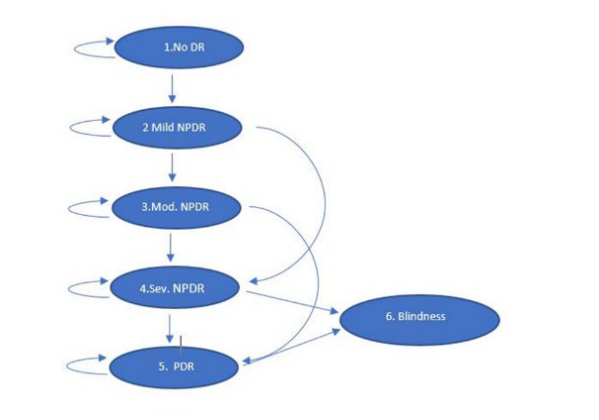


Figure 2a: Transition stages in a Markov Model

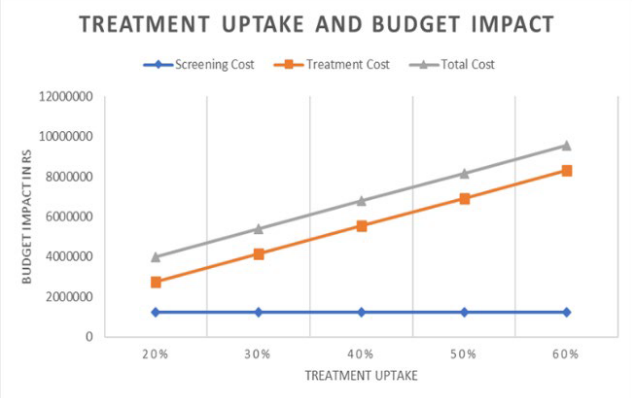


Figure 2b: Treatment uptake and budget impact

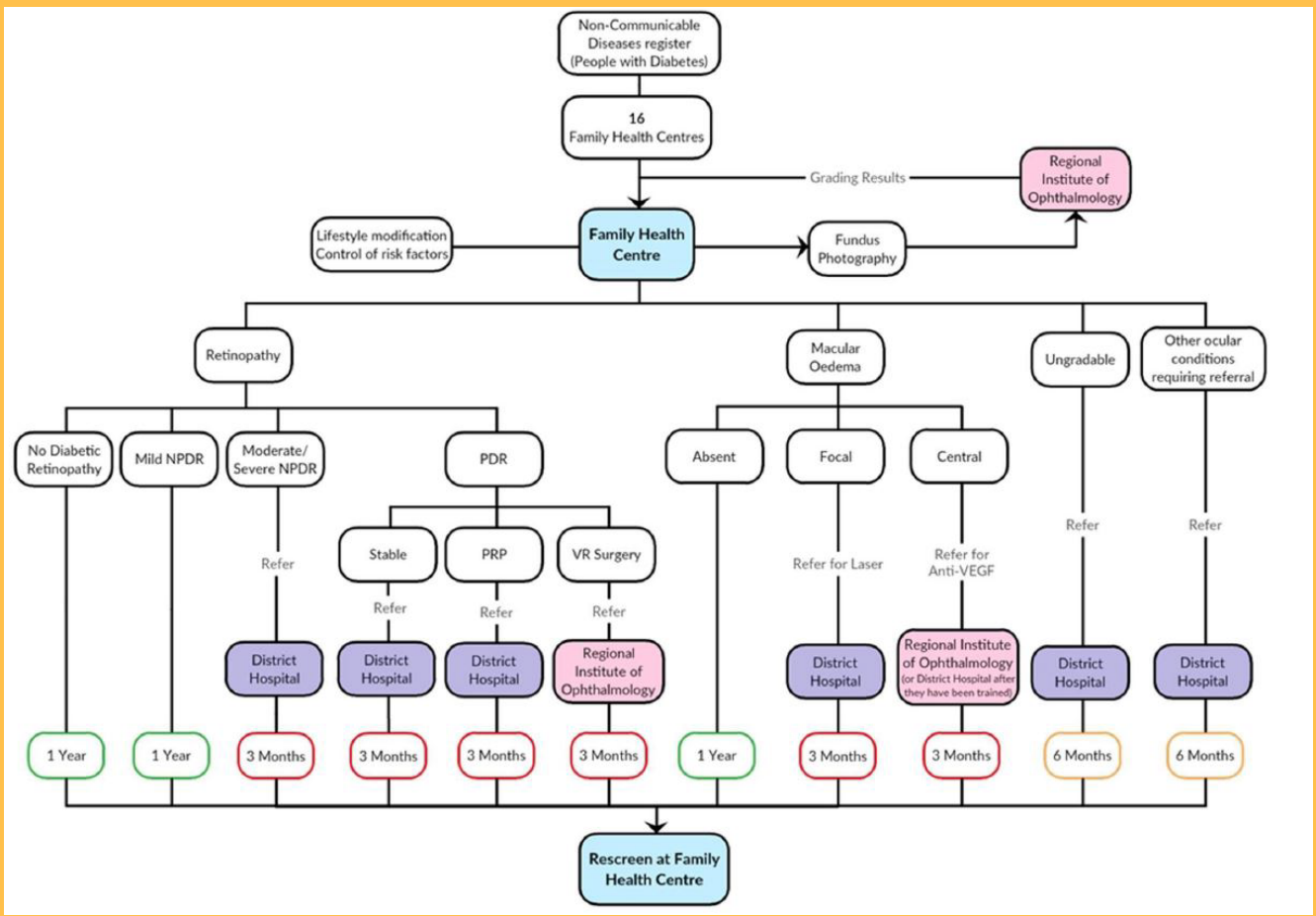


Figure 1: Diabetic retinopathy screening programme in Kerala

Findings

Tele-screening for DR using fundus photography is cost-saving (ICER -717) 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.

Table 1: Treatment Uptake and Budget Impact

Treatment Uptake	Screening Cost (Rs)	Treatment Cost (Rs)	Total Cost/FHC(Rs)	Annual Cost/FHC(Rs)	Annual Cost for Kerala(Rs)
20%	12,42,165	27,72,099	40,14,264	8,02,852	13,64,84,976
30%	12,42,165	41,58,149	54,00,314	10,80,062	18,36,10,676
40%	12,42,165	55,44,198	67,86,364	13,57,272	23,07,36,376
50%	12,42,165	69,30,248	81,72,413	16,34,482	27,78,62,042
60%	12,42,165	83,16,298	95,58,463	19,11,692	32,49,87,742

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.**

Health Technology Assessment on Positron Emission Tomography and Computed Tomography (PET-CT) for Cancer care in India

POLICY BRIEF

Health Technology Assessment in India (HTAIn)
Department of Health Research, Ministry of Health & Family Welfare
Regional Resource Centre for HTA, Kalam Institute of Health Technology-Vizag

Health Technology Assessment on Positron Emission Tomography and Computed Tomography (PET-CT) for Cancer care in India

Introduction

Every year, new cancer patients registered in India are over 11,57,294 lakhs. The risk of developing cancer before the age of 75 years in males is 9.81% and in females it is 9.42 %. The top five cancers in men and women account for 47.2% of all cancers; these cancers can be prevented, screened for and/or detected early and treated at an early stage. This could significantly reduce the death rate from these cancers.

The concept of PET imaging which originated in the mid-1970s as a research tool in cardiology and neurology has in the past four decades evolved into the most sophisticated medical imaging system with its largest application in oncology. India is one of the largest markets for the fast-growing sector of medical devices. The medical device industry in India is presently valued at USD 5.2 Billion and is growing at 15.8% CAGR. Due to the rising costs associated with introducing of new medical devices and procedures into the healthcare system, payers have started to pay more attention to the clinical and cost effectiveness of such technologies in advance.

Objective

In this context, health technology assessment of positron emission tomography and computed tomography (PET-CT) for cancer care in India healthcare system was given by Govt. of Kerala, as they wanted to know the evidence-based indications for PET–CT in support of facilities planning and to describe a project in which this information can be applied for an investment decision in India. The growth for this imaging modality has been slow owing to issues related to high cost of PET scanner, ready availability of useful biomolecules, and trained technical workforce as well as the cost of establishing and operating PET-CT scan facility is quite substantial.

Recommendations

Discussion on number of PET- CT units

- States having maximum number of PET-CT units are in Maharashtra-48
- States & union territory having only one PET-CT unit- Manipur, Tripura, Uttarakhand, Jharkhand, Puducherry.
- States and union territory not even having one PET-CT unit are-Himachal Pradesh, Arunachal Pradesh, Goa, Mizoram, Meghalaya, Nagaland, Sikkim, Andaman & Nicobar Islands, Dadra and Nagar Haveli, Lakshadweep, and Ladakh.
- In Kerala we have 13 PET-CT units, and is not suggestive of adding another PET-CT unit for Kerala, rather recommend it for states having higher cancer incidence and lesser PET-CT units.

Public Private Partnership Model for Service Delivery only for PET- CT

- PET-CT diagnostic service can be provided in Public Private Partnership model across India following National Free Diagnostic Scheme (section radiology services).
- It will help to - Provide accessible, affordable and quality PET-CT diagnostic service in all public health facilities up to district hospitals. Leading to reduction of direct cost for PET-CT scan causing a remarkable impact on out-of-pocket expenditure by general public.
- Utilizing the capacity of private service providers in supporting government to provide PET+ CT scan. will lead to strengthening PET-CT diagnostic service network across the country.
- Cost of PET-CT PET scans are conducted for around Rs 11,000 - 15,000 in private sector which are suggested to be included free of cost under PMJAY scheme.

Cyclotrons

We suggest cyclotron should be under public sector as –

- If the cost of raw material for PET-CT is maintained the cost for PET-CT scan will also be maintained otherwise if it is under private sector the cost might increase according to market fluctuations.
- Private companies are more interested in installation of PET-CT units as they will get return on investment soon, unlike the case of cyclotron.
- We need to focus on even distribution of cyclotron units across the country, as the shelf life of the radioisotopes used for PET-CT is very less

PET- CT for Cancer Treatment

(a) Early diagnosis-

PET-CT should be used for early diagnosis of cancers as they are treatable and cost effective to treat if diagnosed early and the patient goes back to lead a normal routine life.

(b) Treatment Planning

It also plays an important role in treatment planning for the patient to assess the effectiveness of the treatment and to evaluate the recurrence of the cancer.

Nuclear Medicine infrastructure in India and other countries

Table 4: Installed base of Computerized tomography, magnetic resonance imaging, and Positron emission tomography in India and other countries versus cancer statistics (24)						
Country	Australia	France	New Zealand	United States	India	Japan
Total CT units	1782	1222	76	14750	5324	14126
Units per million population	70.25	18.24	15.44	44.94	**3.93**	111.49
Total MRI Units	375	1034	76	13275	1800	6996
Units per million population	14.78	15.43	15.44	40.44	**0.69**	55.21
Total PET Units	102	167	5	1790	279	586
Units per million population	4.02	2.49	1.02	5.45	**0.20**	4.62
Total Population in Millions	25.0	66.9	4.9	327.2	1354.1	126.4
New cancer cases	197876	455618	35897	2129118	1157294	883395
Units per thousand cancer cases	0.51	0.36	0.13	0.84	**0.24**	0.66
5-year prevalent cases	755062	1390878	133716	7279710	2258208	2127559
Units per/thousand 5-year cancer prevalent cases	0.13	0.12	0.037	0.24	**0.12**	0.27

Findings

Clinical Effectiveness

A Systematic Review and Meta Analysis was conducted to evaluate the diagnostic accuracy of positron emission tomography and computed tomography (PET-CT) in oncology (Head and neck, breast, lung, gastric and cervical cancer) compared to positron emission tomography (PET), computed tomography (CT) and magnetic resonance imaging (MRI).

Diagnosis and detection of different cancers by PET-CT, PET, CT and MRI varies based on the region, recurrence and different stages of cancer.

The forest plot was plotted for all five different cancers with a total of 345 studies and their sensitivity and specificity was calculated. It is concluded that PET-CT as a diagnostic tool is highly sensitive and specific in all fields of diagnosis, staging, and treatment in oncology. PET-CT intervention during staging, restaging, may lead to timely changes in the treatment of the patient. .

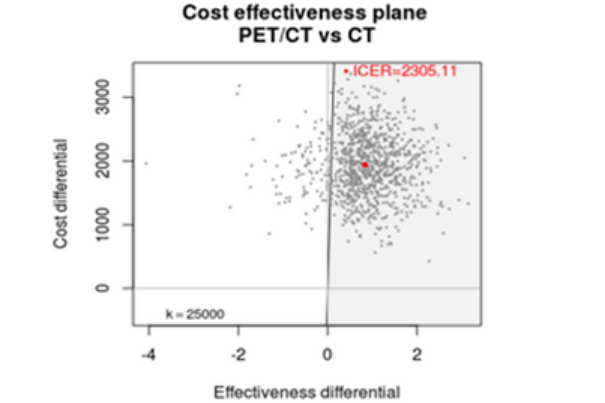
Cost Effectiveness

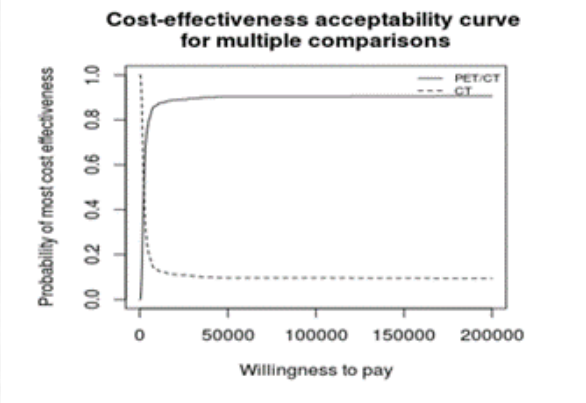
To evaluate the cost effectiveness of positron emission tomography and computed tomography (PET-CT) in oncology, cost and Quality Adjusted Life Years (QALYs) were chosen as outcomes and individuals with high risk aged between 30 and 80 are considered to be eligible for diagnosis.

The base-case results of model analyses, which revealed that PET-CT as diagnostic modality gains 4.19, 6.42 and 6.99 QALYs, in the time horizon of 5 years, 10 years and lifetime respectively.

A deterministic and probabilistic Markov model was developed with a cohort of 1,000 patients. We chose a cycle length of one year and ran the model for 50 cycles (i.e., 50 years). Cost effectiveness of PET-CT was assessed from societal perspective with time horizon of 5 years, 10 years and lifetime. Direct medical cost, Direct Non-Medical cost and Indirect cost were calculated and depicted as mean along with its standard error and distribution type. Costs are presented in IN Rupees. The costs and Quality Adjusted Life Years (QALYs) were discounted by 3% per year.

Cost Effectiveness

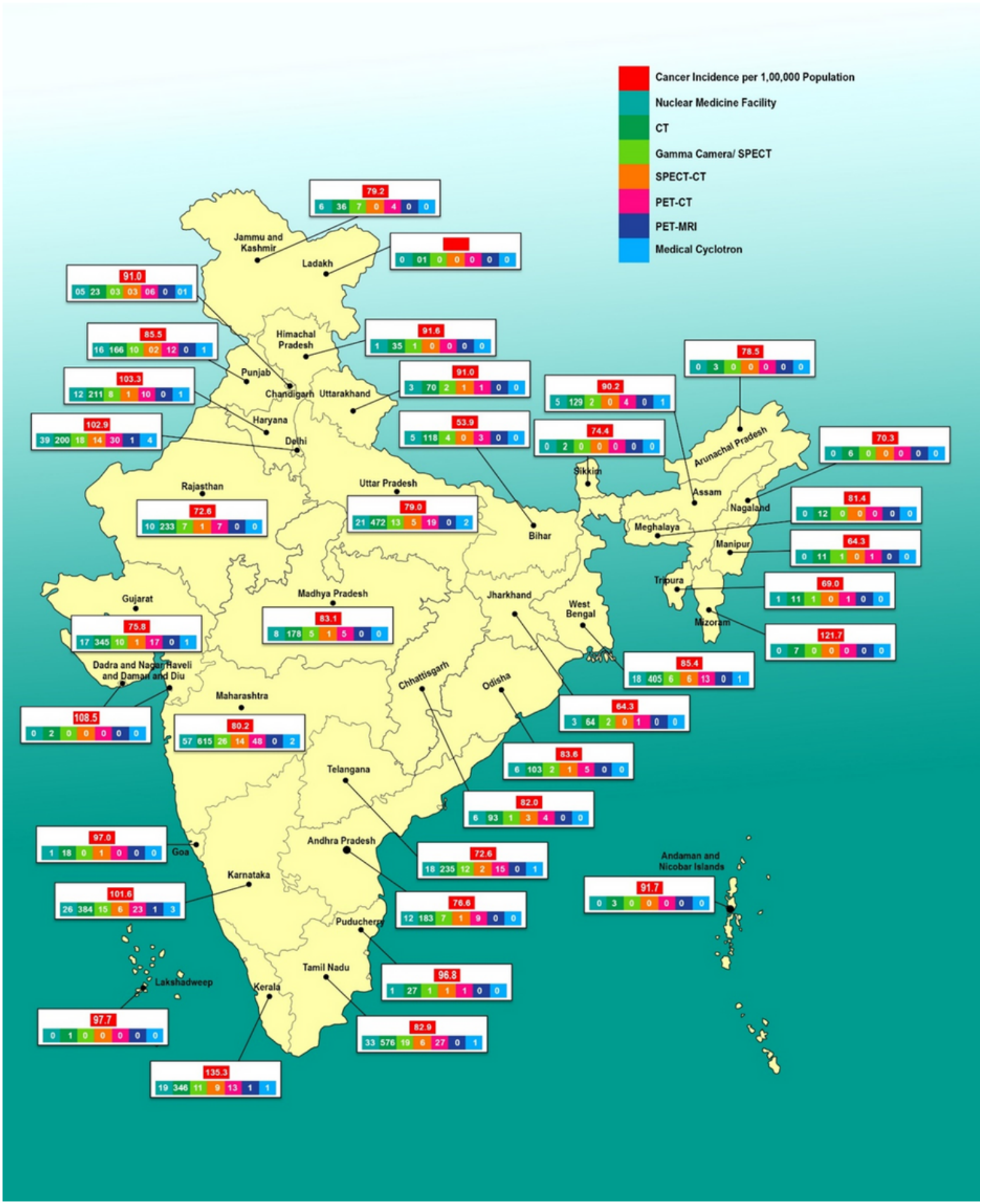




The ICER for PET-CT compared to CT were 617, 1783 and 2337 respectively for different time horizons. The ICER values obtained from PSA are all somewhere close to the base-case lifetime horizon ICER value.

Up to the willingness to pay of ₹9000, CT is cost-effective. When the willingness to pay is high, patients opt for better interventions that give better outcomes. Here, in our study, when the WTP is greater than ₹9000, PET-CT is almost 80% cost-effective.

One-way sensitivity analysis reveals that the uncertainty in the utility of diseased patient, total hospitalization cost with length of stay for PET-CT and CT, total diagnostic cost for PET-CT and CT and utility of health population has the greatest impact on the ICER.



Mapping of Nuclear medicine infrastructure in India vis-a-vis Cancer Incidence

Conclusion

- It has been observed that PET- CT is clinically as well as cost effective in diagnosing cancers. It can actually create an impact as cancer treatment delay is the actual problem, whereas diagnosing them at an earlier stage using the appropriate diagnostic modalities such as PET-CT can help solve the issue at a greater extent.
- Total cost of establishing PET-CT scan facility without cyclotron was calculated to be INR 17.08 Cr (USD 2,339,048.75), we propose additional 13 units of PET-CT, which is still very less than what is required to meet the current demand and the total cost of setting up of cyclotron facility was calculated to be INR 58.63 Cr (USD 8,026,734.1), we propose additional 4 cyclotrons via phase wise implementation to meet the current demand.
- A PPP model is suggested where cyclotron can be provided by the public sector and PET-CT by the private sector.
- Another model that can be implemented is by providing private sectors with land or infrastructure and private sectors investing on equipment's and other facilities required. Services will be provided by the private sector and the bills can be reimbursed by the government.
- Limited availability of the radiotracer FDG currently creates high-cost barriers for cancer-care programs integrating PET technology as there are only 20 cyclotrons producing FDG for oncologic PET imaging across India and FDG loses one-half of its activity every two hours (approximately) from the time it is produced. Much of the difference in cost can be attributed to variable distance from the cyclotron facility to the PET clinics. Addressing this major challenge can be a stepping stone to dealing with the whole issue of meeting the demand across the country.
- Regulation of FDG is viewed as a major hurdle to the efficient use of PET resources, geography also makes it difficult to transport FDG over long distances.
- We also propose an evaluation of the existing SPECT imaging facilities for possible conversion into PET as the only difference is the detector which is possible according to literature.
- India does not have a national approach or national policy for the use of PET/CT as a clinical tool for cancer care or for expansion of PET-CT facilities in India. Coordinated action, based on evidence- based guidelines, is required as a national approach for optimal utilization of the nuclear medicine resources in India.
- It may be time for governments to develop a systematic approach to assess the proper utilization of CT and MRI, rather than limit the expansion, and utilization, of PET technology in clinical care. Governments should consider the merits of PET technology based on its own capabilities, not on the possible overuse of other technologies.

Reference: *HTA on Health Technology Assessment on Positron Emission Tomography and Computed Tomography (PET+ CT) for Cancer care in India by Kalam Institute of Health Technology, Vizag, Andhra Pradesh.*

Acknowledgment- *HTAIn Secretariat, Department of Health Research, Ministry of Health &Family Welfare, GOI*

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

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 Gandhinagar

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.

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, disea se 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.

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 toprioritize their resources towards patient adherence

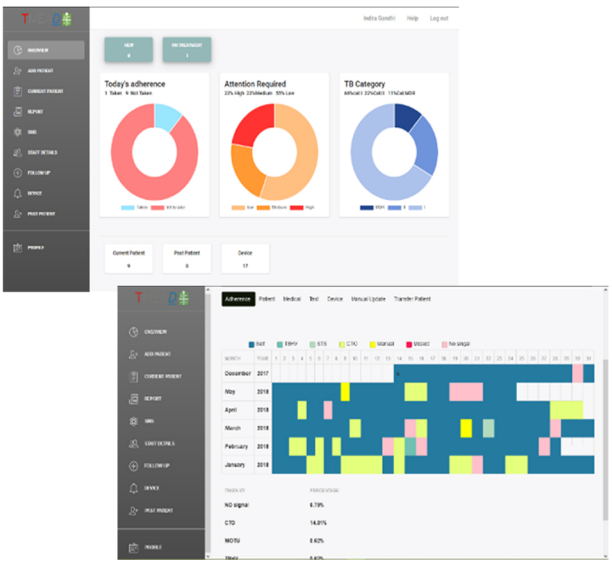


Figure 1: Daily Regime Monitoring and Real Time Tracking

Figure 2: TMEAD Device

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.

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.

Policy Implications and Novelty

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

Methods

The study was undertaken prospectively at Nasik districts of Maharashtra during 2020-21. The target population for the study were All 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

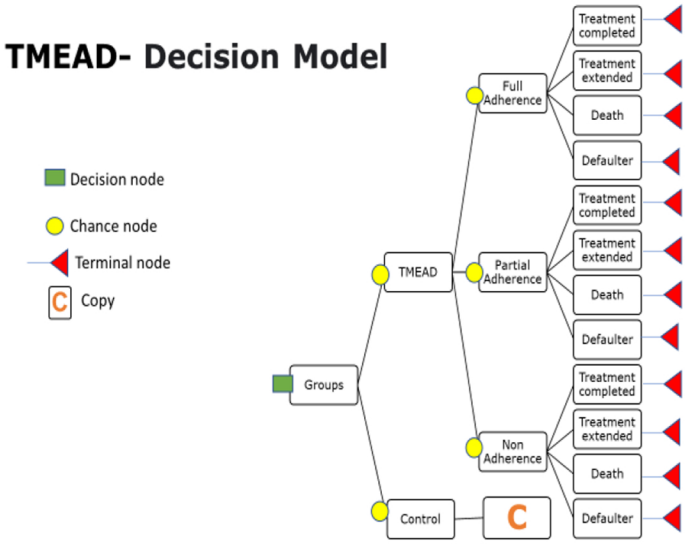


Figure 3: Decision tree model

Results

Overall adherence was 94% among those who completed treatment. Adherence in the intervention arm was 99% compared to 90% in the control arm. The average adherence reported by TMEAD devices was 88.2% in intervention group. Point adherence among those who are on treatment was 97.4% with higher adherence reported in the intervention arm (98.7%) compared to 95.24% in control arm. The adherence reported by urine rifampicin analysis was 76% in the intervention arm and 72% in the control arm.

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)

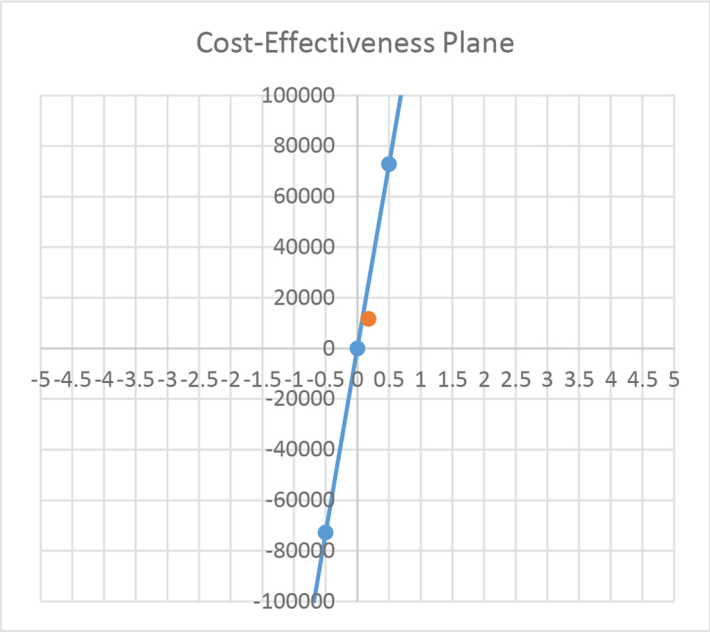


Figure 4 illustrates cost-effectiveness plane. Orange dot indicates ICER value which falls in the North East quadrant. It means intervention is costly than comparator but highly effective.

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.

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 regimen.

Acknowledgement

This study was supported through India Health Fund - A Tata Trust Initiative.

DHR provided a supplementary grant for urine rifampicin analysis.

Health Technology Assessment of TECHO+ Programme in Gujarat

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

Health Technology Assessment of TeCHO+ Programme in Gujarat

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-centres across 24 Primary Health Centres 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 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-centres 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 Taluka was done purposively based on their distance to their respective headquarters. However, a simple random sampling method was adopted to select the PHC and Sub-Centre using a table of random numbers.

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. For morbidity and its management related indicators, all the high-risk women suffering from severe maternal anaemia and pregnancy-induced hypertension (PIH) and children suffering from severe acute malnutrition and low birth weight reported at the selected PHCs was surveyed.

Cost data

Cost data was collected from a health systems perspective. An incremental costing approach was adapted for the study. Financial record of *TeCHO+* project involved in delivering intervention activities remained a key source of information.

In addition, a time usage study was conducted to assess the true cost incurred by the State and assess any time saved as a result of the TeCHO plus programme through interviewing key stakeholders and programme staffs at every level.

Cost of time spent by various technical partners of TeCHO+ programme towards capacity building, resource utilization was assessed through interviews and financial records. Cost of service delivery (cost of ANC care, immunization, cost of PHC & CHC level care, cost of institutional delivery, cost of specialist care (Gynaecologist and Paediatrician) were inferred from secondary literature. All costs are presented in local currencies. Costs were converted to constant values and reported as annualized cost in 2019- 2020 price.

Cost-effectiveness

Transition probabilities were derived from primary data for clinical indicators for both the intervention and control arms. 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. A tornado chart is presented using ICER values to depict changes in selected variables that influence the results.

Budget Impact Analysis was performed to estimate the cost of implementing TeCHO+ programme at the National levels at 2020 prices. The Budget Impact Analysis depicted the allocation of budget for 1st year to 5th year.

Findings

The annualized cost incurred for the TeCHO+ was estimated to be INR 291,99,69,103. With this investment, around 12,04,590 beneficiaries, the

calculated cost per beneficiary amounted to (INR) 2424. Similarly, for eMamta, the programme cost was estimated to be INR 334,01,06,631. With this investment, around 14,06,252 beneficiaries, the calculated cost per beneficiary amounted to (INR) 2375. For the management of high-risk cases, the total calculated cost per beneficiary for high-risk management in TeCHO+ programme was (INR) 4827 and (INR) 4778 for eMamta based on secondary literature.

For management of high-risk cases, we added cost of receiving services at Community Health Centre and cost of specialist care (Gynaecologist) proposed by Prinja et al 2016 & 2017. The total calculated cost per beneficiary for high-risk management was (INR) 4827. Similarly, cost per beneficiary for high-risk management in eMamta was calculated as (INR) 4778. For children, calculated cost per beneficiary for high risk management was (INR) 3080 and (INR) 2732 for TeCHO+ and eMamta respectively.

Scenario analysis

We have two scenarios 1) 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 is INR 95,73,72,441.

Quality of data

Quality of data reporting in 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 (IFA) 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 IFA tablets (16.3 % 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 (80.1% vs 77.9%, p-value=<0.0001), consumption of at least 180 iron-folic acid tablets (93.5 % vs 77.2 %, p-value<0.0001), 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 HBV0 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-centres 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 is 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.

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

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 OI group. IV iron sucrose was found to be costly but more effective than the oral therapy for the treatment of moderate and severe anaemia. 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.

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 in establishing effect of rise in haemoglobin level on maternal and birth outcomes.

Introduction

Maternal anaemia is a major public health issue in India. Specifically, iron-deficiency anaemia (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 (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 OI therapy.

Policy Implications and Novelty

- IVIS is indicated in the national guideline (I-NIPI)[5] 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 I-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.

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 haemoglobin level post treatment from baseline.

Secondary objectives:

- To measure incidence of morbidity and mortality associated with iron deficiency anaemia
- To measure treatment compliance to IVIS therapy
- To measure health-related quality of life (HRQoL) using EQ-5D 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 health care 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 anaemia 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 OI 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, IVIS intervention can be concluded to be very cost-effective.

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

Outcomes	IVIS	OI
Cost (in INR) per patient treated as per modelling	6768.28	6503.79
Incremental Cost (in INR)	286.05	
Effects	0.368	0.003
Incremental Effects	0.365	
ICER	783.11	

Figure 1 illustrates cost-effectiveness plane. Orange dot indicates ICER value which falls in the North East quadrant. It means intervention is costly than comparator but highly effective.

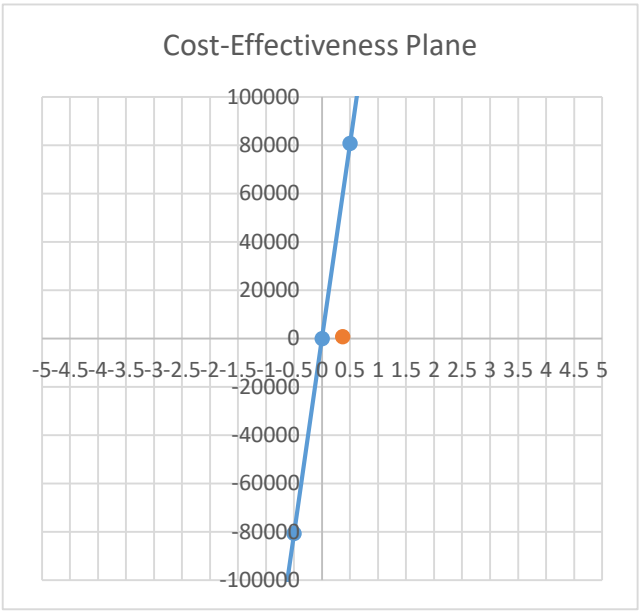
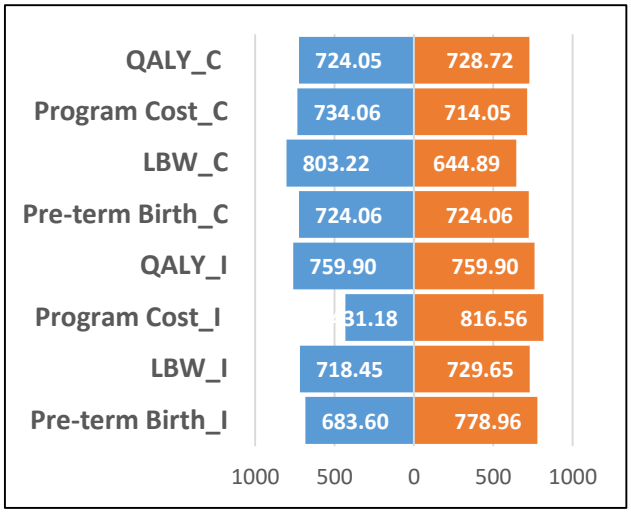


Figure 1: Cost-effectiveness plane of the study.

One-way sensitivity analysis was applied. Figure 2 presents results from simulations done as part of one-way sensitivity analysis. The tornado diagram of one-way sensitivity analysis shows that ICER value is slightly changed when the input parameter is changed in multiple indicators. Programme cost of intervention arm, low-birth weight and pre-term birth in control arm are key parameters that influence the model

Figure 2: Tornado diagram of cost-effectiveness of IVIS and OI therapy



Conclusion

IVIST was found to be cost-intensive but more effective than oral therapy for the treatment of moderate and severe anaemia. Further, it is well tolerated as side effects are less compared to that of oral iron. Considering the limited sample size and lack of blinding, larger studies with robust methodologies are needed to validate the results findings. Future studies on clinical efficacy would be critical in establishing effect of rise in haemoglobin level on maternal and birth outcomes.

References

1. Kumari S, Garg N, Kumar A, Guru PKI, Ansari S, Anwar S, et al. Maternal and severe anaemia in delivering women is associated with risk of preterm and low birth weight: A cross-sectional study from Jharkhand, India. One Heal (Amsterdam, Netherlands) 2019;8:100098.
2. Kalaivani K. Prevalence & consequences of anaemia in pregnancy. Indian J. Med. Res.2009;130(5):627–33.
3. Kriplani A, Mahey R, Dash BB, Kulshreshta V, Agarwal N, Bhatla N. Intravenous iron sucrose therapy for moderate to severe anaemia in pregnancy. Indian J Med Res 2013;138(JUL 2013):78–82.
4. Radhika AG, Sharma AK, Perumal V, Sinha A, Sriganesh V, Kulshreshtha V, Kriplani A. Parenteral Versus Oral Iron for Treatment of Iron Deficiency Anaemia During Pregnancy and post-partum: A Systematic Review. J Obstet Gynaecol India. 2019 Feb;69(1):13-24. doi: 10.1007/s13224-018-1191-8.
5. Ministry of Health and Family Welfare, Government of India. Intensified National Iron Plus Initiative (I-NIPI): Operational Guidelines for Programme Managers. 2018;84.

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

Policy Brief

June 2022

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

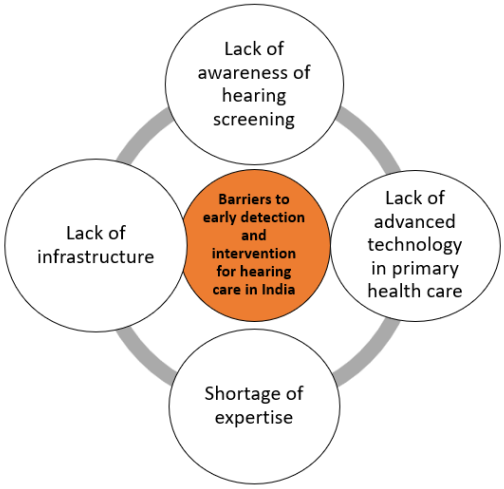
Health Technology Assessment in India, Regional Resource Hub, ICMR-Regional Medical Research Centre, Bhubaneswar

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), educational support costs, lost productivity, and societal costs. 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, anxiety, and depression. The primary barriers to treatment 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 population. 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 Ayushman 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 & Gynaecology and Pediatric patients. However, no such tele-facilities implemented for ENT care.

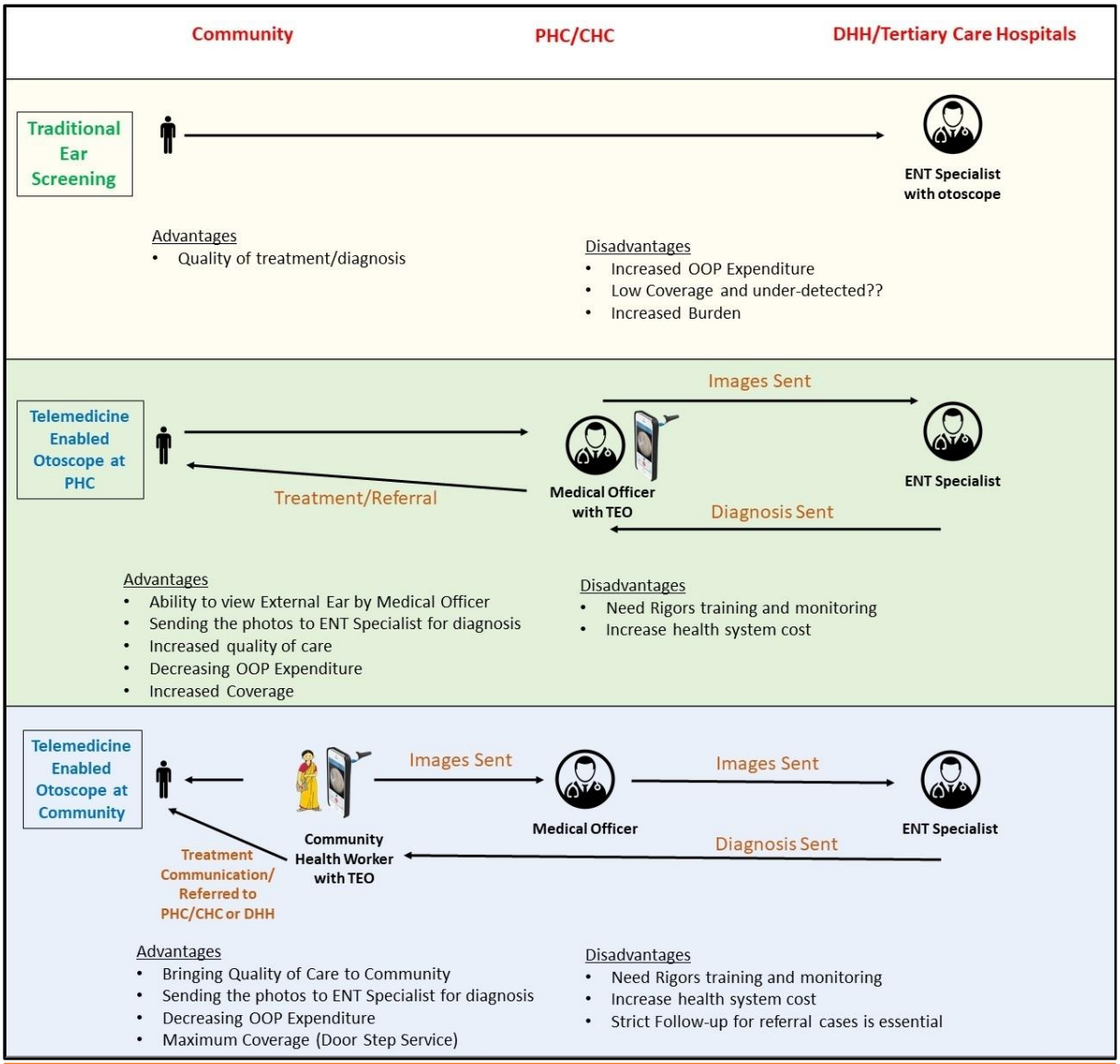
Objective

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.

Figure 1. Proposed model for hearing screening/check-up – traditional ear check-up, telemedicine enabled otoscope at primary health centre and community.



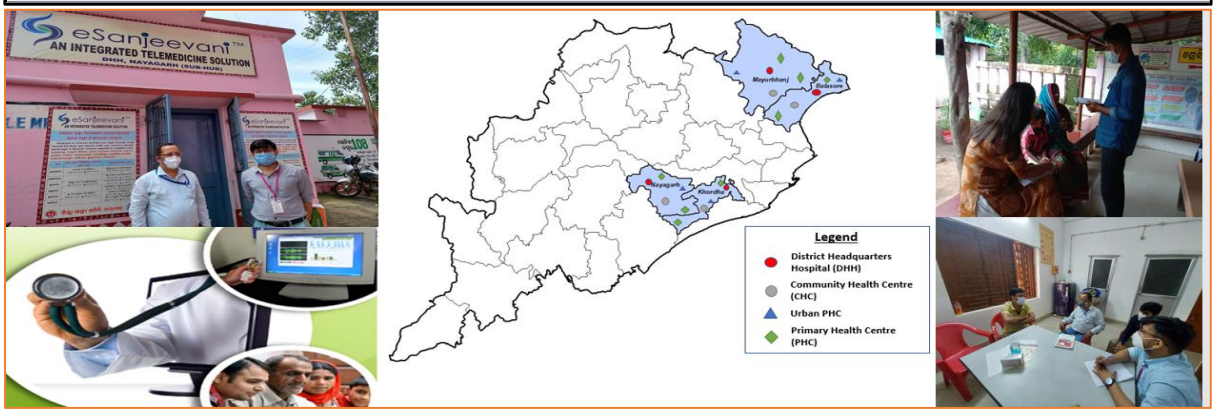


Figure 2. Population, Intervention, Comparator, and Outcome (PICO).

This project approved by the Technical Appraisal Committee (TAC), Health Technology Assessment, Department of Health Research, Ministry of Health and Family Welfare, Government of India. The ethical clearance was obtained from the Institutional Ethical Committee of RMRC Bhubaneswar. Permission was taken from the concerned local authorities, and consent was obtained from the participants.

Findings

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.

Table 2. Implementation cost.

Variables	Telemedicine-enabled Otoscope by Medical Officer at each Primary health centres	Telemedicine-enabled Otoscope by Community 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 3. Budget Implication.

Average number of facilities and annual implementation cost	Telemedicine-enabled Otoscope by Medical Officer at each Primary health centres	Telemedicine-enabled Otoscope 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

- 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 patient.

- 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.

	Variables	TEO at PHC	TEO by CHWs at Community level	Traditional Otoscope by ENT specialist at DHH
QALY	QALYs (per district)	44,08,661	8,55,84,094	9,63,898
	Average annual implementation cost at district level*	₹ 6.9 Crore	₹ 12.5 Crore	₹ 29 Lakhs
ICER		TEO at PHC	TEO by CHWs at Community level	
		Rs 19.19/QALY gained	Rs 1.44/QALY gained	

Conclusions and Implication

Telemedicine has been recommended to bridge the gap in human resources for health to alleviate the shortage of ear care specialists in India and other settings with limited resources. It can significantly enhance access to ear and hearing services, such as screening, community education, and primary treatment. Traditional otoscopes provide less coverage than PHC and CHW models. With TEO, both primary health care and CHW models have a high level of coverage. The community model has a lower QALY than the PHC model. However, the PHC model has a substantially lower implementation cost. The community model would be excellent for universal coverage, but it would overburden CHWs and be expensive to implement. Thus, the PHC model might be prioritised under the eSanjeevani platform for sustainability.

Health Technology Assessment of Strategies for Oral Cancer Screening in India

Health Technology Assessment of Strategies for Oral Cancer Screening in India

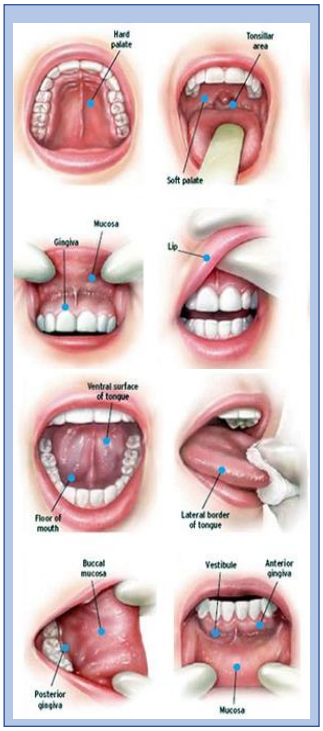
Health Technology Assessment in India (HTA In)

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

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

Background

- GLOBOCAN 2020 estimates showed that the annual number of incident cases for lip and oral cavity cancer was more than 100,000 (1).
- Most patients with oral cancer present at an advanced stage, requiring costly and aggressive combined modality treatment (2).
- This study was designed to evaluate the clinical and cost-effectiveness of commonly used oral cancer screening techniques namely, Conventional oral examination (COE), Toluidine blue staining (TBS), Oral cytology (OC), and Light-based detection (LBD) at various screening intervals.

Objectives

1. To assess the clinical and cost-effectiveness of commonly used screening modalities for oral cancer. i.e., COE, TBS, OC, and LBD.
2. To determine the most appropriate strategy between mass screening and high-risk screening strategy.
3. 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 1 Model A

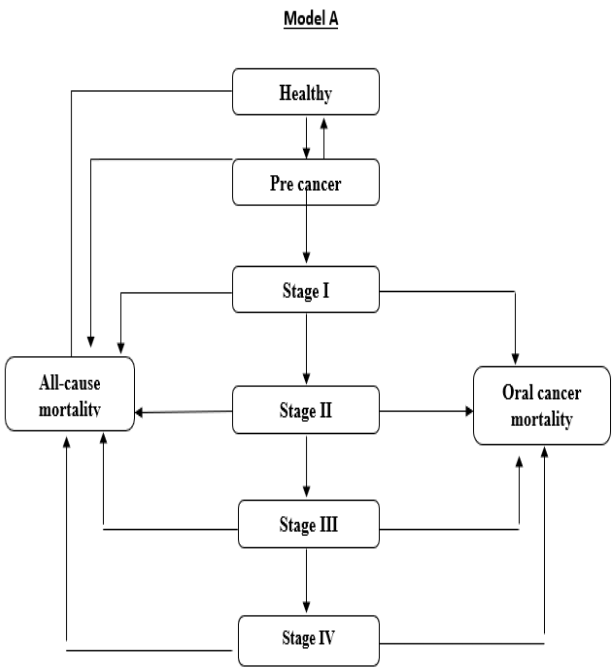
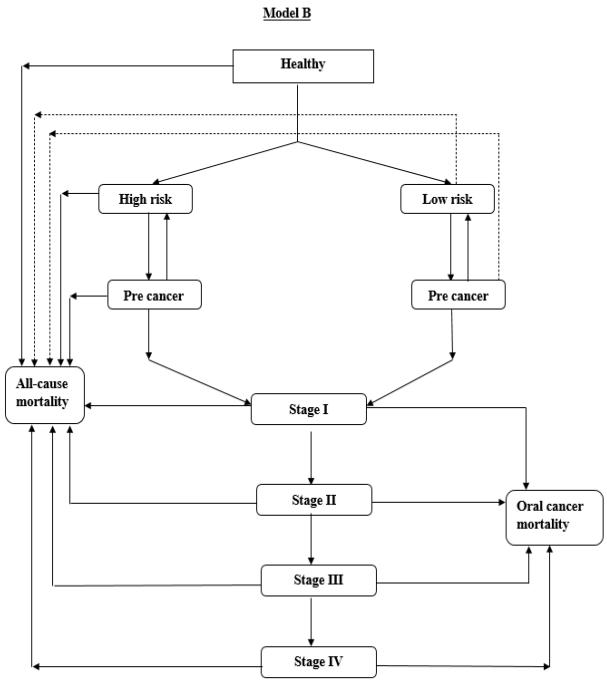


Figure 2 Model B



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 no screening.

•Mass screening using LBD and OC at 3 years interval averted the maximum number of oral cancer deaths (459.76 each).

Table 1 Outcome indicator in 1 lakh cohort (ICER values) for the high-risk (HR) strategies

Screening strategy		ICER
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)

Note: The ICER value in negative denotes dominant strategy (D)

- Across all the strategies, the high-risk screening was cost-saving as compared to mass screening throughout the intervals (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-year was more than 80% cost-effective at the willingness to pay threshold of India (Figure 4) (4).

Figure 3 Base-case cost-effectiveness plane

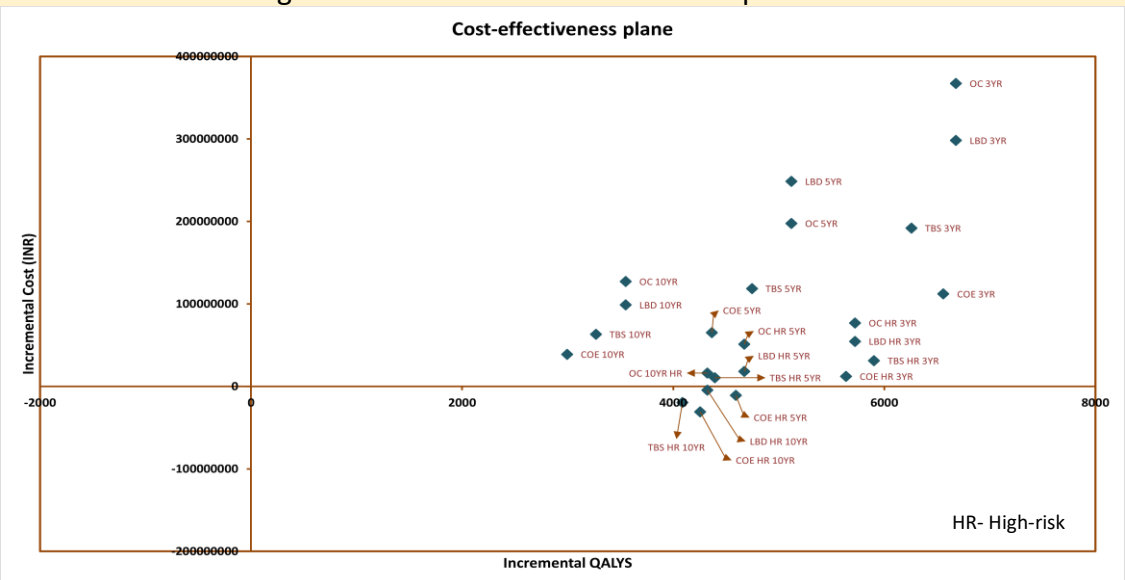
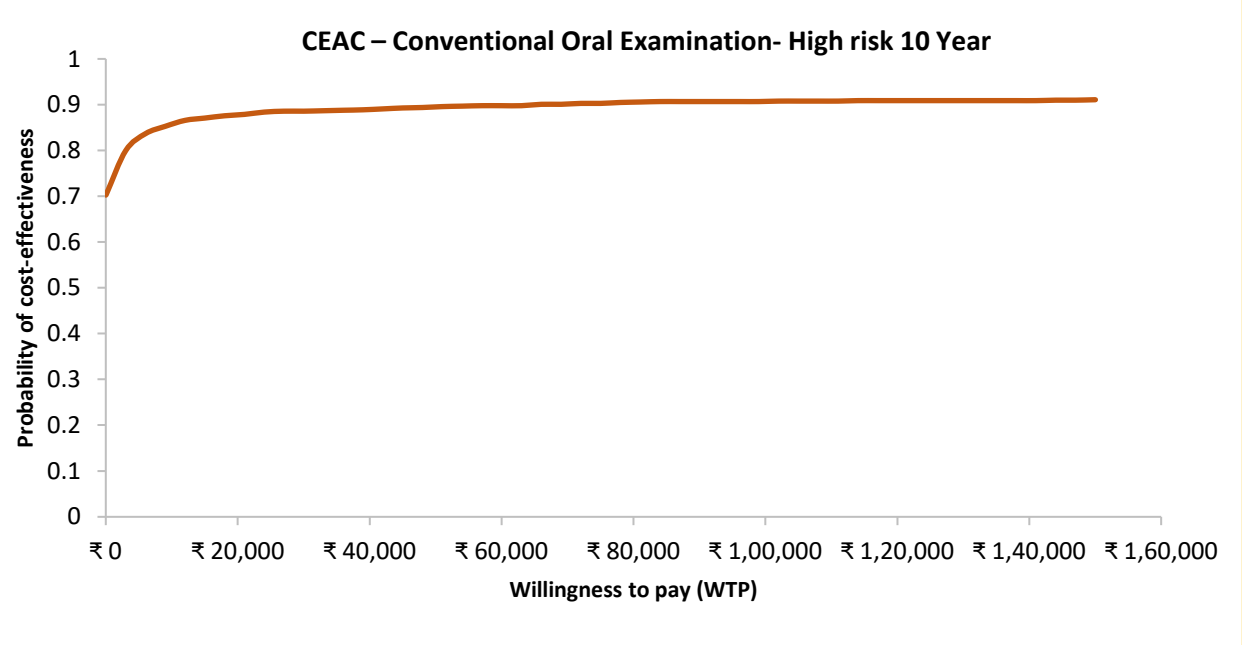


Figure 4 Cost-effectiveness acceptability curve (CEAC)



Conclusion

- 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.

Reference

1. GLOBOCAN, Cancer Today 2020, International Agency for Research on Cancer. World Health Organization.https://gco.iarc.fr/today/onlineanalysistable?v=2020&mode=population&mode_population=regions&population=900&populations=900&key=asr&sex=2&cancer=1&type=0&statistic=1&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&group_cancer=1&include_nmsc=0&include_nmsc_other=1.

2. Rajpal S, Kumar A, Joe W. Economic burden of cancer in India: Evidence from cross-sectional nationally representative household survey, 2014. PloS one. 2018;13(2): e0193320.

3. Sankaranarayanan R, Ramadas K, Thomas G, Muwonge R, Thara S, Mathew B, et al. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomised controlled trial. Lancet (London, England). 2005;365(9475):1927-33.

4. Willingness to pay threshold GDP: https://tradingeconomics.com/india/gdp-per-capita2021.

Inj. Gentamicin in Neonatal Sepsis by ANMs Before Referral

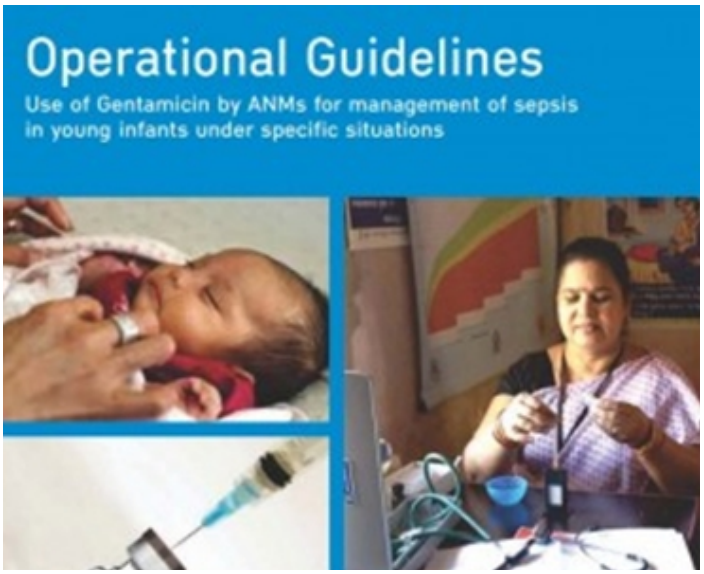
INJ. GENTAMICIN IN NEONATAL SEPSIS BY ANMS BEFORE REFERRAL

Health Technology Assessment in India (HTAIn)
All India Institute of Medical Sciences Jodhpur Rajasthan

EXECUTION 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.



POLICY RECOMMENDATIONS

- 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.

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 newborn where referral is not feasible or refused; pre-referral or for the completion antibiotic treatment.

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.

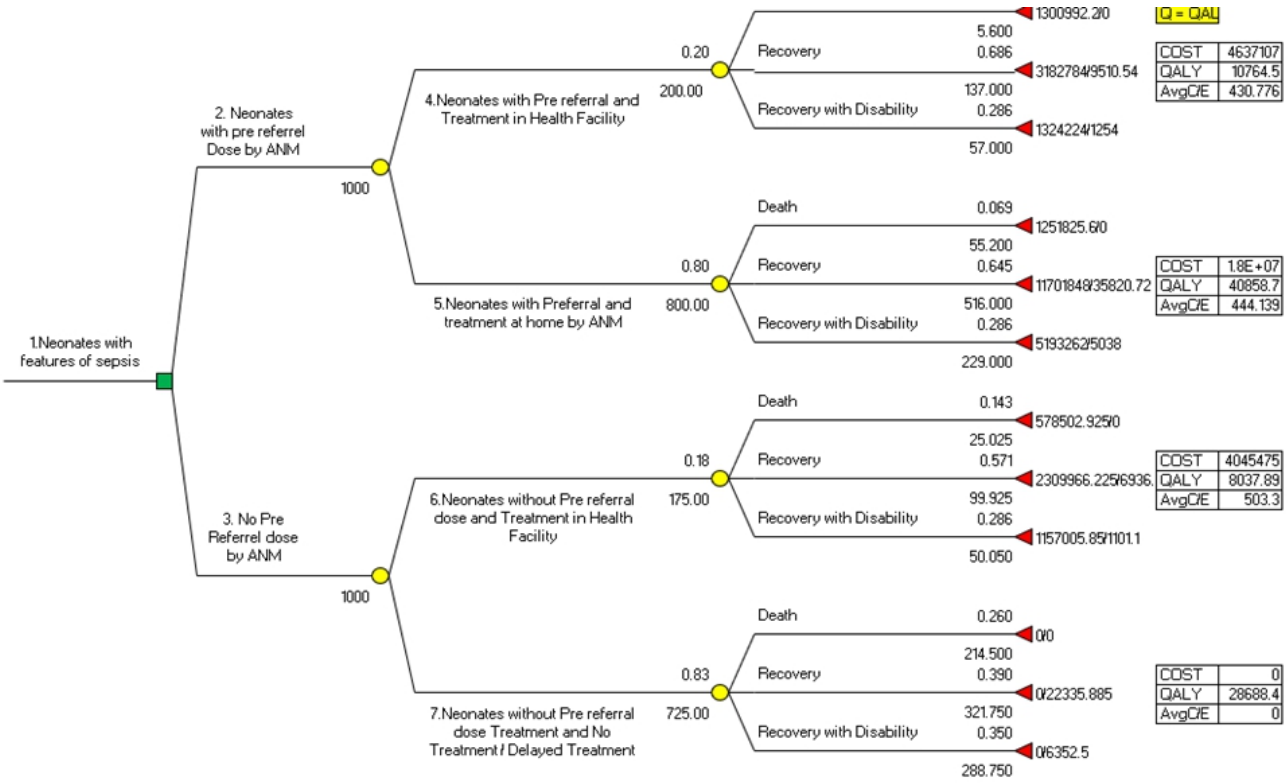


FIGURE 1 DECISION TREE

FINDINGS

A 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 amoxycillin 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 ofin cremental cost-effectiveness ratio (ICER) between intervention and comparator arm.

Literature review was conducted to get the secondary data on effectiveness of the regieme, transition probabilities and health system cost. Feasibility, accessibility, and availability of ANM was determined by consultation exercise.

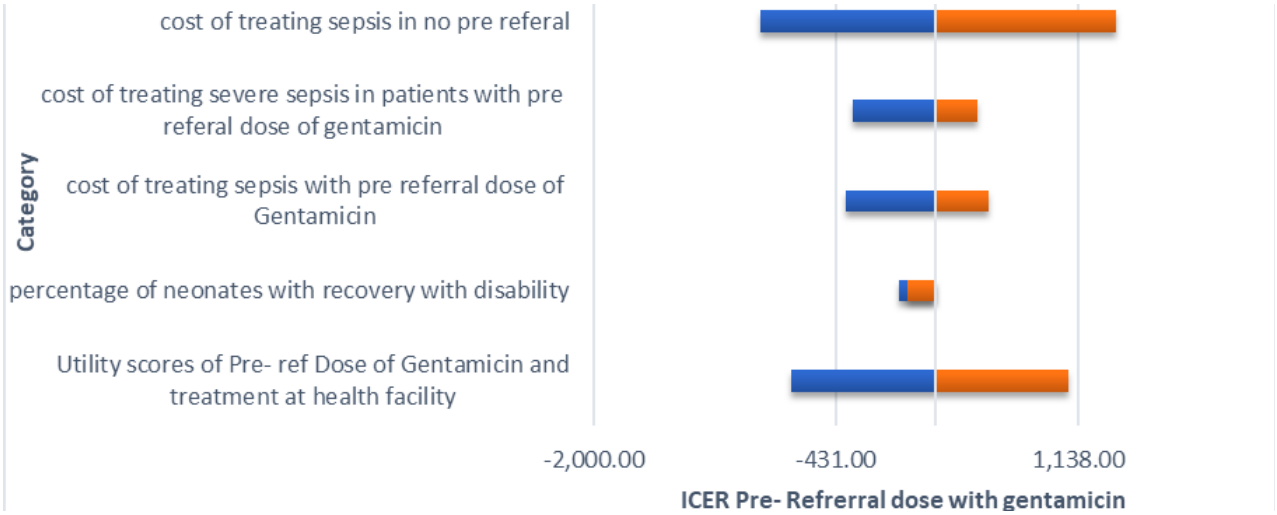


FIGURE 2 TORNADO DIAGRAM

REFERENCES

1. Bang AT, Bang RA, Baitule SB, Reddy MH, Deshmukh MD. Lancet Field Trial. 2005;354:1–7.
2. Welfare F. Operational Guidelines Use of Gentamicin by ANMs for management of sepsis in young infants under specific situations Ministry of Health and Family Welfare Government of India. 2014
3. Jaiswal N, Singh M, Kondel R, Kaur N, Thumburu KK, Kumar A, et al. Feasibility and efficacy of gentamicin for treating neonatal sepsis in community-based settings: a systematic review. World J Pediatr. 2016;12(4):408–14.
4. Awasthi S, Kesarwani N, Verma RK, Agarwal GG, Tewari LS, Mishra RK, et al. Identification and management of young infants with possible serious bacterial infection where referral was not feasible in rural Lucknow district of Uttar Pradesh, India: An implementation research. PLoS One [Internet]. 2020;15(6):1–20. Available from: http://dx.doi.org/10.1371/journal.pone.0234212
5. Coffey PS, Sharma J, Gargi KC, Neupane D, Dawson P, Pradhan Y V. Feasibility and acceptability of gentamicin in the Uniject prefilled injection system for community-based treatment of possible neonatal sepsis: The experience of female community health volunteers in Nepal. J Perinatol. 2012;32(12):959–65.
6. Prinja S, Manchanda N, Aggarwal AK, Kaur M, Jeet G, Kumar R. Cost & efficiency evaluation of a publicly financed & publicly delivered referral transport service model in three districts of Haryana State, India. Indian J Med Res. 2013;138(DEC):1003–11.
7. Pharoah POD, Stevenson RC, Cooke RWI, Sandu B. Costs and benefits of neonatal intensive care. Arch Dis Child. 1988;63(7 SPEC NO.):715–8.

The Health Technology Assessment of a Pediatric Cardiac Surgery Program (Hridyam) For Congenital Heart Disease in Kerala

Policy Brief

The health technology assessment of a pediatric cardiac surgery program (Hridyam) for congenital heart disease in Kerala

HTAIn Secretariat, Dept. of Health Research, Ministry of Health & Family Welfare, New Delhi

Regional Resource Centre for HTAIn, SCTIMST, Trivandrum

National Health Mission, Kerala

July 2022

Summary Conclusions

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 oximeters at all delivery points to screen for CHDs along with the usual physical examination. Early detection, prompt stabilization and expedited referral to a tertiary centre were the program's key components.

How many hospitals are empanelled in the Hridyam programme?

In addition to two public hospitals, five private hospitals with advanced pediatric cardiac surgery capabilities were empanelled (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 oximeter 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?

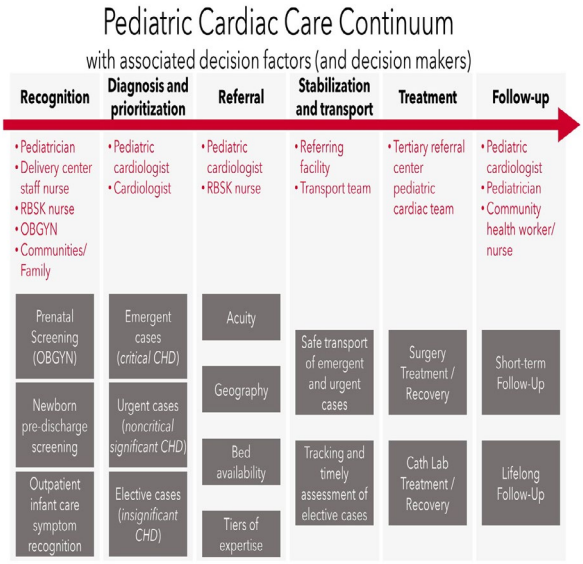
The Hridyam pathway costs Rs 53.6 crores compared to the comparator arm, which costs the health system Rs 44.7 crores. The net increase in the budget because of the Hridyam project on an annual basis is Rs 8.9 crores. This model has potential applications for other conditions and in other jurisdictions, especially LMICs considering building CHD capacity.

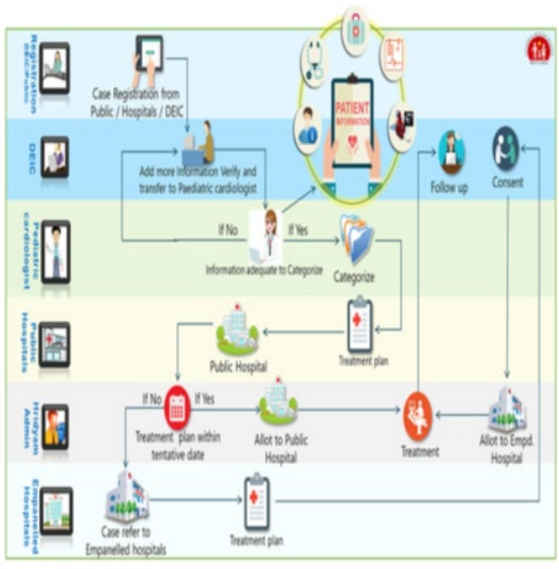
Recommendations

The package of newborn screening includes a pulse oximeter 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 crores 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 burden[1]. Among these, congenital heart disease (CHD) represents the world's most common class of major birth defects, affecting one in 120 newborns[2]. About one-fourth of all CHDs are considered critical congenital heart disease (CCHD), which requires a lifesaving procedure in the first year of life[3]. In 2012, the Government of India started the Rashtriya Bal Swasthya Karyakram (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.

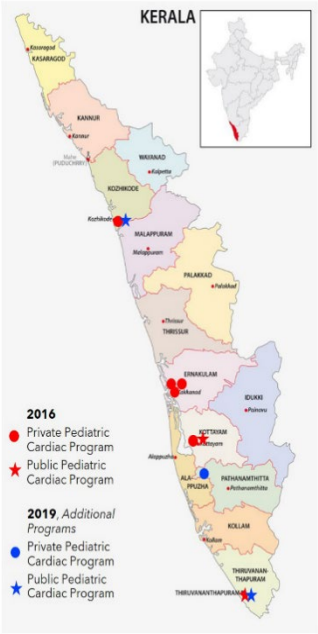




Figures: (1) Hridyam CHD Patient Care Continuum; (2) Hridyam Process Map

Methods

- *Population*
  - 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 centres (2 government, 5 private).



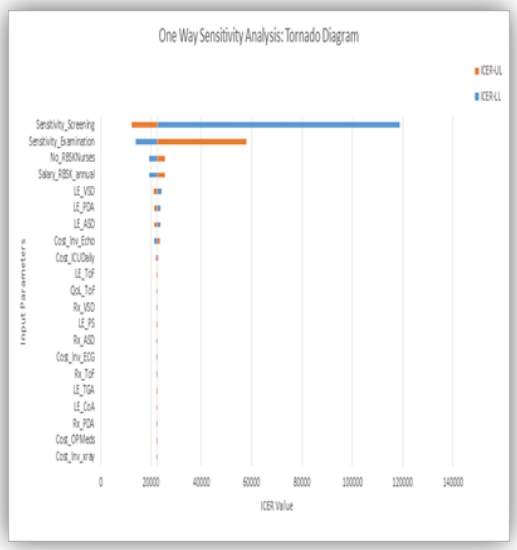
Cost-effectiveness (including sensitivity analysis) and Budget Impact Analysis

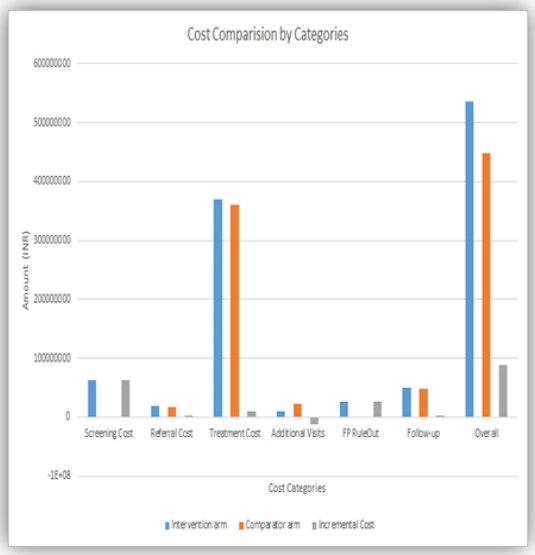
a) ICER Calculation and BIA: The study found that compared to the usual care scenario, the Hridyam program had an incremental cost of INR 8.85 crores and generated 3947 additional QALYs, resulting in an ICER of **22,145**. This makes the program cost-effective at the threshold of one GDP per capita.

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**			

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**.





Figures: (3) Tornado Diagram; (4) Cost comparison by categories

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.

Acknowledgement

The Regional Resource Centre for HTAIn, SCTIMST, Trivandrum, conducted the study and HTAIn, DHR, MoHFW provided the support and funding.

References

1. Sankar MJ, Neogi SB, Sharma J, Chauhan M, Srivastava R, Prabhakar PK, et al. State of newborn health in India. J Perinatol. 2016 Dec;36(Suppl 3):S3–8.

2. Liu Y, Chen S, Zühlke L, Black GC, Choy M kit, Li N, et al. Global birth prevalence of congenital heart defects 1970–2017: updated systematic review and meta-analysis of 260 studies. Int J Epidemiol. 2019 Apr;48(2):455–63.

3. Oster ME, Lee KA, Honein MA, Riehle-Colarusso T, Shin M, Correa A. Temporal Trends in Survival Among Infants With Critical Congenital Heart Defects. Pediatrics. 2013 May 1;131(5):e1502–8.

Decentralized Dengue Screening Strategy at Primary Healthcare 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 health care level. 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.[3] 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. 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 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.

The policy brief is based upon the Health Technology Assessment of " implementation of cell counters (Haematology Analysers) for diagnosing suspected dengue cases at Primary Health Care settings in Tamil Nadu" and can be found on the link: https://dhr.gov.in/sites/default/ files/

Policy Brief

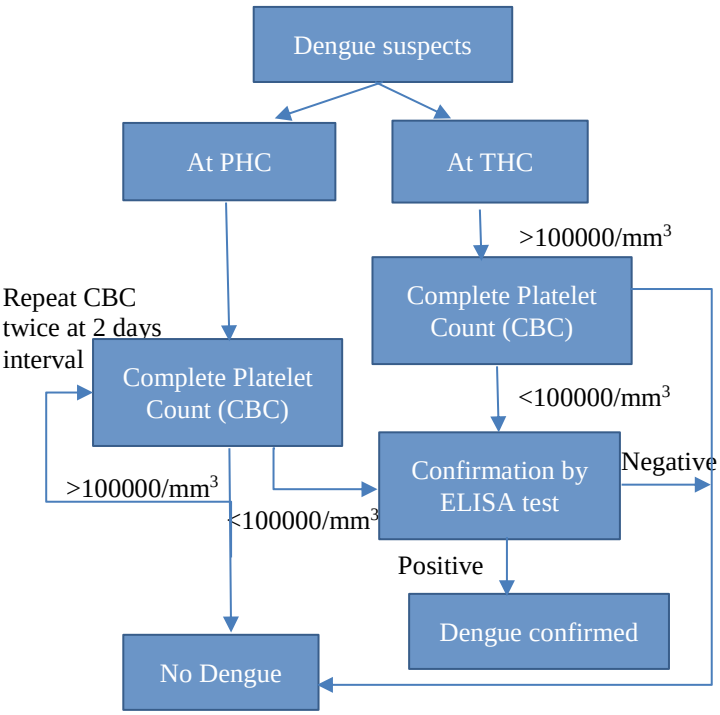
Decentralized dengue screening strategy

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 100000/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-1). 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

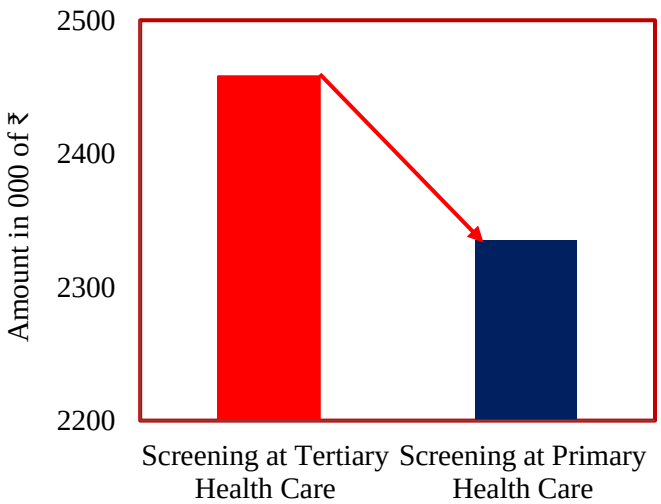
Implementation of haematology analyser at PHC is cost saving. The ICER was estimated to be -41197 for proposed strategy over current strategy. Average incremental net monetary benefit (INMB) for the proposed strategy over control strategy was estimated to be ₹6105504. Sensitivity analysis showed the 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, hospitalisation cost and ambulatory cost of non-fatal cases had higher influence on ICER value.

Current & proposed dengue screening strategy



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.

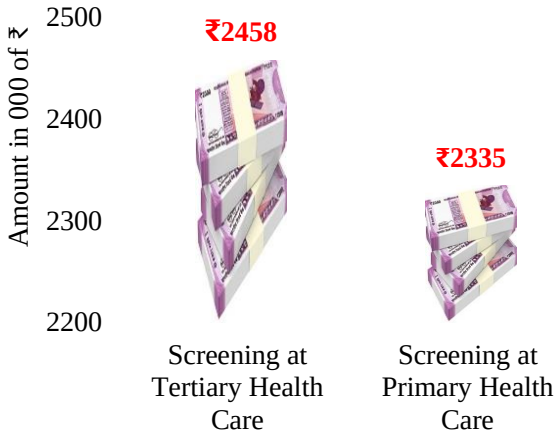
Total cost



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



References

1. World Health Organisation. Dengue and severe dengue. World Health Organisation 2020; https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue
2. Stanaway JD, Shepard DS, Undurraga EA, Halasa YA, Coffeng LE, Brady OJ, Hay SI, Bedi N, Bensenor IM, et al. The global burden of dengue: an analysis from the Global Burden of Disease Study 2013. Lancet Infect Dis 2016;16(6):712-723.
3. Murhekar MV, Kamaraj P, Kumar MS, Khan SA, Allam RR, Barde P, Dwibedi B, Kanungo S, Mohan U, Mohanty SS, et al. Burden of dengue infection in India, 2017: a cross-sectional population based serosurvey. Lancet Glob Health. 2019; 7(8):e1065-e1073
4. Department of Health Research, Government of India. Establishment of a network of Laboratories for managing epidemics and Natural Calamities (VRDL). http://dhr.gov.in/schemes/establishment-networklaboratories-managing-epidemics-and-natural-calamities

Cost Effectiveness of I.V. Tranexamic Acid for Treatment of Postpartum Hemorrhage

Cost-effectiveness of I.V tranexamic acid for treatment of postpartum hemorrhage

Policy Brief

Health Technology Assessment in India (HTAIn)
National Institute for Research in Reproductive Health - Mumbai

Post-partum haemorrhage

Post-partum haemorrhage (PPH) is one of the complications post delivery accounting for 6-7% of maternal mortality cases in India

Standard of care for management of primary PPH as per Indian guidelines includes supportive care, treatment with uterotonics, conservative interventions like uterine balloon tamponade followed by surgical interventions for refractory cases

About Tranexamic Acid (TXA)

TXA is an anti-fibrinolytic drug. It causes competitive inhibition of plasminogen activation. It reduces bleeding by inhibiting breakdown of fibrinogen and fibrin clots.

Recommendations

Addition of intravenous Tranexamic Acid for primary PPH management within three hours of birth is costeffective and is recommended for use in the Indian public health system with an additional dose if required after 30 minutes or within 24 hours if bleeding restarts

The 'Dakshata' checklist and 'LaQshya' (emergency drug tray) and other Indian guidelines should be updated with this recommendation.

Summary

Intravenous Tranexamic acid (TXA) use in all women with primary PPH is now recommended by the World Health Organization. This HTA answers the policy question of whether the Indian public health system should consider TXA intervention for all PPH management from a cost-effectiveness perspective.

The analysis suggests that from a disaggregated societal perspective, a per patient cost of INR 6,607 with a discounted health gain of 20.25 QALYs is associated with TXA intervention as compared to INR 6,486 incurred with 20.16 QALYs gained with standard care (i.e. without TXA).

At base-case, an ICUR value of INR 1,470 per QALY gained and 94.5% simulations favouring the intervention across sensitivity analysis, TXA addition for PPH management in the Indian context is cost-effective.

Approximately 389 maternal deaths, 177 surgeries, and 128 ICU admission per 1,00,000 PPH cases respectively in India can be averted with TXA intervention.

Budget impact analysis indicates an additional financial allocation of 2.3% for PPH management in case TXA intervention is considered.

Context and gap analysis

India's guidance note on PPH management follows the WHO 2012 guidelines

2012 WHO recommends using TXA only in refractory atonic or traumatic PPH cases within 3 hours of delivery. Based on this, there is no clarity in Indian guidelines over dosage or timing of administration [1]

'Dakshata' checklists and the 'LaQshya' guidelines to improve quality of care have no mention about use of TXA and is not part of the emergency tray [2]

This HTA will help in justifying whether India should adopt the latest WHO recommendation of adding IV TXA to all PPH cases by considering both clinical and cost-effectiveness perspectives.

Policy Brief

Aim and Objectives

This study aimed to address the policy question of whether India should consider adding IV tranexamic acid for all primary PPH case management in the Indian public health system.

Objectives

- **To estimate cost-effectiveness of addition of IV Tranexamic acid to standard care treatment in the Indian public health facilities.**
- **To assess budget impact of introducing tranexamic acid in the Indian public health program**

Methods and Approach

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 (100mg/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

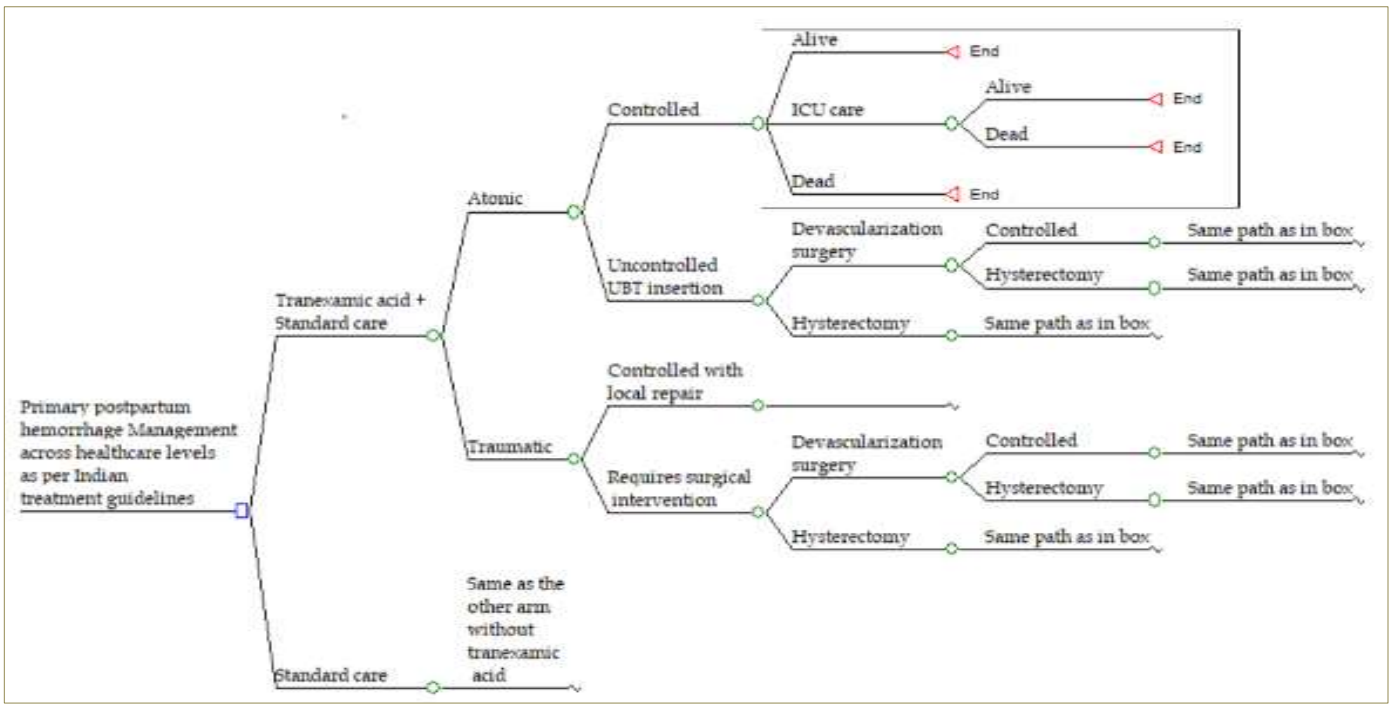
Clinical and epidemiological input parameters were obtained from WOMAN trial study and literature relevant to the Indian context.[4]

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 undertaken

Budget impact was analysed for a 5 year period using phased bottom-up uptake of intervention from primary to tertiary care level

Diagrammatic representation of the model



Policy Brief

Results

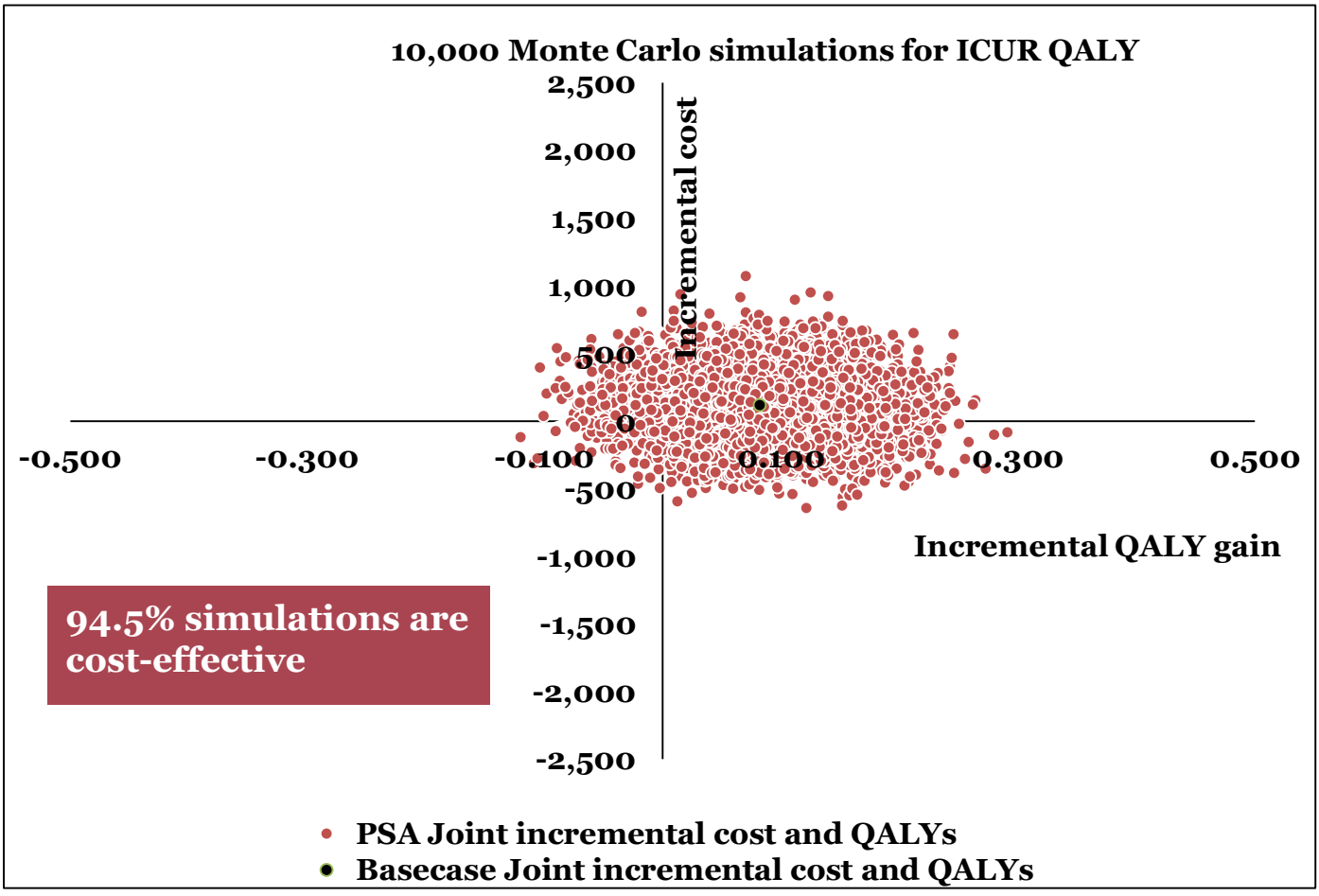
For an estimated annual cohort of 5,10,915 women who experience primary PPH in Indian public health facilities, a disaggregated societal cost of INR 6,607 is incurred per patient for PPH management with an associated gain of 20.25 discounted QALYs. Similarly, management without TXA i.e. current standard 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 likely to prevent 389 maternal deaths, 177 surgeries, and 128 ICU admissions per 1,00,000 PPH cases. These outcomes as shown in the table below favor addition of TXA to the Indian public health system.

	TXA+SOC	SOC	Increment /Averted with TXA
Health system cost per patient	INR 5,934	INR 5,782	INR 152 (increment)
Societal cost per patient	INR 6,607	INR 6,486	INR 121 (increment)
Total surgeries (for annual cohort)	19,387	20,293	905 (averted)
Total number of ICU admissions	27,181	27,836	655 (averted)
Total number of maternal deaths	13,923	15,913	1990 (averted)

The study findings were robust across sensitivity analysis. Probabilistic sensitivity analysis suggested that 94.5% simulations across 10,000 Monte Carlo simulations favored IV TXA addition as a cost-effective intervention indicating low error probability.



Policy Brief

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 Tranexamic 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

References

1. *Guidelines- MH :: National Health Mission.* *https://www.nhm.gov.in/index1.php?lang=1&level=3&sublinkid=839&lid=377. Accessed 18 Nov 2019*
2. *DAKSHATA Implementation Package :: National Health Mission.* *https://www.nhm.gov.in/index1.php?lang=1&level=3&sublinkid=838&lid=449. Accessed 18 Nov 2019*
3. *HTA in India Manual. https://htain.icmr.org.in/index.php/documents/*
4. *Shakur H et al., (2017) Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage : an international, a double-blind, placebo-controlled RCTl. The Lancet 389:2105–2116*

Cost-Effectiveness of Population-Based Screening for Chronic Kidney Disease Among Adults Aged 40 Years and Above with Type 2 Diabetes Mellitus in Kerala and Puducherry

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 Diabetes Mellitus in Kerala and Puducherry

SUMMARY

Chronic Kidney Disease (CKD) is a major public health problem with increasing incidence and 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 next ten 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**

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

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.

Acknowledgment: The study was conducted by Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) Pondicherry, in collaboration with Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvanthapuram.

References

1. Varughese S, Abraham G. Chronic Kidney Disease in India: A Clarion Call for Change. Clin J Am Soc Nephrol. 2018 May 7;13(5):802–4.
2. Ohta M, Babazono T, Uchigata Y, Iwamoto Y. Comparison of the prevalence of chronic kidney disease in Japanese patients with type 1 and type 2 diabetes. Diabet Med. 2010;27(9): 1017-1023.
3. Pradhan Mantri National Dialysis Programme | National Health Portal of India [Internet]. [cited 2021 Jun 1]. Available from: https://www.nhp.gov.in/pradhan-mantri-national-dialysisprogramme_pg
4. Varughese S, Abraham G. Chronic Kidney Disease in India: A Clarion Call for Change. Clin J Am Soc Nephrol. 2018 May 7;13(5):802–4
5. Bhuwania, S., Saxena, S., Bansal, R., & Goel, R. (2020, July). Gender Bias in Kidney Donation in India: Has It Changed Over the Past 2 Decades? In Transplantation proceedings (Vol. 52, No. 6, pp. 1665-1670). Elsevier.

Cost effectiveness of RapidDiagnostic Tests (Hemo Type Sc., Sickle Scan andGazelle) in Comparison to Solubility Test Followedby HPLC for Sickle Cell Disease/ Trait Diagnosis Among High Risk Population in India

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

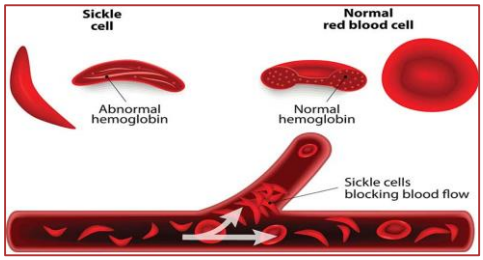
Sickle Cell Disease (SCD) is a common genetic disorder prevalent in Sub-Saharan Africa, the Mediterranean, the Middle East, and the Indian subcontinent. Three nations, including India, bear over half of the world's SCD burden. SCD has a large impact on childhood morbidity and mortality. In India, where 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

Policy Brief

Tests for Sickle Cell Disease Screening

Introduction

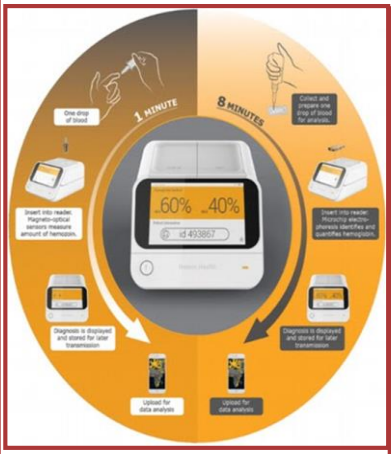
Sickle cell disease (SCD), an autosomal recessive disorder of the red blood cell, is the most common monogenic disease with more than 300 000 affected births annually worldwide, mostly in low- and middle-income countries. An estimated 7% of the world population carry an abnormal hemoglobin gene, while 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 diseased or carriers, as low-cost screening tests with high negative predictive value are available. Genetic counseling, community education and awareness play a very important role in successful implementation of prevention programs.

Hemotype Sc:

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 includes the inability to detect hemoglobin variants like HbD, HbE and HbF. It also cannot differentiate between HbSS and sickle- β0-thalassemia. Misinterpretation of the result in cases with recent blood transfusion is also reported.

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, HbE and HbF and also cannot differentiate between HbSS and sickle- β0-thalassemia.



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 interpretation and web-based image processing application for automated results.

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:

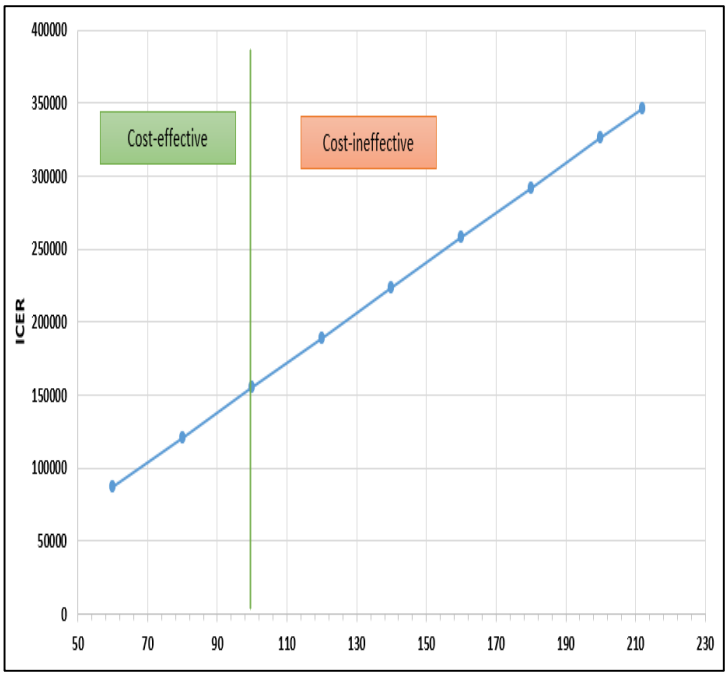
The population to be screened was considered in a Decision Tree analytical model and analysed in three different age groups. The cohort size for age group 0 to 2 years, 2 to 30 years and 0 to 30 years was 1.37 crores, 3,07 crores and 3,41 crores, respectively. These populations were selected from the 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:

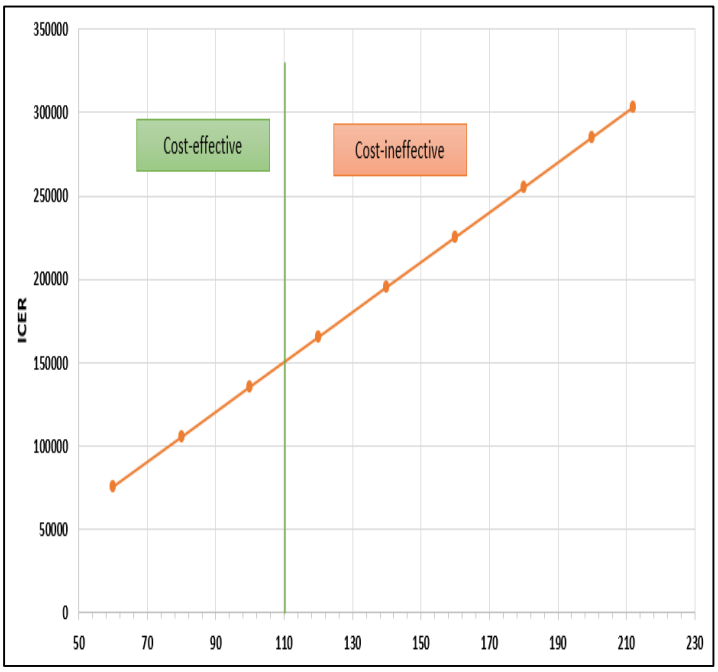
ICER per case detected suggests that if Hemotype SC Kit can be procured below INR 100 it will become cost effective. Similarly, if Sickle SCAN Kit can be procured below INR **110,** it will become cost-effective.

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

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 screening program with Sickle SCAN	89.59 (84.04 – 95.43) Crores	795.38 (846.40 – 846.40) Crores	885.53 (836.66 - 938.24) Crores
Cost of rolling out screening program with Solubility + HPLC	Solubility can still be used for children above 9 months of age	175.08 (167.25 – 183.12) Crores	194.64 (185.74 – 203.10) Crores

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.

References:

1. Kaur M, Das GP, Verma IC. Sickle cell trait & disease among tribal communities in Orissa, Madhya Pradesh & Kerala. Indian J Med Res. 1997;105:111–6.
2. Dash BP, Das RK: Age, sex and seasonal variations of sickle cell disorder cases in Orissa. J Hum Ecol 1998, 9:281–284.
3. Mukherjee MB, Surve RR, Gorakshakar AC, et al.: Symptomatic presentation of a sickle cell heterozygote: an evaluation of genetic factors. Am J Hematol 2001, 66:307–308.
4. Mohanty D, Mukherjee MB. Sickle cell disease in India. Current Opinion in Hematology 2002;9:117–122.
5. Mohanty PK, Meher S. Mortality risk factors in hospitalised late adolescent and adult sickle cell disease patients. J Evid Based Med Health Care 2018;5:135–9.
6. Shah P, Bhagat VM, Patel K, Patel C. Pattern of mortality in sickle cell disease: an autopsy study. International Journal of Research in Medical Sciences. 2017;5(5):2115-2119. doi:10.18203/2320-6012.ijrms20171853
7. Newborn Screening and Clinical Profile of Children With Sickle Cell Disease in a Tribal Area of Gujarat | SpringerLink. Accessed August 4, 2022. https://link.springer.com/article/10.1007/s13312-022-2476-7
8. Upadhye DS, Jain DL, Trivedi YL, Nadkarni AH, Ghosh K, Colah RB. Neonatal Screening and the Clinical Outcome in Children with Sickle Cell Disease in Central India. PLoS One. 2016;11(1):e0147081. doi:10.1371/journal.pone.0147081
9. Purohit P, Mantri S, Nayak J, Mahapatra B. Factors responsible for mortality in patients with sickle cell disease: A hospital-based study. Natl J Physiol Pharm Pharmacol. 2019;(0):1. doi:10.5455/njppp.2020.10.0932225102019
10. Thaker P, Colah RB, Patel J, et al. Newborn Screening for Sickle Cell Disease Among Tribal Populations in the States of Gujarat and Madhya Pradesh in India: Evaluation and Outcome Over 6 Years. Front Med (Lausanne). 2022;8:731884. doi:10.3389/fmed.2021.73188
11. Balgir RS. The spectrum of haemoglobin variants in two scheduled tribes of Sundargarh district in north-western Orissa, India. Annals of Human Biology. 2005;32(5):560-573. doi:10.1080/03014460500228741
12. Jain DL, Apte M, Colah R, et al. Efficacy of fixed low dose hydroxyurea in Indian children with sickle cell anemia: a single centre experience. Indian Pediatr. 2013;50(10):929-933. doi:10.1007/s13312-013-0264-0
13. Bhatwadekar SS, Deshpande SV, Khadse SV, Shah B, Desai D. Morbidity Pattern in Sickle Cell Disease in Central Gujarat, India — Single Centre Perspective. Blood. 2017;130:4785. doi:10.1182/blood.V130.Suppl_1.4785.4785
14. Silva-Pinto AC, Costa FF, Gualandro SFM, et al. Economic burden of sickle cell disease in Brazil. PLoS One. 2022;17(6):e0269703. doi:10.1371/journal.pone.0269703

Estimation of Recurrent Cost for Institutional Delivery at Different Levels of Facilities Under JSSK Scheme

POLICY BRIEF

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

Health Technology Assessment in India - Secretariat
Department of Health Research, Ministry of Health and Family Welfare
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 various 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.

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.**

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:

1. Rates of diagnostics were taken from the CGHS list or from published literature.
2. 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.

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

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.

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

CONCLUSION

The study estimates the recurrent cost (excluding cost of human resource and transportation) of providing comprehensive maternal and new born care services included in JSSK through different public healthcare facilities. It intends to help decision makers in the process of budgetary allocation to different healthcare facilities in respective states and districts, according to their patient load and spectrum of services provided in a year.

Meghalaya's Megha Health Insurance Scheme (MHIS): An assessment of the enrolment and claims data

Meghalaya's Megha Health Insurance Scheme (MHIS)

An assessment of the enrolment and claims data

January 2021

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 ₹ 31 in 2012 under MHIS-I. 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 Megha Health Insurance Scheme (MHIS) was initiated by the Regional Resource Hub (RRH-HTAIn) 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 analysed 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 spending 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-I through 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 6-18 years.

- 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 for duplicate expenditure by the Government. Consolidating these schemes and revising clinical criteria for rabies injection towards more stringent evidence-based provision could leverage significant funds for the wider health sector.*

- *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.*

- *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*

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 III.

Acknowledgement

This policy brief is a part of the collaborative efforts between the Regional Resource Hub HTAIn, Indian Institute of Public Health – Shillong1, Directorate of Health Services, Government of Meghalaya, and the George Institute for Global Health, Imperial College, London, UK2. The Department of Health Research (DHR), MoHFW, were a constant source of support and encouragement throughout the study.

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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

Policy Brief

Executive Summary:

Multiple myeloma (MM) is the second most frequent haematological malignancy (~15%), accounting for nearly 20% of all haematological cancer-related deaths [1–3]. 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.

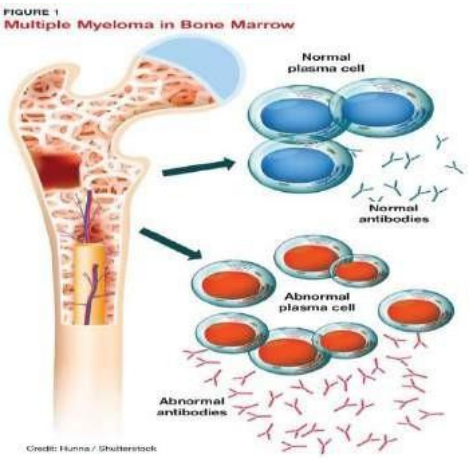


Image source: Internet

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 publicly financed health insurance 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 tothese 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 tocompare the costs and consequences of different induction regimens. According to a systematic review, few studies have evaluated the cost-effectiveness of regimens based on novel agents, including bortezomib, thalidomide and lenalidomide [10] but 3 of them have included only the transplant-ineligible MM population [11-13].

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 a Economic evaluation study on various NDMM treatment regimens, conducted by the HTA Resource Hub, PGIMER, Chandigarh.

Treatment arms:

(1) Bortezomib, lenalidomide, dexamethasone (VRd) alone
(2) Bortezomib, thalidomide, dexamethasone (VTd) alone
(3) Bortezomib, cyclophosphamide, dexamethasone (VCd) alone
(4) VRd followed by AHSCT
(5) VTd followed by AHSCT
(6) VCd followed by AHSCT
(7) 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:

1. **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).
2. 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].
3. 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.
4. 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.

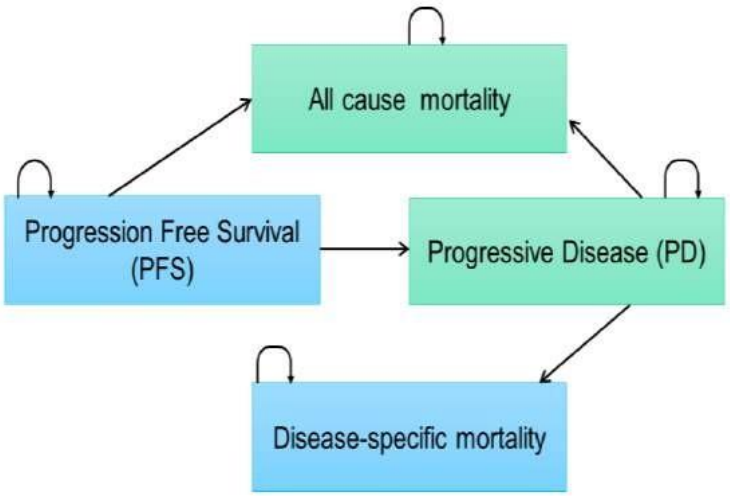


Figure 1: Schematic diagram for the Markov state transition model.

***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.

References:

1. Palumbo, K. Anderson, Multiple myeloma, N. Engl. J. Med. 364 (2011) 1046–1060, https://doi.org/10.1056/NEJMra1011442.
2. S. Zweegman, A. Palumbo, S. Bringhen, P. Sonneveld, Age and aging in blood disorders: multiple myeloma, Haematologica 99 (2014)1133–1137, https://doi. org/10.3324/haematol.2014.110296.
3. C. Röllig, S. Knop, M. Bornhäuser, Multiple myeloma, Lancet 385 (2015) 2197–2208, https://doi.org/10.1016/S0140-6736(14)60493-1. K. Bora Cancer Epidemiology 59 (2019) 215-220 219.
4. J. Ferlay, I. Soerjomataram, R. Dikshit, S. Eser, C. Mathers, M. Rebelo, et al., Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012, Int. J. Cancer 136 (2015) E359–86, https://doi.org/10.1002/ijc. 29210
5. F. Bray, J. Ferlay, I. Soerjomataram, R.L. Siegel, L.A. Torre, A. Jemal, Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA Cancer J. Clin. (2019), https://doi.org/10.3322/caac. 21492 n.d.;0.
6. Kumar SK, Rajkumar SV, Dispenzieri A et al. Improved survival in multiple myeloma and the impact of novel therapies. Blood 2008;111:2516–2520.
7. Laubach JP, Mitsiades CS, Mahindra A et al. Novel therapies in the treatment of multiple myeloma. J Natl Compr Canc Netw 2009;7:947–960.
8. Moreau P, San Miguel J, Ludwig H, et al. Multiple myeloma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.Ann Oncol. 2013;24 Suppl 6:vi133–vi137.
9. Palumbo A, Rajkumar SV, San Miguel JF, et al. International Myeloma Working Group consensus statement for the management, treatment, and supportive care of patients with myeloma not eligible for standard autologous stem-cell transplantation. J Clin Oncol. 2014;32(6): 587–600.
10. Fu S, et al. Cost Effectiveness of Transplant, Conventional Chemotherapy, and Novel Agents in Multiple Myeloma: A Systematic Review. PharmacoEconomics : 7 Aug 2019. Available from: URL: https://doi.org/10.1007/s40273-019-00828-y
11. Garrison LP Jr, Wang ST, Huang H, Ba-Mancini A, Shi H, Chen K, et al. The cost-efectiveness of initial treatment of multiple myeloma in the U.S. with bortezomib plus melphalan and prednisone versus thalidomide plus melphalan and prednisone or lenalidomide plus melphalan and prednisone with continuous lenalidomide maintenance treatment. Oncologist. 2013;18(1):27–36.
12. Kim MY, Sposto R, Swaika A, Asano H, Alamgir A, ChananKhan A, et al. Pharmacoeconomic implications of lenalidomide maintenance therapy in multiple myeloma. Oncology. 2014;87(4):224–31.
13. Usmani SZ, Cavenagh JD, Belch AR, Hulin C, Basu S, White D, et al. Cost-efectiveness of lenalidomide plus dexamethasone vs. bortezomib plus melphalan and prednisone in transplant-ineligible U.S. patients with newly-diagnosed multiple myeloma. J Med Econ. 2016;19(3):243–58.
14. Prinja S, Dixit J, Gupta N, Mehra N, Singh A, Krishnamurthy MN, et al. Development of National Cancer Database for Cost and Quality of Life (CaDCQoL) in India: a protocol. BMJ Open. 2021 Jul 1;11(7):e048513

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

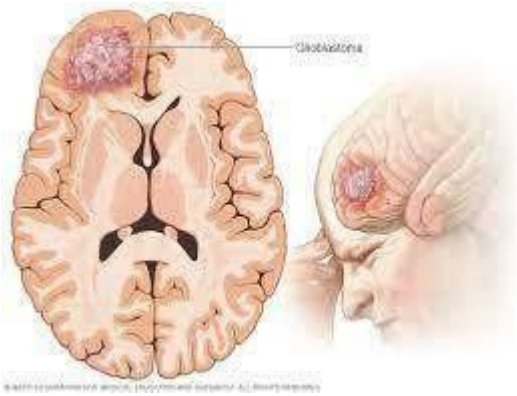
Policy Brief

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.



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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.

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.

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.

Intervention and control arms:

1. 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
2. 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)	-

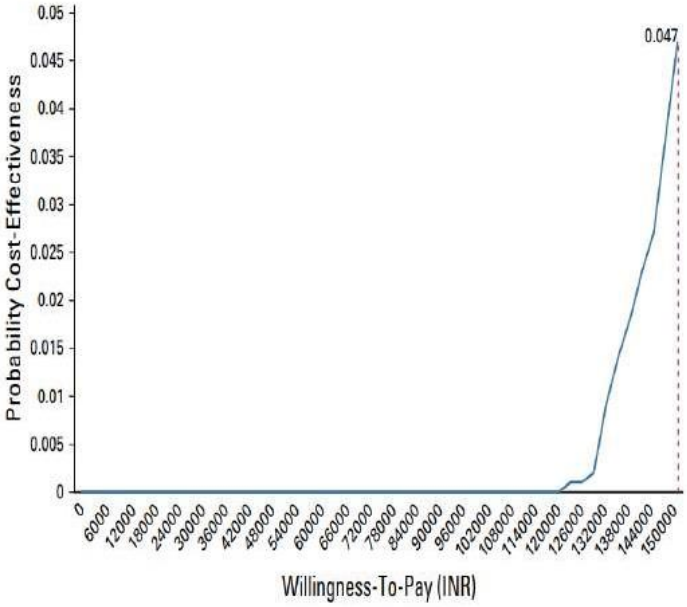


Figure 1: Probability of temozolamide use being cost-effective at varying willingness-to-pay thresholds.

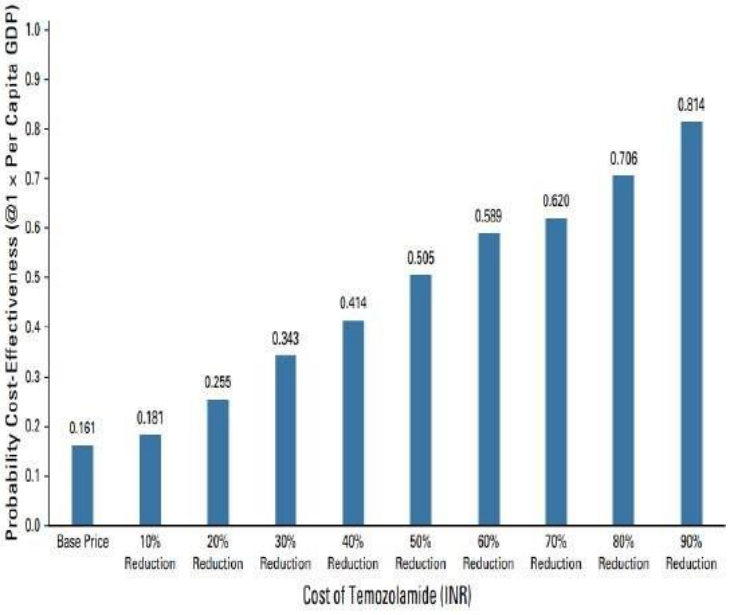


Figure 2: Price threshold analysis: Temozolamide

References:

1. Wen P, Kesari S: Malignant gliomas in adults. N Engl J Med 359:492-507, 2008 2.
2. Cabrera A, Kirkpatrick J, Fiveash J, et al: Radiation therapy for glioblastoma: Executive summary of an American Society for radiation oncology evidence-based clinical practice guideline. Pract Radiat Oncol 6:217-225, 2016
3. Fine H, Dear K, Loeffler J, et al: Meta-analysis of radiation therapy with and without adjuvant chemotherapy for malignant gliomas in adults. Cancer 71:2585-2597, 1993
4. Lamers L, Stupp R, Van Den Bent M, et al: Cost-effectiveness of temozolomide for the treatment of newly diagnosed glioblastoma multiforme: A report from the EORTC 26981/22981 NCI-C CE3 Intergroup Study. Cancer 112:1337- 1344, 2008
5. Uyl-de Groot C, Stupp R, Bent M: Cost–effectiveness of temozolomide for the treatment of newly diagnosed glioblastoma multiforme. Expert Rev Pharmacoecon Outcomes Res 9:235-241, 2009
6. Wu B, Miao Y, Bai Y, et al: Subgroup economic analysis for glioblastoma in a health resource-limited setting. PLoS One 7:e34588, 2012
7. Indiamart. https://www.indiamart.com/proddetail/temcad-temozolomide-250-mg-capsule-20047686333.html
8. Prinja S, Brar S, Singh MP, et al: Process evaluation of health system costing–Experience from CHSI study in India. PLoS One 15:e0232873, 2020 31.
9. Prinja S, Singh MP, Guinness L, et al: Establishing reference costs for the health benefit packages under universal health coverage in India: Cost of health services in India (CHSI) protocol. BMJ Open. 10:e035170, 2020
10. Stupp R, Mason W, Van Den Bent M, et al: Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Eng J Med 352:987-996, 2005
11. Garside R, Pitt M, Anderson R, et al: The effectiveness and cost-effectiveness of carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma: A systematic review and economic evaluation, in NIHR Health Technology Assessment programme: Executive Summaries 2007. NIHR Journals Library. United Kingdom

Cost Effectiveness of Tyrosine Kinase Inhibitors for The Treatment Newly Diagnosed Chronic Myeloid Leukemia: Is Imatinib Old News?

Cost-effectiveness of Tyrosine-kinase Inhibitors for the treatment newly diagnosed Chronic Myeloid Leukemia: Is Imatinib old news?

Health Technology Assessment in India (HTAIn)

Policy Brief

Executive Summary:

Chronic Myeloid Leukaemia (CML) is the commonest adult leukaemia in India and the annual incidence ranges from 0.8-2.2/100,000 population and 0.6-1.6/100,000 population in females in India (1). The introduction of tyrosine-kinase inhibitors (TKIs) such as Imatinib, has drastically changed the treatment and natural history of the disease with an improvement in the 5-year survival rate from approximately 20% to over 90% (1,2). Also, second-generation TKIs such as Dasatinib and Nilotinib have also demonstrated efficacy for treating incident CML patients in chronic phase (CP).

In this analysis, we aimed to determine the most cost-effective treatment option for newly diagnosed CML-CP patients in India. Using a Markov model, the clinical effectiveness and costs of Imatinib, Nilotinib and Dasatinib were estimated. Incremental cost per QALY gained with a given treatment option was compared against the next best alternative, and assessed for cost-effectiveness.

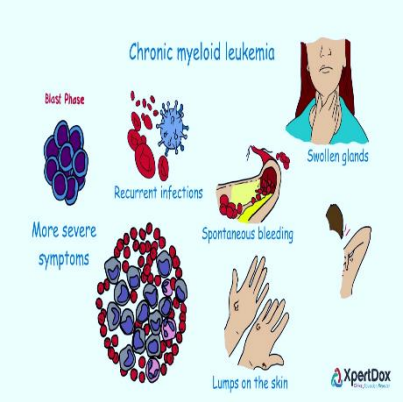


Image source: Internet

We found that imatinib is a non-dominated treatment option with an average cost of ₹ 64,323 per QALY lived which is cost-effective in the Indian scenario.. Moreover, Dasatinib patients incurred an incremental cost of ₹ 237,583 per QALY gained as compared to Imatinib treatment.

Policy Recommendations:

- As per the current reimbursement rates, Imatinib is the most cost-effective treatment option for CML-CP patients.
- Dasatinib offers better health outcomes than imatinib and a 21% reduction in the reimbursement rate is required to make it a cost-effective treatment option for India.
- The use of Nilotinib is currently not value for money in the Indian context.
- There is a need to produce significant clinical literature with respect to Nilotinib and Dasatinib in the Indian context.

Background and Gap in Literature:

National Cancer Grid (NCG) guidelines recommend the use of first-generation Tyrosine-kinase Inhibitor (TKIs): Imatinib as the first-line therapy for newly diagnosed CML-CP patients. In the past decade, second-generation TKIs such as Dasatinib and Nilotinib have demonstrated efficacy for treating incident CML-CP cases and were therefore granted approval for the first-line treatment globally (3,4). The second-generation TKIs produce more rapid molecular responses than imatinib at standard doses of 400 mg daily, but five-year OS does not differ between the three TKIs (3,4).

Most incident CML-CP patients require life-long, daily TKI-based care. This causes an immense financial burden on the cancer patients and their families. The launch of generic imatinib in the market, reimbursement of imatinib in the health benefit package (HBP) and introduction of Glivec International Patient Assistance Program (GIPAP) have provided some relief to the patients in terms of better health outcomes at lower costs. Dasatinib is also a part HBP under India's publicly financed national health insurance scheme – Ayushman Bharat Pradhan Mantri Jan Aarogya Yojana (ABPM-JAY) (5). Therefore, the health system spending on incident CML-CP after generic versions of TKIs (Imatinib and Dasatinib) becomes available is the subject of great interest among patients, physicians, and payers.

Policy Brief

Aims and Objective

This policy brief addressed the policy question of the most cost-effective treatment option for newly diagnosed CML-CP 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 CML treatment regimens, conducted by the HTA Resource Hub, PGIMER, Chandigarh.

Treatment arms:

1. Imatinib 400mg once daily;
2. Nilotinib 300mg twice daily;
3. Dasatinib 100mg once daily.

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 Imatinib, Nilotinib and Dasatinib from the societal perspective. 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. **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 monthly cycle length and lifetime horizon was considered (Figure 1).
2. Reimbursement rates (for Imatinib and dasatinib) and market prices (for Nilotinib) were used to estimate the treatment cost in each health state (5).
3. In order to obtain the Out-of-Pocket Expenditure (OOPE) incurred on out-patient consultations, the primary data for 602 CML patients was analysed as the part of **CADCQoL database** (6).
4. Transition probabilities and effectiveness parameters were obtained from the published Indian literature and pivotal clinical trials for each of the drugs – DASISION and ENESTnd trials (3,4,7).
5. The Quality of Life (QoL) scores were also estimated for all the health states from the primary data from **CADCQoL database** (7).

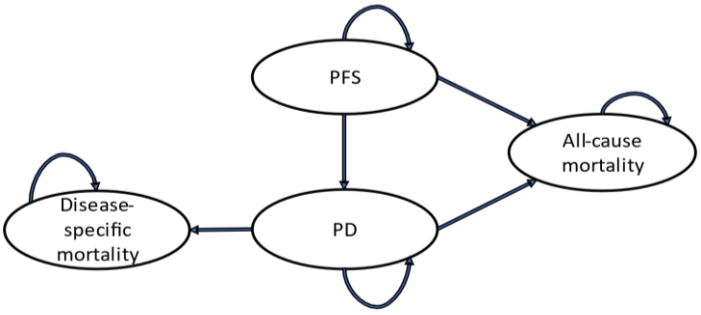
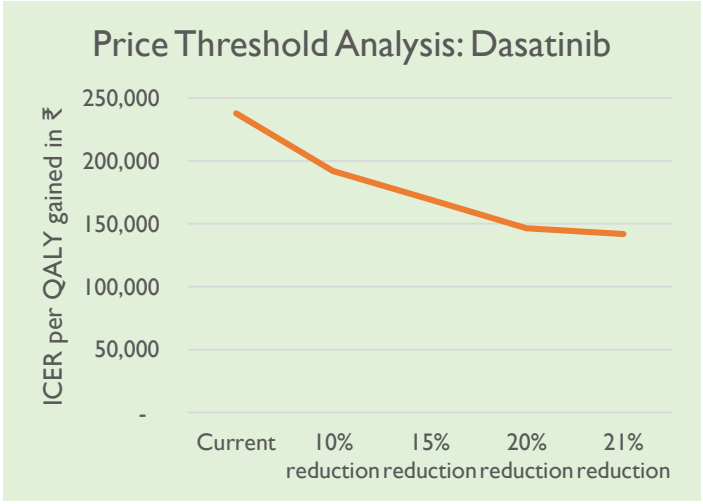


Figure 1: Schematic diagram for the Markov state transition model. PFS: Progression-Free State; PD: Progressive Disease

***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.
- EQ-5D is the most utilised tool worldwide to measure QoL.

Treatment strategy (in ₹)	Cost (in ₹)	QALYs	Incremental cost per QALY gained (in ₹)
Imatinib	746,939	11.61	-
Dasatinib	1,147,877	13.30	237,583
Nilotinib	3,590,493	13.68	6,499,642



Policy Brief

Price Threshold Analysis

- At the current WTP threshold of one-time per capita GDP (₹ 141,225) of India, Dasatinib has a 27.7% probability of being cost-effective as compared to Imatinib in the Indian context.
- Dasatinib offers slightly better health outcomes than imatinib.
- A 21% reduction in the reimbursement rate of dasatinib will make it a cost-effective treatment option.

Results:

- Imatinib is the is the most cost-effective treatment option and incurs an average cost of ₹ 64,323 per QALY lived in the Indian context.
- Dasatinib offers better health outcomes at an incremental cost of ₹ 237,583 per QALY gained as compared to imatinib which is not cost-effective at the current WTP threshold of 1-time per capita GDP.
- Nilotinib is also not cost-effective and incurs an incremental cost of ₹ 6.5 million per QALY gained as compared to Dasatinib.

References:

1. Bhutani N. Chronic myeloid leukemia in India: a review. Int J Sci Healthc Res. 2020;5(1):6–11
2. Ganesan P, Kumar L. Chronic Myeloid Leukemia in India. J Glob Oncol. 2016 Jul 20;3(1):64–71.
3. Cortes JE, Jiang Q, Wang J, Weng J, Zhu H, Liu X, et al. Dasatinib vs. imatinib in patients with chronic myeloid leukemia in chronic phase (CML-CP) who have not achieved an optimal response to 3 months of imatinib therapy: the DASCERN randomized study. Leukemia. 2020 Aug;34(8):2064–73.
4. Kantarjian HM, Hughes TP, Larson RA, Kim DW, Issaragrisil S, le Coutre P, et al. Long-term outcomes with frontline nilotinib versus imatinib in newly diagnosed chronic myeloid leukemia in chronic phase: ENESTnd 10-year analysis. Leukemia. 2021;35(2):440–53
5. Health Benefit Package - 2.0 | Official Website Ayushman Bharat Pradhan Mantri Jan Arogya Yojana | National Health Authority. Available from: https://pmjay.gov.in/node/1128
6. Prinja S, Dixit J, Gupta N, Mehra N, Singh A, Krishnamurthy MN, et al. Development of National Cancer Database for Cost and Quality of Life (CaDCQoL) in India: a protocol. BMJ Open. 2021 Jul 1;11(7):e048513
7. Medhi K, Raina V, Kumar L, Sharma A, Bakhshi S, Gupta R, et al. Response assessment of patients with chronic myeloid leukemia receiving imatinib mesylate (Glivec) therapy: experience from a single center in a developing country. Leuk Lymphoma. 2010 Oct 1;51(10):1850–4

'Value' of new drug therapies for the treatment of Chronic Lymphocytic Leukemia (CLL).

'Value' of new drug therapies for the treatment of Chronic Lymphocytic Leukemia (CLL)

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

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.

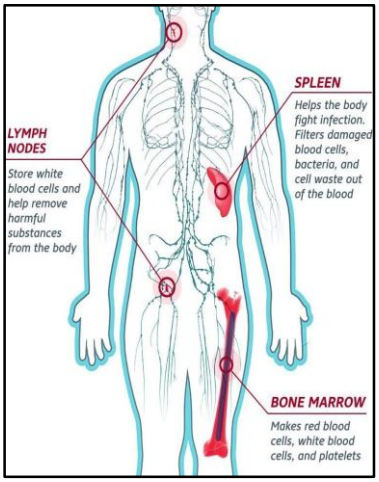


Image Source: https://www.gazyva.com/first-line-cll/about-cll/what-it-is.html

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.

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.

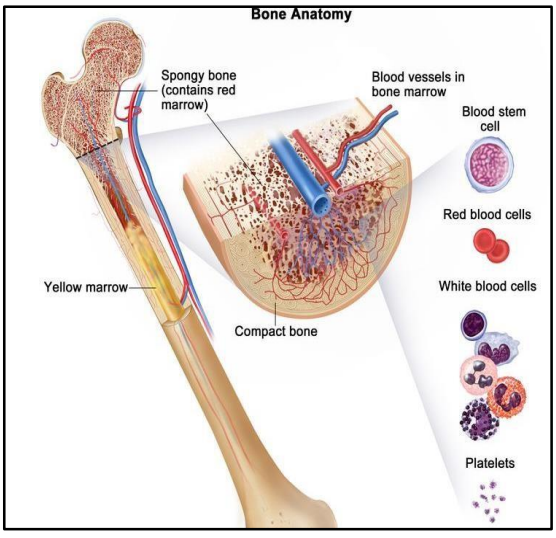
Context:

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.



https://www.cancer.gov/types/leukemia/patient/cll-treatment-pdq

Policy Brief

Aims and Objectives:

This policy brief addresses the policy question of whether different combination therapies of newer drugs, Bendamustine plus Rituximab (BR) and ibrutinib are cost- effective options for treatment of CLL in India. It summarizes the results of a HTA study on BR and Ibrutinib conducted by HTA Resource Hub PGIMER.

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 Ibrutinib

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 leukemia. Treatment done with different combination therapies (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 incremental cost 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 60 mg/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, along 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.

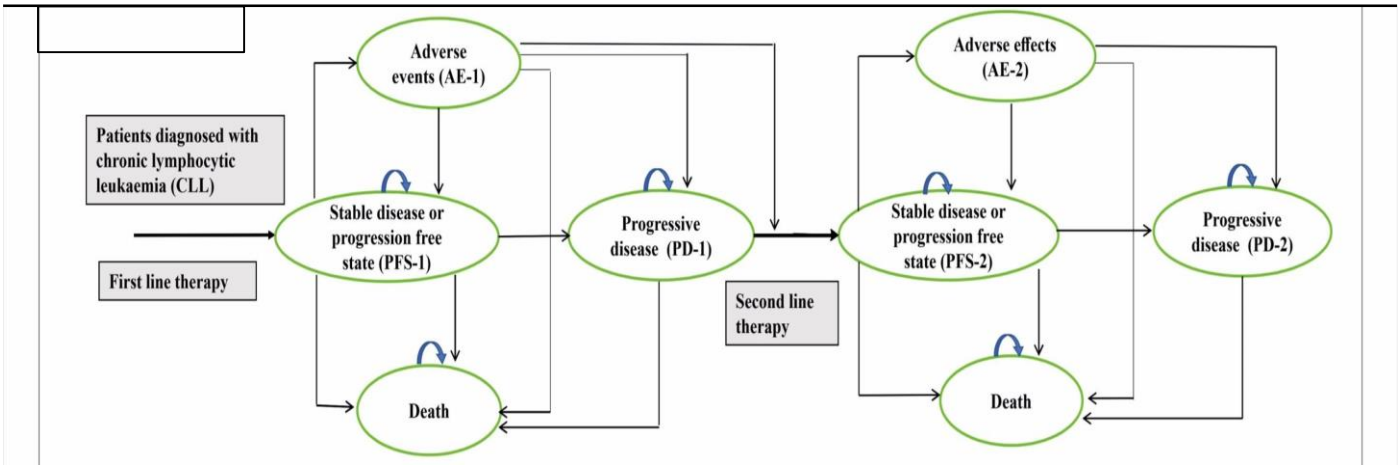


Fig. 1 : Markov Model

Policy Brief

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.

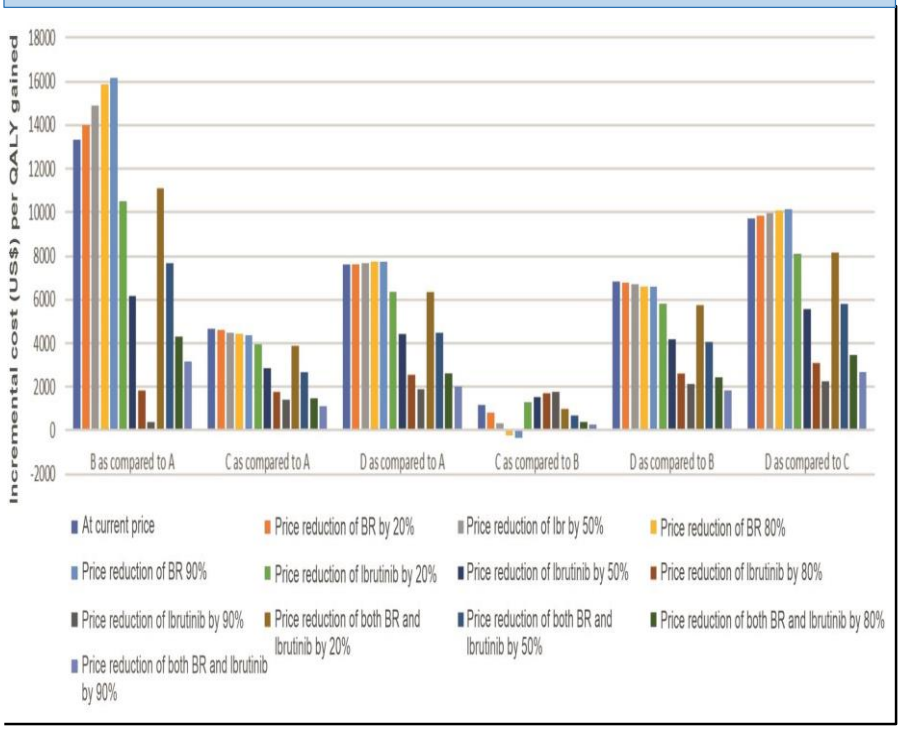


Fig. 2 Threshold Analysis

References:

1. GBD Results Tool | GHDx [Internet].
2. Tejaswi V et al, Chronic Lymphocytic Leukemia: Real-World Data From India. JCO Glob Oncol. 2020;(6):866–72.
3. Lad DP et al, Establishment of a comprehensive chronic lymphocytic leukemia clinic at a tertiary referral center in India. Blood Adv;2(Suppl 1):33.
4. Gogia A et al. Assessment of 285 cases of chronic lymphocytic leukemia seen at single large tertiary center in Northern India. Leuk Lymphoma [Internet]. 2012;53(10):1961–5.
5. Knauf WU et al. Phase III randomized study of bendamustine compared with chlorambucil in previously untreated patients with chronic lymphocytic leukemia. J Clin Oncol. 2009;27(26):4378–84.
6. Burger JA et al. Long-term efficacy and safety of first-line ibrutinib treatment for patients with CLL/SLL: 5 years of follow-up from the phase 3 RESONATE-2 study. Leukemia [Internet]. 2020;34(3):787–98.
7. Soini E et al. Cost-effectiveness of First-line Chronic Lymphocytic Leukemia Treatments When Full-dose Fludarabine Is Unsuitable. Clin Ther [Internet]. 2016;38(4):889-904.e14.
8. Woyach JA, Ruppert AS, Heerema NA, Zhao W, Booth AM, Ding W, et al. Ibrutinib Regimens versus Chemoimmunotherapy in Older Patients with Untreated CLL. N Engl J Med. 2018;379(26):2517–28
9. Woods B et al. Bendamustine versus chlorambucil for the first-line treatment of chronic lymphocytic leukemia in England and Wales: A cost-utility analysis. Value Heal [Internet]. 2012;15(5):759–70.
10. Patel K et al. Cost-Effectiveness of First-Line Ibrutinib versus Third-Line in Patients with Untreated Chronic Lymphocytic Leukemia. Blood. 2020

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

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.

Image source: Internet

We found that CDK4/6 inhibitors are not cost-effective in the Indian scenario even if the cost of Ribociclib and Palbociclib are reduced by 95%. In contrast, a 78% and 72% respectively reduction in the price of Fulvestrant monotherapy in both the scenarios, is required to make it the most cost-effective treatment option for MBC patients in India.

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.

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** in order to determine the most cost-effective treatment modality for MBC among post-menopausal Indian women.

Table 1: Description of scenarios

Scenario	Cost assumptions	Effects
Market price scenario (I)	• Market Prices and procurement prices for all the treatment arms • OOPE: Direct non-medical expenditure (including user/procedure fees) for OPD consultation and day-care visit • Diagnostics: CGHS reimbursement rates	• LYs • QALYs
Publicly financed health insurance scenario (II)	• Reimbursement rates as per AB PM-JAY HBP • Direct non-medical expenditure for OPD consultation and day-care visit	• LYs • QALYs

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 Resource Hub, PGIMER, Chandigarh.

Treatment arms:

1. Tab. Ribociclib 600mg OD daily + Inj. Fulvestrant 500mg monthly
2. Tab. Palbociclib 125mg OD daily + Inj. Fulvestrant 500mg monthly
3. Inj. Fulvestrant 500mg monthly
4. Inj. Paclitaxel 175mg/m^2 three weekly
5. Tab. Capecitabine 1250mg/m^2 OD daily for two weeks

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:

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 (PD2) and death. A monthly cycle length based on the treatment schedules in the MONALEESA-3 trial was considered (Figure1).
2. Costs related to the treatment and the adverse effects were estimated for all the health statesfor both the scenarios using secondary sources. In order to obtain the Out-of-PocketExpenditure (OOPE), the primary data was analyzed from 843 MBC patients as a part **CADCQoL database** (4).
3. 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. (2017)** (5).
4. The Quality of Life (QoL) scores were estimated from the **CADCQoL** primary data collected from 843 breast cancer patients which was thenadjusted to obtain the utility scores for different health states and adverse effects.

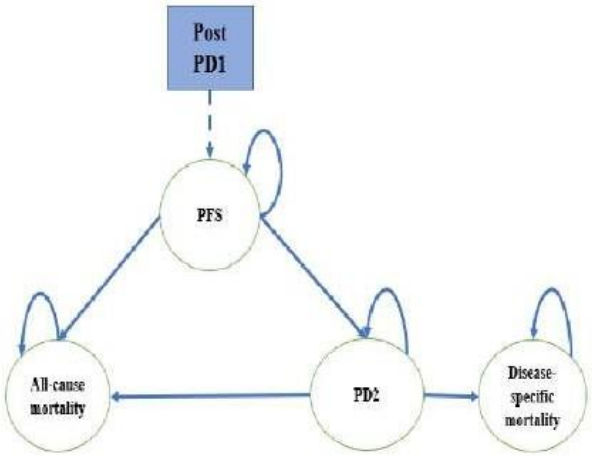


Figure 1: Schematics of the Markov state transition model. PFS: Progression-free state; PD: Progressive Disease

*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 and Price Threshold analysis:

- None of the treatmentstrategies are cost-effective at the current WTP threshold of1-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).
- CDK 4/6 inhibitors: Palbociclib and Ribociclib are not cost- effective even after a current market price reduction of 95%.

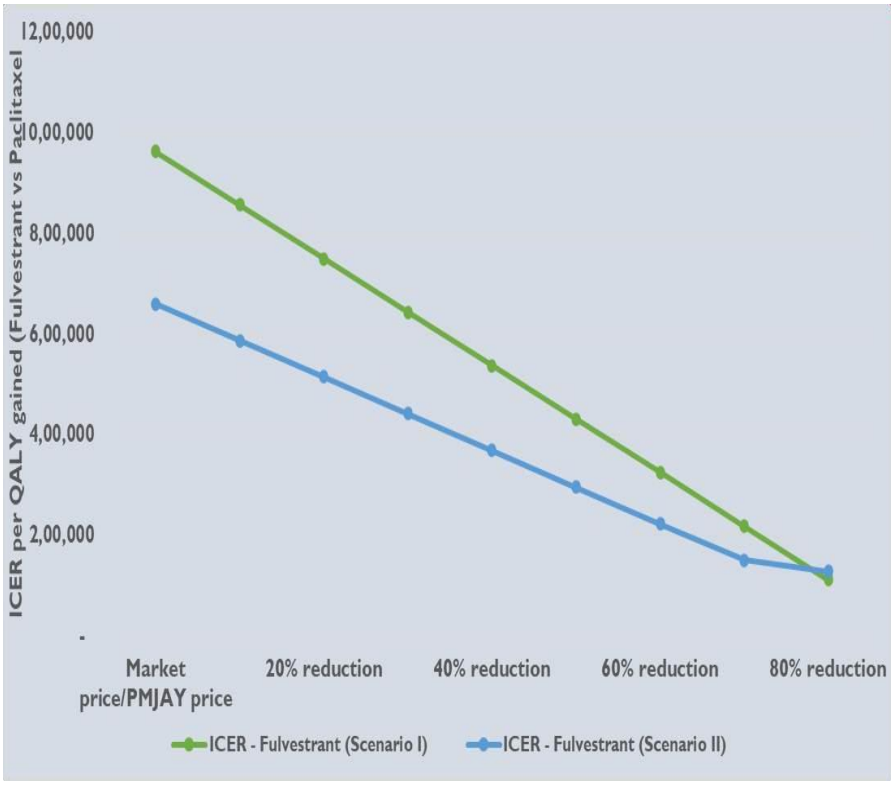


Figure 2: Price Threshold Analysis (Fulvestrant)

References:

1. India Factsheet: GLOBOCON 2020 [Internet]. The Global Cancer Observatory; 2021. Available from: https://gco.iarc.fr/today/data/factsheets/populations/356-india-fact-sheets.pdf
2. Slamon DJ, Neven P, Chia S, Fasching PA, Laurentiis MD, Im S-A, et al. Overall Survival with Ribociclib plus Fulvestrant in Advanced Breast Cancer. N Engl J Med. 2019 Dec 11
3. Cristofanilli M, Turner NC, Bondarenko I, Ro J, Im S-A, Masuda N, et al. Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial. Lancet Oncol. 2016 Apr 1;17(4):425–39
4. Prinja S, Dixit J, Gupta N, Mehra N, Singh A, Krishnamurthy MN, et al. Development of National Cancer Database for Cost and Quality of Life (CaDCQoL) in India: a protocol. BMJ Open. 2021 Jul 1;11(7):e048513
5. Wilson FR, Varu A, Mitra D, Cameron C, Iyer S. Systematic review and network meta-analysis comparing palbociclib with chemotherapy agents for the treatment of postmenopausal women with HR-positive and HER2-negative advanced/metastatic breast cancer. Breast Cancer Res Treat. 2017 Nov;166(1):167–77

Cost Effectiveness of Trastuzumab for Management of Breast Cancer in India

Cost Effectiveness of Trastuzumab for Management of Breast Cancer in India

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

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

Image source: https://pixels.com/featured/3-human-breast-cancer-sebastian-kaulitzki.html

- 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%.

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) by 30% [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-yearuse 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.

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.

Intervention and control arms:

1. 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.
2. Adjuvant chemo- therapy (comprising anthracycline and taxane-based drugs).

Methods and Approach

We undertook this cost-effectiveness analysis (CEA) usinga 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).

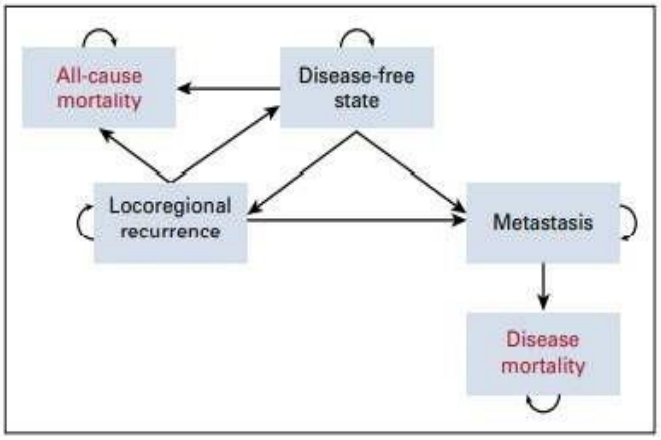


Figure 1: Model schematic

The analysis was performed under the following components:

1. 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.
2. A cycle length of 1 year was considered appropriate based on the available literature. Lifetime horizon was considered in the model.
3. 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.
4. 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]
5. 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%.

	1 Year Trastuzumab Use		
Finding (discounted)	HERA Trial	Joint Analysis of NSABP B-31 and NCCTG N9831 Trials	SC
Lifetime cost per patient, INR	3,41,046	3,37,935	1,10,151
Health consequences per patient			
LYs	8.3	8.7	6.8
QALYs	6.6	7	5.3
Incremental cost, INR	2,30,895	2,27,784	
Incremental benefit			
LYs	1.48	1.93	
QALYs	1.29	1.69	
ICER			
INRs per person LY gained	1,56,291	1,18,096	
INRs per person QALY gained	1,78,877	1,34,413	

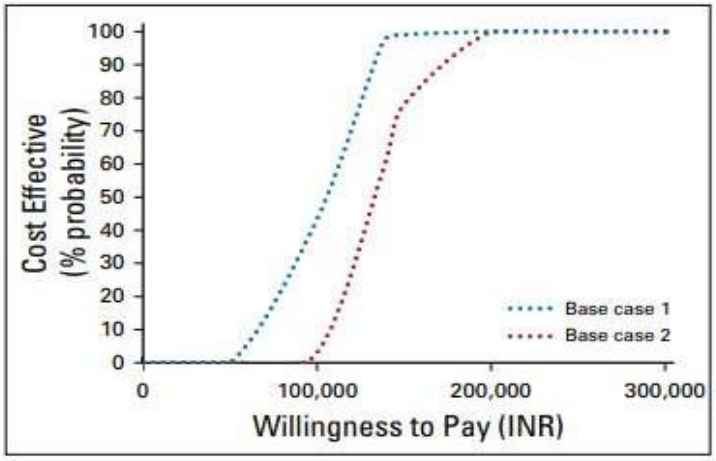


Figure 2: Probability of 1-year trastuzumab use being cost effective at varying willingness-to-pay thresholds. INR, Indian national rupees

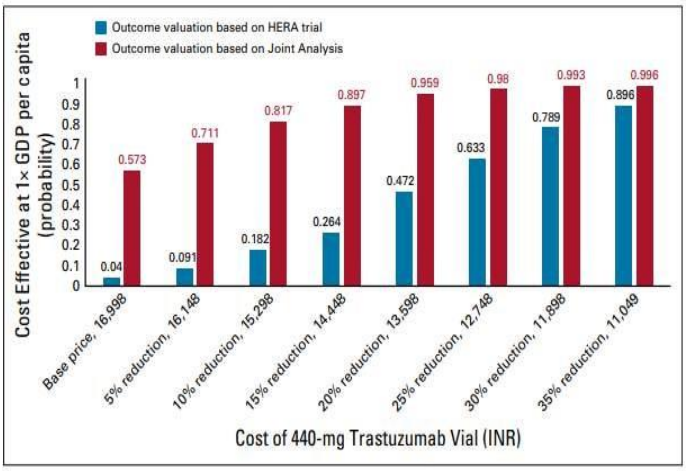


Figure 3 Price sensitivity analyses for cost-effectiveness of 1-year trastuzumab use. GDP, gross domestic product; INR, Indian National Rupee

References:

1. Romond EH, Perez EA, Bryant J, et al: Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. N Engl J Med 353:1673-1684, 2005
2. Perez EA, Romond EH, Suman VJ, et al: Trastuzumab plus adjuvant chemotherapy for human epidermal growthfactor receptor 2-positive breast cancer: Planned joint analysis of overall survival from NSABP B-31 and NCCTG N9831. J Clin Oncol 32:3744-3752, 2014
3. Cameron D, Piccart-Gebhart MJ, Gelber RD, et al: 11 years' follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive early breast cancer: Final analysis of the HERceptin Adjuvant (HERA) trial.Lancet 389:1195-1205, 2017
4. Ghosh J, Gupta S, Desai S, et al: Estrogen, progesterone and HER2 receptor expression in breast tumors of patients, and their usage of HER2-targeted therapy, in a tertiary care centre in India. Indian J Cancer 48:391-396, 2011
5. Garrison LP Jr, Lubeck D, Lalla D, et al: Cost-effectiveness analysis of trastuzumab in the adjuvant setting fortreatment of HER2-positive breast cancer. Cancer 110:489-498, 2007.
6. Hedden L, O'Reilly S, Lohrisch C, et al: Assessing the real-world cost-effectiveness of adjuvant trastuzumab inHER-2/neu positive breast cancer. Oncologist 17:164-171, 2012
7. Liberato NL, Marchetti M, Barosi G: Cost effectiveness of adjuvant trastuzumab in human epidermal growthfactor receptor 2-positive breast cancer. J Clin Oncol 25:625-633, 2007
8. Hall PS, Hulme C, McCabe C, et al: Updated cost-effectiveness analysis of trastuzumab for early breast cancer: AUK perspective considering duration of benefit, long-term toxicity and pattern of recurrence. Pharmacoeconomics29:415-432, 2011
9. Lidgren M, Jo¨ nsson B, Rehnberg C, et al: Cost-effectiveness of HER2 testing and 1-year adjuvant trastuzumabtherapy for early breast cancer. Ann Oncol 19:487-495, 2008
10. Chen W, Jiang Z, Shao Z, et al: An economic evaluation of adjuvant trastuzumab therapy in HER2-positive earlybreast cancer. Value Health 12:S82-S84, 2009 (suppl 3)
11. Shiroiwa T, Fukuda T, Shimozuma K, et al: The model-based cost-effectiveness analysis of 1-year adjuvant trastuzumab treatment: Based on 2-year follow-up HERA trial data. Breast Cancer Res Treat 109:559-566, 2008
12. Aboutorabi A, Hadian M, Ghaderi H, et al: Cost-effectiveness analysis of trastuzumab in the adjuvant treatmentfor early breast cancer. Glob J Health Sci 7:98-106, 2014
13. Buend´ıa JA, Vallejos C, Picho´ n-Rivie` re A: An economic evaluation of trastuzumab as adjuvant treatment ofearly HER2-positive breast cancer patients in Colombia. Biomedica 33:411-417, 2013
14. National Cancer Grid: National Cancer Grid Mumbai. https://tmc.gov.in/ncg/index.php/overview/about-us
15. National Centre for Disease Informatics and Research: Consolidated Report of Hospital Based Cancer Registries2007-2011. https://icmr.nic.in/sites/default/files/reports/Preliminary_Pages_0.pdf
16. Central Government Health Scheme: CGHS rate list. https://cghs.gov.in/index1.php?lang=1&level=3&sublinkid=5948&lid=3881
17. Chauhan A, Prakash G, Gupta N, et al: Cost-effectiveness of rituximab for the treatment of non-Hodgkin'slymphoma in India. XXXX (in press)
18. Prinja S, Sharma Y, Dixit J, et al: Cost of cardiac care at tertiary hospital in North India. Indian Heart J (in press)
19. Tamil Nadu Medical Services, Government of Tamil Nadu: Essential drug list. https://www.tnmsc.tn.gov.in/user_pages/drugtender.php?drugcat=T18028

Is Bevacizumab a Cost-Effective Option for Treatment of Advanced Cervical Cancer?

Is Bevacizumab a cost-effective option for treatment of Advanced Cervical Cancer

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

Policy Brief

Executive Summary:

Patients with advanced and metastatic cervical cancer have a poor survival. Assessment of the cost-effectiveness of a new drug, bevacizumab for the treatment of patients with advanced and metastatic cervical cancer in India is undertaken here. Bevacizumab has shown better effectiveness but is associated with great increase in health care costs. We find out whether the incremental cost is worth the potential health gains with the new drug. Health Technology Assessment (HTA) has been chosen approach to explore this question. Literature review, primary data collection, and economics evaluation via Markov model was done for the HTA. Treatment incorporating Bevacizumab to treat advanced cervical cancer patients would need around INR 25.75 lakhs for gaining 1 QALY.

Chemotherapy along with bevacizumab is not a cost-effective alternative when compared to chemotherapy alone.

Context:

Cervical cancer is the 2nd most common cancer affecting women in LMICs. India alone accounts for around one-fourth of world's cervical cancer deaths.

Most of the cervical cancer cases in India are diagnosed in fairly advanced stages. Nearly 15% to 61% of affected women will develop recurrence or metastasis usually within the first 2 years of completing the treatment. Patients with advanced and metastatic cervical cancer usually have poor 1-year survival.

Presently, chemotherapy of cisplatin and paclitaxel is recognized to be the standard of care for the management of these patients. The only randomized controlled trial, GOG 240, has shown clinical benefits with the addition of bevacizumab to the chemotherapy in advanced and metastatic cervical cancer patients.

Recommendations:

- Chemotherapy along with bevacizumab is not a cost-effective alternative when compared to chemotherapy alone at a threshold of 1-times GDP per capita (₹ 1,45,679 during the year 2020) or 3-times GDP per capita for treating advanced cervical cancer patients in India.
- Doublet chemotherapy with paclitaxel and cisplatin has a tolerable toxicity profile, reasonable disease control, and cost effective, hence should be continued to be prescribed in standard treatment guidelines for resource limited countries like India.

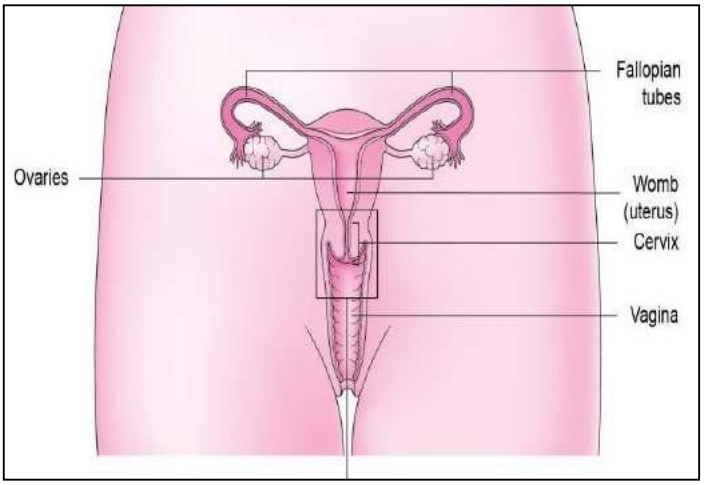


Image source: https://www.rgcirc.org/wp content/uploads/2019/03/FIG.3.jpg

About Bevacizumab:

Cervical cancers are associated with increased levels of VEGF, which is associated with poor prognosis and is the target of antiangiogenesis therapy.
Bevacizumab is an antiangiogenic humanized monoclonal antibody drug, an inhibitor of vascular endothelial growth factor (VEGF) and has shown to improve the survival of patients with advanced cervical cancer.

Policy Brief

Aims and Objectives:

This policy brief addresses the policy question of whether adding a new drug Bevacizumab in standard chemotherapy treatment of advanced cervical cancer will be cost-effective. It summarizes the results of a HTA study on Bevacizumab conducted by HTA Resource Hub PGIMER.

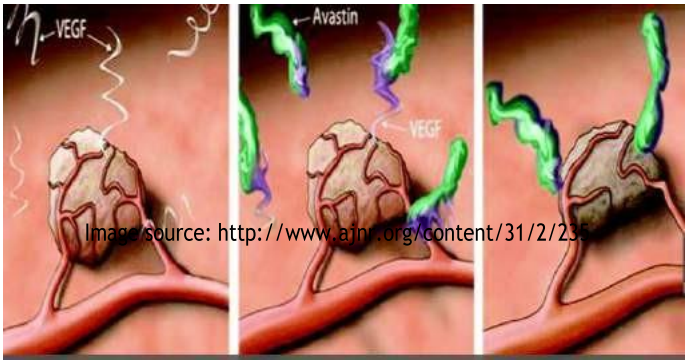


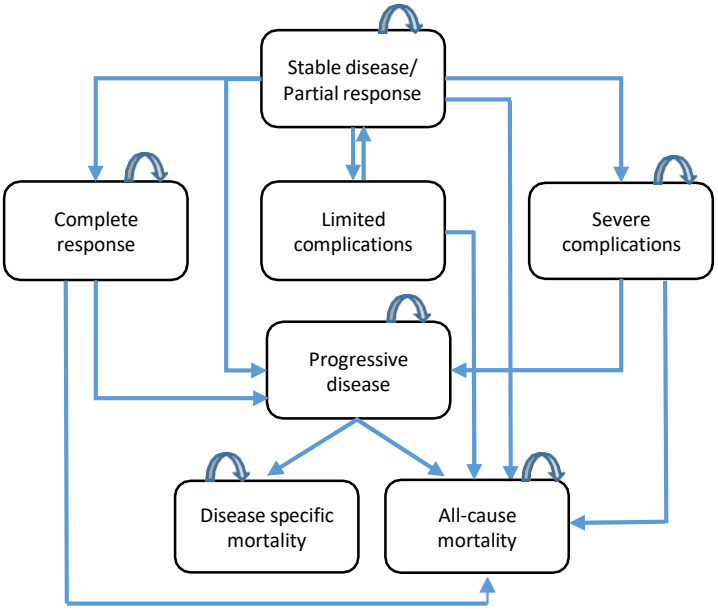
Image source: http://www.ajnr.org/content/31/2/233

Methods and Approach:

HTA was done using Markov modelling technique (Fig 1) to estimate the lifetime costs and health consequences for patients in advanced and metastatic cervical cancer treated. Treatment done with Bevacizumab plus chemotherapy was compared with chemotherapy alone.

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 incremental cost effectiveness ratio (ICER) between the intervention and control arm.

Literature review was done, data was collected on OOPE and quality of life values. The health system costs were derived from the previously undertaken costing studies from India. Clinical effectiveness data was taken from the only trial available, GOG 240.



Data Used:

Out-of-Pocket Expenditure (OOPE), the primary data was obtained as a part of developing CADCQoL database.
Transition probabilities and effectiveness parameters were obtained from the GOG-240 trial (Tewari et al)
Utility scores for calculating QALYs, the primary data was obtained as a part of developing CADCQoL database.

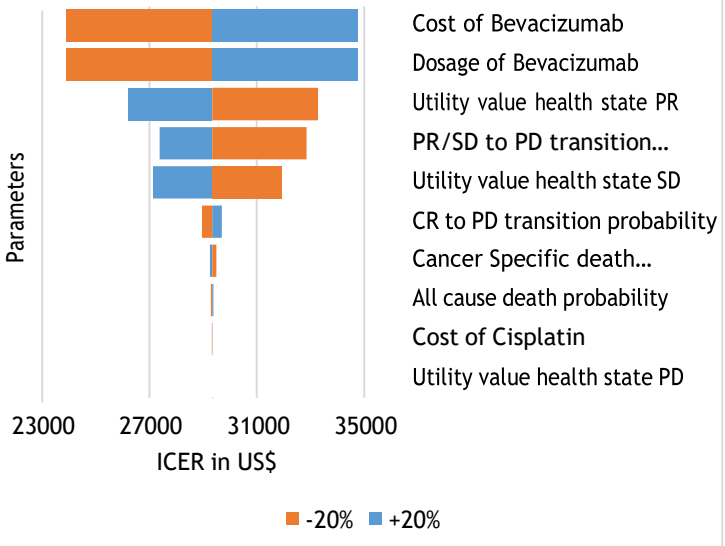
Results and Discussion:

Over the lifetime of a patient of advanced and metastatic cervical cancer, treatment with bevacizumab results in a gain of 3.30 life months 1.55 quality adjusted life months at an additional cost of INR 2.82 lakhs as compared to standard chemotherapy alone. Incremental cost effectiveness ratio of 25.75 lakhs per 1 QALY gained with using Bevacizumab along with standard chemotherapy.

The cost of treating adverse events of this intervention is high, as a result of which the drug remains cost-ineffective even after reducing its prices similar to the prices of control arm drugs.

The sensitivity analysis (Fig.2) showed that the results could vary highly on varying the cost and dosage of Bevacizumab.

Fig. 2: UVA- Tornado Diagram



References:

1. Bray F. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018 Nov 394–424.
2. Bray F. Global cancer transitions according to the Human Development Index (2008-2030): A population-based study. Lancet Oncol. 2012 Aug:790– 801.
3. Gupta N. Impact of COVID-19 on Outcomes for Patients With Cervical Cancer in India. JCO Glob Oncol. 2021;(7):716–25.
4. Ries L. SEER cancer statistics review, 1975-2003. 2006
5. Jayant K. Improved survival of cervical cancer patients in a screened population in rural India. Asian Pacific J Cancer Prev. 2016; 4837–44.
6. Kumar L. Chemotherapy and targeted therapy in the management of cervical cancer. Vol. 42, Current Problems in Cancer. Mosby Inc.; 2018 120–8.
7. Minion LE. A Markov model to evaluate cost-effectiveness of antiangiogenesis therapy using bevacizumab in advanced cervical cancer. Gynecol Oncol. 2015;490–6.
8. Tewari KS. Improved survival with bevacizumab in advanced cervical cancer. N Engl J Med. 2014; 734–43.
9. Phippen NT. Bevacizumab in recurrent, persistent, or advanced stage carcinoma of the cervix: Is it cost-effective? Gynecol Oncol. 2015;43–7.
10. CONSENSUS DOCUMENT FOR THE MANAGEMENT OF CANCER CERVIX.
11. Ferrara N. Vascular Endothelial Growth Factor: Basic Science and Clinical Progress. Endocr Rev. 2004:581–611

A Model-based Analysis for First-line Treatment of Metastatic Renal Cell Carcinoma: Implication from Perspective of PM-JAY

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. Sunitinib incurs an average cost of ₹ 143,269 ($ 1,939) per QALY lived which has a 94.6% probability of being cost-effective at the willingness to pay threshold of 1-time per capita GDP in the Indian context. The immunotherapeutic agents such as Nivolumab, Pembrolizumab are not cost-effective at the current prices in India.

Image source: Internet

Policy Recommendations:

- From the perspectiveof current reimbursement rates,sunitinib is a cost-effective treatment option for first-line metastatic renal cell carcinoma patients in India.
- The use of combination therapies are currently not value for money in the Indian context.
- Further research on the effectiveness and application of these agents among various subgroups should be done.

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.

Treatment arms:

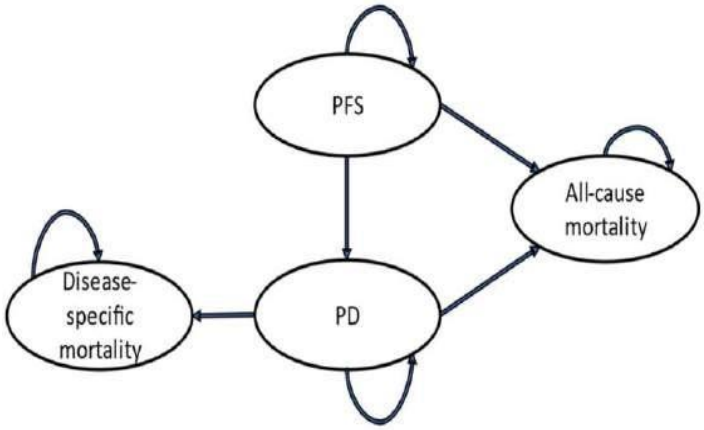
1. Sunitinib (50 mg orally once daily for 4 weeks of treatment followed by 2 weeks with no treatment);
2. Pazopanib (800 mg orally once daily);
3. Pembrolizumab (200 mg intravenously 3-weekly) plus Lenvatinib (20 mg orally once daily);
4. Nivolumab (240 mg intravenously 2-weekly) plus Ipilimumab 50 mg (4 doses intravenously once every6 weeks)

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).

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, 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 and systematic reviews and network meta-analysis (4,5,6).
5. The Quality of Life (QoL) scores were estimated from the published studies (8).



transition model. PFS: Progression-Free State; PD: Progressive Disease

*Quality Adjusted Life-years:

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

Treatment strategy	Cost in ₹	QALYs	Incremental cost per QALY gained in ₹	Interpretation
Sunitinib	273,846	1.91	-	ND
Nivolumab / Ipilimumab	6,686,526	1.97	115,885,317	ND
Pembrolizumab / Lenvatinib	9,744,330	2.75	3,953,457	ND
Pazopanib	348,537	1.86	-	D

Results:

- Sunitinib is the most cost-effective treatment option and incurs an average cost of ₹ 143,269 ($ 1,939) per QALY lived in the Indian context.
- At the current WTP threshold of one-time per capita GDP (₹ 168,300) of India, sunitinib has 94.6% probability of being cost-effective.
- Pazopanib is a dominated treatment strategy in the Indian context as it offers similar health outcomes at a significantly higher cost than sunitinib.
- None of the combination therapies are cost-effective at the current WTP threshold of 1-time per capita GDP of India.

References:

1. Ljungberg B, Campbell SC, Choi HY, Cho HY, Jacqmin D, Lee JE, et al. The epidemiology of renal cell carcinoma. Eur Urol. 2011 Oct;60(4):615–21.
2. Abraham GP, Cherian T, Mahadevan P, Avinash TS, George D, Manuel E. Detailed study of survival of patients with renal cell carcinoma in India. Indian J Cancer. 2016 Oct 1;53(4):572.
3. Pallagani L, Choudhary GR, Himanshu P, Madduri VKS, Singh M, Gupta P, et al. Epidemiology and Clinicopathological Profile of Renal Cell Carcinoma: A Review from Tertiary Care Referral Centre. J Kidney Cancer VHL. 2021 Jan 20;8(1):1–6
4. Motzer RJ, Tannir NM, McDermott DF, Arén Frontera O, Melichar B, Choueiri TK, et al. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. N Engl J Med. 2018 Apr 5;378(14):1277–90
5. Motzer R, Alekseev B, Rha SY, Porta C, Eto M, Powles T, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. N Engl J Med. 2021 Apr 8;384(14):1289–300
6. Motzer RJ, Hutson TE, Cella D, Reeves J, Hawkins R, Guo J, et al. Pazopanib versus Sunitinib in Metastatic Renal-Cell Carcinoma. http://dx.doi.org/10.1056/NEJMoa1303989. Massachusetts Medical Society; 2013
7. Prinja S, Dixit J, Gupta N, Mehra N, Singh A, Krishnamurthy MN, et al. Development of National Cancer Database for Cost and Quality of Life (CaDCQoL) in India: a protocol. BMJ Open. 2021 Jul 1;11(7):e048513
8. de Groot S, Redekop WK, Versteegh MM, Sleijfer S, Oosterwijk E, Kiemeney LALM, et al. Health-related quality of life and its determinants in patients with metastatic renal cell carcinoma. Qual Life Res. 2018;27(1):115–24

Impact of Price and Trade Margin Regulation On Cancer Medicine in India? An Interrupted Time Series Analysis

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

Health Technology Assessment in India
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 strengthen our research design.

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 sales.

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.

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 studyalso 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

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.

Policy Brief

Methods and Approach

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

Equation:

$$Y_t = \alpha + \beta 1 \text{ time t} + \beta 2 \text{ intervention t} + \beta 3 \text{ time after intervention t} + \epsilon_t$$

- 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.

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'

Results

Impact	Impact of Price Regulation on sales of anti-cancer medicines		Impact of Trade Margin Regulation on sales of anti-cancer medicines	
	Number of medicines	Medicine names	Number of medicines	Medicine names
Immediate increase followed by a sustained decline	3	Bicalutamide, Dacarbazine, Etoposide	10	Bevacizumab, Crizotinib, Sunitinib, Pomalidomide, Azacitidine, Decitabine, Epirubicin, Mitomycin, Exemestane, Cabazitaxel
Immediate increase followed by a sustained increase	7	Capecitabine, Asparaginase, Gefitinib, Mycophenoate Mofetil, Tacrolimus, Trustuzumab, Temozolamide	2	Erlotinib, Pegfilgrastim
Immediate decline followed by a sustained decline	6	Arsenic Trioxide, Chlorambucil, Docetaxel, Letrozol, Methotrexate, Cyclosporin	5	Osimertinib, Carfilzomib, Everolimus, Enzalutamide, Triptorelin
Immediate decline followed by a sustained increase	1	Pegylated Interferon Alpha 2b	9	Irnotecan, Lenolidomide, Regorafenib, Lapatinib, Pemetrexed, Bendamustine, Fulvestrant, Estramustine, Nilotinib
Total medicines under study	17		26	

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 prices leading to an increase in sales- both immediate and sustained or in the interest of pharmaceutical (substitution effect). In order to generate higher revenues for pharmaceutical companies as well as hospitals, higher priced drugs outside regulation may be pushed leading to an immediate as well as sustained decline in sales regulated drugs. Only the dose forms and strengths of molecules identified in the NLEM are price-controlled allowing companies to promote various dosage forms, strengths, and competing molecules, restricting the supply of price-controlled drugs. Some drugs are indispensable for treatment of particular cancers and any price reduction for these drugs led to an immediate and sustained increase in sales (e.g. trastuzumab). Standards of care are routinely updated as a result of drugs with improved effectiveness being made available in the market and may have led to prescription of drugs outside regulation which may have led to an immediate increase followed by a sustained decline in sales of certain drugs. Differences in the effects of the policies may be explained in terms of the type of use for individual drugs i.e. whether a drug is used for curative or palliative care use.

National Cancer Database for Costs and Quality of Life (CaDCQoL)

National Cancer Database on Costs and Quality of Life

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

Policy Brief

Open access Protocol

BMJ Open Development of National Cancer Database for Cost and Quality of Life (CaDCQoL) in India: a protocol

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ABSTRACT

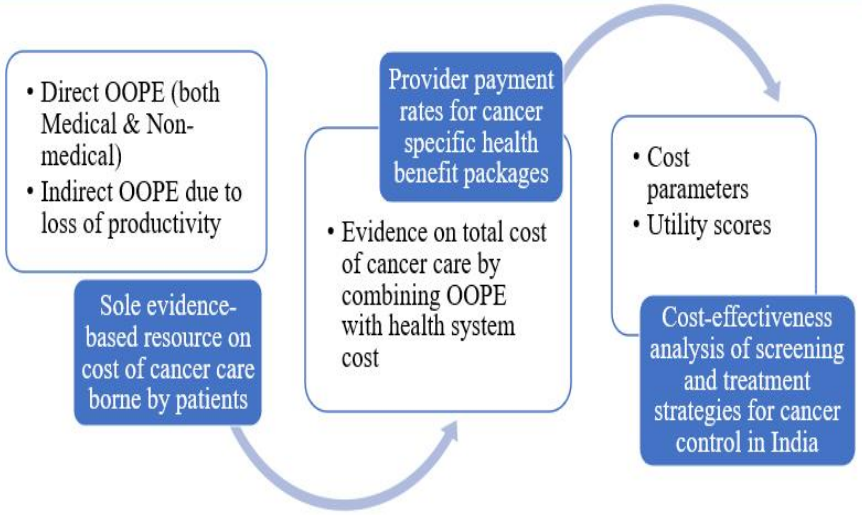
Introduction The rising economic burden of cancer on healthcare system and patients in India has led to the increased demand for evidence in order to inform policy decisions such as drug price regulation, setting reimbursement package rates under publicly financed health insurance schemes and prioritising available resources to maximise value of investments in health. Economic evaluations are an integral component of this important evidence. Lack of existing evidence on healthcare costs and health-related quality of life (HRQOL) makes conducting economic evaluations a very challenging task. Therefore, it is imperative to develop a national database for health expenditure and HRQOL for cancer.

Methods and analysis The present study proposes to develop a National Cancer Database for Cost and Quality of Life (CaDCQoL) in India. The healthcare costs will be estimated using a patient perspective. A cross-sectional

Strengths and limitations of this study

- This study would lead to development of the first national database for costs and quality of life among patients with cancer in India.
- The patient costs and health-related quality of life scores will be determined by cancer site, stage of disease and type of treatment.
- The economic impact of cancer care on household financial risk protection will be assessed.
- Being a hospital-based study, we will not capture quality of life of cancer patients who do not seek care.
- The health system costs on cancer care will not captured in this study, as these are available in National health system cost database.

- First National Cancer Database for Costs and Quality of Life in India.
- This database would serve to build an open-access data repository to derive estimates of cancer-related medical care costs borne by the patients, indirect costs due to loss of productivity and Health-related quality of life (HRQOL).
- Estimates would be generated by type of cancer, stage or severity, as well as by treatment approach.



Policy Brief

Aims and Objective

This policy brief addressed the policy question of economic burden and health-related quality of life among caner patients in India. The results would be useful to inform policy decisions in the field of cancer such as informing health technology assessments for assessing the cost-effectiveness of anticancer drugs and price regulation

Selection of health-care facilities

Classification of states as per Cancer Disability adjusted Life Years

High (less than 0·31)	Middle (0·31–0·55)	Low (0·56–0·75)

Selection of states from each group (random)

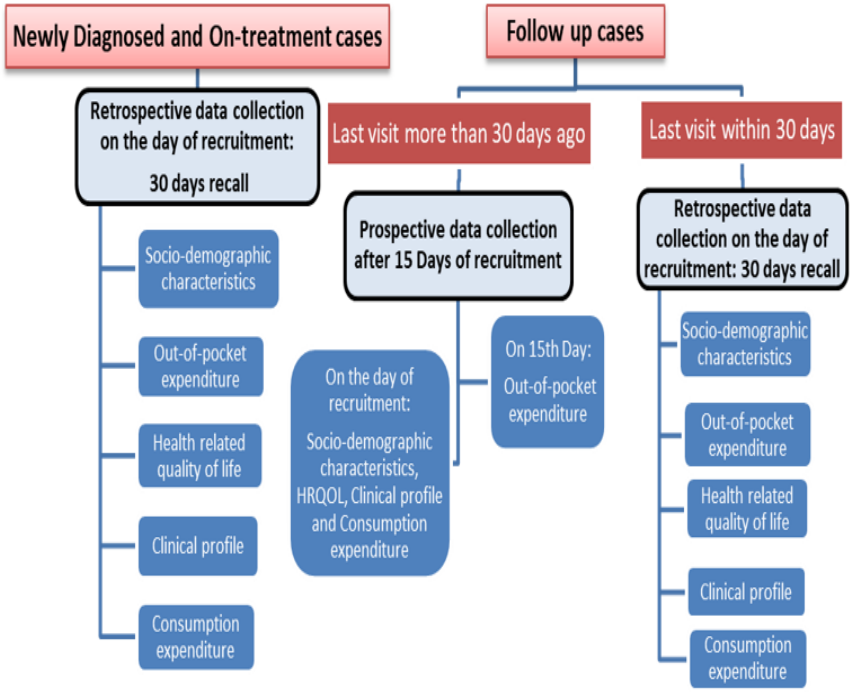
High	Middle	Low
Chandigarh (Punjab) and Tamil Nadu	Delhi & Maharashtra	Assam

Selection of 7 health-care facilities (purposive)

Post Graduate Institute of Medical Education and Research , Chandigarh	All India Institute of Medical S, New Delhi	Christian Medical College, Vellore	Adyar Cancer Institute, Chennai	Govt. Medical College and Hospital, Chandigarh	Tata Memorial Centre, Mumbai

Selection of patients using Systematic random sampling (common cancer clinics) and probability proportional to size (PPS) in case of different disease management groups

Data collection plan



- The study sample would be sufficient to provide valid estimates of OOPE, CHE and HRQOL for top 3, 6 and 12 cancers respectively in India, with a 5% margin of error and 95% CI.
- At 10% margin of error and 95% CI, our study would be powered to give valid estimates of OOPE, CHE and HRQOL for top 11, 17 and 20 cancers respectively in India

Margin of Error	Sample size			Number of cancers with valid estimates		
	OOPE	CHE	HRQOL	OOPE	CHE	HRQOL
5%	1690	845	398	3	6	12
10%	422	211	99	11	17	20

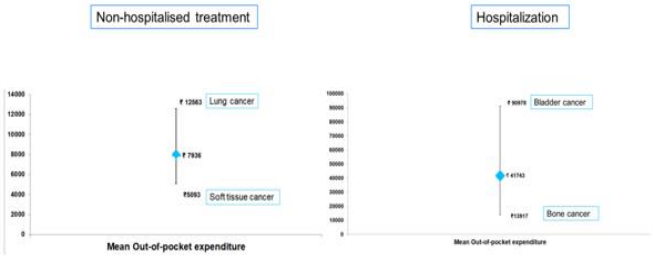
Policy Brief

Preliminary findings

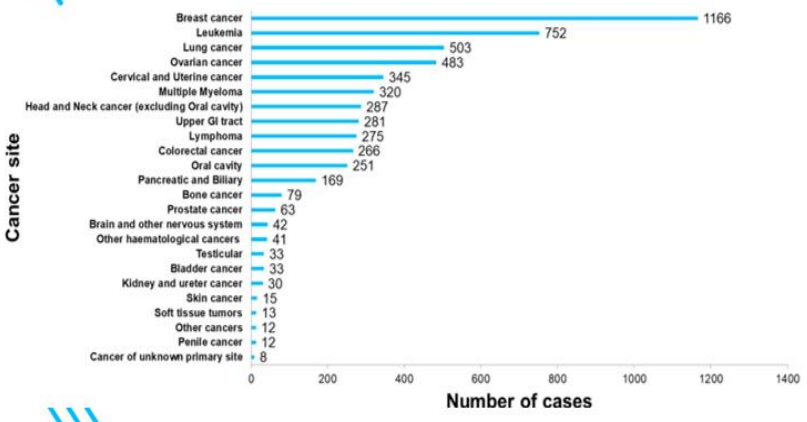
Out-of-pocket expenditure incurred per visit for non-hospitalised treatment of cancer in India

Components of OOPE	Mean (in ₹)	Standard Error (SE)
User fees/Hospital charges	353	46
Medicines	2591	139
Diagnostics	2777	96
Total Medical Expenditure	5722	181
Total Non-medical Expenses	2420	51
Overall OOPE (all cancers)	8142	192

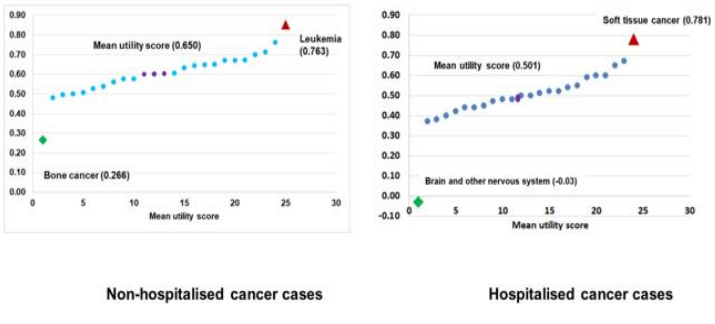
Out-of-pocket expenditure incurred for non-hospitalised and hospitalised cancer treatment



Distribution of cancers in India (Outpatient)



Health-related quality of life among cancer patients



Establishing Proton Technology Equipment for Cancer Treatment, Is this Treatment cost effective: A Rapid Health technology Assessment

Establishing Proton Technology Equipment for Cancer treatment- Is this treatment cost-effective: A Rapid Health technology Assessment

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

Policy Brief

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, SBRT.
- Indian literature suggests that even IMRT and 3D-CRT are not cost-effective at current threshold.

Image source: Internet

Proton beam therapy in comparison to existing current clinical practice 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 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.
- 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, 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 tumor 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 tumor cells. Unlike x-rays (regular radiation treatment), it uses protons to sends beams of high energy that can target tumors 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 pediatric 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) Carbonion therapy Photon radiotherapy Enucleation and plaque brachytherapy

Outcomes of 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.

Policy Brief

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.
NCCN 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 TARGETING CANCER CARE	• 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 conventional 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 GOOD SCIENCE BETTER MEDICINE BEST PRACTICE	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 2-year 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.

Impact of Proton beam therapy on quality of life among cancer patients

Quality of life (Qol) did not deteriorate during PBT in case skull base cancers and after PBT in brain tumors. PRO higher for PBT than photon therapy in case of head and neck and lung cancers. Patient reported breast cosmesis was appropriate after PBT and comparable to photon modalities.

Health Technology Assessment in India (HTAIn)

Department of Health Research

Ministry of Health & Family Welfare

Government of India