RRH-Health Technology Assessment in India

Cost Effectiveness Analysis of Hypothermia Detection Devices (BEMPU, ThermoSpot and Fever Watch) for Premature and Low Birth Weight Neonates in India

INDIAN INSTITUTE OF PUBLIC HEALTH SHILLONG

GOVERNMENT OF INDIA MINISTRY OF HEALTH & FAMILY WELFARE

DEPARTMENT OF HEALTH RESEARCH

Report

Cost Effectiveness Analysis of Hypothermia Detection Devices (BEMPU, ThermoSpot and Fever Watch) for Premature and Low Birth Weight Neonates in India

The Regional Recourse Hub for HTA India, North East Region,

The Indian Institute of Public Health Shillong (IIPHS)

In collaboration with

The Department of Health Research (DHR),

Ministry of Health and Family Welfare (MoH&FW),

Government of India

Indian Institute of Public Health Shillong
Lawmali, Pasteur Hills
Shillong- 793001
Meghalaya
Ph- 0364-2592014
Email: iiphshillong@phfi.org

Department of Health Research
IInd Floor, IRCS Building
1, Red Cross Road
New Delhi- 110003
Ph- 011-23736085

Suggested citation:

Ghosh R, Pde Y, Jana I, Das T, Jain S, Chauhan A, Albert S. Cost Effectiveness Analysis of Hypothermia Detection Devices (BEMPU, ThermoSpot and Fever Watch) for Premature and Low Birth Weight Neonates in India. Indian Institute of Public Health Shillong and Department of Health Research, Ministry of Health and Family Welfare, Government of India. 2019

Acknowledgements

We sincerely thank Dr N Wanswett, Medical Superintendent & Joint Director Health Services, Ganesh Das Hospital, Shillong for granting the team permission to interview the health care professionals in the Special Newborn Care Unit (SNCU) and to photograph a few images related to the treatment of premature and low birth weight neonates in the SNCU[1].

We thank Sister Noreen, Administrator, Nazareth Hospital, Shillong for granting the research team permission to carry out interviews with the Neonatal Intensive Care Unit nurses, related to the standard protocol of treating hypothermic neonates.

We thank Dr Maria De Francesco, Imperial College London for her technical support in developing the decision tree model for this study.

We thank Dr Himesh Barman, Paediatrician, NEIGRIHMS who has spared his time for discussions on treating neonates with hypothermia and the daily challenges that comes with it.

We thank Prof. Vikram Datta, Neonatologist, Lady Hardinge Medical College for taking the time to discuss concerns on under-reported neonatal hypothermia cases in India, and the issues around the treatment and length of stay for neonates with hypothermia.

We thank Dr.Thanigainathan, Neonatologist, JIPMER for inputs on the different techniques used to treat and monitor different stages of neonatal hypothermia.

We gratefully acknowledge the work of Dr Limalemla Jamir and Mr Roshan Ronghang during the early part of the study. We also acknowledge Ms Mary Magdalene Rynjah for supporting the team during her internship.

And finally we would like to express our thanks and acknowledgement to the team at Department of Health Research (DHR), Government of India, for their support and guidance throughout the study.

Ms Rituparna Ghosh MPhil
Ms Ibaplielad Jana MHA
Ms Yoorisabha Mika Pde BSc
Dr Tiken Das PhD
Dr Shalu Jain PhD
Dr Akshay Chauhan BDS MPH
Dr Kavitha Rajsekhar PhD
Prof Sandra Albert MBBS MD DNB DrPH

[1]Verbal consent was taken from health workers and parents before photography.

Table of Contents

List of Figures

List of Tables

Executive Summary

Background:

Hypothermia has been defined by World Health Organization (WHO) as body temperature below the normal range (36.5°C – 37.5°C) and has been sub-classified into three grades; mild (36.0°C – 36 .5°C), moderate (32.0°C – 35.9°C), and severe (<32.0 C) hypothermia. Premature and Low Birth Weight (LBW) neonates are at a greater risk for hypothermia because they lack body fat and have poor thermal regulation system. Often hypothermia goes undetected until it reaches a severe state where several complications arise and can even lead to death. The current standard of care (SoC) for detecting hypothermia includes measuring the body temperature of neonates every six hours with an axillary thermometer at neonatal intensive care unit (NICU). Early detection and continuous monitoring for hypothermia is desirable to prevent progression of hypothermia from the mild range to a more severe condition that can lead to further complications.

BEMPU, ThermoSpot and Fever Watch are hypothermia detecting devices that are specifically designed for neonates. These devices monitor the body temperature continuously and give either a visual or audio-visual alert when the new-born's body temperature drops.

Cost-effectiveness analysis (CEA) are an important part of health technology assessment intended to help decision makers optimize health care spending by making evidence informed decisions based on value for money. By estimating the cost and health gains of alternative interventions it can help prioritize the allocation of resources to interventions that contribute to improvement in health with the resources available.

Aims/objectives:

This study aimed to assess the cost effectiveness of hypothermia detecting devices such as BEMPU, ThermoSpot and Fever Watch in NICU setting for premature and low birth weight neonates in India.

- To assess the incremental costs associated with the use of BEMPU, ThermoSpot and Fever Watch
- To ascertain the difference in life years gained with the use of BEMPU/ThermoSpot/Fever Watch
- To estimate the incremental costs per life years gained with the use of BEMPU/ThermoSpot/Fever Watch

Methods:

A decision tree model was developed for estimating the Incremental Cost Effectiveness Ratio (ICER). For populating the model we required data pertaining to costs, clinical effectiveness and prevalence of hypothermia and its complications. A systematic literature review was conducted using electronic databases such as PubMed, Scopus, Web of Science and Cochrane Library for collating secondary data pertaining to clinical and cost aspects of interventions and comparator. These included data on sensitivity, specificity, clinical accuracy of Bempu, Thermospot, Fever watch and thermometer. For costing, data on treatment cost at NICU in India and treatment cost for hypothermia with or without complications were estimated based on available data. In addition to these epidemiological data such as prevalence of hypothermia among premature low birth weight neonates, neonatal mortality rate from census reports, national survey factsheet and other published studies were collated.

The PICO (Population, Intervention, Comparator and Outcome) framework was used to generate key search terms for developing the search strings for each database and the inclusion and exclusion criteria for the systematic reviews. The PICO framework: Population was premature and low birth weight neonates, Interventions were BEMPU, ThermoSpot or Fever Watch, Comparator was axillary thermometer and the Outcome was the clinical effectiveness and cost effectiveness of the interventions vs the comparator in detecting hypothermia, and also the cost of treating hypothermic LBW neonate in an NICU in India.

There was a paucity of published costing data on management of hypothermic neonates in India. To fill in gaps in information, we reached out to health care professionals such as neonatologists and Neonatal Intensive Care Unit (NICU) staff nurses and administrators for relevant information.

This study particularly focuses on neonatal intensive care cost because hypothermia is believed to be a contributing factor of neonatal mortality and morbidity. NICU cost was measured by multiplying the median duration of NICU stay with the daily NICU cost per patient per day. An assumption that the total hospital cost includes the cost of thermometer as it is part of NICU equipment, was made, hence no additional cost for thermometer was considered. To estimate the treatment cost with the intervention device per day, cost of the device was added to the estimated per day NICU cost. The SoC involves intermittent temperature monitoring rather than continuous monitoring offered by the newer devices; but this was considered to be equivalent as there was no evidence of a comparable nature that could be incorporated into the model. As thermometers were used as the gold standard in most studies we assumed 100% sensitivity in the model in detecting hypothermia by the SoC.

The data and information extracted from the systematic literature reviews and from discussion with experts, were fed into a decision tree model to estimate the incremental cost effectiveness ratio (ICER) for interventions over standard practice. A time-horizon of 30 days was considered to cover all cost and consequences of BEMPU and ThermoSpot. The findings are reported as incremental cost per life year gained of implementing the interventions as compared to standard practice.

A one way sensitivity analysis (OWSA) as well as probabilistic sensitivity analysis (PSA) was carried out to test the effect of uncertainty of the parameters on estimated ICER and to estimate the effect of joint uncertainty in all the parameters. To perform the sensitivity analysis, the demographics and epidemiological parameters such as risk of various morbidities with or without using the preventive interventions were taken into account. For undertaking PSA analysis, a beta distribution for probabilities and proportions, and gamma distribution for costs was assumed. One thousand times simulations were run in order to check the robustness of the model.

Key findings:

There was a paucity of good quality evidence on all the devices in the population of interest namely premature and or low birth weight neonates; no randomised controlled trials were available for any of the devices specifically in premature and LBW. Our literature search did not reveal any suitable published evidence on Fever watch. However, we found one brief research communication (Shafiajn et al, 2018) on fever watch, but the report did not provide details on methodology and other data that were required for our analysis. As per the study, there were 61 false positive cases (16. 2%) along with 5 false negative cases (16. 2%) but authors concluded that there was a good agreement between fever watch and digital thermometer. Due to paucity of good data from India, further analysis of this device was not done.

Cost effectiveness analysis of BEMPU and ThermoSpot were carried out against the standard of care. Both Bempu and ThermoSpot had additional cost (INR 796 for Bempu and INR 5693 for Thermospot) implications without health gain (-0.01 life years for Bempu and -0.06 Lys for Thermospot) in terms of life years. On the cost effectiveness plane BEMPU and ThermoSpot were in the north-west quadrant (less effective). According to the recommended cost-effectiveness threshold of India, both the interventions have ICER (-128207 for Bempu and -102660 for Thermospot) value less than the GDP per capita (as per March 2018, INR 138854.25 INR), so while the slightly higher cost could be acceptable in certain circumstances this was not balanced with gain in life years.

The simulation performed by using Probabilistic Sensitivity Analysis (PSA) showed that majority of the points in the scatter plot concentrated around the base case of the cost-effectiveness plane, considering all the uncertainties in the analysis. As the base case result appeared above the threshold line, it further indicates no cost effectiveness.

The effectiveness of any of these hypothermia detecting devices in preventing complications or death depends on the action taken after the early detection of hypothermia. If proper preventive care is not taken after detection, it cannot prevent morbidity or mortality due to hypothermia. In our model, we assumed there is 100% response after the detection, i.e. Kangaroo mother care (KMC)has been practiced in all cases after Bempu/ThermoSpot alert. If response rate is less than 100%, we assumed it would increase neonatal mortality due to hypothermia and related complications; we varied mortality post hypothermia detection by twenty percent on each side. But it was not found to be cost effective in either scenario.

Limitations:

The systematic review showed a paucity of good quality studies on costing and clinical effectiveness of BEMPU, ThermoSpot and Fever watch. There were just three studies on clinical efficacy of ThermoSpot and BEMPU and none were available for Fever watch in the databases searched. Most studies were funded by the manufacturers. Specific cost of treating a hypothermic neonate in an NICU in India was also not available in the existing literature. Hence general cost of NICU treatment was obtained. The assumption of intermitted temperature monitoring to be equivalent to continuous monitoring and high sensitivity of SoC assumed in the model are limitations. These limitations in data availability posed challenges in populating the decision tree model.

Recommendations:

Based on the ICER value estimated using the rather limited data that was available, the CEA shows that Bempu and Thermospot are not cost-effective devices for detecting hypothermia in premature and low birth weight neonates in India. Considering that in practical terms these devices provide continuous monitoring as opposed to intermittently by the standard of care, we could have accepted the marginally higher cost if they resulted in an increase in life years, but this was not the case. The values need to be interpreted with caution as there was a lack of good quality published evidence in the population of interest for all these devices. A key assumption made in the model is that once hypothermia is detected it will be treated appropriately so that complications are averted. This study considered LBW newborns in a hospital setting. The hypothermia detecting devices are likely to be provided to mothers of neonates on their discharge from a hospital as the devices can monitor body temperature and detect hypothermia in a home/community setting. But for such an analysis we would ideally require sensitivity, specificity of the comparator and interventions in a home settings which is currently not available. When data becomes available of its use in a community setting; with the device being worn by discharged/at home pre-term babies, then the CEA could be re-visited with the fresh data.

It is worth remembering that the device will not be a remedy for societal barriers like gender based discrimination, neglect of female new-borns that exist in some parts of the country nor of poor awareness of post detection care of new-borns. Additionally, it has been claimed that neonatal hypothermia is more due to the lack of knowledge about hypothermia and its prevention rather than lack of equipment. In a cluster-randomised controlled efficacy trial of a community-based behaviour change management on neonatal mortality in Uttar Pradesh, one arm of which used a Thermospot, the authors concluded that addition of the hypothermia detecting device did not provide an advantage over the package of essential new-born care.

List of Abbreviations

CEA	Cost-effectiveness analysis
CEAC	Cost-effectiveness Acceptability Curve
CEIC	Census and Economic Information Centre
CFRs	Case Fatality Rates
CPI	Consumer Price Index
DALYs	Disability Adjusted Life Years
GoI	Government of India
GPD	Gross Domestic Product
HTA	Health Technology Assessment
ICER	Incremental Cost Effectiveness Ratio
INR	Indian Rupee
KMC	Kangaroo Mother Care
LBW	Low Birth Weight
LONS	Late-onset Neonatal Sepsis
LY	Life Years
MeSH	Medical Subject Headings
NHM	National Health Mission
NICU	Neonatal Intensive Care Units
OOPE	Out-of-Pocket Expenditure
OWSA	One way Sensitivity Analysis
PHC	Primary Health Centre
PICO	Population Intervention Comparator Outcome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSA	Probabilistic Sensitivity Analysis
QALY	Quality Adjusted Life Years
SNCU	Sick Newborn Care Unit
SoC	Standard of Care
UNICEF	United Nations International Children’s Emergency Fund
WHO	World Health Organization

Glossary notes

Clinical effectiveness - Applying the best knowledge and practices to achieve optimum process and outcome for patient care. An intervention is considered clinically effective when it provides the best outcome among the other alternatives.

Cold Stress - When the extremities or periphery of the body are cold but the central part of the body is warm and the body temperature is between 36°C and 36.5°C.

Consumer Price Index (CPI) - CPI measures the average changes in price paid by the consumers for goods and services.

Cost effectiveness – The degree to which something is effective or productive in relation to its cost.

Cost effectiveness analysis - Is defined as an analytical technique intended for the systematic comparative evaluation of the overall cost and benefit generated by an alternative therapeutic interventions for the management of a disease (WHO Guide to Cost-effectiveness Analysis, 2003)

Cost effectiveness acceptability curve – A graph that summarizes the impact of uncertainty on the result of an economic evaluation in relation to the possible values of the cost-effectiveness threshold. It is usually expressed as ICER (incremental cost-effectiveness ratio). The graph represents a range of cost effectiveness thresholds on the horizontal axis against the probability that the intervention will be cost effective at that threshold on the vertical axis. This helps in understanding the uncertainty whether to approve or reject a particular health technology.

Cost of treatment - The amount which has to be spent for treating a patient in this case a neonate with hypothermia in the hospital.

Decision tree model - A tool used in decision making, by making a tree shape diagram to represent a course of action or a statistical probability analysis.

Equity – Equity is the absence of avoidable or remediable differences among groups of people, whether those groups are defined socially, economically, demographically, or geographically. Health inequities therefore involve more than inequality with respect to health determinants, access to the resources needed to improve and maintain health or health outcomes. (WHO)

Gross Domestic Product - Measures the value of the final goods and services produced within the geographic boundaries of a country per year. According to WHO, an Intervention with an ICER less than the current GDP is considered 'very cost effective' and if less than three times the per capita GDP, it is 'cost effective'.

Health Technology Assessment (HTA) - Refers to a systematic evidence based evaluation of properties, effects, and/or impacts of a health technology or intervention. It is useful in providing recommendation to policy makers for optimization of resource allocation in health.

Hypothermia detecting devices - Devices which monitor the body temperature of a baby and produce an alert when the temperature drops below normal, example: BEMPU Bracelet device, ThermoSpots, Fever Watch monitoring system.

Incremental Cost Effectiveness Ratio (ICER) - A measurement which represents the economic value of an intervention against an alternative. It is a result of an economic evaluation and It is calculated as ICER = C1 − C2 /E1 − E2 = ΔC/ΔE (Where C1, C2 are the respective cost of an interventions and E1, E2 are the respective effectiveness of using the intervention)

Kangaroo Mother Care (KMC) - Refers to the practice of providing continuous skin-to-skin contact between mother and baby, exclusive breast feeding, and early discharge from hospital.

Length of stay - The number of days the baby stayed in the hospital for treatment from the time of admission till discharge.

Life years gain – The additional number of years of life that a person lives as a result of receiving a treatment or any other intervention.

Low Birth Weight - When the birth weight of a new-born is less than 2500 g.

Mortality rate - The number of deaths due to a specific cause in a particular population, scaled to the size of that population, per unit of time.

Neonatal hypothermia - When the core body temperature of a neonate is below 36.5°C (97.7°F)

Neonates - A new-born baby less than 4 weeks after birth.

Neonatal intensive care unit (NICU) - A unit specializing in the care of ill or premature new-born infants.

Out-of-Pocket Expenditure (OOPE) – All expenses borne by the patient themselves be they direct payment to the healthcare providers while availing the health services or indirect expenses in form of travel costs or loss of wages, etc.

Premature - When a baby is born alive before 37weeks of gestational age. They are more likely to have health issues and to require longer hospital stay.

Prevalence - A measurement of individuals affected by a particular disease at a specific time.

Radiant warmer - An equipment used to maintain the body temperature of a new-born baby. It has a biocompatible bed where the baby is kept and an overhead heater that provides radiant heat along with a skin probe that adjust the heater and audio-visual alarm when the body temperature drops below normal rate.

Room temperature - A range of air temperature that is neither too hot nor too cold, where most people feel comfortable. Usually set between 20-25°C.

Sensitivity –Sensitivity of a clinical test refers to the ability of the test to correctly identify a condition or status (true positives)

Sensitivity Analysis - A technique used to determine what impact, values of an independent variable have on a particular dependent variable under a given set of assumptions.

Sick New-born Care Units (SNCU) - Units in district level hospitals specifically catering to reduce the mortality among the sick new-born, either born within the hospital (inborn) or outside the hospital (out-born)

Specificity - Also known as true negative rate measures the proportion of actual negatives that are correctly identified.

Standard of care – A diagnostic and treatment process that a clinician should follow for a certain type of patient, illness or clinical circumstances. In tort law it is the level at which the average, prudent provider in a given community would practice.

Systematic review –Systematic review is a type of literature review that uses a systematic approach to collect available evidence/ secondary data, critically appraise research studies, and synthesize findings to answer a specific question/s.

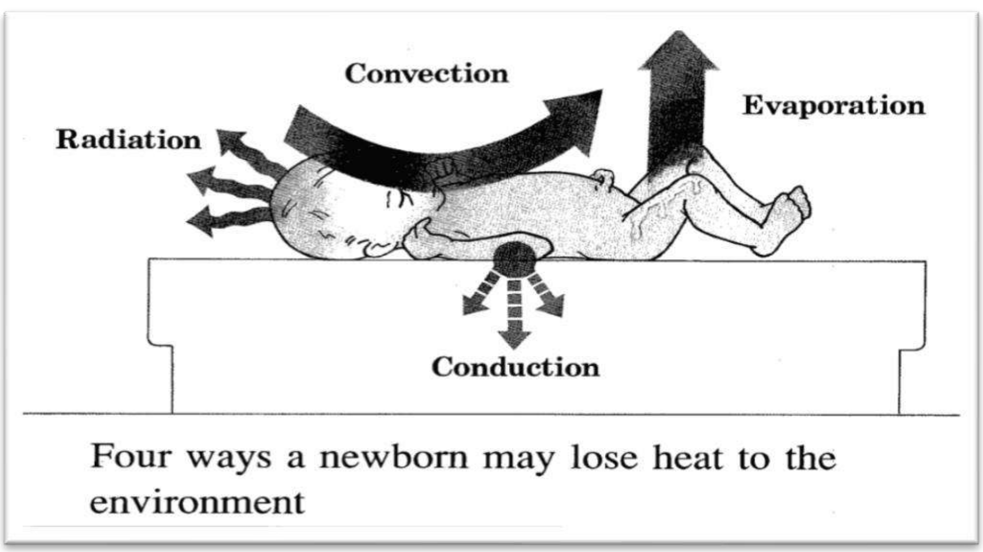
Weight gain - An important indicator of prognosis in neonates. When the body temperature is low, the body uses energy to generate heat therefore hinders weight gain and inversely when the baby does not have adequate weight it affects the heat production mechanism (Non-shivering thermogenesis) and those babies are at risk of getting hypothermia.

1. Introduction

Human beings have evolved to function within a narrow temperature range of 36.5 –37.5˚C. When the body temperature falls below this range the body's immune system is compromised and a condition called hypothermia occurs in which the core body temperature drops below what is required for normal metabolism and body function — putting an individual at risk. Hypothermia has been defined by World Health Organization (WHO) as body temperature below the normal range (36.5°C – 37.5°C) and has been sub-classified into three grades; mild (36.0°C – 36 .5°C), moderate (32.0°C – 35.9°C), and severe (<32.0 C) hypothermia.

From the early 1990s, warm environment was recognized as an essential component in the care of low birth weight (LBW) neonates and since then many measures have evolved to prevent neonatal death and illness due to abnormal body temperature. Thermal protection to a new born is a series of processes adopted at the time of delivery as well as initial days after birth to ensure that the baby does not become either too cold or too hot and maintain a normal body temperature of 36.5-37.5^{o} C (97.7-99.5^{o}F) (WHO). Newborns cannot regulate body temperature as adults would and hence they tend to cool down or heat up much faster. Hypothermia particularly affects neonates (children less than 1 month old) and those with a low birth weight are at greater risk. LBW babies often suffer from hypothermia due to lack of body fat and poor thermal regulation system. In addition to this, independent risk factors for hypothermia are preterm infants, low gestational age and low admission temperature (Mank et al., 2016). As seen in the image below (Fig 1.), there are four ways by which a new born can lose its body temperature; evaporation, conduction, convection and radiation (WHO).

Figure -0-1: Schematic illustration of four different ways in which heat loss can occur



Source: *WHO: Thermal Control of the Newborn: A practical guide (1997).*

Hypothermia causes metabolic changes in the body resulting in poor weight gain, feeding and poor organ development. Hypothermia has been associated with development of complications such as metabolic acidosis, jaundice, respiratory distress, hypoxia, hypoglycemia, disseminated intravascular coagulopathy and pulmonary haemorrhage (Chang, et al., 2015; Zayeri et al., 2005; Nayeri et al., 2006). Prolonged hypothermia is linked to impaired growth (Glass et. al, 1968), makes the new born more susceptible to infection (Dagan & Gorodischer, 1984) and increases the risk of death among low birth weight (LBW) neonates. Hypothermia makes the baby weak, it suckles poorly, feeding process gets disturbed and hence body loses heat further worsening the hypothermia condition. Hypothermia is recognized as a serious complication for babies with severe acute malnutrition (SAM) (Brook, 19 72; Manary, 2008). In an attempt to conserve calories, the metabolic rate is reduced, leading to an inability to generate sufficient heat.

Often hypothermia goes undetected until it reaches a severe state where several complications arise and can even cause the death of many infants. If hypothermia is detected early stage it can be easily reversed back to normothermia.

1.1 Hypothermia and its Relevance in Public Health

Hypothermia is common in infants born at hospital (prevalence range, 32% to 85%) and at home (prevalence range, 11% to 92%), even in tropical environments with the highest prevalence among LBW newborns (Lunze et al., 2013). A major risk factor is being Low Birth Weight (LBW), which contributes 60% to 80% of all neonatal deaths (WHO, 2017). India alone accounts for 40% of LBW newborns in the developing world and many of these newborns are discharged before gaining adequate weight (UNICEF and WHO, 2004). In India 43.7%, 20.8% and 19.2% neonatal deaths are due to preterm birth complications, infections and intra-partum related causes respectively (Sankar et al., 2016). According to the Global Burden of Disease Study 2016, neonatal preterm birth is the seventh leading cause of disability-adjusted life-years [DALYs] in India (Dandona et al., 2017).

Neonatal hypothermia is recognized as a factor contributing to significant morbidity and mortality in newborns (WHO, 1997). Its contribution to neonatal mortality is primarily as a comorbidity of severe neonatal infections, preterm birth, and asphyxia (Lunze et al., 2013). Both mortality and hypothermia are strongly correlated with age of the infant, and overall risk of hypothermia can vary substantially by season (Mullany, 2010 and Sodemann et al., 2008). High prevalence of newborn hypothermia (44%-85%) has been reported over the years from several developing countries (Tafari et al., 1973; Christensson et al., 1988; Christensson et al., 1995; Byaruhanga, 2005; Ogunlesi et al., 2008). In community-based studies (conducted in Nepal or India), hypothermia prevalence range from 11% to 92% (Lunze et al., 2013). In a large study conducted in Uttar Pradesh, almost half (45%) of the 1732 infants studied were found to be hypothermic (Darmstadt et al., 2006).

While neonatal causes of death are associated with neonatal hypothermia, the direction of causality is unclear (Lunze and Hamer, 2012). Neonatal sepsis also often presents as hypothermia in infants and every year sepsis causes approximately 250,000 infant deaths in India, alone (Lawn et al., 2005). Although infections (mostly sepsis and pneumonia) are usually listed as cause of death rather than hypothermia, it is unclear whether hypothermia is the underlying cause or the consequence of severe infections (Lunze et al., 2013). Case fatality rates (CFR) for newborn hypothermia globally range from 8.5% to 52% (Bang, et al., 2005; Christensson et al., 1995; Kambarami and Chidede, 2003; Johanson et al., 1993). In hospital settings, CFRs of 39.3% and 80% have been reported for mild and moderate hypothermia respectively (Mathur, et al., 2005). Even in community settings, risk of death increases substantially for every degree decrease in axillary temperature (Mullany et al., 2010).

Hypothermia in new-born occur throughout the world and in all climate types and is more common than perceived. There is some evidence for a strong association between season and hypothermia; the prevalence of hypothermia is higher in the coolest months of the year (Dec-Feb) (Luke et al, 2010). However, even among babies in the highest ambient temperature exposure quintile, the proportion with hypothermia in the first week of life was almost one in five (18.2%), suggesting the continuing importance and relevance of hypothermia risk even in the hot season of a tropical climate. The estimates of hypothermia depends on the age of the new born at the time of measurements. Babies whose serial measures began within the first day of life had significantly higher risk of meeting the criteria for moderate hypothermia compared with those whose measures were initiated later (Luke et al, 2010). It is highly prevalent in warm tropical regions as well. Therefore nowadays it is an essential package given to every new born. Strategies to prevent and manage hypothermia are extensively studied in developed countries (Sauer et al, 1991) but sincere care is needed in the case of developing countries. Specific data on hypothermia is scarce (Lawn et al, 2005; Bhutta et al, 2005) and mostly limited to hospital based data. A number of hospital based studies revealed that thermal stress is common (Ellis et al, 1996; Byaruhanga et al, 2005) and more than one half of new borns experience hypothermic episodes (Tafari & Olsson, 1973; Byaruhanga et al, 2005; Kambarami, 2003). While these studies indicate that hypothermia may be an important contributor to neonatal mortality, they are limited by lack of adjustment for age of infants at measurement and are predominately focused on sick infants presenting to tertiary care units.

1.2 Government Programmes and Policy

The Government of India (GoI) is building on a series of programmes and policy decisions introduced over the past two decades to address maternal and new-born health. Major milestones include launch of the Child Survival and Safe Motherhood Programme (1992); Reproductive and Child Health Programme (1997); National Health Mission (formerly National Rural Health Mission-2005); *Janani Shishu Suraksha Karyakram* in 2011; Reproductive, Maternal, Newborn, Child and Adolescent Health strategic framework (2013); and *Rashtriya Bal Swasthya Karyakram* (2013) (Paul et al., 2011; Tripathi, et al., 2014; Srivastava et al., 2018). GoI has now developed the India New-born Action Plan in response to the global Every New-born Action Plan launched at the World Health Assembly in June 2014 (India New-born Action Plan, 2014). It is envisioned to significantly reduce preventable new-born deaths and stillbirths and bring down the Neonatal Mortality Rate and Still Born Rate to "single digits" by 2030 (India New-born Action Plan, 2014). In 2017, GoI introduced Labour Room Quality Improvement Initiative which aims to reduce preventable maternal and new-born mortality, morbidity and stillbirths associated with care around delivery in Labour room (National Health Mission, 2017).

1.3 Rationale

Neonatal Hypothermia being a contributing factor to the mortality and morbidity of newborns, it would require frequent or continuous temperature monitoring to prevent this condition from progressing. Currently the Standard of Care (SoC) for temperature monitoring of newborns is carried out by axillary thermometer, where the new-born's body temperature is measured every six hours. If the new-born is hypothermic, then the baby is kept under a radiant warmer with a thermostat continuously monitoring the new-born's body temperature, however this SoC is largely designed for facility level care, which requires health-literate caregivers. Non-invasive newly introduced hypothermia detecting devices specifically designed for newborns, monitor the neonate's body temperature around the clock and gives either a visual or audio-visual alert. They can potentially cater to low resource health care centers as well as for caregivers with limited education. These devices include BEMPU hypothermia alert device, ThermoSpot sticker and Fever Watch.

For appropriate planning and allocation of resources, it is important to understand the cost effectiveness of a health technology before introduction into the health system. Cost-effectiveness studies are an important part of health technology assessment intended to help decisions makers optimize health care spending by basing decisions on value for money (Jonsson, 2015). This study attempted to assess the cost effectiveness of BEMPU hypothermia alert device, ThermoSpot and Fever Watch against the standard of care; axillary thermometer for detecting hypothermia in premature and low birth weight neonates in India.

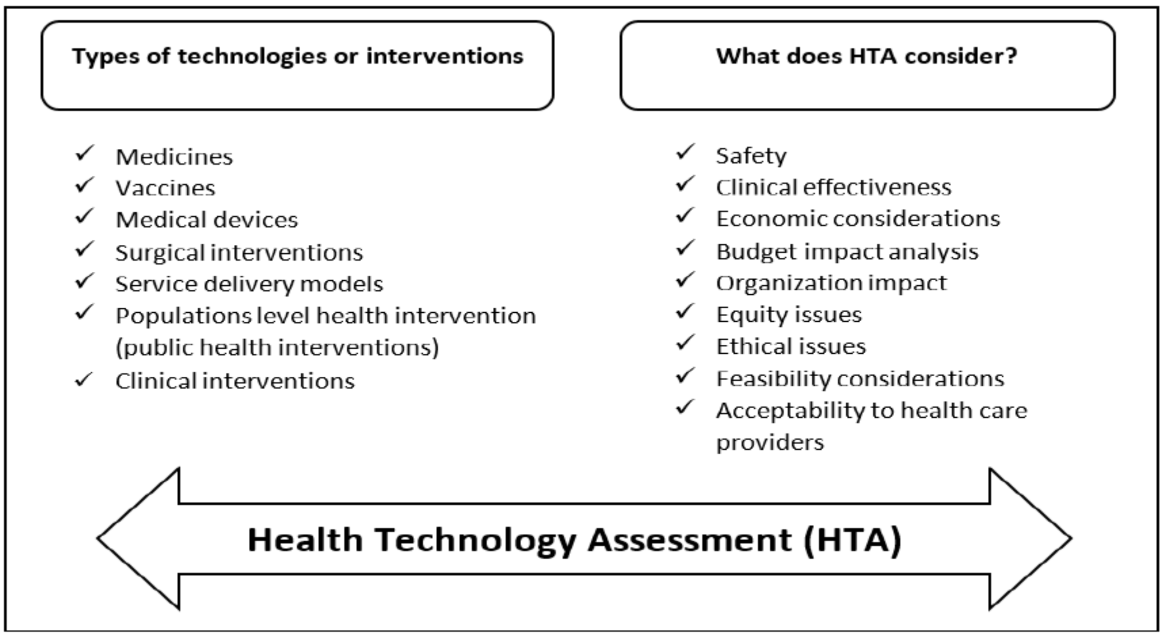
2. Literature Review

2.1 Health Technology Assessment

Health Technology Assessment (HTA) is 'the systematic evaluation of properties, effects and/or impacts of health technologies and interventions (WHO, 2016). The word 'health technology' includes the application of organized knowledge and skills in the form of devices, health programs, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of life (WHO, 2016). There are three ways to describe health technology: the physical nature (such as drugs, equipment, medical and surgical procedures, Public health programs), its purpose (such as prevention, screening, diagnosis, treatment, rehabilitation, palliation) and its stage of diffusion (HTA being experimental, investigational and established) (Goodman C.S., 2015).

HTA paves a way to scientific solutions for complex problems and aids in taking transparent and judicious decisions (Health Technology Assessment Manual, 2018). HTA also addresses the direct and intended consequences of technologies as well as their indirect and unintended consequences (WHO, 2016). The main purpose of HTA is to inform policy makers in making evidence-based decisions in terms of technology for healthcare which includes decision making at the individual or patient level, the healthcare provider and the institution level or at the regional, national and international level. HTA is a widely used methodology at a global level for optimization of resource allocation in health. It strives to identify the most effective strategy among the varied alternatives available by employing scientific and evidence-based methodology so that the greatest amount of health can be bought for every rupee spent (Health Technology Assessment Manual, 2018).

Figure -0-2: Aspects considered in HTA for different types of technologies and interventions



Source: *2015 Global Survey on Health Technology Assessment by National Authorities (WHO)*

2.2 Cost Effectiveness Analysis

Cost-effectiveness analysis (CEA) is a tool which aid decision makings about which medical care should be offered (‘HERC: Cost-Effectiveness Analysis’, n.d.). It estimates the cost and health gains of alternative interventions and it helps prioritize the allocation of resources to health interventions by identifying those which will lead to exceptional improvement in health for the least resources (‘WHO | Cost-effectiveness analysis for health interventions’, 2010). CEA is increasingly important in making public health decisions especially in a growing economy like India. India with its rapid healthcare inflation, increasing rates of chronic conditions, ageing population and increasing technology diffusion, will certainly need to adopt greater economic efficiency in the healthcare systems (Dang A. et al, 2016). It is making strategic efforts in improving healthcare services which is appropriate and of assured quality at the population level and at a feasible cost by employing CEA as one strategy. This study aims to do a CEA of different types of hypothermia detecting devices.

2.3 Hypothermia Detecting Techniques/Devices

Hypothermia can be measured using a thermometer or other devices designed for this purpose or simply by touching the baby's skin (hand touch). One study found that the accuracy of measurement by hand touch depends on the person who is checking; it was 96%, 34.4% and 23.4% sensitive when assessed by paediatricians, community health volunteers (CHVs) and mothers, respectively (Agarwal *et al*, 2007). According to WHO guidelines, taking the axillary temperature is better than the rectal temperature because of safety, hygiene and ease. However rectal temperature is considered to provide an accurate measure of body core temperature. Cold feet of the new born could be a sign that the baby is hypothermic.

A WHO practical guide and a study by Qazi et al (2019) states that neonatal hypothermia is more due to the lack of knowledge rather than lack of equipment(Qazi, Saqib, & Raina, 2019; WHO, 1997). Incorrect baby care is one of the influencing factors for the occurrence of hypothermia. No adequate warm delivery room, new born left wet and uncovered after delivery, delayed initiation of breastfeeding and separation of the baby and mother makes it more difficult to keep the baby warm.

Continuous temperature monitoring can help prevent neonatal hypothermia. For at least two hundred years, concerted efforts have been made to maintain the optimal new-born temperature, particularly premature new-born's body temperature (Stern, 1980; Scopes and Ahmed, 1966). However, in low-resource settings, it is still difficult to ensure that newborns are kept warm. Preventive measures include maintenance of the Warm Chain -: Warm delivery room, immediate drying, skin-to-skin contact/ Kangaroo Mother Care (KMC), breast-feeding, bathing and weighing postponed, appropriate clothing/ bedding, mother and baby together, warm transportation, warm resuscitation, training and awareness raising (WHO, 1997), warm clothing and use of warming mattress. Temperature monitoring of newborns is done by axillary thermometer measurement in routine care (Smith, 2004).

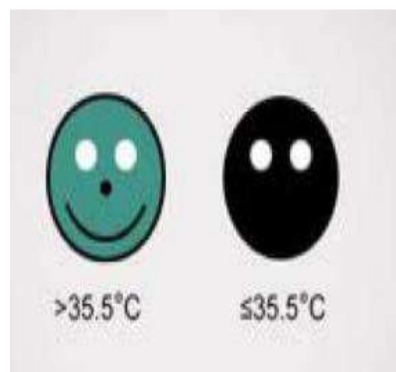
In this section, existing literature on BEMPU, Fever Watch, ThermoSpot and Digital Axillary thermometer have been briefly reviewed.

2.3 a. BEMPU Hypothermia Alert Device

BEMPU bracelet is a hypothermia-detection and alert device in the form of a bracelet that is relatively easy to use in a normal to low birth weight new born. The device alerts the caregiver through an audio-visual alarm. When the neonate's temperature drops or becomes hypothermic, the body respond by restricting the blood flow to the limbs and peripheries, through vasoconstriction. This allows for the conservation of warm blood in the core for the functioning of vital organs and therefore the limbs of the new-born becomes cold first. BEMPU bracelet depends on this principle to accurately detect the drop in temperature of the new-born and in doing so, alerts the caregiver to warm the baby (Morgan & Dave, 2017). The bracelet flashes a blue light every 30 seconds indicating normothermia. If the baby is hypothermic, the bracelet flashes an orange light every five seconds and beeps for one minute with repetition every 5 to 15 minutes. Depending on the severity of the baby's hypothermia, the frequency of the sound alarm would increase or decrease accordingly (Morgan & Dave, 2017). It is claimed that the audio-visual alarm of the bracelet makes it easy to use and detect in low-resource settings where thermal monitoring is limited in home settings (Tanigasalam et al, 2018). The device can monitor the new-born temperature continuously throughout the neonatal period.

2.3 b. ThermoSpot

WHO has recommended the use of low reading thermometer to detect hypothermia in newborn infants, however, these thermometers are fragile and cannot be sterilized, and thus it cannot be used without proper training. They are difficult to obtain especially in developing countries therefore mercury-in-glass thermometers are widely used. Colour contact thermometer called ThermoSpot manufactured by TALC, UK is being studied to be used as an alternative. It (Hallcrest, Glenview, IL, USA) is a continuous temperature monitoring sticker designed for neonates (Mole et al., 2012). It is a liquid crystal thermometer in the form of a sticky disc (12 mm in diameter) that adheres to the skin placed on the axilla or the abdomen. Its liquid crystals are designed to turn black with hypothermia and remain green with normothermia (Mole et al., 2012).). It costs USD 12.50/pack and INR 32.5/Sticker.



2.3 c. Fever Watch

Fever Watch is a compact continuous temperature monitoring device. The device is used by placing in the axilla and secure by using a sticking tape with a patch. First, the Fever Watch App must be downloaded in the smartphone (Android 4.4 iOS 8 onwards). Switch-on the Bluetooth and Click-on the app in order to register and connect to the 98.6 Fever Watch device. When the device is connected with the smart phone via Bluetooth, the temperature reading will be continuously displayed on the smartphone in a tabular as well as graphical form. The temperature threshold can be set and when the temperature decreases or increases beyond the set values an alarm will ring on the phone. Through the Carenet feature, a group of up to 3 people can be created, where the alert is shared even when

they are away from the baby. It also stores the data in the internal memory in case the Bluetooth link of the devices are disconnected and shares the data once it is back in range. The data can also be shared by email and stored for future use.

It is made up of Medical grade plastic and has a replaceable Battery (CR 201 Button Cell). The patch is said to be extremely thin, non-allergic, soft, breathable, nontoxic, anti-bacterial, non-residual and mild. It is water resistant and can be wiped clean and reusable. It is a certified product (European Certification) for safety and has also met “EN 71” standard so that the child cannot swallow it. Other smart feature of the device is it also gives vaccination reminders for the child based on the child’s date of birth (‘Fever Watch Details | Helyxon’, n.d.).

2.3 d. Digital Axillary Thermometer

For more than a century, mercury thermometer was considered as the standard instrument for measuring body temperature. However, due to the hazardous effect of mercury many developed countries has replaced it with an alternative method viz. Axillary digital thermometer (ADT), infrared thermometer.

Axillary temperature measurement by using a thermometer is the standard method of temperature monitoring (Smith et al., 2004). Digital thermometer, which is faster and easier to read has been recommended for routine use over the traditional glass mercury thermometer with increasing safety concerns and the hazardous effects of mercury on the environment (Gerensea et al., 2016). Axillary rather than rectal temperature is safer for neonates as it avoids the risk of rectal perforation (Haddadin & Shamoon, 2007). Temperature measurement by the axillary method has become the accepted neonatal nursing care. Because of the greater surface vasculature, increased body fat and thermal uniformity, temperature measured in the axillary area is considered reliable and used as a standard measurement site in newborns. The National Institute for Health and Clinical Excellence (NICE) UK guidelines recommend the following for paediatric populations: (a) avoid using an mercury thermometer because of risk of rupture; (b) measure only the axillary temperature with a ADT for children up to 4 weeks of age; (c) measure temperature using an ADT and infrared tympanic thermometer for children 4 weeks to 5 years of age, even though this is not recommended at home because this measurement is operator dependent; and (d) do not measure oral and rectal temperatures of children up to 5 years of age because of the invasiveness (Franconi, La Cerra, Marucci, Petrucci, & Lancia, 2016).

2.4 Equity Issues in Health Services

Gender and economic class are two major dimensions of socio-economic inequality and injustice (Sen et al., 2002). In the health sector, urban areas and economically developed regions have attracted a larger share of health institutions, qualified doctors and health workers, than warranted by their share in the total population (Duggal et al., 1995a; Nandraj and Duggal 1997; Sule, 1999). The coverage of health services was lowest among the disadvantaged groups including those belonging to Muslim community, Scheduled Caste, Scheduled Tribes, and those without literacy and/or formal education (Prinja et al., 2016). Joe et al. (2010)

by analysing the Indian National Family Health Survey (2005-2006) data found that the poorer sections of the population were beleaguered with ill health whether in the quest for child survival or due to anxieties pertaining to child nutrition. Balarajan (2011) argued that the key challenges to equity in health service delivery in India include imbalanced resource allocation, limited physical access to quality health services and inadequate human resources for health, high out-of-pocket health expenditures, health spending inflation, and behavioural factors that affect the demand for appropriate health care. Socioeconomic inequality in neonatal mortality seems to have decreased in the past two decades (McKinnon et al., 2014) but substantial survival advantage remains for babies born into wealthier households with a high educational level (McKinnon et al., 2014). Socioeconomic factors remain main predictors of differences in maternal and child health services utilization and outcomes (Memirie et al., 2016). Community-based interventions delivered by female community health volunteers are reported to improve equity in levels of facility delivery and other new-born care behaviours (Nonyane et al., 2016). Moreover, interventions effective in reducing inequity include strengthening outreach activities, using local human resources or provision of services nearest to residents and the provision of financial or knowledge support (Yuan et al., 2014).

3. Policy Question

Are BEMPU/ThermoSpot/Fever Watch hypothermia detecting devices cost effective enough to reduce neonatal mortality through early detection of hypothermia in premature LBW newborns in India?

4. Research Question

What is the cost effectiveness of BEMPU/ThermoSpot/Fever Watch in detecting hypothermia in premature LBW newborns in India?

5. Aims and Objectives

5.1 Aim

This study aimed to do a cost effectiveness analysis of BEMPU Hypothermia Alert Device, ThermoSpot and Fever Watch when compared to the standard of care using an axillary thermometer for detecting hypothermia in premature LBW newborns in India.

5.2 Objectives

The objective of this HTA study was to assess the cost effectiveness of BEMPU Hypothermia Alert device, ThermoSpot and Fever Watch against the standard of care i.e. thermometer in early detection of hypothermia among premature and low birth weight neonates in India. The main indicator for the analysis is incremental cost effectiveness ratio (ICER) which considers life years gained as its main outcome.

- To estimate the incremental costs associated with the use of BEMPU/ThermoSpot/ Fever Watch.
- To ascertain the difference in life years gained between BEMPU /ThermoSpot/ Fever Watch.
- To estimate the incremental costs per life years gained with the use of BEMPU/ThermoSpot/ Fever Watch.

6. Methodology

A decision tree model was developed for estimating the Incremental Cost Effectiveness Ratio (ICER). For populating the model we required data pertaining to costs, clinical effectiveness and prevalence of hypothermia and its complications. A systematic literature review was conducted using electronic databases such as PubMed, Scopus, Web of Science and Cochrane Library for data pertaining to clinical aspects of interventions and comparator and cost aspects. These included data on sensitivity, specificity, clinical accuracy of Bempu, Thermospot, Fever watch and thermometer. For costing, data on treatment cost at NICU in India and treatment cost for hypothermia with or without complications were also obtained through the systematic review. In addition to these epidemiological data such as prevalence of hypothermia among neonates, neonatal mortality rate from census reports, national survey factsheet and other published studies were used.

Initially a Markov model was attempted for this study in which four different temperature states i.e. normal temperature, mild, moderate and severe hypothermia are considered. The model assumes that hospitalization may be required for any stage of hypothermia along with the possibility of complications and different outcomes in each state. Hence each state will accrue different costs and QALYs. It also takes into consideration that mortality can happen due to hypothermia or due to causes other than hypothermia, utilizing a Markov transition state model. But Markov Model was not feasible to use due to lack of data regarding the transition from one state to another either forward and backward and hence was dropped in favour of a decision tree model.

6.1. Data Collection: Systematic Review

To collate required data for the analysis, two separate systematic literature reviews were carried out to capture data regarding clinical effectiveness and cost of the hypothermia detecting devices in the Indian context.

6.1.1 Clinical Effectiveness data

Methods

Research Question: What is the clinical effectiveness of hypothermia detecting devices (BEMPU/Fever Watch/ ThermoSpot) as compared to Digital Thermometer in terms of sensitivity, specificity and QoL in Premature and Low birth weight Neonates?

Selection Criteria

Only studies in the English Language were included. No time period restriction was applied in any of the electronic databases. We used the PICO (Population Intervention Comparator Outcome) framework to generate the inclusion criteria as well as the key words (Annexure 13.1, Concept Table). The following were inclusion criteria used for this review: study participants are premature or/and Low Birth weight neonates (28 days old), diagnostic tests are Digital Thermometer/BEMPU/Fever Watch/ ThermoSpot, the target condition was restricted to neonatal hypothermia (temp below 36.5^{o}C), government reports, comparative studies, cohort studies and ongoing studies that provided sufficient information and data.

Population (P)	Premature and Low birth weight Neonates
Intervention (I)	Bempu, ThermoSpot, Fever Watch
Comparator (C)	Standard of Care (Thermometer)
Outcome (O)	Clinical effectiveness in terms of sensitivity, specificity, quality of life Cost effectiveness (done separately)

INCLUSION CRITERIA	EXCLUSION CRITERIA
Peer-reviewed articles Government reports Working papers English language Low birth weight (lbw) neonates Hypothermia detecting devices Expert opinions Commentaries	Abstracts Conference papers Narrative reviews Case reports

We excluded abstracts, expert opinions, narrative reviews, new paper articles, commentaries and conference papers. We also excluded studies that used different hypothermia detecting devices, other than the devices listed as intervention and comparator, participants that were infants, adults and or premature and low birth weight (LBW) neonates suffering from other comorbidities.

Search Strategy

Electronic database used in this review were PubMed, Cochrane Library, Web of Science and Scopus. Other sources searched were from references of included studies and studies provided by manufactures, such as BEMPU. The PICO framework (Annexure 13.1, Concept Table) helped generate the key search terms for developing the search strings for each database. These key terms include; sensitivity, specificity, diagnostic accuracy, digital thermometer, neonates, premature, low birth weight, BEMPU and ThermoSpot. A search string (Fig.3) was developed for the study selection for PubMed and the search string was then adapted accordingly for each of the other electronic databases (Annexure 13.1, Search Strings). Unlike PubMed and Cochrane, Web of Science and Scopus do not support controlled vocabulary, therefore a concept table (Annexure 13.1, Concept Table) was made, which includes all the MeSH words and their synonyms.

Figure -0-3: PubMed Search String

Search: ((((((((sensitivity) OR diagnosis)) AND ((Neonate*) OR Newborns)) OR Premature) OR Low Birth Weight) AND hypothermia*) AND ((((((digital thermo met* [Mesh]) OR axilla* digital thermo met*) OR ThermoSpot) OR liquid crystal thermomet* [Mesh] OR BEMPU) OR novel bracelet device) OR Fever watch)) Filters: Humans; English

Study Selection

Two reviewers independently searched the electronic databases to identify relevant studies and assess all studies for inclusion. The studies derived from all four databases and other sources were combined and duplicates were removed using Mendeley refernce managing software. Following this, selection of studies was carried out based on screening of titles and abstracts of the studies against the inclusion and exclusion criteria. Next, selection of studies was carried out independently by two reviewers by screening of full text against the inclusion and exclusion criteria. Any disagreements were resolved by discussion in consultation with a third reviewer. This process is outlined in Fig.4, the PRISMA flow chart.

Data Extraction and Management

One reviewer extracted the following data from the included studies: Name of first author, year of publication, sample size, type of diagnostic test, negative predictive value, positive predictive value, accuracy, and sensitivity and specificity values. Management of included and excluded studies and references was supported with Mendeley.

Results

Fig 4 is a PRISMA flow chart summarizing all the different stages carried out during the screening for the studies from the different electronic database and the number of included and excluded studies at each stage. As seen in the flow chart 55 and 18 studies were initially selected from the different electronic databases and other sources respectively A total of 55 studies were obtained through the systematic review, 12 studies from PubMed, 18 from Scopus, 24 from Web of Science and one from Cochrane. An additional 20 studies were obtained through other sources like search of reference lists of studies initially identified, hand search in Google by using the keywords, grey literature (unpublished studies) from the manufacturer of the devices. Out of 75 total studies, 16 were found to be duplicates and were removed. The next phase was screening of the title and abstract of the studies, where only studies of our interest were taken into consideration. Out of the 59 studies, only 27 studies were included for the next phase due to various reasons such as irrelevant studies, not related to our PICO framework study being a presentation or a newspaper article. After scrutiny of full text 3 studies were selected for data extraction as shown in the table below.

Figure -0-4: PRISMA Flow chart: A summary of the process for study selection

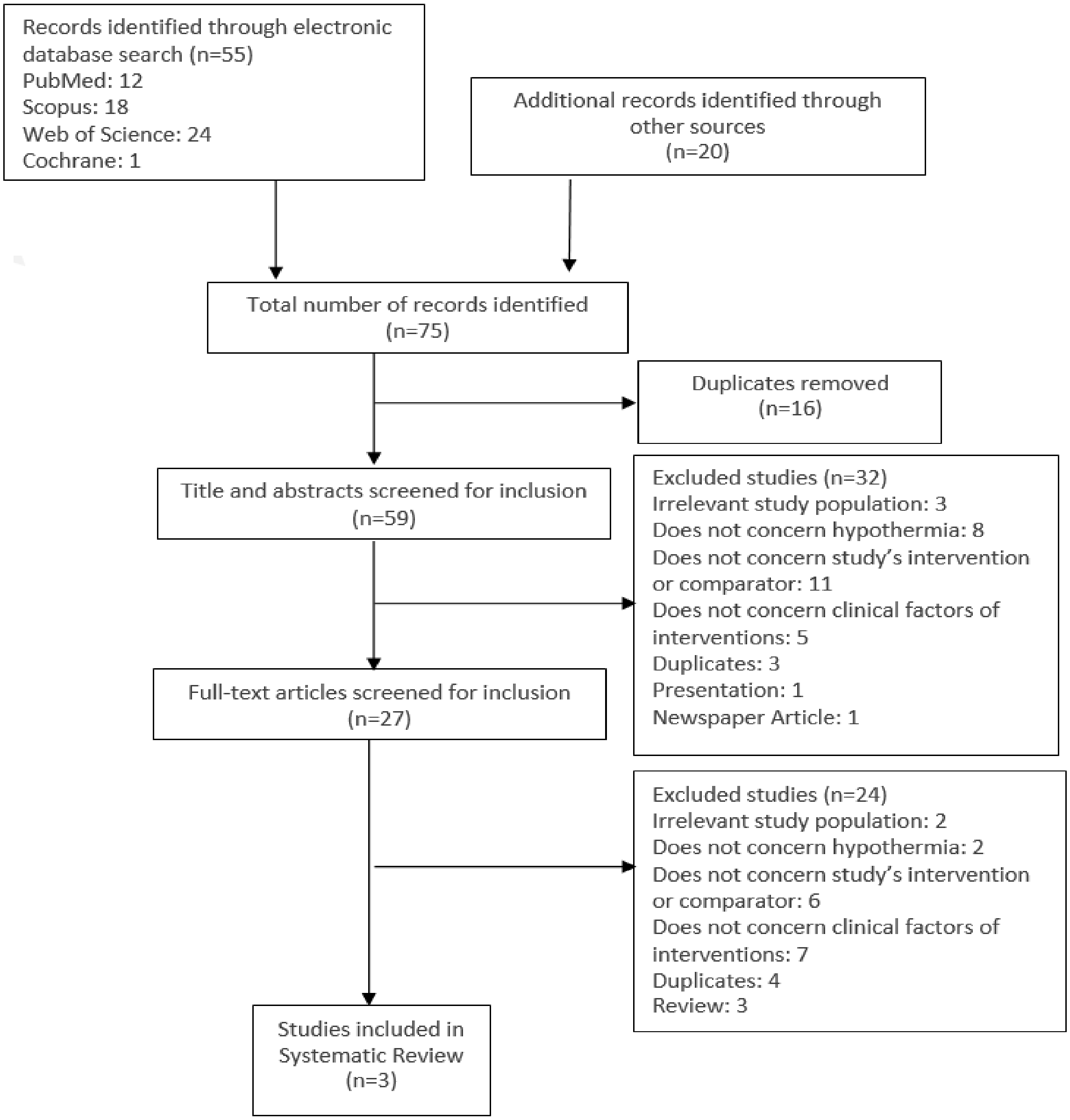


Table 1: Extracted clinical data of the different hypothermia detecting devices from the included studies

First Author	Year	Diagnostic Test	Sample size	Study design	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)
R. Kambarami	2002	ThermoSpot	313	Cross-sectional study	98%	68%	43.7	100
T. Vasanthan	2018	BEMPU	461	Controlle d	83.6	99.6	98.6	95

				prospective study				
D A Green	2006	ThermoSpot	180	Comparative study	29 (ratio)	0.13 (ratio)	88	97

Table 1 shows out of the three studies included for data extraction; two were for ThermoSpot and one for BEMPU. We used the study by Green in 2006 in our model input as the other study on Thermospot by R. Kambarami in 2002 considered 100% specificity of Thermospot.

There are a few other studies (Turab et al, 2014; Pejaver et al, 2004; Shrestha et al, 2010; Manadhar et al, 1998) on Thermospot conducted at different part of the country. We considered some elements of these studies but not the data for clinical effectiveness to support our model development. We did not consider data from these studies for clinical effectiveness in our analysis as the target population was different from our population of interest and they mainly focused on weight gain in newborns as an outcome measure. These studies are summarized in annexure Table-7.

We found one cluster-randomised controlled efficacy trial of a community-based behaviour change management on neonatal mortality in Uttar Pradesh, India by Kumar et al. (Kumar et al, 2008) The primary intervention was a package of preventive essential new-born care, including skin-to-skin care between the infant and a family member, promoted through behaviour change management, layered on existing services available to the control group. One arm of this study used a Thermospot in addition to the behaviours change programme and kit that was provided. Adjusted neonatal mortality rate was 54% lower in the essential new-born care arm than the control arm (RR 0·46, 95% CI 0·35–0·60, p=0·0001) and 52% lower in the essential new-born care plus ThermoSpot arm than the control arm (RR 0·48, 95% CI 0·35–0·66, p=0·0001). The authors concluded that the intervention that included the use of the ThermoSpot did not seem to have an advantage over the package of essential new-born care.

The studies identified did not provide the sensitivity, specificity or accuracy of axillary thermometer as the device is almost always used as a gold standard.

Some limitations of this review include the language restriction to English and publication bias, where some meaningful yet unpublished data could've been missed out.

There was limited data available in the existing literature, on clinical effectiveness of ThermoSpot, BEMPU and Fever Watch. We found one research letter on fever watch (not in the systematic review) conducted by Safijan et al. in 2018. They considered post neonatal period till 90 days which was different from our population of interest. The report did not provide details on methodology and other data that were required for our analysis. There were 16. 2% false positives reported but authors concluded that there was a good agreement between fever watch and digital thermometer. Due to paucity of relevant data from India, further analysis on fever watch was not done.

There were a few studies/reports regarding how BEMPU device promotes Kangaroo Mother Care (KMC), weight gain and health seeking behaviours.(example: *Pilot of the BEMPU Device for Reduction in Hypothermia and Infection Related Neonatal* Mortality *and Morbidity in Rajasthan NHM Rajasthan and WISH Pilot of BEMPU Bracelet*, 2017). Thus even if the devices is clinically effective in detecting hypothermia early it is the response rate by caregivers by swaddling or KMC that determines the prevention of hypothermia related complications. These studies did not focus on determining the diagnostic test accuracy of these interventions or include the digital thermometer as comparator, nor was the study population premature and Low Birth Weight (LBW) neonates.

6.1.2 Cost Effectiveness data

Research Question: What is the cost of hypothermia detecting devices (BEMPU/Fever Watch/ ThermoSpot) as compared to Digital Thermometer in terms of out-of-pocket expenditure and health system cost for premature and low birth weight neonates?

Household Out of Pocket Expenditure (OOPE) in India was Rs.3,02,425 crores (62.6% of Total Health Expenditure, 2.4% of GDP, Rs.2,394 per capita) for the year 2014-2015 whereas for private Health Insurance expenditure was Rs.17,755(3.7% of Total Health Expenditure) (*National Health accounts estimates for india*, 2017). Hence if hypothermia is detected earlier, it can reduce the cost of hospitalization of the neonate by preventing the need of hospital admission or decrease the length of stay in NICU. Therefore determining the cost of NICU care is necessary in order to estimate the cost of expense saved by using such devices.

Methods

This part of the literature search focused on extracting studies concern about the cost and cost effectiveness of temperature monitoring devices such as BEMPU bracelet devices, ThermoSpot and Fever Watch and the cost benefit of using these devices to prevent hypothermia against the cost of being admitted into NICU due to hypothermia.

Selection Criteria

PICO (Population, Intervention, Comparator, and Outcome) framework was used to generate selection criteria as well as the keywords as mentioned in the annexure 13.2 (Concept Table).There was no restriction on the years of publication of the studies. The inclusion and exclusion criteria applied to the type of articles and studies for this systematic review are listed in Table 2.

Table 2: Inclusion and exclusion Criteria

INCLUSION CRITERIA	EXCLUSION CRITERIA
Peer-reviewed articles	Abstracts
Government reports	Conference papers
Working papers	Narrative reviews
English language	Case reports
Low birth weight (lbw) neonates	
Hypothermia detecting devices	
Expert opinions	
Commentaries	

Search Strategy

The electronic databases included in this review were PubMed, Scopus, Web of Science and Cochrane. The search strategies were a combination of controlled vocabulary (MeSH) terms and free text terms. Keywords used during search are cost effectiveness analysis, cost of treatment, NICU, SNCU, fever watch, Thermospot, Bempu, thermometer, neonate, hypothermia, preterm. MeSH terms used are Cost benefit analysis, economic evaluation, new-born, and Liquid crystal thermometer. A search strategy was developed for PubMed and was then adapted to each of the other electronic databases accordingly. (Annexure 13.2, Search Strings)

Study Selection

The studies were screened in three phases, in the first phase studies identified from all the sources were screened for removal of duplicates. Selecting the studies based on the relevant title and abstracts was done next and then they were further screened by reading the full papers and included for the final review if relevant.

Results

The literature searched identified a total of 171 studies from all the sources, 147 studies from PubMed, Scopus, web of Science and Cochrane and 24 studies were obtained from other sources through hand-search, reference search, studies from the manufacturers. Fig 5 is a PRISMA flowchart demonstrating the process of study selection. After removing the duplicates 162 studies remained for further screening In the next phase, 12 studies were selected after screening the title and abstract of the studies while the rest were discarded due to various reasons (studies did not consider the cost of the devices or NICU cost but only the clinical efficacy, some studies considered infants as a population, some studies were not relevant, while few considered the cost of NICU but were done in developed countries like Canada, Mexico. Six studies were selected for extraction of data for analysis

Figure -0-5: PRISMA Flow diagram of literature review process on cost

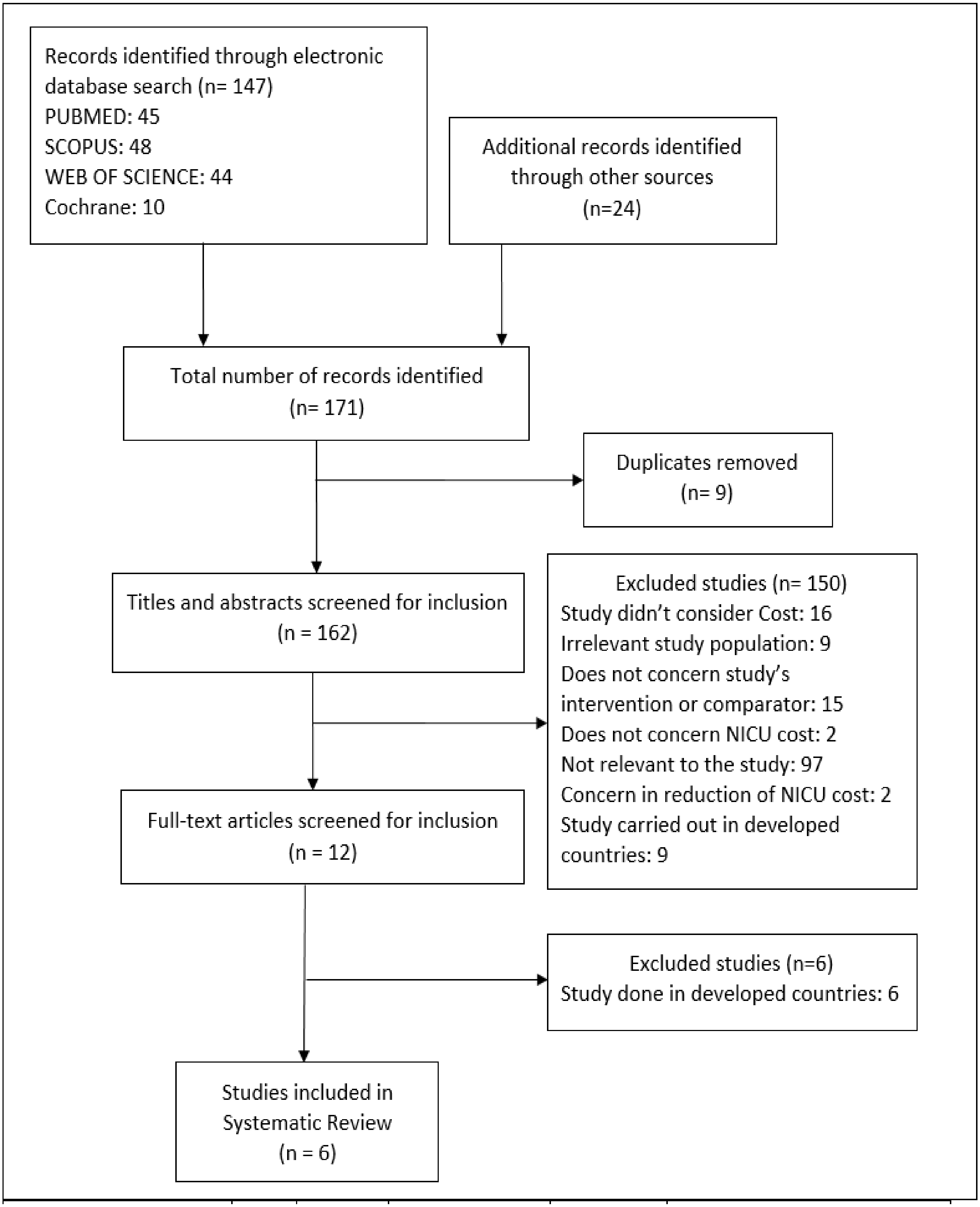


Table 3: Summary data extracted for assessment of included papers

Author	Year	Country	Methodological approach	Population	Key findings
Gini Morgan , Janan Dave	2017	India	HTA based on literature review (grey literature, not peer reviewed)	Neonates	BEMPU Bracelet claimed to save 327,180 neonatal lives per year and alert for 7,433,394 incidences of hypothermia per year. BEMPU Bracelet monitor newborns 24/7 for 30 days for Rs. 2000, a daily price of Rs. 67 a day. Saving life at a cost of INR 49390 and averting an illness is INR 2020. concluded the bracelet as cost effective
(Narang, Sandesh Kiran, & Kumar, 2005)	2005	India	Cost analysis	Neonates	To establish a 16 bedded level III tertiary care neonatal unit was Rs.3.78 crore. The cost for one ventilation bed is Rs30.5 lacs and for a non-ventilation bed is Rs16.9 lacs.
Kannan Venkatnarayan, M Jeeva Sankar, Ashok Deorari, Anand Krishnan and Vinod K Paul	2014	India	micro-costing analysis	neonates	basic cost of NICU calculated by micro-costing is Rs. 4969 as compared to gross costing which is Rs. 6315 per bed per day
Geeta Karambelkar, Sudhir Malwade and Rajendra Karambelkar	2016	India	prospective cost analysis study		The mean cost of care per patient per day was US $90.7 and the median total cost of care for the whole group was US $272.4.
Shankar Prinja, Neha Manchanda, Pavitra Mohan, Gagan Gupta, Ghanashyam Sethy, Ashish Sen, Henri Van DEN Homebergh and Rajesh Kumar	2013	India	cost analysis study	neonates	Overall, SCNU neonatal treatment costs is INR 4581(USD 101.8) per neonate treatment and INR 818(USD 18.2) per bed-day treatment. Standardized treatment cost of INR 5090(USD 113.1) per neonate and INR 909(USD 20.2) per bed-day treatment were estimated. In the event of entire direct medical

					expenditure being borne by the health system, the cost was found as INR 4976 (USD 110.6) per neonate and INR 889(USD 19.8) per bed-day.
R.Shanmugasundaram, E.Padmapriya and J.Shyamala	1998	India	cost analysis study	Neonates	average total cost of hospitalisation of neonates in NICU are INR 3,080.00 with birth weight of less than 1000 , INR 8 ,962.25 with birth weight between 1000-1499 , INR 6,896.90 (birth weight between 1500-1999), INR 5104.15(birth weight between 2000-2499) and INR 6,576.50 with birth weight more than 2500 grams.

There were no peer reviewed published studies that reported cost-effectiveness or cost-benefit analysis of these devices (Bempu, Thermospot and fever watch) or the cost of neonatal intensive care particularly for Neonatal Hypothermia. The studies simply had costs e.g., 'cost of the NICU in India' and not specific for cost of treating hypothermia. The review also revealed studies on cost effectiveness of therapeutic or induced hypothermia which is not relevant here, hence these were disregarded. Likewise, those on the efficacy of interventions like Kangaroo Mother Care or plastic wraps soon after delivery to prevent hypothermia in neonates.

Costs from the more recent study reporting on NICU costs was used in the model. The future value (FV) and inflation rate was taken into consideration while estimating the current cost of NICU in India.

6.2 Decision tree model for estimating ICER

A decision tree was parameterized on Microsoft-Excel to estimate the incremental cost effectiveness ratio (ICER) for implementing the hypothermia detecting interventions over standard practice. A time-horizon of 30 days was considered to cover all cost and effectiveness of BEMPU and ThermoSpot. This time horizon is justified as it covers the neonatal period and the BEMPU device works 24X7 for one month. The cost of treatment at public sector hospital generally varies with duration of stay at hospital. To capture the cost difference, we considered one episode of hypothermia per neonate (i.e. one episode in 30 days).

Details of the decision tree model and the assumptions made are shown in Annexure 11.4.

The SoC involves intermittent temperature monitoring with a thermometer usually supplemented with hand touch rather than continuous monitoring offered by the newer devices; but SoC was considered to be equivalent to continuous monitoring as there was no evidence of a comparable nature that could be incorporated into the model. Thermometers were used as the gold standard in most studies on hypothermia in neonates, where thermometers always provided 'accurate' temperature measurements. Hence we assumed 100% sensitivity in detecting hypothermia by the SoC (thermometer) in LBW neonates.

The cost-effectiveness can be measured from three perspectives- health system perspective, patient perspective and or societal perspective. In health system perspective, only cost to the health system is considered while in patient perspective expenditure incurred by patient party is taken into consideration. Total treatment cost, i.e. health system cost and out-of-pocket expenditure together is considered in societal perspective. In the current study, cost effectiveness is measured from a societal perspective. In addition to the health system cost, the out-of-pocket expenditure (OOPE) incurred by the patients to measure the societal cost is also included. Health system costs includes the resources spent by the government department of health. These include resources like building space, staff salary, equipment cost. The OOPE incurred for purchasing medicines, medical or surgical procedures, boarding, lodging, and transportation as a result of any health care sought during pregnancy, intra-partum care, or neonatal period. The measurement of indirect costs in terms of productivity loss to the household as a result of absenteeism due to illness was not considered. Effect was measured in terms of life years gained.

The findings are reported as incremental cost of implementing our interventions per life year gained as compared to standard practice. An incremental cost-effectiveness ratio (ICER) is a summary measure in economic evaluations to represent the economic value of an intervention in comparison with an alternative (comparator). The ICER is expressed as the ratio of the difference in costs between two strategies to the difference in effectiveness.

There are several thresholds which could be used for decision making in a cost-effectiveness analysis (Bertram et al, 2016). Thresholds can be defined from supply side, demand side and based on Gross Domestic Product (GDP) per capita. Supply-side threshold is a measure of health benefits forgone due to reduced funding for current interventions as a result of allocating resources for a new intervention from provider's perspective. A demand-side threshold describes the willingness to pay for an individual to gain additional health benefits in view of other competing demand of their resources. Lastly, the per capita GDP threshold of a country recommended by several guidelines in the absence of evidence over other threshold measures (WHO, 2003). Most of the cost related studies in India, follows the thumb rule for an intervention to be cost effective, i.e., an intervention is considered as "very cost-effective" if the incremental cost-effectiveness ratio (ICER) is less than the per capita national GDP; "cost-effective" if it is between one–three times the per capita national GDP; and "not cost-effective" if the value of ICER is more than three times the GDP per capita (Prinja et al,2016; Goldie et al, 2010).

6.2.1. Estimation of hospital stays

To fill the data gaps regarding duration of hospital stay, we consulted with paediatricians from different part of the country. We also discussed with experienced nurses who are working at NICU. According to health care personnel the period a neonate with hypothermia without complications would need to be at an NICU ranged from 2-7 days. In the model we considered 7 days of hospital stays for a neonate with hypothermia without complications. All of the experts said that hypothermia cases with other complications would needs to be treated for 44-45 days at NICU. Bempu works for 30 days only and our target population is neonates. Hence we considered 30 days of hospital stays for a neonate with severe hypothermia and complications.

6.2.2. NICU Costing

The treatment cost of neonatal intensive care unit at per day per patient basis was obtained from the study conducted by Narang ET. al (2005) in Nehru Hospital, Postgraduate Institute of Medical Education and Research, Chandigarh - a tertiary care teaching hospital catering to north Indian states. The number of NICUs in the country is increasing but the current status of these units is not known (Sundaram et al, 2014). There are very few studies on the cost of an NICU, all previous studies focused on paediatric treatment cost for particular disease and in focal geographical areas (Mendelsohn et al, 2008; Sur et al, 2009). Moreover the methodology of these studies do not follow the true economic cost (Narang et al, 2005; Shanmugasundaram et al, 1998). In addition to this, low birth weight is one of the characteristics of our study population, but most of the studies in the existing literature did not estimate the cost in LBW neonates.

NICU cost was measured by multiplying the median duration of NICU stay with the daily NICU cost per patient per day. The daily cost of intermediate level II nursery care in the hospital was estimated to be Rs. 1000 per patient per day on the basis of 1:5.5 weightage in comparison with level III NICU care. The daily cost to the family in level II nursery was Rs. 100 per patient per day. The study also showed that for each subsequent 250g increments in birth weight, the cost of care decreased by 50% among babies that weigh <1500g. (Narang et al, 2005)

Adjusting for inflation:

The Narang et al study was conducted in the year 2005. Money value changes over time due to inflation, thus treatment cost will also likely change over the period of 13 years. Inflating is the process of converting a value expressed in the currency of a given point in time into a value with an equivalent amount of purchasing power expressed in the currency of a later time. The treatment cost from 2005 to 2018 was inflated using Consumer Price Index (CPI) of these two time points. CPI accounts for variations in the inflation rate over time and indicate the appropriate amount of inflation for any historical period. In order to inflate a past value to current dollars, the past value should be multiplied by the ratio of the current price index over the price index for the time at which the past value occurred.

Hence, we converted the cost using the below formula by McDill (1999):

Treatment cost in 2018 (in Rupees) = Treatment cost in 2005 (in Rupees)*(CPI in 2018/ CPI in 2005)

Table 4: Cost of treatment at NICU in India:

Birth weight(grams)	Hospital stay	Total cost	No of neonates
<1000	44	1,68,600	80
<1500	41	1,30,000	243
<2500	19	50,150	1385
Total			1708
Average cost(2005)			2770.904164
Average cost(2018)			3779.3844

6.2.3. Costing of hypothermia detecting devices

The model incorporates the intervention scenario as comprising monitoring of body temperature of premature and LBW neonates using the different hypothermia detecting devices with all other medical services at NICU remaining unchanged.

To estimate the treatment cost with the interventions, the device per day cost was added to per day NICU cost estimated. The BEMPU bracelet monitors the new born for one month for 1250 rupees which leads to a per day cost of 41 rupees per neonate. The cost of ThermoSpot is 852 rupees for a pack of 25 stickers and these stickers are reusable. According to the product webpage, a sticker can be used for up to 10 days, which gives us a value of Rs. 38.05 per sticker and therefore Rs. 4.87 per sticker per day.

The routine care scenario comprised of monitoring body temperature of neonates using thermometer. As per operation guidelines on Maternal and New born health by Ministry of Health and Family welfare, Government of India, thermometer is one of the essential equipment for neonatal intensive care unit. Therefore an assumption that the total hospital cost included the cost of thermometer as an equipment was made and no additional cost due to thermometer was considered.

6.2.4 Costing in scenarios with and without complications

In the study's model, it was assumed that neonates with mild hypothermia will not have any complications and this is because complications and body temperature share a U-shaped curve. As per experts' opinion hypothermic babies can be reversed to normothermia by simple means such as KMC, rapid warming, wrapping the baby which does not incur any extra cost for treating hypothermia. Therefore treating hypothermia without any other complications results in no extra cost. NICU per day cost was used as treatment cost for hypothermia without complications in both interventions and routine care. We considered 7 days hospital stays for a neonate without complications.

According to the existing literature and expert opinions, in public hospital treatment cost mainly depends on the number of days of hospital stay which in turn depends on the severity of the disease. As per expert suggestions, a mild hypothermic baby needs to be kept in a NICU for approximately 4-5 days while a baby with severe hypothermia and other complications needs to be under treatment for more than one week and ventilation may extend the stay further. Hence the number of hospital days was considered as the main factor which differentiated the treatment cost of hypothermia with and without complications. The per day treatment cost at NICU was multiplied with the number of hospital stays to estimate the total treatment cost of hypothermia with complications. We considered 30 days hospital stays for a neonate with complications.

According to health care professionals, hypothermia is not considered as a severe disease as it can easily be reversed back to normothermia and hence cases of hypothermia are not properly documented in case sheets. The research team also observed this during discussions with health workers regarding hypothermia. Only one hypothermia case was found among 30 low birth weight neonates who were born within the previous two months in a large public sector hospital on the day of our inspection of case records.

6.2.5 Valuing Effectiveness of BEMPU and ThermoSpot Intervention

Early detection of hypothermia by the mother or health worker is crucial to institute corrective actions to improve the survival rate of new born babies (Anto et al, 2018). Post detection of hypothermia, KMC can be practiced to avoid severe complications and death. It is a simple, practical and inexpensive method which has been promoted for preventing cold stress in low income or resource poor countries.

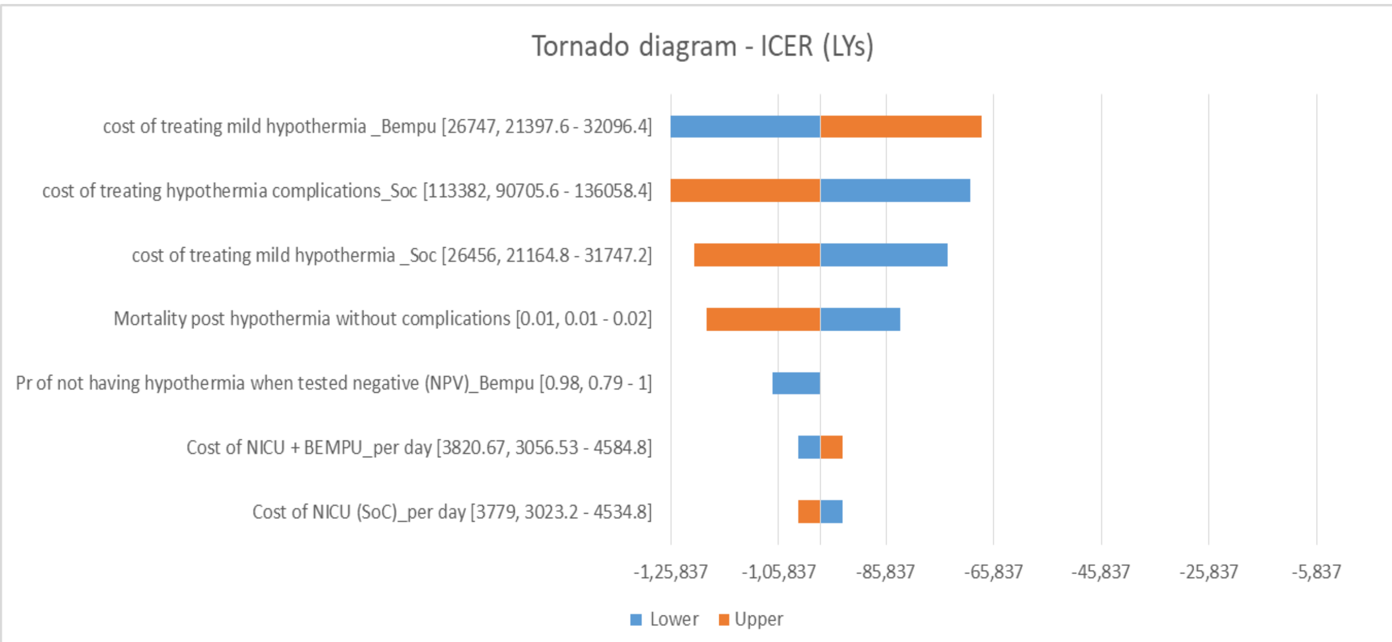
In this study, we model the effect of BEMPU and ThermoSpot interventions on early detection of hypothermia cases among premature and low birth weight neonates. In the long run, this contributes to reduction in neonatal death due to hypothermia - ultimately resulting in averting life lost to premature mortality and gain in life years.

In terms of complications due to hypothermia which leads to death, it was assumed that neonates with moderate and severe hypothermia would have at least one or more complications due to hypothermia while neonates with mild hypothermia are assumed as early detected cases and hence having no complications. Evidence indicates a U-shaped relationship between body temperature and the composite outcome (defined as mortality or any of the major neonatal morbidities (Lyu et al, 2015). According to the health care professionals interviewed, hypothermia can be treated easily with KMC practice if detected at an early stage and the baby's body temperature can be reversed to normal body temperature. Hence mild hypothermia cases was used as a proxy of early detected hypothermia cases to populate the decision tree model in this study. (For a log of interactions with health care professionals please see annexure)

6.2.6 Sensitivity Analysis

A one way sensitivity analysis (OWSA) as well as probabilistic sensitivity analysis (PSA) was carried out to test the effect of parameters uncertainty on the findings of the analysis and to estimate the effect of joint uncertainty in all the parameters (Andronis et al, 2009). OWSA can be used to investigate the sensitivity of the results from a model-based analysis to variations in a specific input parameters. Results of OWSA are presented in a Tornado Diagram (Figure.6) which enables simultaneous visualization of variation in model parameters and in order of their influence on the model output. PSA is used to quantify the level of confidence in the output of the analysis, in relation to uncertainty in the model inputs.

Figure -0-6: Tornado diagram for OWSA



To perform the sensitivity analysis, the demographics and epidemiological parameters such as risk of various morbidities with or without use of preventive interventions, we varied the base estimate obtained from literature 20% on either side. We varied the cost of intervention by 50% on lower side and 20% on higher side (Prinja et al, 2018). For undertaking PSA analysis, a beta distribution for probabilities and proportions, and gamma distribution for costs was assumed. To check the robustness of the model, the results were simulated 1000 times.

7. Results

7.1. Incremental cost using devices

We did the cost-effectiveness analysis from societal perspective, i.e. considering both out-of-pocket expenditure and health system cost. From a societal perspective, it was found that use of BEMPU incurs an additional cost of INR 796 and for ThermoSpot INR 5693 per new-born. Table-5 shows that, per head treatment cost is INR 15344 using Thermometer which increased to 16141 INR with Bempu and for Thermospot per head treatment cost is 21038.

According to MoHFW guidelines, thermometer is one of the essential equipment for setting up an NICU unit. Therefore, it was assumed that the treatment cost includes thermometer cost as part of NICU equipment cost. It was assumed that Bempu and Thermospot can detect hypothermia at an earlier stage which causes less number of cases with severe hypothermia and complications. And the corollary being that with early detection, preventive practice like KMC will take place thus reducing the number of severe hypothermia episodes in the intervention scenario and hence decreased demand for curative care at NICU.

Table 5: Estimated incremental cost and effects of interventions vs. standard of care

standard of care	
Cost for treating 100 neonates	1534431
Cost for treating per neonates	15344
Life years gained	55.540
BEMPU	
Cost for treating 100 neonates	1614096
Cost for treating per neonates	16141
Life years gained	55.537
Thermospot	
Cost for treating 100 neonates	2103779
Cost for treating per neonates	21038
Life years gained	55.490
Incremental cost in compared to SoC	
BEMPU	796
Thermospot	5693
Incremental life years gained	
BEMPU	-0.010
Thermospot	-0.060
Incremental cost effectiveness ratio	
BEMPU Vs. SoC	-128207
Thermospot Vs. SoC	-102660

*We measured the cost in INR

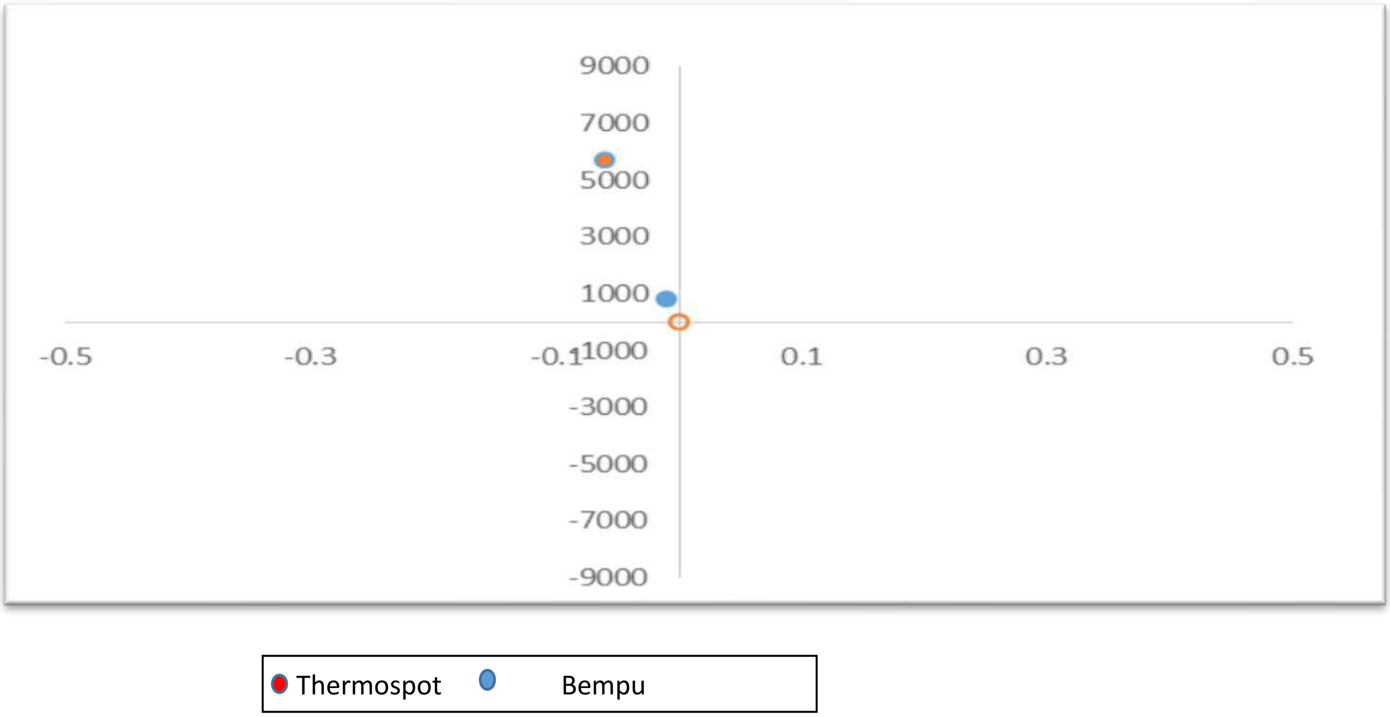
7.2 Incremental cost per life year gained

The clinical effectiveness of the interventions and standard of care were measured in terms of life years gained. Health adjusted life expectancy in India was used, which is currently 56.2 years (WHO). Accordingly, an assumption was made that if a neonate survived beyond 28 days after birth, he/ she gained life years of 56.2 years. On the other hand if the neonate dies within the neonatal period of 28 days, no years of life were gained. In an intervention scenario, life years per patient was 55.54 years for BEMPU and 54.49 years for ThermoSpot. While in comparator scenario, life years for a neonate was 55.55 years. Hence there is not much gain in life years for neonates as a result of implementing the interventions (Table 5).

7.3 Estimation of ICER

Results show that hypothermia detecting interventions; BEMPU and ThermoSpot are not cost saving from a societal perspective (Table 4). Standard decision rule for considering the cost-effectiveness of an intervention, compared with a given comparator focus on the difference in effect and the difference in cost. If the incremental cost is negative and the incremental effect is positive, the intervention is unequivocally cost-effective. In this study both interventions result in slightly higher cost without much gain in life years. Both interventions lie in north-west quadrant of the cost-effectiveness plane which implies that the interventions are not cost-effective when compared to optimum use of standard of care with Thermometer (Fig 7).

Figure -0-7: Cost effectiveness plane for BEMPU and ThermoSpot against Thermometer

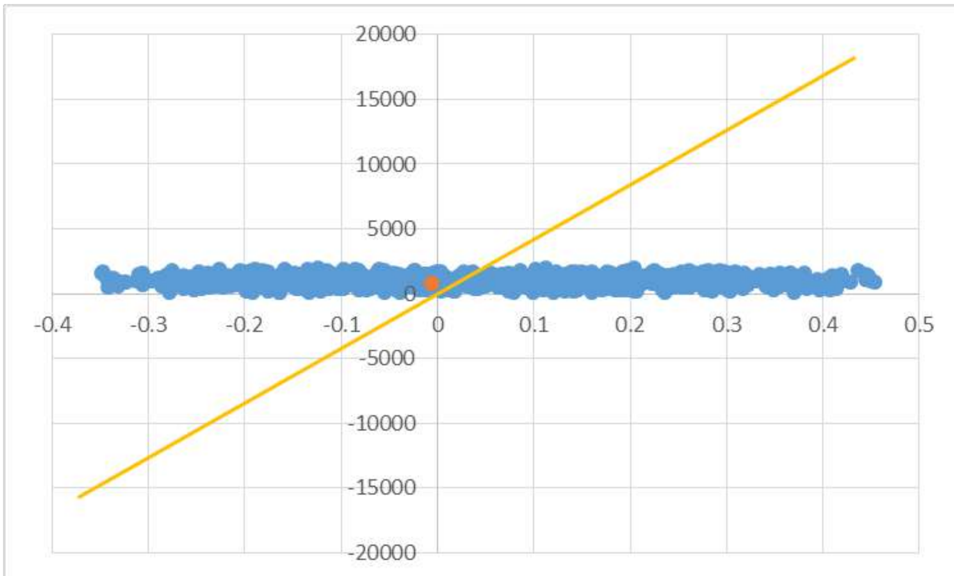


In March 2018, India's per capita GDP was 138854.25 INR (2015.228 USD). According to the cost-effectiveness threshold rule in India, both the interventions have less ICER value than the per capita GDP in India (Table 4).

Fig 8 shows results from a simulation performed as part of the probabilistic sensitivity analysis (PSA). The points in the scatter plot indicates that, considering all the uncertainties in the analysis, majority of the simulated results are concentrated around the base case results and lies just above the cost-effectiveness threshold line.

We conducted a threshold analysis varying cost of BEMPU to see at what price it becomes cost-effective while other parameters remain constant. Currently the price of one BEMPU device is 1250 INR. We considered the price as 1200, 1000, 500, 100 INR. The device did not demonstrate cost-effectiveness in either case.

Figure 0-8: Cost effectiveness plane with incremental cost effectiveness ratio for BEMPU, PSA Analysis



Thus neither intervention can be considered to be dominant.

8. Conclusion and recommendations

Neonatal hypothermia is recognized as a factor contributing to significant morbidity and mortality in new-borns (WHO, 1997). The range of prevalence of Hypothermia at the hospital and at home varies from 32% to 85% and from 11% to 92% respectively. Its contribution to neonatal mortality is primarily as a comorbidity of severe neonatal infections, preterm birth, and asphyxia (Lunze et al., 2013). The independent risk factors for hypothermia are preterm infants, low gestational age and low admission temperature (Mank et al., 2016). A major risk factor is being Low Birth Weight (LBW) that contributes to 60% - 80% of all neonatal deaths (WHO, 2017); a major public health concern. LBW neonates are highly prone to hypothermia due to lack of body fat and a poor thermal regulation system. India accounts for 40% of LBW babies in the developing world (WHO, 2017) while 43.7%, 20.8% and 19.2% neonatal deaths are due to preterm birth complications, infections and intra-partum related causes respectively (Sankar et al., 2016). Moreover, approximately 2,50,000 infant deaths occurs every year due to sepsis whereby neonatal sepsis is often presented as hypothermia in infants.

We undertook the present economic evaluation to compare the cost effectiveness of implementing hypothermia alert devices- BEMPU, ThermoSpot and Fever Watch in the existing set-up of routine health services, compared to routine care. In our analysis, we report findings from societal perspective. We used per capita gross domestic product of India as on April 2019 as threshold for determining the cost-effectiveness. India had a GDP per capita of INR. 1, 42,034 (2045.794 USD) in April, 2019 as per Census and Economic Information Centre (CEIC) data.

In order to overcome the information gap as there were limited data for the estimation of ICER, we also carried out in-depth interviews with nurses and doctors for their expert opinions. Expert opinions were used to supplement data gaps in the model building relevant to this study.

The analysis carried out in this study shows that neither of the interventions are cost saving from a societal perspective. BEMPU and ThermoSpot are primary or preventive care interventions that prevent neonates from falling ill and seeking tertiary care. The model suggests that the increase in preventive services can lead to a reduction of illness during neonatal period. The overall cost for treatment was lower in the counterfactual scenario of routine care which can detect hypothermia if used appropriately and adequately. In practice temperature is monitored continuously in NICU settings and it is supposed to be monitored every six hours using axillary thermometers in neonates. But it is worth remembering that the latter may not happen as frequently as desirable in practice.

For benefits to accrue post detection of hypothermia at an early stage implementation of warming practices such as KMC is crucial. Raising awareness of other protective measures such as wrapping the baby after birth and maintaining appropriate room temperature continues to be important.

The following excerpts from treating doctors in the Rajasthan pilot study flag an important point: "However there is an urgent need to strengthen processes to ensure that the importance of KMC is effectively communicated to mothers of infants, many of whom are unaware of the correct method of performing KMC. The Bracelet's impact on Hypothermia related issues with infants will be maximized only if good KMC practices are adopted by caregivers". "One of the biggest challenges continues to be effective communication of KMC practices to mothers and family members, many of whom do not perform KMC in a proper manner". The study also reported few instances where mothers chose not to perform KMC, such as mother was unable to care for twins after giving birth or mother did not want a female child and neglect.

According to one of the experts consulted "In a NICU unit with almost 70 neonates there are many beeping sounds from different electrical equipment. Hence it is not always possible for a nurse to identify the alarm of BEMPU device in NICU and take the needful action immediately".

Based on the ICER value, this CEA shows that Bempu and Thermospot are not cost-effective devices for detecting hypothermia in premature LBW neonates. These conclusions were made based on very limited evidence. Well-designed primary that generate good quality evidence would enable revisiting the CEA especially in community settings, which is potentially the setting where the use of such devices is needed. It is worth keeping in mind that such devices will not be a remedy for societal barriers like gender based discrimination and neglect of female new-borns that exist in some parts of the country nor for poor awareness of post detection care. Hence for lasting effectiveness, any device used to detect hypothermia needs to be combined with initiatives that will address good post hypothermia detection care. Improving quality of routine care can significantly reduce hypothermia episodes and complications as reported in a recent study; the proportion of neonates who were norm thermic on admission increased from 27% to 75%, the number of cases of late-onset neonatal sepsis decreased from 15.2 to 5 cases/1000 patient days, and all-cause mortality fell from 4.2 to 2.6 neonatal deaths per week (Dutta 2017).

9. Study Limitations

Data constraint was one of the major limitations for this study. The present analysis relied on modelled estimation in life years gained as a result of early detection of hypothermia among premature low birth weight neonates. There exists no data on life expectancy specific to hypothermia hence health adjusted life expectancy was considered.

The SoC involves intermittent temperature monitoring rather than continuous monitoring offered by the newer devices; but this was considered to be equivalent as there was no evidence of a comparable nature that could be incorporated into the model. As thermometers were used as the gold standard in most studies we assumed 100% sensitivity in detecting hypothermia by the SoC.

This study considered LBW newborns in a hospital setting. The hypothermia detecting devices are likely to be provided to mothers of neonates on their discharge from a hospital as the devices can monitor body temperature and detect hypothermia in a home/community setting. But for such an analysis we would ideally require sensitivity, specificity of the comparator and interventions in a home settings which is currently not available.

It is evident from previous studies that prevalence of hypothermia varies seasonally and was also supported by health care personnel in a public sector hospital “the number of hypothermia cases increases during winter season”. Lack of taking this fact into consideration in the model could result in some bias in this study as only 30 days’ time horizon was considered for the model irrespective of the season.

10. References

Agarwal, S., Sethi, V., Pandey, R.M., & Kondal, D. (2008): Human Touch vs. Axillary Digital Thermometry for Detection of Neonatal Hypothermia at Community Level. *Journal of Tropical Pediatrics*, 54, (3).

Andronis L, Barton P, Bryan S. Sensitivity analysis in economic evaluation: an audit of NICE current practice and a review of its use and value in decision-making. Perth: Prepress Projects Limited; 2009.

Anto A., Mathew S., Shekharappa C.B., (2018). Accuracy of touch method for assessing temperature in newborn. *Indian J Child Health.* 5(7), 477-480.

Aryeetey, Genevieve C., Jehu-Appiah, C., Spaan, E., Agyepong, I., & Baltussen, R. (2011): Costs, Equity, Efficiency and Feasibility of Identifying the Poor in Ghana's National Health Insurance Scheme: Empirical Analysis of Various Strategies. *Tropical Medicine and International Health*, 17 (1), pp. 43-51.

Balarajan, Y., Selvaraj, S., & Subramanian, S.V. (2011): Health care and equity in India. *Lancet*, 377, pp. 505–515.

Bang, A.T., Reddy, H.M., Baitule, S.B., Deshmukh, M.D., Bang, R.A (2005): The incidence of morbidities in a cohort of neonates in rural Gadchiroli, India: seasonal and temporal variation and a hypothesis about prevention. J Perinatol, 25(Suppl 1):S18-28.

Bhat R., & Jain N. (2004): Analysis of public expenditure on health using state level data. Ahmadabad: Indian Institute of Management.

Bhutta Z.A, Darmstadt G.L, Hasan B.S, Haws R.A. (2005). Community-based interventions for improving perinatal and neonatal health outcomes in developing countries: A review of the evidence. Pediatrics;115(2 Suppl):519–617.

Brooke O.G (1972). Influence of Malnutrition on the Body Temperature of Children. British Medical Journal, 1: 331–332. [PMC free article] [PubMed]

Byaruhanga, R., Bergstrom, A., & Okong, P. (2005): Neonatal hypothermia in Uganda: prevalence and risk factors. *J Trop Pediatr*, 51 (5), pp. 212–215.

Chang, H. Y., Sung, Y. H., Wang, S. M., Lung, H. L., Chang, J. H., Hsu, C. H., Hung, H. F. (2015). Short-and long-term outcomes in very low birth weight infants with admission hypothermia. PloS one, 10(7), e0131976. 21

Cheah IG, Soosai AP, Wong SL, et al. Cost-effectiveness analysis of Malaysian neonatal intensive care units. J Perinatol 2005;25:47–53.

Christensson, K., Bhat, G.J., Eriksson, B., Shilalukey-Ngoma, M.P., & Sterky, G. (1995): The effect of routine hospital care on the health of hypothermic newborn infants in Zambia. *J Trop Pediatr*, 41, pp. 210–214. doi: 10.1093/tropej/41.4.210.

Christensson, K., Ransjo-Arvidson, A.B., Kakoma, C., Lungu, F., Darkwah, G., Chikamata, D., Sterky, G. (1988): Midwifery care routines and prevention of heat loss in the newborn: a study in Zambia. *J Trop Pediatr*, 34 (5), pp. 208–212.

Dagan R, Gorodischer R. Infections in hypothermic infants younger than 3 months old. Am J Dis Child 1984;138(5):483- 5

Dandona, L., Dandona, R., Kumar, G. A., Shukla, D. K., Paul, V. K., Balakrishnan, K. & Nandakumar, A. (2017). Nations within a nation: variations in epidemiological transition across the states of India, 1990–2016 in the Global Burden of Disease Study. The Lancet, 390(10111), 2437-2460.

Dang, A., Likhar, N., & Alok, U. (2016). Importance of economic evaluation in health care: An Indian perspective. *Value in health regional issues*, *9*, 78-83.

Darmstadt, G.L., Kumar, V., Yadav, R., Singh, V., Singh, P., Mohanty, S., Baqui, A.H., Bharti, N., Gupta, S., Misra, R.P., Awasthi, S., Singh, J.V., Santosham, M. (2006): Introduction of community-based skin-to-skin care in rural Uttar Pradesh. *India. J Perinatol*, 26 (11), pp. 597–604.

Department of Health Research Ministry of Health &Family Welfare, Government of India, (2018), *'Health Technology Assessment in India: A Manual'.*http://dhr.gov.in/

Derosas, R. (2009). The joint effect of maternal malnutrition and cold weather on neonatal mortality in nineteenth-century Venice: An assessment of the hypothermia hypothesis. *Population Studies, 63*(3), 233-251. Retrieved from http://www.jstor.org/stable/40646423

Duggal, R. (2007): Poverty and Health: Criticality of Public Financing. *Indian Journal of Medical Research*, 126 (4), pp. 309-317.

Duggal, R., Nandraj, S., & Vadair, A. (1995a): Health Expenditure across States: Part I. *Economic and Political Weekly*, 30, pp. 834-844.

Ellis M., Manandhar N., Shakya.U., Manandhar D.S., Fawdry.A., Costello A.M. (1996).Postnatal hypothermia and cold stress among newborn infants in Nepal monitored by continuous ambulatory recording. Arch Dis Child Fetal Neonatal Ed; 75(1):F42–F45. [PMC free article] [PubMed]

Franconi. I., La Cerra. C., Marucci A. R., Petrucci. C., Lancia. L., (2018). Digital Axillary AND Non-contact Infrared Thermometers for Children. Clinical Nursing Research, 27(2):pp. 180-190

Gerensea, H., & Murugan, R. (2016). Is There Significant Difference between Digital and Glass Mercury Thermometer? Advances in Nursing, 2016.

Goldie SJ, Sweet S, Carvalho N, Natchu UCM, Hu D (2010) Alternative Strategies to Reduce Maternal Mortality in India: A Cost-Effectiveness Analysis. PLoS Med 7(4): e1000264. doi:10.1371/journal.pmed.1000264

Goodman C.S., (2015), NIH: U.S National Library of Medicine, '*National Information on Health Science research And Health Care Technology (NICHSR)'*, https://www.nlm.nih.gov/nichsr/hta101/ta10102.html

Green, D. A., Kumar, A., & Khanna, R. (2006). Neonatal hypothermia detection by ThermoSpot in Indian urban slum dwellings. *Archives of Disease in Childhood: Fetal and Neonatal Edition*, *91*(2). https://doi.org/10.1136/adc.2005.078410

Haddadin, R.B., & Shamoon, H.I. (2007): Study between Axillary and rectal temperature measurements in children. *Eastern Mediterranean Health Journal*, 13 (5).

India Newborn Action Plan (2014): Ministry of Health & Family Welfare. Government of India.

Jayakrishnan, T., Jeeja, M. C., Kuniyil, V., & Paramasivam, S. (2016): Increasing Out-Of-Pocket Health Care Expenditure in India- Due to Supply or Demand? Pharmacoeconomics, doi: 10.4172/2472-1042.1000105.

Joe, W., Mishra, U.S., &Navaneetham, K. (2010): Socio-economic inequalities in child health: Recent evidence from India. *Glob Public Health*, 5, pp. 493-508.

Johanson, R.B, Malla, D.S, Tuladhar, C., Amatya, M., Spencer, S.A., Rolfe, P (1993): A survey of technology and temperature control on a neonatal unit in Kathmandu, Nepal. J Trop Pediatr, 39:4-10.

Jonsson, B. (2015): Bringing in health technology assessment and cost-effectiveness considerations at an early stage of drug development. *Molecular Oncology*, 9, pp. 1025-1033.

Kambarami, R., Chidede, O. (2003): Neonatal hypothermia levels and risk factors for mortality in a tropical country. Cent Afr J Med, 49:103-106.

Kambarami, R., Chidede, O., & Pereira, N. (2002). ThermoSpot in the detection of neonatal hypothermia. Annals of tropical paediatrics, 22(3), 219-223.

Lawn J.E, Cousens S, Zupan J., Lancet Neonatal Survival Steering Team (2005). 4 million neonatal deaths: When? Where? Why? Lancet, 365(9462):891–900. [PubMed]

Lunze, K., Bloom, D. E., Jamison, D. T., & Hamer, D. H. (2013): The global burden of neonatal hypothermia: Systematic review of a major challenge for newborn survival, *BMC Medicine,* pp. 11-24.

Lunze, K., Hamer, D.H. (2012): Thermal protection of the newborn in resource-limited environments. *J Perinatol*, 32 (5), pp. 317–324.

Lyu Y, Shah PS, Ye XY, et al. Association Between Admission Temperature and Mortality and Major Morbidity in Preterm Infants Born at Fewer Than 33 Weeks' Gestation. *JAMA Pediatr.* Published online April 01, 2015169(4):e150277. doi:10.1001/jamapediatrics.2015.0277

Manandhar, N., Ellis, M., Manandhar, D. S., Morley, D., & Costello, A. D. L. (1998). Liquid crystal thermometry for the detection of neonatal hypothermia in Nepal. *Journal of tropical pediatrics*, *44*(1), 15-17.

Manary M.J., Sandige H.L (2008). Management of acute moderate and severe childhood malnutrition. British Medical Journal. 13;337: a2180. [Pub.Med]

Mank, A., van Zanten, H.A., Meyer, M.P., Pauws, S., Lopriore, E., te Pas, A.B. (2016): Hypothermia in Preterm Infants in the First Hours after Birth: Occurrence, Course and Risk Factors. *PLoS ONE* 11(11): e0164817. doi:10.1371/journal. pone.0164817.

Mathur, N. B., Krishnamurthy, S., Mishra, T. K. (2005). Evaluation of WHO classification of hypothermia in sick extramural neonates as predictor of fatality. Journal of tropical pediatrics, 51(6), 341-345.

Mauta, L., Vince, J., & Ripa, P. (2009). Comparison of the Use of Liquid Crystal Thermometers with Glass Mercury Thermometers in Febrile Children in a Children's Ward at Port Moresby General Hospital, Papua New Guinea. *Journal of tropical pediatrics*, *55*(6), 368-373.

McDill, M. E. (1999). Forest resource management. *Penn State Univ*.

McKinnon, B., Harper, S., Kaufman, J.S., Bergevin, Y. (2014): Socioeconomic inequality in neonatal mortality in countries of low and middle income: a multicountry analysis. Lancet Glob Health, 2, www.thelancet.com/lancetgh.

Memirie, S. T., Verguet, S., Norheim, O.F., Levin, C., Johansson, K.R (2016): Inequalities in utilization of maternal and child health services in Ethiopia: the role of primary health care. BMC Health Services Research 16 (51). DOI 10.1186/s12913-016-1296-7.

Mendelsohn AS, Asirvatham JR, Mwamburi DM, TV S, Malik V, J M, *et al*. Estimates of the economic burden of rotavirus-associated and all-cause diarrhoea in Vellore, India. Tropical Medicine and International Health. 2008;13:934-42.

Mole, T.B., Kennedy, N., Ndoya, N., & Emond, A. (2012) ThermoSpots to Detect Hypothermia in Children with Severe Acute Malnutrition. *PLoS ONE* 7(9): e45823. https://doi.org/10.1371/journal.pone.0045823.

Morgan, G., & Janan, D. (2017): Health technology assessment on the BEMPU hypothermia alert device for critical neonates. NHSRC HTA Training.

Morley D, Blumenthal I. A new neonatal hypothermia indicator. Lancet.2000: 355: 659-660. 24

Mullany, L. C., Katz, J., Khatry, S. K., LeClerq, S. C., Darmstadt, G. L., Tielsch, J. M. (2010). Risk of mortality associated with neonatal hypothermia in southern Nepal. Archives of pediatrics & adolescent medicine, 164(7), 650-656.

Mullany, L.C. (2010): Neonatal hypothermia in low-resource settings. *Semin Perinatol*, 34(6), pp. 426–433.

Nandraj, S., & Duggal, R. (1997): Physical Standards in the Private Health Sector: A Case Study of Rural Maharashtra, Centre for Enquiry into Health and Allied Themes, Mumbai.

Narang A, Kiran PS, Kumar P. Cost of neonatal intensive care in a tertiary care center. Indian Pediatr. 2005;42:989–97

National Health accounts estimates for India. (2017). Retrieved from https://mohfw.gov.in/sites/default/files/National Health Accounts Estimates Report 2014-15.pdf

National Health Mission. LaQshya. Labour Room Quality Improvement Initiative (2017). Ministry of Health and Family Welfare. Government of India. Available from: http://nhm.gov.in/New_Updates_2018/NHM_Components/RMNCH_MH_Guidelines/LaQshya-Guidelines.pdf on Accessed 18 March 2018).

Nayeri, F., & Nili, F. (2006). Hypothermia at Birth and its Associated Com-plications in Newborn infants: a Follow up Study. Iranian Journal of Public Health, 35(1), 48-52.

NHM Rajasthan and WISH Pilot of BEMPU Bracelet (2017): Pilot of the BEMPU Device for Reduction in Hypothermia and Infection Related Neonatal Mortality and Morbidity in Rajasthan.

Nonyane, B. A.S., Ashish, K.C., Jennifer, A., Callaghan, K., Guenther, T., Sitrin, D., Syed, U., Pradhan, Y.V., Khadka, N., Shah, R., Baqui, A.H (2016): Equity improvements in maternal and newborn care indicators: results from the Bardiya district of Nepal. Health Policy and Planning, 31, pp. 405–414, doi: 10.1093/heapol/czv077. 25

Ogunlesi, T.A., Ogunfowora, O.B., Adekanmbi, F.A., Fetuga, B.M., Olanrewaju, D.M. (2008): Point-of-admission hypothermia among high-risk Nigerian newborns. *BMC Pediatr*, 8 (40). doi: 10.1186/1471-2431-8-40.

Paul, V. K., Sachdev, H. S., Mavalankar, D., Ramachandran, P., Sankar, M. J., Bhandari, N & Kirkwood, B. (2011). Reproductive health, and child health and nutrition in India: meeting the challenge. The Lancet, 377(9762), 332-349.

Prinja S, Bahuguna P, Mohan P,Mazumder S, Taneja S, Bhandari N, etal.(2016) Cost Effectiveness of Implementing Integrated Management of Neonatal and Childhood Illnesses Program in District Faridabad, India. PLoSONE 11(1):e0145043.doi:10.1371/journal.pone.0145043

Prinja, S., Bahuguna, P., & Duseja, A. (2017): Cost of Intensive Care Treatment for Liver Disorders at Tertiary Care Level in India. https://doi.org/10.1007/s41669-017-0041-4.

Prinja, S., Bahuguna, P., Balasubramaniam, D., Sharma, A., & Kumar, R. (2016): Analyzing Inequality in Use of Healthcare Services: Implications for Targeting Within Universal Health Coverage Reforms. DOI: 10.1136/bmjgh-2016-EPHPabstracts.32.

Prinja, S., Gupta, A., Verma, R., Bahuguna, P., Kumar, D., Kaur, M., &Kumar, R. (2016): Cost of Delivering Health Care Services in Public Sector Primary and Community Health Centres in North India. 10.1371/journal.pone.0160986.

Prinja, S., Kaur, G., Malhotra, P., Jyani, G., Ramachandran, R., Bahuguna, P., &Varma, S. (2017): Cost-Effectiveness of Autologous Stem Cell Treatment as Compared to Conventional Chemotherapy for Treatment of Multiple Myeloma in India. *Indian J Hematol Blood Transfus*, 33, pp. 31-40.

Prinja, S., Manchanda, N., Mohan, P., Gupta, G., Sethy, G., Sen, A. & Kumar, R. (2013). Cost of neonatal intensive care delivered through district level public hospitals in India. Indian pediatrics, 50(9), 839-846.

Rahman, N., Kasem, F. B., Islam, M. R., Islam, M. R., Sultana, R., & Matin, A. (2012). Comparison between mercury and liquid crystal forehead thermometers for measurment of body temperature. *Journal of Shaheed Suhrawardy Medical College*, *4*(2), 60-61.

Russell RB, Green NS, Steiner CA, et al. Cost of hospitalization for preterm and low birth weight infants in the United States. Pediatrics 2007;120:e1–9. 26

Sankar, M.J., Neogi, S.B., Sharma, J., Chauhan, M., Srivastava, R., Prabhakar, P.K., Khera, A., Kumar, R., Zodpey, S., & Paul, V.K. (2016): State of newborn health in India. *Journal of Perinatology*, 36, pp. S3–S8.

Sauer PJ. Neonatal thermoregulation. In: Cowett RM, editor. Principles of Perinatal-Neonatal Metabolism. New York: Springer-Verlag; 1991.

Scopes, J. W., & Ahmed, I. (1966): Range of critical temperatures in sick and premature newborn babies. *Arch Dis Child*, 41, pp. 417-419.

Sen, G., Iyer, A., George, A. (2002): Structural Reforms and Health Equity: A Comparison of NSS Surveys, 1986-87 and 1995-96. *Economic and Political Weekly*, 37, pp. 1342-1352

Shafijan, S. M., Chandrasekaran, A., Balakrishnan, U., Ninan, B., & Abiramalatha, T. (2018). Continuous Temperature Monitoring Using Bluetooth-enabled Thermometer in Neonates. *Indian pediatrics*, *55*(10), 914-915.

Shanmugasundaram, R., Padmapriya, E., & Shyamala, J. (1998). Cost of neonatal intensive care. The Indian Journal of Pediatrics, 65(2), 249-255.

Singh, M., Rao, G., Malhotra, A. K., & Deorari, A. K. (1992). Assessment of newborn baby's temperature by human touch: a potentially useful primary care strategy. Indian Pediatrics, 29(4), 449–452. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=1506096

Smith, A.B. (1963): Paying for Health Services: A Study of the Costs and Sources of Finance in Six Countries. Public Health Papers No. 17. Geneva: World Health Organization.

Smith, L. (2004). Temperature monitoring in newborns: A comparison of thermometry and measurement sites. Journal of Neonatal Nursing-London, 10, 157-165).

Sodemann, M., Nielsen, J., Veirum, J., Jakobsen, M. S., Biai, S., & Aaby, P. (2008): Hypothermia of newborns is associated with excess mortality in the first 2 months of life in Guinea-Bissau, West Africa. *Tropical Medicine and International Health*, 13 (8), pp. 980-986.

Srivastava, A., Singh, D., Montagu, D., & Bhattacharyya, S. (2018). Putting women at the center: a review of Indian policy to address person-centered care in maternal and newborn health, family planning and abortion. BMC public health, 18(1), 20.

Stern, L. (1980): Thermoregulation in the Newborn Infant: Historical, Physiological and Clinical Considerations In: Historical Review and Recent Advances in Neonatal and Perinatal Medicine. In: Smith, George F.; Vidyasagar, Dharmapuri, editors. *Mead Johnson Nutritional Division.*

Sule, M. (1999): 'Health Manpower in the District' in S Kavadi (ed), Health Resources, Investment and Expenditure: A Study of Health Providers in a District in India, Foundation for Research in Community Health, Pune.

Sundaram V, Chirla D, Panigrahy N, Kumar P (2014) Current Status of NICUs in India: A Nationwide Survey and the Way Forward. Indian J Pediatr (November 2014) 81(11):1198–1204

Sur D, Chatterjee S, Riewpaiboon A, Manna B, Kanungo S, Bhattacharya SK. Treatment Cost for Typhoid Fever at Two Hospitals in Kolkata, India. Health Popul Nutr 2009;27:725-32.

Tafari, N. & Olsson, E.E. (1973): Neonatal cold injury in the tropics. Ethiop Med J, 11 (1), pp. 57–65.

Tanigasalam, V., Bhat, V., Adhisivam, B., Balachander, B., & Kumar, H. (2017): Hypothermia detection in low birth weight neonates by bracelet device in Indian setting-novel method. Department of Neonatology and Department of Biostatistics, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry.

Tanigasalam, V., Vishnu Bhat, B., Adhisivam, B., Balachander, B., & Kumar, H. (2018, March 5). Hypothermia detection in low birth weight neonates using a novel bracelet device. *Journal of Maternal-Fetal and Neonatal Medicine*, pp. 1–4. Taylor and Francis Ltd. https://doi.org/10.1080/14767058.2018.1443072

Tripathi, N., Saini, S. K., & Prinja, S. (2014). Impact of Janani Shishu Suraksha Karyakram on out-of-pocket expenditure among urban slum dwellers in Northern India. Indian pediatrics, 51(6), 475-477.

Turab, A., Pell, L. G., Bassani, D. G., Soofi, S., Ariff, S., Bhutta, Z. A., & Morris, S. K. (2014). The community-based delivery of an innovative neonatal kit to save newborn lives in rural Pakistan: design of a cluster randomized trial. *BMC pregnancy and childbirth*, *14*(1), 315.

UNICEF and WHO (2004): Low birth weight country, regional, and global estimates. WHO Publications, 1211 Geneva 27, Switzerland.

WHO (1997): Thermal protection of the newborn: A practical guide, *WHO/RHT/MSM/97.2*.

WHO maternal, newborn, child and adolescent health (2017): Care of the preterm and/or low-birth-weight newborn.

World Health Organization (WHO), (2015), *'2015 Global Survey on Health Technology Assessment by National Authorities'*https://www.who.int/health-technology-assessment/MD_HTA_oct2015_final_web2.pdf?ua=1

World Health Organization (WHO), (2016), '*Health Technology Assessment',*https://www.who.int/health-technology-assessment/en/

Yuan, B., Målqvist, M., Trygg, N., Qian, Xu., Ng, N., Thomsen, S. (2014): What interventions are effective on reducing inequalities in maternal and child health in low- and middle-income settings? A systematic review. BMC Public Health 2014 14:634, http://www.biomedcentral.com/1471-2458/14/634.

Zayeri, F., Kazemnejad, A., Ganjali, M., Babaei, G., Khanafshar, N., & Nayeri, F. (2005). Hypothermia in Iranian newborns. Incidence, risk factors and related complications. Saudi medical journal, 26(9), 1367-1371

11. Annexures

11.1 Clinical Effectiveness: Systematic Review details

Table 6: Clinical Effectiveness: Concept Table

	Population	Interventions	Comparator	Outcome
Mesh Terms/Key words	Premature and Low Birth Weight Neonates	1.BEMPU, 2.ThermoSpot 3.and Fever Watch	Axillary Thermometer	1.Diagnostic Accuracy and 2.Hypothermia
Text words	Preterm Low Birthweight, LBW, Low Weight Neonatal, Newborn	1.Novel bracelet device 2. Liquid crystal thermometer/ thermometry 3. Feverwatch	Digital thermometer and Axillary Digital thermometer	1.Sensitivity, Specificity and Accuracy 2. Hypothermic, cold stress and cold shock

Search Strings

Figure -0-6: Clinical effectiveness Search Strings- Web of Science

Search: (ALL FIELDS: (sensitivity) *OR* ALL FIELDS: (accuracy) *OR* ALL FIELDS: (specificity) *OR* ALL FIELDS: ("diagnostic accuracy")) *AND* ((ALL FIELDS: (BEMPU) *OR* ALL FIELDS: ("novel bracelet device")) *OR* (ALL FIELDS: ("Digital Thermomet*") *OR* ALL FIELDS: ("Digital Axilla* Thermomet*") *OR* ALL FIELDS: ("Axilla* Thermomet*)) *OR* (ALL FIELDS: (Feverwatch) *OR* ALL FIELDS: ("Fever Watch"))) *AND* ((ALL FIELDS: ("Low Birth Weight") *OR* ALL FIELDS: (LBW) *OR* ALL FIELDS: (Premature) *OR* ALL FIELDS: (Preterm) *OR* ALL FIELDS: ("Low Birthweight") *OR* ALL FIELDS: ("Low weight")) *OR* (ALL FIELDS: (Neonat*) *OR* ALL FIELDS: (Newborn)) *OR* (ALL FIELDS: (Hypotherm*) *OR* ALL FIELDS: ("low body temperature") *OR* ALL FIELDS: ("cold stress") *OR* ALL FIELDS: ("cold shock"))) Refined by: LANGUAGES: (ENGLISH) Timespan: All years

Figure -0-7: Clinical effectiveness Search Strings-Scopus

Search: **(ALL (sensitivity OR accuracy OR specificity OR {diagnostic accuracy})) AND ((ALL (BEMPU OR {novel bracelet device})) OR (ALL (ThermoSpot OR {Liquid crystal thermomet*})) OR (ALL ({Digital Thermomet*} OR {Axilla* Thermomet*} OR {Digital Axilla* Thermomet*})) OR (ALL ({Fever Watch} OR feverwatch))) AND ((ALL (hypotherm* OR {Low body temperature} OR {cold stress} OR {cold shock})) OR (ALL ({Low Birth Weight} OR LBW OR premature OR preterm OR {Low birthweight} OR {Low weight})) OR (ALL (neonat* OR newborn))) AND (LIMIT-TO (LANGUAGE , "English"))**

Figure -0-8: Clinical effectiveness Search Strings- Cochrane

Search: {AND ({OR ("Diagnostic accuracy" OR accuracy), ([Sensitivity and Specificity])}), ({OR ([Hypotherm*]), (Preterm OR Premature), ([Low Birth Weight]), ([Newborn])}), ({OR (BEMPU OR "novel bracelet device"), (Feverwatch OR "Fever Watch"), (ThermoSpot OR "Liquid crystal thermomet*"), ("Digital Thermomet*")})} Limit to English

Table 7: Relevant studies on Thermospot

No	Title	Journal	Year of publishing	Place of study	objectives	Study Design	Exposure measurement	Outcome measurement	Method used for analysis	Finding	Additional comments
	Comparison Between Mercury and Liquid Crystal Forehead Thermometers for Measurement of Body Temperature	J Shaheed Suhrawardy Med Coll, 2012;4(2) :60-61 ISSN 2226-5368	2012	Dhaka, Bangladesh	recordings of normal body temperature using liquid crystal forehead thermometer and compare with gold standard oral mercury thermometer	Cross-sectional study. All first year MBBS medical students at the age of eighteen (18) to twenty (20) years of either sex were selected randomly by selecting every third student.		Oral-temperature was recorded with Chinese made mercury thermometer and the forehead temperature was recorded using liquid crystal.	Student t test	Mercury thermometer remains the gold standard	Excluded as the target group is not relevant

	COMPARISON OF LIQUID CRYSTAL DEVICE (THERMOSPOT) WITH LOW READING AXILLARY THERMOMETER IN DETECTING NEONATAL HYPOTHERMIA	http://www.pediatriconcall.com	2010	Maharajgunj, Kathmandu	To assess the efficacy of a liquid crystal device (ThermoSpot) in detecting neonatal hypothermia.	Hospital based, cross sectional study.	Babies were assessed thrice in first 24 hours of life i.e. within 4 hour, 4-12 hours and 12-24 hours.	colour in the Thermo Spot	univariate analysis	Mercury in glass thermometer remains the gold standard.	Not for low birth weight babies
	Comparison of the Use of Liquid Crystal Thermometers with Glass Mercury Thermometers in Febrile Children in a Children's Ward at Port Moresby General Hospital, Papua New Guinea	Published by Oxford University Press	2009	Port Moresby by General Hospital, Papua New Guinea	Comparison of the Use of Liquid Crystal Thermometers with Glass Mercury Thermometers in Febrile Children	Prospective study. It involved a convenience sample of 200 children who were admitted with fever.	Authors measured the temperature with thermometer, nurses measured using LCT		Bland Altman plots &box-plot	The LCT such as NextempR and TraxitR devices can have a significant place in Hospital and clinic practice in resource-poor environments.	Target population is of upto 13 years. Children admitted with high fever were only considered.
	Hypothermia and the use of ThermoSpots	NA									

	Liquid crystal thermometry for early detection of hypothermia in newborns in neonatology ward, Sardjito Hospital, Yogyakarta	Paediatr Indones	2008	Sardjito Hospital	To evaluate the ability of liquid crystal thermometry (LCT) in early detection of newborn hypothermia	Cross-sectional study.	measurement was carried out three times after the babies were recruited within 8 hours interval		univariate analysis	LCT exhibits good accuracy and is safe to diagnose hypothermia in newborn in the neonatology ward, Sardjito Hospital.	All term babies. The ThermoSpot® reading was done at the time when the digital thermometer showed the body temperature showed hypothermic
	Liquid Crystal Thermometry for the Detection of Neonatal Hypothermia in Nepal	Journal of Tropical Paediatrics	1998	Kathmandu, Nepal	To assess the sensitivity, specificity and likelihood ratio of a low cost liquid crystal strip thermometer (LCT) compared with axillary mercury thermometry for the detection of neonatal hypother	Cross-sectional study.				Liquid crystal thermometry is a simple, low-cost, and valid method for identifying core hypothermia in newborns. It is ideal for isolated rural communities	Healthy, term, new born infants (n = 76) were recruited

					mia in Nepal.					where LCT strips could be added to delivery kits.	
	Temperature Monitoring in Newborns Using Thermospot	Indian Journal of Pediatrics	2004	Bangalore, India	To monitor temperature using Thermospot	Cross-sectional study.	Temperature was measured by termospot and thermometer	Agreement between thermospot and thermometer	No statistical analysis	ThermoSpot device is a simple accurate device allowing continuous thermal monitoring of low birth weight infants, especially in resource poor setting. conclusion is not based on any statistical measure	conclusion is not based on any statistical measure

	The Community-based delivery of an innovative neonatal kit to save newborn lives in rural Pakistan: Design of a cluster randomized trail	BMC; Study protocol	2014	Pakistan	efficacy of an innovative neonatal kit	cluster randomized study	primary outcome was NMR					It's a study protocol, no findings reported.
	THE EFFICACY OF THERMO SPOT IN DETECTING NEONATAL HYPOTHERMIA COMPARED TO RECTAL TEMPERATURE	Journal of Evidence based Medicine and Healthcare	2014	Tamaka, Kolar	Assess the efficacy of Thermospot	Prospective study.	Hypothermia			Univariate and Bivariate	The study showed a sensitivity of 96.9% and specificity of 99.8% by thermo spot in detecting hypothermia compared to standard rectal temperature among normal babies only	newborns admitted to NICU were excluded from the study

0	ThermoSpotinthedetectionofneonatalhypothermia				to determine the Vectiveness of ThermoSpot in detecting hypothermia in newborn infants in a developing country	6 week cross sectional study			% analysis	There is a need to improve the sensitivity and accuracy of ThermoSpot in detecting hypothermia before its widespread use.	It considered 100 % specificity of thermospot but in practice there were 16 cases who were normal by thermometer but hypothermic by thermospot
1	Effect of community-based behaviour change management on neonatal mortality in Shivgarh, Uttar Pradesh, India: a cluster-randomised controlled trial	Lancet	2008	UP	Effect of community-based behaviour change management on neonatal mortality in Shivgarh,	cluster randomized study	Neonatal mortality	Behaviour change	conservative analytical methods	Compared with controls, neonatal mortality rate was reduced by 54% in the essential newborn-care intervention and by 52% in the	No comparison of neonatal mortality rate between the two intervention arms was planned. The intervention that included the use of the ThermoSpot did not seem to have an advantage over the package

										essenti al newbo rn care plus Therm oSpot arm	of essential newborn care.

11.2 Cost of hypothermia detecting devices and NICU Cost- Systematic Review

Table 7: Cost effectiveness Concept Table

PICO	MeSH terms	Text words
POPULATION	Hypothermia Preterm Neonate	Hypothermia OR low body temperature OR rewarming OR cold Stress OR cold shock Preterm OR premature OR low birth weight Neonate OR Newborn OR babies
INTERVENTION	ThermoSpot BEMPU Fever Watch	ThermoSpot OR Liquid Crystal Thermometer BEMPU OR Novel bracelet device Fever Watch OR Fever Watch monitoring system
COMPARATOR	Thermometer	Thermometer OR Digital thermometer OR Axillary thermometer OR mercury thermometer
OUTCOME	Cost effectiveness analysis NICU cost	Cost effectiveness analysis OR cost benefit analysis OR Cost Minimization OR Economic evaluation NICU OR SNCU OR cost of treatment

Search Strings

Figure -0-9: Cost Effectiveness Search String - Web of Science

Search: ((((ALL=(hypothermia) OR ALL=("cold shock") OR ALL=(rewarming) OR ALL=("cold stress") OR ALL=("low body temperature")) AND (ALL=("low birth weight") OR ALL=("preterm") OR ALL=(premature) OR ALL=("premature low birth weight")) AND (ALL=(neonat*) OR ALL=(newborn) OR ALL=(babies))) AND ((ALL=(thermomet*) OR ALL=("digital thermometer") OR ALL=("axilla* thermometer")) OR (ALL=(BEMPU) OR ALL=("novel bracelet device") OR ALL=("BEMPU bracelet device) OR (ALL=(ThermoSpot*) OR ALL=("liquid crystal Thermomet*")) OR (ALL=(thermomet*) OR ALL=("digital thermometer") OR ALL=("mercury glass thermometer") OR ALL=("axilla*thermometer"))) AND (ALL=("cost effectiveness analysis") OR ALL=("cost benefit analysis") OR ALL=("cost minimization analysis") OR ALL=("economic evaluation") OR ALL=("marginal analysis"))) OR (((ALL=(India) OR ALL=("low income countries") OR

ALL=("developing countries)) ((ALL=(cost) OR ALL=("cost of treatment") OR ALL=("cost analysis")) AND (ALL=("neonatal intensive care unit") OR ALL=("NICU") OR ALL=("Sick newborn care unit") OR ALL=("SNCU")) AND (ALL=(neonat*) OR ALL=(newborn) OR ALL=(babies))))

Figure -0-10: Cost Effectiveness Search String - Scopus

Search: (((ALL (cost) OR ALL ({cost of treat*}))) AND ((ALL (neonat*) OR ALL (newborn))) AND ((ALL (hypothermia) OR ALL ({low body temperature}))) AND ((ALL (nicu) OR ALL (sncu))) AND ((ALL (india) OR ALL ({Developing Countries}) OR ALL ({Low income countries})))) OR ((ALL ({cost effectiveness analysis} OR {cost benefit analysis} OR {cost minimization} OR {economic evaluation})) AND ((ALL (BEMPU OR {novel bracelet device})) OR (ALL (ThermoSpot OR {Liquid crystal thermomet*})) OR (ALL ({Digital Thermomet*} OR {Axilla* Thermomet*} OR {Digital Axilla* Thermomet*})) OR (ALL ({Fever Watch} OR feverwatch))) AND ((ALL (hypotherm* OR {Low body temperature} OR {cold stress} OR {cold shock})) OR (ALL ({Low Birth Weight} OR lbw OR premature OR preterm OR {Low birthweight} OR {Low weight})) OR (ALL (neonat* OR newborn)))) AND (LIMIT-TO (LANGUAGE , "English"))

Figure -0-11: Cost Effectiveness Search String - Cochrane

Search: (((NICU in All Text OR SNCU in All Text AND cost in All Text) AND (neonate in All Text) AND (hypothermia in All Text AND neonate in All Text)) AND (("cost effectiveness analysis" in All Text OR "cost-benefit analysis" in All Text OR "cost minimization analysis" in All Text OR economic evaluation in All Text) AND (Thermometer in All Text OR ThermoSpots in All Text OR BEMPU bracelet device in All Text) AND (hypothermia in All Text AND neonate in All Text)))

Figure 0-12: Cost Effectiveness Search String - PubMed

Search: ((((((((((NICU) OR SNCU) OR neonatal intensive care unit) OR sick newborn care unit) OR newborn care)) AND hypothermia)) AND ((cost) OR cost analysis)) AND (Humans[Mesh])) OR (((((((((thermometer) OR body temperature thermometer)) OR Fever Watch device) OR (((BEMPU) OR BEMPU bracelet) OR novel bracelet device)) OR ((ThermoSpots) OR liquid crystal thermometer))) AND ((((((neonate) OR premature neonate) OR low birth weight neonate) OR premature low birth weight neonate)) AND hypothermia))) AND ((((((cost effectiveness analysis) OR cost benefit analysis) OR cost minimization) OR cost utility) OR economic evaluation) OR marginal analysis)) AND (Humans[Mesh])

11.3 Interview Log with Health Care Professionals

Table 8: Interview/Meeting logs with Physicians:

Unique ID	Date	Mode of meeting	Meeting Mins
Peds_GD_GovtS_008	8/02/2019	In Person	Dr M advised us to look at individual case sheets because the SNCU admission register does not record the temperature of the neonate on admission. Also, they consider hypothermia as a sign of other underlying conditions e.g. neonatal sepsis and therefore do not record if the neonate is hypothermic but rather record the diagnosis as "neonatal sepsis" only. The case sheets will provide us with the temperature recording of the neonate admitted into SNCU and state if the neonate is hypothermic.
Peds_NEG_MC_009	1/022019	In Person	Dr. B said that NICU cases are not the right subject to look at. Since hypothermic neonates admitted to NICU are being kept under a radiant warmer which has a Thermistor that continuously monitors the neonate's temperature. Therefore BEMPU or ThermoSpot will not be useful in the hospital setting but could be useful to those neonates who can be with their mother; either admitted to postnatal ward or discharge from the hospital. Ganesh Das hospital and I along District Civil hospital would be the best area to explore since they have limited man power and facilities either at the post natal ward or SNCU. He mentioned that hypothermic neonates are only admitted to the NICU when they have other complications and they treat hypothermia as a sign of some underlying diseases such as sepsis, otherwise they are being treated in the postnatal ward keeping the neonate with the mother and instructed to provide KMC. He also mentioned that calculating the cost related to the NICU care or maintenance will give a biased results since they have sophisticated equipment which are not specifically just for treating hypothermic babies and moreover the cost of manpower will also mislead the results since the NICU staff and doctors are not only paid to treat hypothermic neonates but also for teaching Medical Students. We asked him about the statistics of the low birth weight babies and if we are accessible to their case sheets, he directed us to get the permission letter from the Medical Superintendent and get the information from the Medical record department and Finance department. We asked him about the statistics of the low birth weight babies and if we are accessible to their case sheets, he directed us to get the permission letter from the Medical Superintendent and get the information from the Medical record department and Finance department. Dr H also suggested we get in touch with Prof VD,

			Lady Harding Medical College, Neonatology as he might have papers/research work related to our project.
Neo_LH_MC_010	15th Mar 2019	In Person	Dr D mentions hypothermia is highly under reported in India. He shared his own experience at a public hospital in India that doctors of that unit claimed that they do not have any hypothermia case and they monitor the temperature regularly. But he found 83% hypothermia cases in that same unit when he started monitoring temperature himself for few days. According to him, we need to do primary survey for authentic data. To estimate the treatment cost, he said at public hospitals, cost does not vary much for treatment. It mainly depends on the no of days stayed at hospital. Therefore we can multiply the per day cost with number of stays to estimate complications cost. He told that, yearly around 82-85 lives can be saved by preventing hypothermia. He shared few information on hospital stays for different situations, like a neonate with severe hypothermia needs to stay 2-3 days at NICU without any other complications. But with complications: bleeding: 14days; severe infections: 7-11days; pulmonary hemorrhage: 21 days. He shared his personal opinion regarding BEMPU, "There are a number of beeping in NICU unit, and it is hard to identify the beep of BEMPU. Moreover it is too expensive for most of the people." He also added that any device is not effective in preventing hypothermia and related consequences until and unless people become aware about it. If the caregiver does not know KMC or what action should be performed when the baby is hypothermic, then there is no point of installing a new device. He reported that yearly 2-3 neonates die at his NICU due to negligence, scarcity of staffs etc.
Peds_NZ_CS_012	3rd April 2019	In Person	Dr G mentioned that although he is aware of LBW and premature neonates being at risk for hypothermia he has rarely encountered in-born babies with hypothermia because actions to prevent hypothermia are already being taken before the neonate could experience hypothermia. But among referred cases hypothermia is detected on admission and prompt actions are being taken to maintain normal temperature. He said he will look at records regarding neonatal admission from the last month and get back to us. However after two days, he said he looked at 10-15 cases but did not come across any hypothermia cases.

Neo_JIP_MC_013	10th April 2019	Skype	Babies who are admitted solely for hypothermia are rare. In-born neonates who are referred to NICU- experience episodes of hypothermia transiting between mild and moderate, these neonates are kept under the warmer and their temperature is monitored throughout their NICU stay. There are many underlying cause due to hypothermia such as Sepsis and bleeding→ these cause of these are not direct for treatment of hypothermia. There are no studies or data recorded/documented these days regarding solely due to hypothermia, which would include the number of hospital stays, the transition rate between the different levels of hypothermia, etc. Transition rates are not fixed (these vary) and are therefore not documented. Treatment of hypothermia include: Rapid re-warming: When a neonate's temperature is less than 32oC- 100% heater input until baby reaches 34oC for around 15-30 mins. However rapid re-warming is not good can cause more damage however it is still carried out to avoid transition from one level to another, such as from moderate to severe. Slow re-warming results in 1 degree rise/hour therefore when baby reaches 34oC from the rapid re-warming then slow re-warming is carried out till baby reaches 36oC. Prolong hypothermia → when neonate is admitted and treated for 2-3 days before discharge. Dr N emphasized on: HYPOTHERMIC NEONATEs TAKES ONLY A FEW HOURS TO BECOME NORMOTHERMIC.
Neo_JIP_MC_014	17th April 2019	Email	In continuation with the Skype call held on the 10th April 2019, via email Dr T mentions "usually the baby will be hypothermic at the time of admission. After admission, the baby's temperature will be normalized in few minutes to hour's duration. The baby is then kept under radiant warmer continuously for few days before discharge. In a hospital environment, usually we have not encountered the same problem again. And now a days, no death we see due to hypothermia in hospitalized babies. If at all the baby have any episodes of hypothermia, usually it will be mild to moderate hypothermia and it will be corrected soon."

Table 9: Interview log with NICU and SNCU nurses:

Sl No.	Date	22/04/2019	22/04/2019	23/04/2019	24/04/2019	24/04/2019	25/04/2019	25/04/2019
	Questions/ Unique ID	Nnur_NZ_CS_001	Nnur_NZ_CS_002	Nnur_NZ_CS_003	Snur_GD_GovtS_004	Snur_GD_GovtS_005	Snur_GD_GovtS_006	Snur_GD_GovtS_007
1	Length of experience in NICU/SNCU	5 years	4 months	4 years	4 years	3 years	1 year	11 months
2	How many times in a day is the body temperature of a neonate measured? (The daily routine for temperature monitoring of a hypothermic neonate)	3 times per shift and there are 3 shifts (each shift= 6 hours). In addition to this when the neonate is crying, feeding and while changing the diaper. "Not all temperature readings are recorded, only when we have to make nurse reports when the baby has cold stress"	When needed; assess the body temperature during feeding and diaper changing; when baby cries.	Once in the morning and another in the evening.	Every 4 hours and if the baby is crying.	Every 4 hourly and when the nurse gives care to the baby, she also checks the body temperature.	Every 2 hours in addition to this during diaper change and when the baby is crying.	Temperature monitoring is done at every shift- maximum 5 times in 24 hours. At 6 am, 9/10 AM, 12 pm, evening and night time.
3	At what weight do you consider a	> 2500g	<2500 g	<2000g	<1800g	<2000 g considering the term babies while	<1800g	<1800g

	neonate to be LBW?					for preterm is 1800 g		
4	What is the temperature cutoff for hypothermia in LBW and premature neonates?	> 36oC	<98 F	31-32oC	<36oC for mild, <35oC for moderate and <32oC for severe. Cold stress when only the limbs are cold but the core (stomach) is warm- detect through hand touch.	<97.1 F	<96 F	95-98 F: Mild/Moderate; < 95 F: Severe
5	What is the average number of hospital stays for a hypothermic LBW or premature neonate at different levels of hypothermia? Mild, Moderate or Severe	Mild + moderate= 1-2 days. Severe= 1-2 week without complications and with complications it will be more than 1 week, however these are termed baby that weight >2500g. She mentioned that all LBW and premature neonates always stay for	Depend on the physician and the type of complication.	2-3 days under the warmer for cases without complications.	Hypothermic neonates who weight more than 1800g usually stay in the SNCU for 1 day but those that weigh less than 1800g then it can be up to 1 week on average. With Severe cases who also have complications it is between 45 days to 1 month.	5-6 days without complications and 20 days with complications.	Not sure but for mild and moderate cases the neonates only stay in the warmer for 15-20 mins and for severe 30 mins.	Not sure

		1 month till discharge and not solely because of hypothermia but due to complications.						
6	What are the complications associated with hypothermia?	Hypoglycemia, sepsis, low oxygen saturation and respiratory distress syndrome.	Sepsis, Hypoglycemia.	Low oxygen saturation, mild retraction and asphyxia.	Hypoglycemia, respiratory distress, respiratory rate >60, low oxygen saturation and cyanosis.	Cyanosis, lethargy, hypoglycemia and death.	Hypoglycemia and respiratory distress.	Hypoglycemia, sepsis and takes longer to gain weight.
7	What is the average number of hospital stays for neonates who are hypothermic with the said complications ?	Hypoglycemia: 1 month, Sepsis: 2-3 weeks, low oxygen saturation 2-3 weeks and respiratory distress: 1 month.	1-2 months	Not sure	All premature and LBW neonates that have hypothermia + complications and would stay between 1 month to 45 days.	Within 1 month	Not sure	Not sure
8	Approx. out of 100 LBW or premature neonates with severe hypothermia,	80%	90%	3-4/10 have complications	Almost 100%	5-6 babies out of 10	6 to 7 out of 10	Almost all severe cases of LBW and premature have complications however hypothermia is

	how many will have complications ?							not the "cause" this is due to their low weight.
9	What kind of signs and symptoms do you look for in a hypothermic baby?	Cyanosis, baby crying, not sucking well, limbs are cold.	Cold feet, baby crying, not sucking well.	Cold stress-less perfusion.	Crying, cyanosis, grunting and not sucking well.	Cyanosis, lethargic, limbs are cold, hypoglycemia.	Low glucose infusion rate, cold feet and distress.	Crying and not sucking well.
10	Please can you take me through your treatment protocol for treating hypothermic neonates? (From the time the baby is admitted to the NICU to the time the baby is returned back to the mother in the ward)	When the baby is admitted it is kept under the warmer and wrapped to keep warm. Warming of the baby is continued till it becomes normothermia . But if baby shows signs of distress/ keeps crying such retraction, low oxygen saturation and cyanosis, then different test are carried out	Assess the baby: Check the temperature by touch; check the weight: give colpol medication; sponging and kept on the radiant warmer.	The cold baby is placed under the warmer, which is usually for 2 -3 days and if the baby is responding well then it is moved to the cradle which is in the NICU and these are monitored for 3 hours before they are shifted to the mother in the ward.	Upon admission to the SNCU the neonate is placed in the warmer than the vitals, temperature, fluids, sugar level and oxygen saturation are measured and the neonate is treated for whatever complications it has and vitals are monitored.	Baby is kept in the warmer (temperature set at 36.5 degree Celsius), maintaining the room temperature by using heaters, radiators. When the baby is in cold stress then hot water bag is kept on the lower limbs, and assess the weight gain of the baby.	We place the neonate under the warmer and also put hot water bags on the foot of the neonate in some cases.	On admission the neonate is kept under the warmer. At first the probe is not attached, to allow the warmer to heat up then after the probe is attached to the neonate. The warmer raises an alarm if the temperature drops below the set set temperature.

		such as blood test and x-rays.						
11	Does the protocol vary with the different levels of hypothermia: Mild, moderate and severe	If it is severe then we inform the doctor but if it is just mild and moderate then we just keep the baby under the warmer and wrap it. For babies who have mild and moderate within 20-30 mins if will return to normothermia when actions are taken such as wrapping.	The care for the different levels of hypothermia varies with the temperature set at the radiant warmer. Decrease when the baby's temperature increases.	No it is the same protocol.	Does not vary but severe cases stay in the warmer longer as they take longer to become normothermic. On average the time it takes a hypothermic neonate between 15-30 mins to become normothermic when in the warmer.	No theres no difference because the skin probe attached to the baby's skin adjust the temperature of the warmer accordingly.	It does not vary, the time it takes for the neonate to become normothermic varies. Severe cases take longer.	Does not vary however mild and moderate cases become normothermic within 30 mins after being in the warmer and for severe cases it can take 1 to 1.5 hours.

12	Regarding putting the neonate under the warmer, how do you decide when the neonate needs to be kept under the warmer?	On admission the temperature of the neonate is measured/or hand touch - if the baby is found to be cold then the baby is wrapped and kept under the warmer.	The nurses at NICU will be informed regarding babies from the ward with hypothermia (usually with some other complication). On reaching NICU the baby is assessed. Baby's feet is touched for measuring temperature and weighed. Probe attached to the feet and radiant warmer is set as per the physician's order.	This comes with admission advice, if the neonate is to be kept under the warmer or on doctor's advice.	Mostly through hand touch child is found to be cold and the temperature is measured and neonate is admitted to the SNCU to be kept in the warmer.	All the babies admitted in the SNCU are kept in the warmer.	On admission the neonate is kept under the warmer and through hand touch method to see if the baby is cold.	Since the SNCU only has warmers, the neonate admitted to the SNCU is kept straight under the warmer.

13	When is it appropriate/ when do you decide to take the neonate out of the warmer?	Until doctor's advice. When the baby is stable: baby is maintaing oxygen saturation, temperature is normal, all blood reports are ok, baby is sucking well, no signs of distress, sugar levels are normal and no complications then baby is shifted to craddle. All these factors are monitored for since the day of admission.	When the physician gives an order. Usually when the baby is stable and with normal body temperature.	When the neonate is gaining weight, a preferred weight to discharge is 1.7 - 1.8kgs. The neonate is feeding well, normal temperature and there is also a 1-2 weeks.	Since the warmer is automatic where the probe placed on the side of the neonate's stomach, detects the skin temperature of the neonate therefore once the neonate's temperature is normal above 36.5oC then the warmer is turned off automatically. Therefore when the temperature of the baby is normal, sucking and feeding well, all vitals are normal and the mother is confident with taking care of the neonate.	When the baby' vital sings is stable and has gained appropriate weight.	When the neonate is responding.	The neonate is discharge when it shows weight gain, sucking well, sepsis screening is clear, sugar levels are normal and all vitals are normal.

14	Once the neonate is out of the warmer, where is it shifted to?	Craddle. But for LBW and Premature cases most of the time these are discharge directly from NICU to home.	Ward	From the warmer the baby is shifted to the craddle where it is monitored and if everything is ok, such as it is feeding well then it is moved to the ward with the mother.	Usually back to the ward with the mother but with premature and LBW neonates, once they gain adequate weight and has no complications they are directly discharge. Adequate weigh is equivalent to 1800g however there are cases where neonates that weighed lower than the 1800g were discharged but the minimum weigh of discharge is no less than 1500g.	To the mother or step -down sick babies or observation ward.	To the mother in the baby room.	The neonate is discharge to the baby room to be with the mother.
15	Have there been incidences where a neonate was taken off the warmer but had to be kept back on?	Yes	Yes	Yes	Yes	Yes, 1 out of 20 babies.	Yes	From experience I have not yet encountered such cases.

16	If so, approximately out of 100 neonates that are kept under the warmer and taken out, how many had to be kept back under the warmer and due to what reasons?	Most of the time if the baby is not stable then it will be kept back under the warmer.	Don't know	4 to 5 out of 10	20/100 for mild and moderate hypothermic neonates and those with complications.	5/100. Due to improper care by the mother, room temperature is not maintained.	4 to 5 out of 10 for mild and moderate cases. And 6 to 7 out of 10 for severe cases.	NA
17	What is the period (days) between the time the neonate was taken out of the warmer and the time it had to be kept back under the warmer? Does this period vary regarding the different levels of hypothermia? Mild, Moderate and Severe.	For mild and moderate: 5 to 6 days. And for severe cases: 2-3 days.	Approximately 12 hrs to a day.	5 to 6 hours.	2-3 days for mild and moderate cases.	Within 1-2 days	1 day	NA

18	What temperature is the warmer set to? And what is the room temperature in the NICU or SNCU?	Temperature of the warmer is to 35oC. RT:36oC	Radiant warmer- 10oC; Room AC-30oC	RT: 25- 27oC	36.5oC - the warmer and the room temperature is usually between 25-28oC. There is no AC but temperature is monitored using a room thermometer and during the winter when it gets too cold then heaters are being used.	Warmer is set at 36.5 degree Celsius, room temperature is 25 degree Celsius.	36oC	Skin temperature set to: 30oC and RT: 25-28oC
19	Are all the warmers accompanied with a thermistor that monitors the baby's temperature 24/7?	Yes	Yes	Yes	Yes	Theres a skin probe which continuosly monitors the skin temperature of the baby, however sometimes more than one babies are being kept in the same warmer.	Yes.	Yes but only one skin probe per warmer. The skin probe is attached to the abdomen of one neonate and it adjust the temperature to this neonate accordingly. Therefore when there is more than one neonate under the warmer it puts the other neonates who's skin is not in

								contact with the probe, at risk.
20	How many neonatal referral cases do you get in a month?	Too many. Out of 100 cases, 80 are LBW or premature.	Don't know	Around 10	30-40 cases	3-5 days	3 to 4 neonates referred in a day and 1 LBW neonate per week.	It varies
21	Approx. out of 100 referred neonatal cases what were the number of cases among these who were LBW or premature with cold stress or hypothermia?	80 out of 100. Referral cases always come in with cold stress.	80%	Very rare, maybe around 2-3 out of 10 neonates with hypothermia.	5%	4 out of 10 cases	Very rarely but they do get admitted with hypothermia.	5 out of 10

22	Have you ever encountered death due to a) hypothermia or b) related to hypothermia? If so, approx. out of 100 how many?	A) Yes: 2 or 1 out of 100. Because we are already aware that LBW and premature neonates are at risk of hypothermia, extra percuations are taken for these neonates. B) Yes- 50 out of 100 due to several complications not just one.	Don't know	This is also very rare.	0 due to hypothermia alone	1 out of 10 babies	I have never encountered such cases.	Death due to hypothermic related cases is approx 3 in a month.

23	Additional info	The NICU consist of warmers and craddles. The NICU also has AC that maintains room temperature. The warmer has two modes: manual and baby mode. With the manual mode the temperature of the warmer can be set by the nurse but with baby mode the probe is attached to the feet of the baby and the probe adjust the temperature of the warmer accordingly. In Nazareth manual mode			On discharge the mother is well taught about KMC, breastfeeding, signs of hypothermia and keeping the baby warm and how important all these factors are. Do not admit neonates that are more than 28 days old.			Babies that are more than 28 days old are usually not admitted into SNCU except on doctor's advice.

		is used mostly because most of the time the baby's body is warm but the feet remain cold and with baby mode, it requires the probe to be attached to the feet of the baby.							

11.4. Decision tree model and assumptions used in the model

Figure 0-13: Decision tree model for SoC

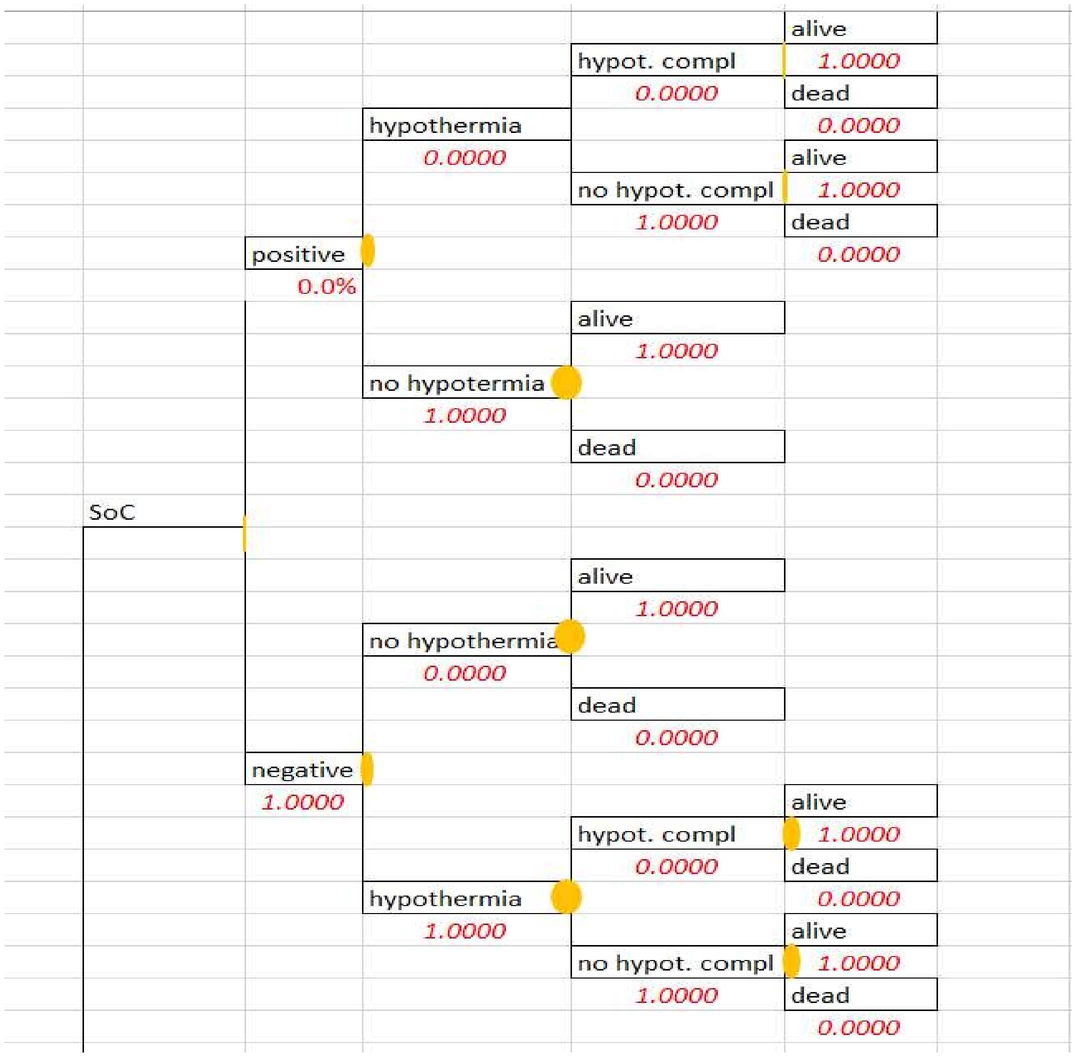


Figure 0-14: decision tree model for Bempu

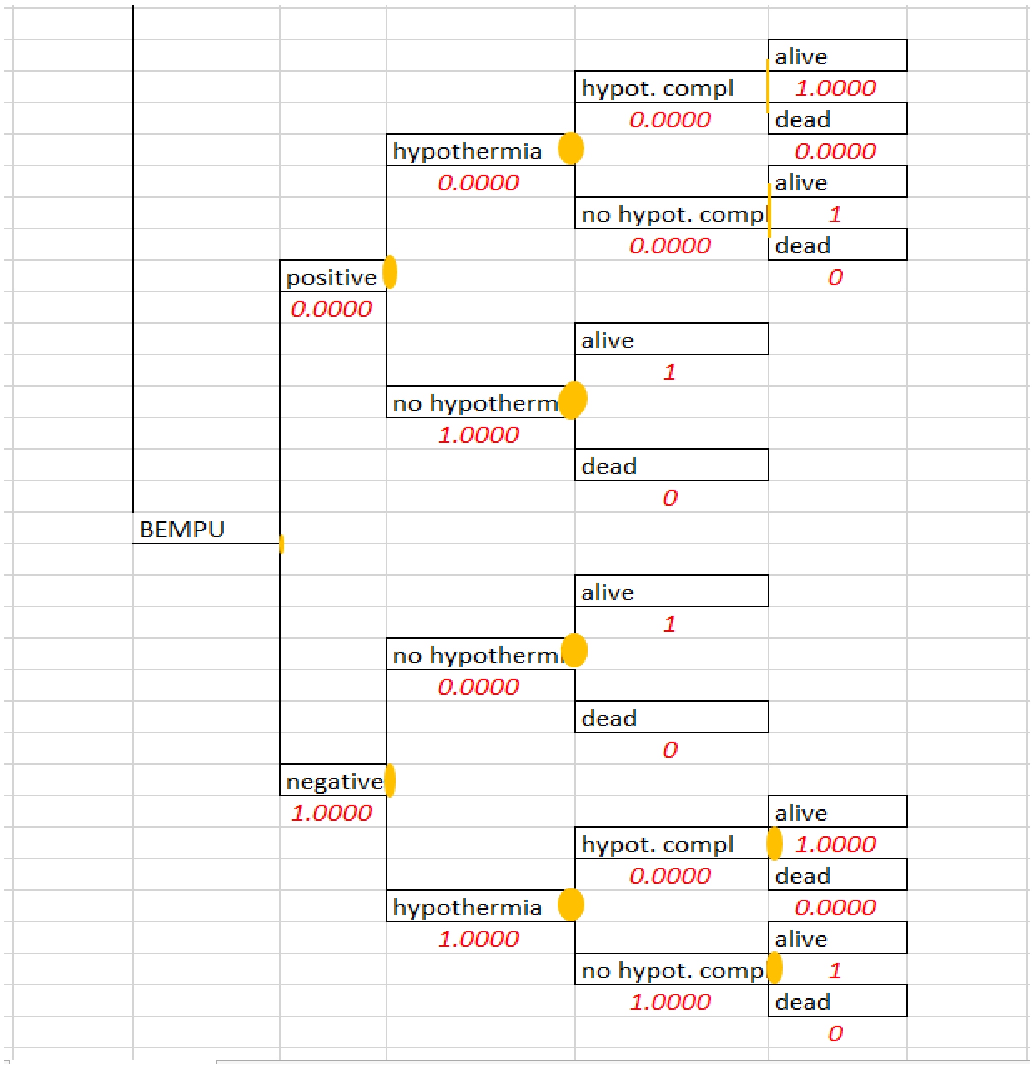


Figure 0-15: Decision tree model for Thermospot:

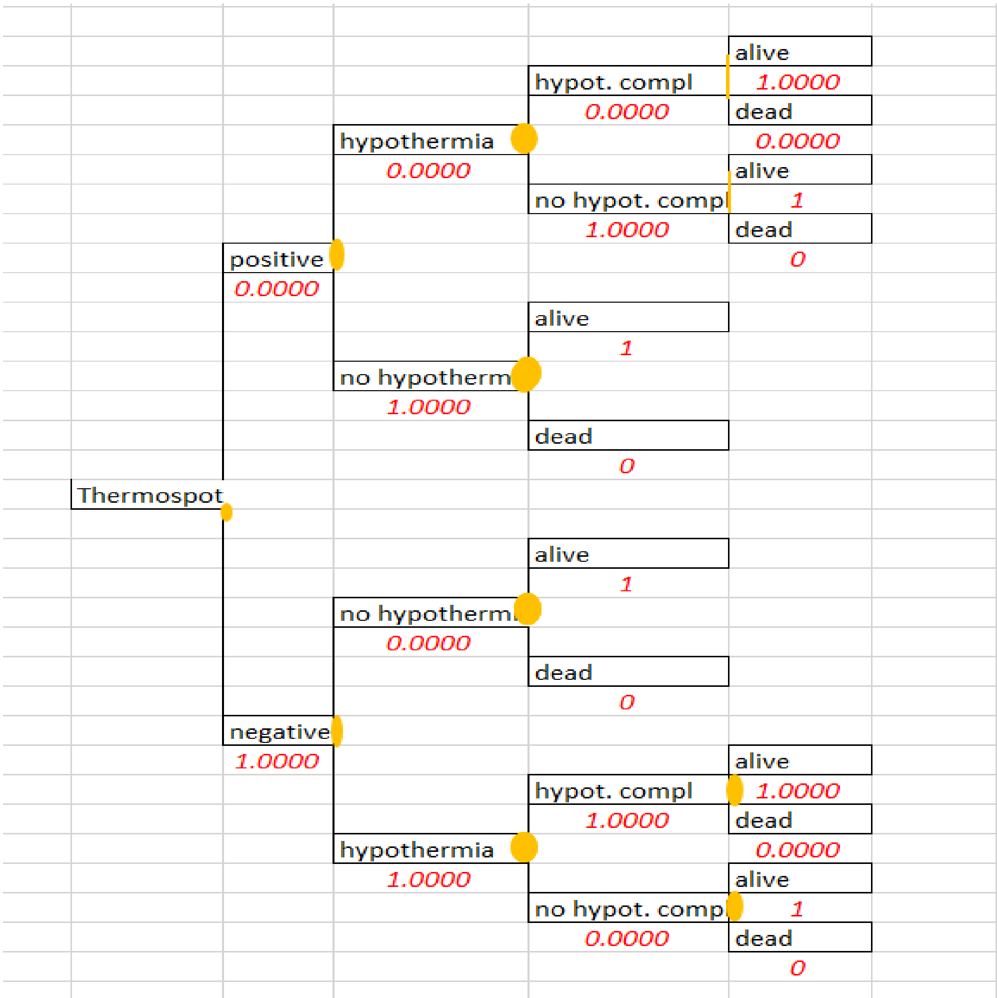


Table 10: Assumptions in the model:

Sl. no	Assumptions
1	Neonates with mild hypothermia are early detection cases
2	Neonates with moderate/severe hypothermia are late detected cases
3	Neonates with mild hypothermia do not have any complications
4	Neonates with severe hypothermia must have at least one hypothermia related complications
5	Thermometer is the gold standard device for detecting hypothermia. Hence it has 100% sensitivity and specificity
6	Response rate after detection of hypothermia, only impact mortality rate due to hypothermia. If response rate decreases, mortality due to hypothermia will increase and vice-versa.