HEALTH TECHNOLOGY ASSESSMENT OF UTERINE BALLOON TAMPONADE FOR MANAGEMENT OF POSTPARTUM HAEMORRHAGE IN INDIA

HTA Regional Resource Hub

National Institute for Research in Reproductive Health
ICMR, Mumbai

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Health Technology Assessment (HTA) Resource Hub

National Institute for Research in Reproductive Health

Indian Council of Medical Research

Mumbai

December 2019

Supervised by: Dr. Beena Joshi
Assisted by: Dr. Oshima Sachin

Compiled by

Dr. Kusum V. Moray, Dr. Siddesh Shetty, Mr. Nazim Mondal, Dr. Akshay Shrinath and Mr. Himanshu Chaurasia

HTA Resource Hub
ICMR- NIRRH Mumbai

LIST OF ABBREVIATIONS

AMTSL	Active Management of Third Stage of Labour
BEmOC	Basic Emergency Obstetric care
CEmOC	Comprehensive Emergency Obstetric care
DALY	Disability Adjusted Life Years
DCGI	Drug Controller General of India
DH	District Hospital
DHR	Department of Health Research
ESM-UBT	Every Second Matters for Mothers and Babies Uterine Balloon Tamponade
FP2020	Family Planning2020
FIGO	International Federation of Gynecology and Obstetrics
GOI	Government of India
GDG	Guideline Development Group
HMIS	Health Management Information systems
HRQoL	Health-related Quality of Life
HTA	Health Technology Assessment
ICER	Incremental Cost Effectiveness Ratio
ICMR	Indian council of Medical Research
ICM	International Confederation of Midwives
ICU	Intensive care unit
ICUR	Incremental cost-utility ratio
IUD	Intra Uterine Device
INR	Indian Rupee
IPD	In Patient Department
IV	intravenous oxytocin
JSY	Janani Suraksha Yojana
JSSK	Janani Shishu Suraksha Karyakaram
LMIC	Low and middle income countries
LSCS	Lower Segment Cesarean Section
MGH	Massachusetts General Hospital
MMR	Maternal Mortality Ratio
MeSh	Medical Subject Heading
mCPR	Modern method couple protection rate
NHB	Net health benefit
NIRRH	National Institute for Research in Reproductive Health
NMB	Net monetary benefit
OBGYn	Obstetrics and Gynaecology
OOP	Out of Pocket (expenditures)
OT	Operation Theatre
PICOS	Population - intervention - comparator - outcomes - study design
PHC	Primary Health Care

PPH	Post-partum haemorrhage
QALY	Quality Adjusted Life Years
QoL	Quality of Life
RCT	Randomized Controlled Trial
RGI	Registrar General of India
SC	Sub Center
SC/ST	Scheduled Caste and Scheduled Tribes
SDH	Sub-district hospital
SRS	Sample Registration System
SDG	Sustainable Development Goals
UBT	Uterine Balloon Tamponade
USD	United States Dollar
USFDA	US Food and Drug Administration
UHC	Universal Health Coverage
UNFPA	United Nations Fund for Population Actions
UNICEF	United Nations International Children's Emergency Fund
WB	World Bank
WHO	World Health Organization
WTP	Willingness to pay

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EXECUTIVE SUMMARY

In the year 2015, there were an estimated 303,000 maternal deaths globally. Nearly 99 % of all maternal deaths occur in developing countries with more than half of them occurring in sub-Saharan Africa and one third occurring in South Asia. Sample Registration System (RGI-SRS) for period 2014-16 states maternal mortality ratio to be at 130 deaths per 100,000 live births. One of the top preventable and treatable causes of maternal death is post-partum hemorrhage.

Operational Guidelines on Maternal and Newborn Health in India (NRHM) for management of PPH, Guidance Note on PPH management and Dakshata Guidelines recommend use of intrauterine balloon tamponade for uterine atony cases or refractory bleeding cases when medical management fails. There are a number of Uterine Balloon Tamponade devices available across the world. The guideline documents in India mention the assembled 'condom uterine balloon tamponade device'. The market offers a few 'packed UBT' devices like Bakri UBT. Some developing countries have also tried out the Ultra-Low Cost ESM-UBT (Every second Matters). This health technology assessment aims to assess the most cost-effective option for use in public health settings in India i.e. Condom UBT, ESM -UBT and Bakri UBT.

Our objectives were to assess clinical effectiveness profile of the three uterine balloon tamponade techniques currently used in India for management of atonic type of postpartum haemorrhage and to evaluate cost-effectiveness of Condom Uterine balloon device (that has been recommended in Govt. of India's guidelines for management of PPH) against ESM-UBT and Bakri uterine balloon tamponade techniques available for management of atonic type of postpartum hemorrhage.

A decision tree model was used for a hypothetical cohort of women with atonic PPH in India. Input parameters for the model were derived from literature review and a primary costing study across five public health centers in Maharashtra centers. The structure of the tree simulated real world settings, at three levels of healthcare in India. Three decision trees for each of the three alternatives (ESM UBT, Condom UBT & Bakri UBT) were constructed and costs, QALYs, DALYs, maternal deaths and surgeries were obtained from these trees. The primary outcomes of ICUR for QALYs and DALYs were calculated. Maternal deaths averted and net health and monetary benefits by each of the three alternatives were calculated. The three alternatives

assumed that all women (100%) who were eligible to get UBT would receive that particular type of UBT.

We have considered the effectiveness of condom UBT, ESM UBT and Bakri UBT to be 93%, 95% and 86% respectively, from available literature. The price of condom UBT, ESM UBT and Bakri UBT were taken to be INR 128, INR 397 and INR 9554 respectively. The total costs from the model from societal perspective for one woman using condom UBT, ESM UBT and Bakri UBT was INR 13,672, INR 12,096 and INR 22,301. The QALYs per woman in condom UBT, ESM UBT and Bakri UBT were 23.767, 23.769 and 23.763 respectively; showing a very minute difference in QALYs.

HTAIn reference case recommends use of QALYs as primary outcome measure. For ESM UBT vs. Condom UBT, the ICUR is -12,05,590 INR /QALY and hence ESM UBT is more cost-effective than Condom UBT. The negative sign indicates that there is a saving of 12,05,590 per QALY gained with the use of ESM-UBT. However the incremental QALYs gained by ESM UBT as compared to condom UBT was very minimal; the incremental cost was negative, as ESM UBT was less expensive(in spite of higher product cost that condom) due to its reported better clinical effectiveness that reduced the probabilities of surgeries and thus the costs. The efficacy of ESM-UBT is based on three case series, the only available published literature on the same. ICUR of Bakri UBT vs. Condom UBT is -17,51,769 indicating that Bakri UBT is not cost-effective as compared to condom UBT.

Maternal deaths that occurred as per the model in each of the three alternatives were compared with the maternal deaths of current scenario (i.e. Condom UBT). Condom UBT, ESM UBT and Bakri UBT were found to avert 10,038, 10,041 and 10,027 maternal deaths respectively; showing minimal difference. One-way sensitivity analysis shows that the efficacy of Condom UBT and ESM UBT are among the top ten factors that influence the ICUR. The probabilistic sensitivity analysis shows that there is some degree of uncertainty around the model results and majority of 57.2% simulations show ESM is not cost-effective. .The cost-effectiveness acceptability curve shows that above the willingness to pay threshold of INR 19,109 the curve plateaus to show that only about 43% of the 1000 simulations will be cost-effective. Hence the final outcome of the model that ESM UBT is cost-effective as compared to condom UBT should be viewed with restraint even though the ICUR is below the GDP per-capita. It is also

noteworthy to observe that the difference of the total costs as well as QALY is marginal between ESM and Condom UBT use.

As there were multiple mutually exclusive UBT alternatives, net health benefits (NHB) and net monetary benefits (NMB) were calculated. NHB of ESM UBT is 23.68, of condom UBT is 23.67 and of Bakri UBT is 23.60. All three UBTs have NHB>0, hence they are all cost effective. Although NHB is highest for ESM UBT, the incremental NHB between condom UBT, ESM UBT and Bakri UBT is minimal. At the WTP threshold of ₹ 1, 38,468.76, ESM UBT, Condom UBT and Bakri UBT provide NMB of ₹ 32,79,133, ₹ 32,77,376 and ₹ 32,68,065 respectively. Again the highest NMB is seen in ESM UBT with very minimal difference between condom UBT and Bakri UBT.

Budget impact analysis shows that, at 100% coverage of ESM-UBT, annual additional budget required for introduction of ESM UBT into India's public health system is estimated to be 0.004% of the total health budget and 0.005% of the total maternal and child health budget. However, if the coverage reduces to 50%, the percentages increase to 0.02% of the total health budget and 0.03% of the total maternal and child health budget.

Limitations of our study:

- The efficacy value of ESM UBT that has been used in the model was derived by taking averages of values from three case series conducted in other LMICs that were of fair quality, due to lack of any robust meta-analysis/ randomized control trials. Also one of the draw backs of ESM UBT is that the health provider cannot assess the amount of blood flow after its insertion, which is an advantage when modified Condom UBT i.e. Chhattisgarh UBT or Bakri UBT is used. The efficacy of ESM-UBT needs to be established with RCTs and better quality evidence in Indian setting is required, as the current evidence for ESM is limited.

- The cost of ESM-UBT has been taken as INR 397 in the model. The exact price of the product if introduced into the public health system in India needs to be estimated.

- The coverage of ESM-UBT in the model has been assumed to be 100%. This needs to be looked at with a pragmatic lens as informal discussions with health providers revealed

that use of UBT is not universal and no reported evidence is available about it's use in India

- Preventing maternal deaths has numerous consequences, and not all can be quantified based on monetary terms. Beyond the obvious benefit of DALYs saved for mothers, the other benefits include the fact that reducing maternal deaths ensures that more children grow up with their mother's care improving their health and education. Our model accounts for only a few benefits of the intervention and comparators; and not all the above mentioned benefits. Hence a complete valuation of costs has been done, but a complete valuation of benefits has not been done underestimating the benefits of the interventions.

- Utility weights used in our model are from studies done in western settings. Indian utility weights would have been more appropriate. Specific utility scores for the use of individual devices are not available.

- Primary health system costing study was done in a few public health centers in the state of Maharashtra. The costs may not be applicable across the different states of India (This was addressed in the sensitivity analysis).

- The group of surgeries that we have included in our model under the heading of "devascularization surgeries" includes the most commonly done ones such as uterine artery/iliac artery ligation and B-Lynch suturing. It does not include embolization of arteries which is a very specialized facility done by intervention radiologists. Hence cost of devascularization group of surgeries excludes cost of embolization.

Recommendations from this HTA:

- QALY gain in ESM UBT and Condom UBT are very similar. ICUR value of ESM UBT against Condom UBT shows that ESM UBT is cost-effective, but the probabilistic analysis shows that a majority of 57.2% of the simulations show that ESM-UBT is not cost-effective. We recommend that good quality efficacy data on ESM-UBT should be

generated by doing RCTs in Indian settings, before any decision regarding the same is undertaken

- Based on net health benefits, there is less than 0.1 difference between the three alternatives; indicating the similarity in health benefits of the three UBTs.
- Considering the above statements, decision-making regarding ESM UBT's introduction into the public health system must be made with caution. Also, studies on ease of use by Indian healthcare providers and qualitative aspects need to be conducted and its actual costs for use in public health system need to be derived.
- If ESM-UBT is considered for introduction, it should be noted that to gain the benefits estimated by the model, a universal coverage needs to be attained (100%) which currently seems to be very challenging given the current poor use of condom UBT in spite of being recommended in the Govt. of India Guidelines .

CHAPTER 1: BACKGROUND

Maternal deaths in Global and Indian context

Every day 830 women around the world die from preventable causes related to pregnancy and childbirth. In the year 2015, there were an estimated 303,000 maternal deaths in the world. Nearly 99 % of all maternal deaths occur in developing countries with more than half of them occurring in sub-Saharan Africa and one third occurring in South Asia (1–3). Major complications accounting for nearly 75 percent of all maternal deaths are severe bleeding, infection, high blood pressure and delivery related complications. Postpartum haemorrhage is the largest direct cause of maternal deaths with about 14 million women around the world suffering from it (4,5). The causes are preventable and treatable; hence managing and taking care of women during and after pregnancy remains the cornerstone of improving overall maternal health. The Sustainable Development Goals – Goal 3 prioritizes reduction of global maternal mortality ratio to less than 70 per 100,000 live births by 2030 and to increase the proportion of births attended by skilled health personnel as its primary target. In the year 2018, 81.1 per cent births in the world had been reported to be attended by skilled health personnel.

India has shown tremendous progress in maternal health in recent years indicated by reducing maternal mortality by 77 per cent from 556 per 100,000 live births in 1990 to 130 per 100,000 live births in 2016. The key actions India focussed on, for such an improvement included institutionalization of deliveries, providing schemes such as the JSSK, improving demand side financing, addressing social determinants such as literacy of women and improving public-private engagements amongst other actions to capitalize on improving maternal health (5). Despite such progress, out of the 303,000 maternal deaths in the world in 2015, 45,000 or nearly one-sixth of the total deaths occurred in India contributing to second highest number of maternal deaths by a country behind Nigeria (6).

Latest figures released by Registrar General of India – Sample Registration System (RGI-SRS) for period 2014-16 states maternal mortality ratio to be at 130 deaths per 100,000 live births (NHM website). Indian National health policy target is to reduce MMR to 100 per 100,000 live births by year 2020. India has set a target value of reducing maternal mortality to 70 deaths per 100,000 live births by 2030 to achieve its SDG target (7).

Indian HMIS report for 2015-16 shows bleeding to be the major contributor to maternal deaths in India accounting for nearly 15.1 per cent of all maternal deaths. Bleeding followed by

hypertension or fits at 10.7 per cent, prolonged labour at 4.3 per cent, high fever at 2.9 per cent and abortion at 1.6 per cent were the direct major causes of maternal deaths in India. Indirect causes such as pre-existing disease accounted for 65.4 per cent of the total maternal deaths (8).

Improving maternal and child health and their survival are central to achievement of the national health goals envisaged by the National Health Mission which ultimately aim for attainment of universal access to equitable, affordable and quality health care services which is accountable and responsive to people's needs by addressing wider social determinants of health. One of the key programmatic components under the NHM is the Reproductive, Maternal, New born, Child and Adolescent Health Services **(**RMNCH + A) which has one of its primary objectives to be reduction in maternal mortality. The RMNCH+A is built upon the continuum of care concept and encompasses all interventions aimed at reproductive, maternal, new born, child and adolescent health. The RMNCH+A strategizes by prioritization of high-impact interventions and increasing effectiveness of investments based on regional, cultural and economic diversity within the Indian population with available limited resources catering to the large population, prioritizing to ensure larger benefits to the entire population (9).

Postpartum Haemorrhage

Postpartum Haemorrhage (PPH) is commonly defined as blood loss of 500 ml or more within 24 hours after birth. Blood loss of more than 1000 ml in the same time frame is labelled as severe PPH. PPH affects approximately 2 per cent of all women who give birth. It is estimated that about 2-4 per cent of vaginal deliveries and 6 per cent of all LSCS suffer from PPH (10). Uterine atony is the most common cause of PPH, but genital tract trauma, uterine rupture, retained placental tissue and coagulation disorders also lead to it. PPH complications have no identifiable clinical or historical risk factors but grand multiparity and multiple gestations are associated with increased risk of bleeding after birth. Further, conditions such as widespread anaemia in pregnant women exacerbate the condition resulting in adverse clinical sequelae thus proving to be a major challenge in the Indian settings. The Indian guidance note on prevention and management of PPH for the year 2015 observed preference for home deliveries to be a key contributory factor for maternal deaths in India. This compounded by poor quality of care at health facilities, late referrals, shortage of necessary drugs and equipment, inadequate transportation and poor decision making adds to women not getting adequate care during this emergency. Interventions

such as birth preparedness, high quality antenatal care, timely detection, referral and appropriate management all collectively play a part in preventing and managing PPH cases.

Guidelines for PPH Management

The Guideline Development Group (GDG) of the World Health Organization (WHO) in 2012 recommended use of uterotonics as the main intervention within active management of third stage labour for prevention of PPH. For settings where skilled birth attendants are not present, misoprostol use by community health care workers has been supported by the WHO guideline (11). The Indian guidance note focuses at community and facility level interventions for prevention of PPH. Birth preparedness, promotion of skilled attendant at birth, early detection of anaemia and misoprostol at community level along with treatment of anaemia, limiting episiotomy and active management of third stage of labour form the mainstay framework for preventing PPH. For treatment the WHO Guideline Development Group (GDG) recommends Oxytocin (first choice uterotonic) to play a central role in PPH management. Supportive measures such as uterine massage and resuscitation with isotonic fluids have also been recommended. For refractory bleeding or in settings where uterotonics are unavailable, tranexamic acid or intrauterine balloon tamponade has been recommended. Measures such as bimanual compression, external aortic compression and non-pneumatic anti-shock garments maybe used as temporizing measures until substantive care is made available. For persistent bleeding where relevant resources are available, uterine artery embolization may be considered. If bleeding persists, despite treatment with uterotonic drugs and other conservative interventions, surgical interventions are to be used without further delay (11).

Indian facility level guidelines for PPH treatment suggests active management of third stage of labour (AMTSL) to be the most important element for preventing PPH in a facility. For treatment, intramuscular oxytocin alone is the recommended uterotonic choice of drug. IV Oxytocin or methergine or tranexamic acid for refractory cases may be considered next. Use of intrauterine balloon tamponade is recommended for uterine atony cases or refractory bleeding cases. This has been observed as a step to avoid surgery and also as a measure to transfer these patients to a higher facility. Use of bimanual uterine compression and external aortic compression has been recommended for uterine atony cases after vaginal birth. Surgical

interventions (Modified B-Lynch) have been recommended if the above measures fail to control bleeding.

The Indian guidance note on prevention and management of PPH recommends use of intrauterine balloon tamponade for treatment of PPH due to uterine atony, for women who fail to respond to uterotonics and in cases where uterotonics are not available. Use of uterine balloon tamponade is seen as surgery avoiding step, and has been found appropriate for women awaiting transfer to a higher facility. This life-saving technique limits the on-going uterine blood loss and is relatively simple and effective approach at managing PPH. The intervention involves inserting a balloon device into the uterus and incrementally filling with liquid which slowly applies pressure to the uterus until bleeding stops. Effective tamponade occurs rapidly within 5 to 15 minutes after insertion and inflation of balloon. The World Health Organization (WHO), the International Federation of Gynaecology and Obstetrics (FIGO), the American College of Obstetricians and Gynaecologists, the Royal College of Obstetricians and Gynaecologists, and the International Confederation of Midwives (ICM) recognize balloon tamponade as a method that could significantly improve the management of intractable PPH, especially in low-resource areas where blood transfusions are not available and surgical interventions are not an option (12,13).

Indian guidance note recommends initial resuscitation and IV oxytocin infusion to be administered followed by options such as uterine massage, bimanual or external aortic compression or a balloon or condom Tamponade before referring the woman. But as Mukherji et al have reported, 58 per cent of maternal deaths occurring due to haemorrhage were actually due to PPH, resulting from lack of provision of emergency transport at community level. Lack of blood transfusion services, anaesthetist availability and operating capabilities further add to the need for a woman to be referred for continuity of care during PPH. As complications associated with PPH are acute and potentially fatal in nature, availability of equipment, medical supplies such as emergency drugs and formal protocols for referral need to be ensured at every level of care.

Types of Uterine Balloon Tamponade:

Bakri balloon tamponade: The concept of intrauterine balloon technology was first published by Bakri for management of haemorrhage due to placenta praevia-accreta during caesarean section (14). It was first used by Bakri in 2001 in 6 women and has been consequently used

extensively (15). Currently used specifically for postpartum haemorrhage, it is an inflatable balloon device made of silicone. It is 54 cms long double lumen shaft and can fill up to 800 ml but it is recommended to not exceed 500 ml of saline. The tip of the silicone tube has two holes for drainage; so on-going blood loss can be detected after insertion of balloon. The Bakri balloon has US Food and Drug Administration (USFDA) clearance for specific application to PPH. The device comes with 60 ml syringe for filling (16–18). The cost of this device in India is approximately INR 9500, and hence is used in private sector.

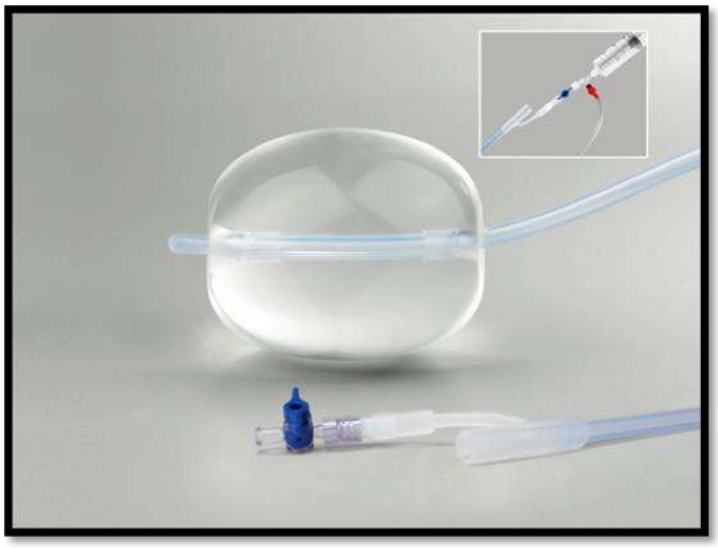


Figure 1: Bakri Uterine balloon tamponade (Image source: Cook Medical Products(19))

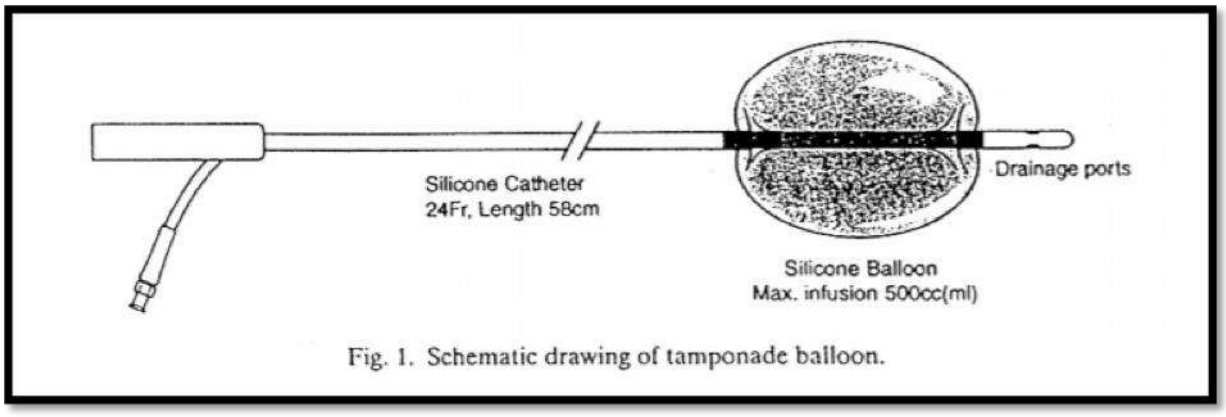


Fig. 1. Schematic drawing of tamponade balloon.

Figure 2: Schematic diagram of Bakri UBT with parts labelled (Image source:(20)**)**

Condom Catheter: The idea of using condom as a balloon tamponade was first generated and evaluated in Bangladesh in 2001 in response to the high cost of commercially available UBT

devices. The condom catheter is assembled at the point of use and consists of readily available components (male latex condom, an 18 or 22+ rubber catheter, and a string to tie the condom to the rubber tube). An IV infusion set can be used to fill the condom catheter, or it can be filled using a plastic syringe (50 cc to 100 cc). The cost of the condom catheter is low, estimated in the range of INR 100- INR 150. The condom catheter is an improvised device that relies on the availability, quality of the components and the skill of the health care provider in assembling and using the device

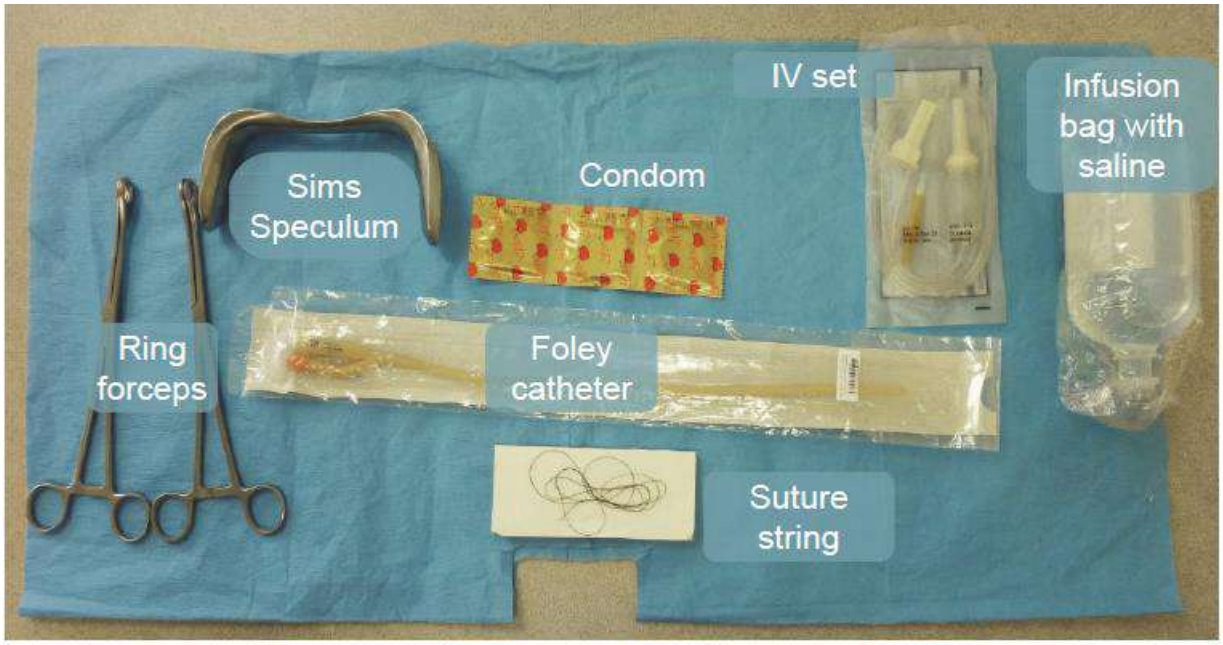


Figure 3: Condom Uterine balloon tamponade (Image source: Jhpiego(21))

CG Balloon: Named as 'CG balloon' as it was invented in Chhattisgarh, India. It is a further modification of condom UBT prepared manually under aseptic precautions. It has added advantages of a drainage port to assess blood loss and lack of need of an additional thread or suture material to tie the condom to the catheter. It instead uses a ring cut from the distal end of the drainage tube of the Foleys catheter

Sengstaken-Blakemore tube: Single or multiple Foleys catheters have been used for management of PPH. However, volume of postpartum uterus was considered too large for effective tamponade. So, Sengstaken-Blakemore tubes, originally designed for management of bleeding oesophageal varices have been used. The distal gastric balloon and subsequently the

oesophageal balloon of this tube have been used. It is relatively the costliest of all the tubes mentioned here and isn't primarily designed for managing PPH (14).

Every Second Matters – Uterine Balloon Tamponade: ESM –UBT is an ultra-low-cost (less than INR 400) device consisting of a condom tied to a Foleys catheter, inflated with clean water through a syringe and a one way valve. It is a low cost alternative to other manufactured balloons which are relatively expensive costing as much as INR 9500 apiece. The MGH Division of Global Health and Human Rights developed this device and have demonstrated its effectiveness (22).

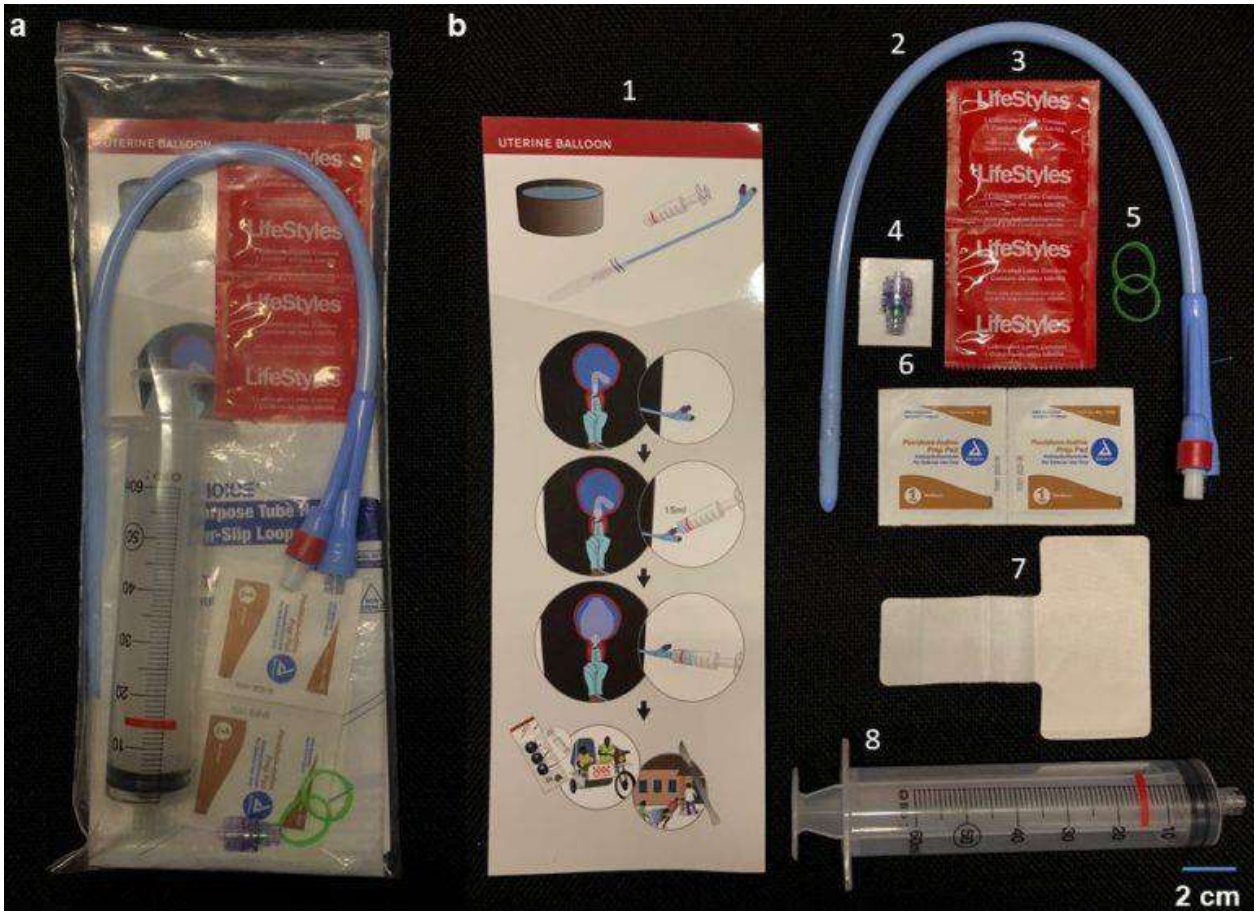


Figure 4: Every second matters Uterine balloon tamponade a) Every Second Matters for Mothers and Babies – Uterine Balloon Tamponade (ESM-UBT) package. b) ESM-UBT package made of 8 components: 1/Instruction card, 2/2-way Foley catheters (retention catheters), 3/Condom, 4/Check valve for injection site, 5/O-Rings, 6/Povidone-iodine prep pads, 7/Catheter Holder, and 8/Syringe**. (Image source:** (23)**)**

BT-Cath®: Is made of silicone and comes equipped with a lumen that allows health providers to monitor intrauterine blood drainage and assess effectiveness of the tamponade. The intrauterine drainage port is flush with the top of the inflated balloon (no tubing protruding from the balloon), allowing placement near the uterine fundus. Check valves simplify and expedite the inflation process. The BT-Cath® is USFDA approved and patents are pending (24).

Rusch tube: Factors such as cost and balloon size have resulted in use of the urological Rusch balloon for tamponade in PPH cases (14).

Need for Health Technology Assessment on Uterine Balloon Tamponade:

Given the availability of different types of uterine balloon tamponade and effectiveness of UBTs in management of PPH, the Indian government is keen on introducing a cost effective uterine balloon tamponade in the public health system. Published evidence highlights clinical efficacy of low cost ESM-UBT device in many developing countries. Literature is also available for clinical effectiveness of Bakri and condom UBT devices across various regions. Cost effectiveness evaluations have been carried out for uterotonic drugs such as oxytocin, misoprostol, etc. (25–27). However, very few studies have been conducted to date which model cost effectiveness of uterine balloon tamponade for controlling PPH in LMICs (32,33). Further, no studies describe cost effectiveness of uterine balloon tamponade in India. Hence, objective of the present study is to evaluate cost effectiveness of uterine balloon tamponade devices (ESM-UBT and Bakri UBT) against standard of care (Condom catheter, recommended in guideline) to aid the policy makers in decision making whether there is a need to introduce a new device into the public health system of India.

The above mentioned devices were taken into consideration after discussion with experts and health care providers in India. These two devices have been used in various centres across the country depending on availability and affordability. None of the experts mentioned using other devices mentioned above. There are many modifications of the condom balloon, like the CG balloon. These have been considered under condom UBT in our HTA.

Research question

Which uterine balloon tamponade is cost effective and can be introduced into the public health system in India?

Aim

Aim of this health technology assessment is to evaluate and compare costs and consequences of uterine balloon tamponade techniques available to identify the most cost-effective treatment for postpartum haemorrhage due to uterine atony in the public health system of India.

Objectives

1. To assess clinical effectiveness profile of various uterine balloon tamponade techniques currently available for management of atonic type of postpartum haemorrhage.

2. To evaluate cost-effectiveness of Condom Uterine balloon device against ESM-UBT and Bakri uterine balloon tamponade techniques available for management of atonic type of postpartum haemorrhage.

PICOT OF THE STUDY

Population

Women with atonic PPH in whom medical management has failed

Intervention

1. Every Seconds Matter-Uterine Balloon Tamponade (ESM-UBT)
2. Bakri Uterine Balloon Tamponade

Comparators

Condom Catheter that is Standard care in India for the management of PPH as per Guidelines

Primary Outcomes

- Incremental Cost Utility Ratio in terms of cost per QALY gained
- Incremental Cost Effectiveness Ratio in terms of cost per DALY averted

Secondary Outcomes:

- Number of surgeries averted
- Number of deaths averted

CHAPTER 2: METHODOLOGY

The Methodology of the study follows the steps of a HTA. We retrieved, in a systematic manner, the available evidence on the HTA topic. A decision analytical model was constructed based on literature and expert opinion. The necessary steps were taken to populate the model. The steps of the HTA are listed and elaborated below.

I) CONCEPTUALISATION OF THE DECISION ANALYTIC MODEL –DECISION TREE

Rationale for decision tree:

Decision tree was deemed to be appropriate because the occurrence of postpartum haemorrhage (PPH) is an emergency situation and the entire event occurs over a short duration after delivery which needs immediate intervention. PPH does not last for a prolonged duration and the flow of events i.e. health states are progressive in nature without possibility of coming back to the previous health state. A woman experiencing PPH can be cured by using available interventions and the events occur in a sequential pattern. For these reasons, a decision tree type of decision analytic model was used over other decision analytical models.

Assumptions made in the Model:

i. UBT is being considered only in atonic PPH cases after ruling out all other causes of bleeding.

ii. UBT is being considered only after all medical management fails. Medical management includes Intramuscular oxytocin which remains the uterotonic drug of choice, bleeding uncontrolled by IM oxytocin should be administered IV oxytocin or IV methergine as the next uterotonic drug. Additional measures such as intravenous isotonic crystalloids, maintaining airway, breathing and circulation are essential. It is expected that these measures are being undertaken for all women experiencing atonic PPH and have been accounted for in our model.

iii. External aortic compression and bimanual uterine massage is carried out simultaneously along with UBT insertion.

iv. Parallel management for complications such as shock, septicemia, etc. with uterotonic, IV fluids, blood transfusion, antibiotics etc. is continued along with regular monitoring of vital parameters and blood loss throughout the course of management of PPH along with and after UBT intervention.

v. Prompt transport arrangements are made for referrals to higher facilities when no surgical infrastructure/manpower is available.

vi. Prompt measures for surgical procedure if needed are made ready at facilities that have infrastructure for surgical interventions.

vii. It is assumed that at primary level, all women after UBT insertion will be referred.

viii. However outcomes and costs incurred after referral are accounted for at that level only

ix. The three UBT alternatives assumed that all women (100%) who were eligible to get UBT would receive that particular type of UBT.

After insertion of UBT, medical management and measures to control PPH are considered to occur concurrently and have been accounted for in costs. A societal perspective was chosen for the model in terms of costs. This societal perspective includes costs incurred by the health system and OOPE as reported by NSSO which does not include cost of losses in daily wages etc.

Structure of the model:

The decision tree starts from the point where medical management has failed in women who experienced atonic PPH. The women could be present to one of the three levels of healthcare at this point. Depending on this, the tree goes forward with interventions appropriate to each level. As per Operational Guidelines on Maternal and New born Health (34) three levels have been described with respect to obstetric care in India. [Level 1: SC and PHC, Level 2: PHCs (24X7), CHC where BEMONC is available (Basic) and Level 3: DH, SDH, RH (Comprehensive Level)]. In this model, following three levels of public health care facilities as per IPHS standards were considered, to take into account ICU and blood storage, as these are an important component of PPH management (35).

- **Primary level of healthcare:** PHC and Sub centers where skilled birth attendants are available but no infrastructure for comprehensive management Emergency Obstetric care (EMOC)
- **Secondary level of healthcare:** CHC and SDH that have an OBGYn specialist, functional OT and blood storage unit but no ICU facilities
- **Tertiary level of healthcare:** DH and medical colleges which have all of the above and ICU

Figure 5: **Structure of the decision tree**

Note: **Devascularization surgeries:** These include B-lynch surgery, uterine artery ligation, and anterior division of internal iliac artery ligation

●= Chance node, ■= Decision node, ◄= Terminal node

Starting point of the decision tree: A square box shown in figure 5 indicates the start of the decision tree at the point of failed medical management where a decision needs to be made on the type of uterine balloon tamponade to be used to control bleeding associated with postpartum hemorrhage.

To compare the three different UBTs under consideration, three separate decision trees estimating costs and consequences (ESM-UBT, Bakri-UBT and condom UBT) have been modeled.

The costs incurred before this decision node will remain the same irrespective of the type of intervention sought (Type of UBT) and thus have been excluded from the analysis.

Branching of the decision tree:

After either a decision node or a chance node, the tree branches out to give the available alternatives/ possibilities. Hence at each node, probabilities are required, called branch probabilities.

Depending on at what level of healthcare, the UBT was inserted, the tree branches into chance nodes for facilities where care maybe sought by women. From this point, the condition of women is depicted through a series of branches representing events occurring in a sequential pattern depending on the resources available in the facility, skill set of the available human resources and based on the medical condition of women experiencing postpartum hemorrhage.

At the primary level: If a woman has PPH then UBT is inserted and she is referred to a higher facility. There is a possibility of death after insertion while being referred or otherwise. This is represented by a chance node after insertion of the UBT device at primary healthcare level. Since no other intervention is expected at that level, terminal node represents referral or death of women at primary facility level due to postpartum hemorrhage. After referral, she may survive with the interventions at secondary level, or she may die. The death before/ during referral has been taken as due to PPH, and a cause-specific mortality rate has been applied. If the woman, moves on to receiving interventions at the secondary level, her costs have been taken into

account here. Also, death after interventions has been taken as "death due to causes other than PPH". An appropriate probability of the same has been calculated and applied here.

At secondary level and tertiary level: Secondary and tertiary health facilities in India are equipped to take measures to manage uncontrolled postpartum haemorrhage using necessary surgical measures in the form of uterine devascularization group of surgeries such as B-lynch compression, uterine artery ligation, ligation of anterior division of internal iliac artery based on the medical condition and need of the patient, skills of the health care provider or availability of resources. Alternatively, a woman may directly undergo hysterectomy procedure to control bleeding.

Management of postpartum hemorrhage after UBT insertion at secondary and tertiary facility will follow a similar pathway at these facilities. Insertion of the UBT device at these levels will result in bleeding either being controlled or uncontrolled represented by a chance node. Those in whom bleeding is controlled will further have a chance node for either remaining alive or dying due to other maternal causes. Some women may develop complications (DIC, shock, sepsis, etc.) which require ICU care. In such cases, referrals will be made from secondary to tertiary facilities which are equipped with ICU facilities. Secondary level, ICU facilities aren't mandated by IPHS, and hence the chance node has an option of 'Referred for ICU'. Following this, woman may remain alive or dead that will be the terminal event in this path. For those in whom bleeding remains uncontrolled after UBT intervention will further be represented by a chance node of either undergoing uterine devascularization surgeries as mentioned above or may undergo hysterectomy directly. In the uterine devascularization group, this intervention may result in woman being controlled or uncontrolled after this surgical intervention. Those controlled by this intervention will further have the possibility of being alive without any associated morbidity or being dead as shown by a terminal event node. Similarly, those being controlled may still have some complications which may need further medical management in the ICU. Secondary level may not have an ICU for which patient may be referred to tertiary facility. In tertiary level, ICU facility is available. Patients in ICU will eventually be alive or dead at its terminal node.
Women uncontrolled by uterine devascularization surgery after UBT insertion may have a chance of undergoing a hysterectomy as a lifesaving indication. Those undergoing a

hysterectomy will have possibilities of being alive without any complications, being alive with complications that require ICU admission or dying after hysterectomy. Death or alive without complications are terminal nodes in this path. Those experiencing complications after hysterectomy will be further managed to eventually be alive or resulting in death as a terminal event. As mentioned earlier, those uncontrolled after UBT insertion have a chance of undergoing hysterectomy directly depending on the need. The future course for those undergoing hysterectomy directly will remain the same as mentioned above.

Probabilities of death applied at all nodes where women have undergone surgery, and the surgery has controlled the PPH, is taken to be "death due to causes other than PPH". If a woman undergoes a surgery to manage PPH, but PPH is not controlled , leading to her death, PPH-cause-specific mortality rates have been applied.

Cohort size going through the model:

An imaginary group of women were run through the model to conduct economic evaluation as a part of this HTA. This cohort was taken as the number of women who experienced atonic PPH; and in whom medical management failed; in a year in India. This was calculated to be 59,862 using Indian HMIS data and reviewed literature on PPH. Parameters included total births in India, PPH incidence and effectiveness of medical management.

II) SEARCH FOR INPUT PARAMETERS

1. Demographic and epidemiological data
    - Incidence of post-partum haemorrhage in India
    - Mortality and complications of post-partum haemorrhage.
    - IPHS standards that facilitate management of PPH at different levels of public health care facilities
    - Average duration of stay in healthcare facility after delivery.
    - Probabilities of events after PPH
    - Total births in India annually
    - Health seeking behavior of women in terms of level of healthcare
    - Effectiveness of the UBTs

All the input parameters used to populate the model are listed in the table 1.

Table 1: List of model input parameters

Sr.no.	Parameter	Default value	Source
1	Probability of delivery at primary level	0.19	NFHS -4 (2015-2016)
2	Probability of delivery at secondary level	0.33	NFHS -4 (2015-2016)
3	Probability of delivery at tertiary level	0.48	NFHS -4 (2015-2016)
4	PPH controlled after Condom UBT insertion	0.934	Targeted Literature Review
5	PPH uncontrolled after Condom UBT insertion	0.065	
6	PPH controlled after Bakri UBT insertion	0.864	
7	PPH uncontrolled after Bakri UBT insertion	0.135	
8	PPH controlled after ESM UBT insertion	0.953	ESM –UBT Systematic review
9	PPH uncontrolled after ESM UBT insertion	0.047	ESM –UBT Systematic review[#]
10	Probability of alive after being controlled with UBT	0.992	PPH mortality calculation[**]
11	Probability of being dead after being controlled with UBT	0.008	PPH mortality calculation[**#]
12	Probability of Devascularization surgery in uncontrolled PPH after UBT	0.85	(36)
13	Probability of DIRECT Hysterectomy in uncontrolled PPH after UBT	0.15	
14	Probability of being controlled after devascularization surgery after UBT	0.74	
15	Probability of being uncontrolled after devascularization surgery and hence undergoing Hysterectomy	0.26	
16	Probability of alive and ICU need in cases controlled by devascularization surgery in UBT	0.025	(37)
17	Probability of ward in cases controlled by devascularization surgery in UBT	0.97	
18	Probability of dead after being controlled by devascularization surgery in UBT	0.008	PPH mortality calculation[**]
19	Probability of alive after ICU after being controlled by devascularization surgery in UBT	0.992	PPH mortality calculation[**#]

20	Probability of dead after ICU after being controlled by devascularization surgery in UBT	0.008	PPH mortality calculation**
21	Probability of ICU after hysterectomy for those uncontrolled by devascularization surgery in UBT	0.769	(37)
22	Probability of death after hysterectomy for those uncontrolled by devascularization surgery in UBT	0.008	PPH mortality calculation**
23	Probability of going to ward after hysterectomy for those uncontrolled by devascularization surgery in UBT	0.223	(37)
24	Probability of alive after ICU after being controlled by hysterectomy following devascularization surgery in UBT	0.992	PPH mortality calculation**#
25	Probability of death after ICU after being controlled by hysterectomy following devascularization surgery in UBT	0.008	PPH mortality calculation**
26	Probability of ICU after DIRECT Hysterectomy in uncontrolled PPH after UBT	0.769	(37)
27	Probability of ward after DIRECT Hysterectomy in uncontrolled PPH after UBT	0.22	
28	Probability of death after DIRECT Hysterectomy in uncontrolled PPH after UBT	0.008	PPH mortality calculation**
29	Probability of being alive after ICU after DIRECT Hysterectomy in uncontrolled PPH after UBT	0.992	PPH mortality calculation**#
30	Probability of death after ICU after DIRECT Hysterectomy in uncontrolled PPH after UBT	0.008	PPH mortality calculation**
31	Maternal mortality rate per thousand	8.8	(7)
32	Total births in India 2017-18	2,07,85,669	Family welfare statistics, HMIS India, 2017
33	Incidence of PPH, weighted	0.036	Amy JJ, India, 1998#
34	Cost of insertion of Condom -UBT at primary level	162.59	Primary costing study#
35	Cost of insertion of Condom -UBT at secondary level	245.06	

36	Cost of insertion of Condom -UBT at tertiary level	525.98	
37	Cost of insertion of ESM -UBT at primary level	432.09	
38	Cost of insertion of ESM -UBT at secondary level	514.56	
39	Cost of insertion of ESM -UBT at tertiary level	795.87	
40	Cost of insertion of Bakri -UBT at primary level	9588.59	
41	Cost of insertion of Bakri -UBT at secondary level	9686.57	
42	Cost of insertion of Bakri -UBT at tertiary level	9951.98	
43	Cost of Devascularization in secondary level	4396.21	
44	Cost of Hysterectomy at secondary level	5872.66	
45	Cost of Devascularization surgery at tertiary evel	4024.04	
46	Cost of Hysterectomy at tertiary level	5400.38	
47	Cost of complications and ICU in tertiary level	3454.02	
48	Cost of post natal ward in secondary level per admission	2026.04	
49	Cost of post natal ward in tertiary level per admission	2117.45	
50	Cost of referral per patient referred	1000.96	(38)
51	Cost of training per beneficiary, Maharashtra state	2068.69	Maharashtra government
52	OOPE per woman per delivery	3578.00	(39)
53	Utility of PPH	0.9918	(40)
54	Utility of devasculuarization surgery	0.75	(41)
55	Utility of Hysterectomy surgery	0.605	(42)
56	Utility of being well in ward	1	(43)
57	Utility of complications after surgery	0.77	(44)
58	Disutility of ICU admission	0.23	(45)
59	Disutility of ward admission	0.105	(45)
60	Number of days for which disutility of PPH is experienced	3	Expert opinion
61	Number of days for which disutility of ICU admission is experienced	10	

62	Number of days for which disutility of ward admission is experienced	5	
63	Number of days of post-partum recovery	42	
64	Number of days for post-operative recovery	14	

Probabilities estimated based on findings of the study

** Calculated based on available data

2. Literature Review

- Systematic review on clinical effectiveness of ESM UBT
- Targeted review of the following:
  - Clinical effectiveness of Condom UBT
  - Clinical effectiveness of Bakri Balloon Tamponade
  - Cost-effectiveness of UBT
  - Health related quality of life
    - Utility of PPH
    - Utility of hysterectomy
    - Utility of ectopic pregnancy
    - Utility of complications after hysterectomy
  - Equity Issues

Systematic review on ESM UBT: Systematic Review to assess Clinical effectiveness of ESM UBT to manage atonic post-partum haemorrhage (Registered with PROSPERO: Registration number is: CRD42019122802). The systematic review was done as per standard protocol. The study included RCTs and observational studies that have abstracts and full text in English language and those that ascertain clinical effectiveness of uterine balloon tamponade for the management of atonic post-partum haemorrhage; done in the last decade. Three databases were used for the search namely PubMed, Cochrane, and Web of science databases for studies published between January 1998- November 2018 and the review was done independently by two researchers. Figure 6 shows the PRISMA flowchart, which shows the three databases searched and the final number of studies reviewed to be three.

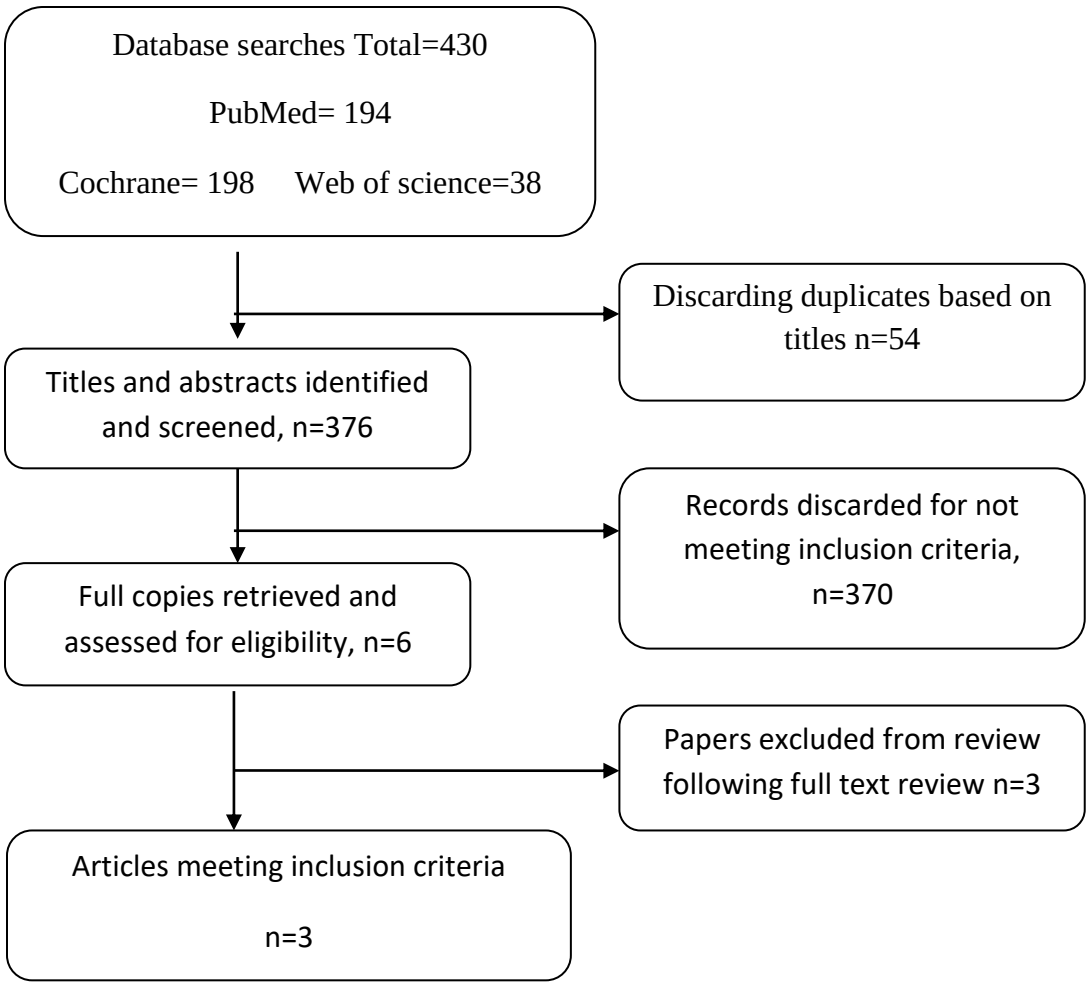


Figure 6: Flowchart of systematic search

Summary findings of the systematic review

An algorithm of search strategy and included excluded studies is presented showing a total of three studies. It is clear from the selected three studies that UBT results in a survival rate that ranges from 94 per cent to 99.4 per cent after placing UBT for uncontrolled post-partum haemorrhage. The ESM-UBT device appears safe for use in women with uncontrolled PPH. The data extracted from the final included studies is presented.

Regarding the effectiveness and adverse events of the first study, Out of 201, total-cause survival was 95% (190/201). However, 98% (160/163) of women survived uncontrolled PPH if delivery occurred at an ESM-UBT online facility. One (1/151) potential UBT-associated complication (postpartum endometritis) was identified and two improvised UBTs were placed in women with

a ruptured uterus. Eleven of the 201 women who underwent UBT placement due to uncontrolled PPH, died.

In the second study, normal vital signs or class I/II shock were reported for 166 (54.2%). In this group, one death occurred and was attributed to PPH (survival rate 99.4%). There were no cases of shock progression. One hundred and eleven (36.3%) were in class III shock and 29 (9.5%) in class IV shock; the respective survival rates were 97.3% (n=108) and 86.2% (n=25).

In the light of the effectiveness and adverse events of the third study, 189 (94.0%) survived out of 201 women. Six week or longer follow-up was recorded in 156 of the 189 (82.5%). A causal relationship between use of an ESM-UBT device and one death, three perineal injuries and one case of mild endometritis could not be completely excluded. Three experts found a potential association between these injuries and an ESM-UBT device highly unlikely.

Authors of this review desired to look at primary outcomes **(**deaths averted and surgical interventions averted) and secondary outcomes (procedure-related Complications/ Adverse events: Infections, tears. Uterine rupture; time to arrest of bleeding, time to stabilization, time to UBT device removal). But the three studies that were selected, looked at only death averted and adverse events. They did not look at surgical interventions averted, time to arrest of bleeding, Time to stabilization, time to UBT device removal.

The ESM-UBT package is a clinically promising and safe method to arrest uncontrolled postpartum hemorrhage and save women's lives. The UBT was successfully placed by all levels of facility-based providers. It appears safe for use in women with uncontrolled PPH. It arrests hemorrhage, prevents shock progression, and is associated with high survival rates among women with uncontrolled PPH from uterine atony. Future studies are needed to further evaluate the effectiveness of ESMUBT.

The limitation is that all the three studies are observational studies done by the same research group without any comparator in different population across several countries (Kenya, Sierra Leone, Nepal, Senegal, and Tanzania). The only three published studies available in ESM UBT are authored by the developer of the product. In the course of this review, we discovered that there is use and experience of ESM UBT in India; however, none of it is published.

Table 2: Summary of Studies selected in systematic review on ESM UBT

Sl.no	Authors And Year of Publication	Country	Type of study design and method	Intervention	Results
1	TF Burke et al. 2015	Kenya, Sierra Leone, Senegal, and Nepal	Prospective multi-centre case series.	Use of ESM-UBT device for uncontrolled PPH due to uterine atony.	Total 201 UBT were placed for uncontrolled vaginal haemorrhage refractory to all other interventions. All-cause survival was 95% (190/201). However, 98% (160/163) of women survived uncontrolled PPH if delivery occurred at an ESM-UBT online facility
2	Thomas S Burke, Sundra Danso-fanbo et al 2017	Kenya, Sierra Leone, Senegal, and Tanzania	Prospective multi-centre case series.	Use of ESM-UBT device for uncontrolled PPH due to uterine atony	Data for 306 women with uncontrolled PPH from uterine atony across 117 facilities were analysed. Normal vital signs or class I/II shock were reported for 166 (54.2%). In this group, one death occurred and was attributed to PPH (survival rate 99.4%). There were no cases of shock progression. One hundred and eleven (36.3%) were in class III shock and 29 (9.5%) in class

					IV shock; the respective survival rates were 97.3% (n=108) and 86.2% (n=25).
3	Aparna Ramanathan et al 2018	Kenya and Sierra Leone	Prospective multi-centre case series.	Use of ESM-UBT device for uncontrolled PPH due to uterine atony	Of the 201 women treated with an ESM-UBT device in Kenya and Sierra Leone, 189 (94.0%) survived. Six weeks or longer follow-up was recorded in 156 of the 189 (82.5%). A causal relationship between use of an ESM-UBT device and one death, three perineal injuries and one case of mild endometritis & 2 hysterectomies could not be completely excluded. Three experts found a potential association between these injuries and an ESM-UBT device highly unlikely.

Critical appraisal of the above three studies was done using National Institute of Health Tool, USA. Two of three studies fared as poor and one as good. None of them met all criteria for a robust observational study.

Targeted review for use of uterine balloon tamponade in management of atonic postpartum hemorrhage (Condom UBT & Bakri balloon UBT)

Targeted review was conducted to enlist effectiveness profile of various UBT devices used for atonic PPH treatment. This review forms basis of a comprehensive comparison to help understand clinical profile of UBT devices currently being used. The review highlights usage of these devices, processes involved, outcomes observed and any other factor that may affect use of these devices. The review focuses on condom catheters or its modifications and Bakri uterine balloon tamponade technique which are being actively used in the Indian settings. We have reviewed studies of the past ten years, conducted or relevant to the use of technique in Indian context to develop an evidence profile on usage of condom catheters and Bakri balloons.

Condom Catheter Uterine balloon tamponade:

Condom catheter uterine balloon tamponade is an assembled device made using condom and urinary catheter (Foley's catheter) which are available even in low resource settings, thus ensuring availability of second-line treatment measure for PPH management. The underlying functioning of any condom catheter used for PPH treatment is to have a condom tied to the proximal end of the urinary catheter using a string or a suture and allowing flow of IV fluid from distal end to ensure application of continued hydrostatic pressure in a controlled manner thus reducing bleeding associated with atonic uterus. Several modifications to this principle of condom catheter tamponade have been tried and practiced to achieve hemostasis in atonic PPH cases. In the following section, we have attempted to give a summary of factors related to success or failure of usage of condom UBT, methodological aspects associated with its use, adverse events if any and causes for failure to use of this condom device. This review includes two RCTs, one systematic review, four prospective studies of which two were observational, one was descriptive and one did not mention the type and two case series studies. One RCT compares Condom UBT with Bakri UBT and hence has been used in targeted review of both the devices.

Table 3 summarizes the effectiveness of Condom UBT from the different studies in the targeted review.

Table 3: Effectiveness of Condom UBT, A targeted review

Sr. No.	Author Year of publication Country	Methodology Sample Size	Effectiveness
1.	Darwish et al. 2017 Egypt	Single blinded RCT comprising 66 women divided randomly into Bakri and condom group	Success rate in Bakri – 91 % Success rate in condom – 85 %
2.	Tindell et al. 2012 -	Systematic review of 13 studies from resource poor tertiary settings Total of 241 cases with C-UBT inserted in 193 women	Success rate in condom UBT – 95 %
3.	Santhanam et al. 2018 India	Prospective descriptive study with Condom UBT inserted in 61 women	Success rate – 96.7 %
4.	Rathore et al. 2012 India	Single arm prospective study with a sample size of 18 patients with Condom UBT insertion	Success rate – 94 %
5.	Tort J et al. 2013 Benin	Multicentre randomized parallel RCT in 3 public hospitals with 5 patients each in intervention(Condom UBT plus medical management) and control group (only medical management)	-
6.	Aderoba et al. 2016 Nigeria	Prospective observational study with singleton pregnancies in 229 women with PPH having UBT insertion	Success rate – 88.6 %
7.	Mishra et al. 2015 India	Prospective case series with 13 atonic PPH patients in which CG balloon was used as an intervention	Success rate in CG balloon – 92 %
8.	Mishra et al. 2017 India	Prospective observational case series with 60 women in whom CG balloon and condom UBT inserted Reports 12 studies with 277 cases relevant to Indian context where condom UBT was used	Overall success rate for 60 women – 98.33 % Overall success rate for 277 cases – 97 %
9.	Kandeel et al. 2016 Egypt	Prospective observational study with condom UBT being inserted in 50 cases of PPH	Success rate – 96 %

Brief extracts from key studies on Condom UBT

Darwish et al conducted a single blinded randomized control trial comparing Bakri Balloon catheter in comparison to condom loaded Foley's catheter in Egypt between October 2014 to December 2015 with 66 women experiencing atonic PPH after vaginal delivery. The primary outcome measured was success of tamponade to stop bleeding. This RCT found Bakri balloon to be effective in 91 percent cases as compared to 85 percent for Condom catheter. Those failing to be controlled beyond 15 minutes were considered to be failures. Failures were seen in 3 cases of Bakri balloon insertion and 5 cases of condom catheter which were managed by further surgical interventions. There was no statistical significance between both groups with regards to the surgical intervention following failure. It was noted that five cases of condom balloon ruptured after inflation wherein reinsertion was undertaken. Bakri balloon needed statistically significantly shorter time duration to stop bleeding as compared to condom tamponade (9.09 minutes and 11.76 minutes respectively. No statistically significant differences were found with regards to need for blood transfusion, ICU admission, DIC development and postpartum fever between the two groups. Safety aspect of the tamponade in terms of complications associated with use of UBT was not observed in the study. The authors acknowledged Bakri balloon to be a very expensive device thus making condom UBTs an attractive alternative especially for developing countries. Soft condom material has been attributed as a possible reason for delay in arrest of bleeding comparatively to Bakri balloon. However, low price of condom UBT results in outweighing disadvantages associated with condom catheter use according to the authors. They call for missing cost effectiveness evaluation to be an integral limitation of their study.

Tindell et al. (2012) reviewed 13 studies conducted in resource poor tertiary facilities comprising devices such as condom UBT, Foley's catheter, Sengstaken – Blakemore tube accounting for a total of 241 cases. 193 of these cases had condom UBT insertion. UBT insertion was carried out after failed medical management in all the studies considered. The success rate observed in condom UBTs was 95 % with time taken to control PPH after insertion ranging between 4 to 15 minutes for all the studies. It was reported in 7 out of 8 condom UBT studies that vaginal packing was used to prevent condom expulsion. The review reported no case of sepsis, fever or endometriosis to be reported in any of the 8 reviewed condom studies. No increased infection

was noted in any of the 8 condom UBT studies. The authors suggest condom UBT to be effective in resource poor settings.

Santhanam et al. (2018) conducted a prospective descriptive study in Kerala, India in 2015 over a period of 15 months wherein a total of 5742 deliveries had taken place with 487 mothers developing PPH. The study had a sample size of 61 patients in whom condom tamponade insertion was done. The condom tamponade was successful in controlling bleeding in 96.7% cases. Bleeding continued in 3.37% cases and needed further surgical intervention. Blood transfusion was required in 55.7% cases and 1.63% or 1 case underwent hysterectomy. No maternal deaths were reported in the study. Condom catheter insertion was done in 6.6% of cases after having delivered by caesarean section. Bleeding was controlled within 15 minutes of insertion of condom UBT in 80.3% of the cases. Of the study population, 4.9% cases continued bleeding beyond 30 minutes of condom UBT insertion. The condom UBT was retained for a duration of 12-24 hours in 96.7% cases. The study stated condom tamponade to be cheap, safe, easily available, lifesaving less expertise requiring intervention to be used especially in low resource settings at times of referral of such patients.

Rathore et al. (2012) conducted a prospective study in Delhi, India in 2009 over a period of 17 months to witness 160 cases of non-traumatic PPH out of 14,680 deliveries. Of these 160 cases, 18 patients had condom tamponade inserted and were included in the study. Condom tamponade was successful in controlling bleeding in 94.4% of the cases. Remaining 5.6% or 1 case had to undergo surgical intervention in the form of hysterectomy as a lifesaving procedure. There were two deaths in the maternal group but they were not related to PPH. 27.8% cases had condom catheter insertion after having delivered by caesarean section. Average time taken to control bleeding was 6.2 minutes with a range of 4 to 12 minutes. Average blood lost in the study population was 1330 ml. Mean duration for which condom UBT was left in situ was 27.5 hours. None of the cases had to be re-inflated after deflating the balloon. On following up 12 patients for 6 weeks, none had developed endometriosis. Difficulty in insertion of condom UBT was observed in 11%cases wherein the balloon was getting expelled. This was overcome by holding the lips of cervix by sponge holder. The limitations of the study included a small sample size and no consideration of the long term outcome of use on future fertility.

Tort et al. (2013) carried out a multicenter randomized parallel-group controlled trial between October and February 2013 in three maternity units of Cotonou, Benin where 3279 vaginal deliveries were reported. 35 women were diagnosed with PPH and of the eligible women; two groups of 5 patients each were divided into intervention and control group respectively. The primary outcome under consideration was recourse to surgical intervention. No maternal deaths were reported in the study. Total estimated mean blood loss was 800 ml. The average time taken to assemble the device in this study was found to be 5 minutes. The condom UBT was retained for a mean duration of 9 hours 11 minutes. Patients having condom UBT inserted did not complain of any associated pain. All patients randomized had induction of labor and controlled cord traction before being categorized. The study stated the two groups to be comparable thus demonstrating no selection bias in the study.

Aderoba et al. (2017) conducted a prospective observational study in Akure, Nigeria between 2012 and 2014 to witness 1788 cases of PPH out of 20,551 deliveries that took place in the unit of study. 229 eligible women treated with condom UBT were included in the study. Successful treatment of PPH occurred in 88.6% cases. Remaining 11.4% needed further intervention primarily in the form of uterine packing and hysterectomy in 53.8% of the unsuccessful cases. A total of 6.11% cases of the study population underwent hysterectomy. The study found that advanced maternal age and caesarean section were associated with lower likelihood of successful treatment with condom UBT. Infective morbidity was observed in 4.4%cases with higher prevalence in the unsuccessful condom UBT group. The mean time to control bleeding in this study was 12.76 minutes. Total blood lost in the study after delivery was 1496 ml. On an average, the total time for which device was retained for 12.84 hours. The large sample size broadened the range of possible findings in the study, thus making it generalizable by giving insights on factors associated with successful use of the device. The limitation reported in the study was ability to uncover impact of explanatory variables in case of unsuccessful cases due to small sample size.

Mishra et al. (2016) presented a case series of 13 patients with use of a modification of condom catheter for atonic PPH treatment amongst women who delivered between December 2014 and August 2015 in India. The success rate observed in this study was 92.3%. One case or 7.69% cases needed further intervention in the form of devascularisation surgery. This patient

succumbed to disseminated intravascular coagulopathy and has been reported as a case of failure of uterine tamponade. 3 patients or 23.3% cases in this report had delivered by caesarean section. Average blood lost in the series was observed to be 1611 ml. On an average, the time taken to assemble this device was 7 minutes. The condom UBT (CG balloon) was retained for a mean duration of 14.38 hours. The modification undertaken in this case series was to further reduce cost associated with assembling such condom catheters.

Mishra et al (2017) carried out a prospective observational case series of 60 women in India whom had CG – balloon (Chhattisgarh balloon) a modification of condom UBT and conventional condom UBT was inserted. 46 women had CG balloon insertion whereas remaining 14 had conventional condom UBT insertion. The overall success rate for these women was reported to be 98.33 % with findings of greater blood loss, higher inflation volume of balloon and technical delays to be higher in condom UBT as compared to CG balloon. Failure of inflation due to technical problems was noted in 2 cases of condom UBT and in 1 case of CG balloon. The study further described studies related to condom UBT carried out in the past 10 years in Indian or related settings to compile results for 277 cases of condom UBT use. It was reported that overall success rate for all these studies was 96.75 %. The study concludes both conventional and CG balloon to be easy to use, feasible and effective with added advantages of drainage and less cost to be added advantages in CG balloon.

Kandeel et al (2016) undertook a prospective observational study in Egypt in 2016 in patients with failed medical management for PPH. 57 women out of enrolled 151 were found to be unresponsive to uterotonics and bimanual compression. Of these 57, 7 were excluded due to failed inflation, failed insertion and displacement reasons. Out of the 50 included finally, a success rate of 96 % was observed. The study had 28 cases of atonic PPH and all cases were successfully controlled. Maternal fever was recorded in 10 % cases, and 4 % underwent hysterectomy. Lack of comparator group and small sample size were reported to be the limitations of this study.

Summarizing key findings of this targeted review for use of condom catheters suggests that success rate of condom catheters in the above mentioned studies ranged from 84.84 to 98.33% with a mean of 93% in studies (RCT and systematic review inclusive) included in the review. Out of the total respective study populations, women with caesarean section deliveries

undergoing condom UBT insertion ranged from 6.5 to 64% wherein one study reported a very high prevalence of caesarean deliveries included in the study. Women not controlled by condom UBT insertion needing further intervention or surgery ranged from 0 to 15.2%. On an average, 6.26 % overall cases needed some form of higher intervention. A mean of 3.12% cases underwent hysterectomy with a range of 0 to 7.14% undergoing hysterectomy in the above mentioned studies. The mean time taken to control bleeding with condom UBT varied between 8.75 to 15 minutes with mean time of 11.74 minutes. The mean blood loss observed in condom UBT patients was 1475 ml ranging between 800 to 2200 ml. Data for assembling the condom UBT was mentioned in two studies as 5 and 7 minutes respectively. The condom UBT was retained for a mean duration of 17.81 hours ranging from a minimum average of 9.11 to maximum mean of 27.5 hours in the above mentioned studies. The balloon in condom UBT was inflated with an average of 340.6 ml of saline on an average ranging from 222 to 443 ml. Table X.X given below shows comparison of these figures with those of Bakri balloon tamponade as seen in the studies. In the studies included in the review, one study reports maternal death due to DIC. The studies suggest efficient use of condom UBT in treatment of atonic PPH especially in low resource settings.

Targeted review on Bakri Balloon Tamponade:

Bakri first published the concept of intrauterine balloon technology in management of haemorrhage secondary to placenta praevia. Eventually, a surgical obstetric silicone balloon with capacity of 500 ml was used to achieve pressure and tamponade effect to control bleeding site. This is how the Bakri balloon came into being used. Currently, Bakri balloon is the only device specifically designed for control of PPH bleeding. Bakri balloon allows for drainage of the uterine cavity which is with a relatively larger bore as compared to other UBT devices. Condom catheter and Rusch balloon do not allow drainage of the uterine cavity. The balloon in case of Bakri balloon UBT is made of silicone material. Following are the studies included in this targeted review to get a clinical effectiveness profile associated with use of Bakri balloons. Table 4 summarizes clinical effectiveness of Bakri UBT from the studies under review.

Table 4: Clinical effectiveness of Bakri UBT

Sr.no.	Type of study Sample size	Author, Country and year	Effectiveness of Bakri balloon (%)
1	Systematic review. 28 studies, 17 retrospective, 6 prospective observational, 2 intervention	Said Ali, Muti-Country, 2019	??
2	Retrospective case series n=50	Gro¨ nvall et al, Finland, 2012	86
3	Retrospective cohort	Oslen et al, USA, 2013	67.57
4	Prospective cohort	M Revert, France, 2016	83.20
5	Retrospective chart review	Tahaoglu, Turkey, 2017	89.9
6	Retrospective case series n=24	Aibar et al,Spain, 2012	87.50
7	Retrospective case series n=47	Alkis et al, Turkey, 2015	91.40
8	Retrospective n=9 of placenta previa accrete	Arduini et al, Italy, 2010	-
9	Prospective n=6	Bakri, Saudi Arabia, 2001	100
10	Prospective interventional observational n=58	Brown, Kenya, 2016	95
11	Retrospective n=20 (Out of 24 medical Mx failures, 20, they used UBT)	Diemert, Germany, 2011	60
12	Prospective interventional with comparator n=50, 25 in "traction stitch group" and 25 in non-traction group; only LSCS	Khalil, Saudi Arabia, 2010	96 in stitch group 80 in non-stitch group
13	Retrospective n=25, placenta praevia	Kumra, Turkey, 2012	88
14	Before and after study (change in protocol)	Laas, France, 2012	86
15	Prospective n=16	Patacchiola, Italy, 2012	100
16	Prospective n=5, Uterine sandwich technique	Nelson, USA, 2016	-
17	Retrospective Case series n=15	Vitthala, UK, 2009	80
18	N=11 Uterine sandwich	Yoong, UK, 2010	100
19	Retrospective, n=36	Emanuelle Vintejoux, France	69
20	Case study, n=10	Nagai S, Japan, 2015	90
21	Retrospective review, n = 49	Mathur M, Singapore,	81.6

		2017	
22	Retrospective case series, n = 49	Martin E, France, 2015	65
23	Retrospective cohort, 43 cases	Anderson Lo, USA, 2016	81
24	Retrospective study, n= 305	Guo Y, China, 2017	87.3
25	Single blinded RCT, Bakri Vs Condom,	Darwish, Egypt, 2017	91.00 (Bakri)
26	Retrospective case series n=18	Vrachnis, Greece,2013	94.4
27	Multicentre Cohort N=407	Wang, China, 2018	91.65
28	Retrospective Placenta praevia with LSCS n=70	Soyama, Japan, 2019	87

Brief extracts of key studies on Bakri UBT:

Said Ali et al conducted a non-Cochrane systematic review in 2019. The study identifies 28 studies on Bakri Balloon. Meta-Analysis has not been done. Hence a summary measure for effectiveness could not be used for our model; instead an average was taken of all effectiveness measures. Below, are extracts of a few key studies:

Revert et al. (2017) conducted a prospective cohort study from July 2010 to March 2013 in France. A total of 226 cases of severe PPH were managed with intrauterine balloon tamponade. The Bakri balloon was used for 87.6% cases while the rest had ebb balloon insertion. The global success rate was 83.2%. Caesarean section delivery followed by severe PPH treated with balloon tamponade was seen in 24.3% cases. A total of 16% of the study population needed further surgical intervention with 2.65% eventually needing hysterectomy. Higher amount of blood loss and coagulopathies were found as factors associated with failure of balloon insertion. No maternal deaths were reported in the study however one woman developed endometritis which resolved with antibiotics. The mean estimated blood loss before insertion of IUBT in this study was found to be 1508 ml. The study cites literature to point out possibility of sub optimal filling of the balloon due to fixed capacity of Bakri balloon thus resulting in lower efficacy rate. Large sample size and observation of standard treatment protocol were the strengths identified by the

study. Lack of control group leading to overestimation of efficacy was observed as the limitation of this study.

Lo et al. (2017) conducted a retrospective cohort study from January 2002 to March 2013 in Massachusetts, USA to compare rates of postpartum hysterectomy before and after Bakri balloon introduction using statistical tools. The study period had a total of 43 Bakri balloons and 21 hysterectomies being performed for PPH secondary to uterine atony. The study found rate of postpartum hysterectomy to decrease from a rate of 7.8 per 10,000 deliveries to 2.3 per 10,000 deliveries after availability of Bakri ($p=0.01$). Also, use of B-Lynch decreased from a rate of 5.6 per 10,000 deliveries to 1.6 per 10,000 deliveries in this period after Bakri was available ($p=0.03$). Of total 43 Bakri insertions, 8 or 18.6%required further intervention in the form of uterine artery embolization. None of these needed hysterectomy. The success rate of this study was 81 percent. The rates of uterine artery embolization were found to have increased in post Bakri period. No maternal deaths were reported in the study. Large baseline population for such uncommon procedure was identified as the strength by the authors whereas limitations included the retrospective nature of the study design, long duration of study leading to changes in treatment measures and lack of generalizability of the study.

Vintejoux et al. (2015) conducted a retrospective cohort study in 6 French hospitals between May 2010 and August 2011 to witness 622 PPH cases of 19,440 deliveries. A total of 36 women had Bakri balloon inserted and were included in the study. The success rate observed in this study was 69%while 31%needed additional procedures with uterine artery embolization being the commonest. Hysterectomy had to be performed in 5.5% cases. Eleven women or 31% women were hospitalized in the ICU. No medical deaths were reported. Mean time taken for controlling the bleeding was 2 minutes with a range of 0-30 minutes. Blood loss reported in this study was an average of 1130 ml. The balloon was retained for a mean duration of 23 hours. The study noted 5.5%insertion failure but the cases did not need any additional care. No early complications were noted after balloon use. Only observed predictive factor in the study for Bakri failure was haemorrhage greater than 1000ml. The study identified its homogeneity in terms of use of only Bakri balloon and uterine atony cases as it strength while retrospective design was identified as the limitation of this study.

Brown et al. (2016) carried out a prospective observational intervention study between January 2013 and May 2015 at two sites in Kenya and Eldoret. Bakri balloon was used in 55 cases with uterine atony. Successful control of bleeding was seen in 95% cases. Of the total atony cases, 5.4% needed further surgical interventions. A total of 3.63% cases underwent hysterectomy. There was one maternal death reported in the atonic PPH group. The death that occurred was due to coagulopathy before surgical intervention was initiated. Average blood loss reported in this study was 1385 ml. The duration or which Bakri device was retained ranged from 5.3-14.2 hours. The reported failure of device occurring in caesarean section group had Bakri device placed for 3 and 5 hours respectively. Strengths of the study were standardized protocols and training of providers, while small sample size, selection bias and study area limited to resourceful tertiary centres were identified as limitations of this study.

To summarize findings of studies included in Bakri balloon review, success rate for Baki UBT averaged to 82.05% in our review with a range of 69 to 95% across different studies. Women having delivered by caesarean section accounted for 22.22 and 24.3% respectively in two of the studies. Failure of Bakri UBT in controlling bleeding leading to further intervention or surgeries ranged from 5.4 to 31% with an average of 17.75% of all cases needing further intervention. Of the studies reviewed here, a mean of 2.95% cases had to undergo hysterectomy. Hysterectomy ranged from 0 to 5.55% cases in Bakri UBT use. Mean time to control bleeding was reported by one study at a mean duration of 2 minutes. Blood lost in Bakri UBT insertion cases were reported to be 1130 and 1385 in two studies. Mean retention time for Bakri UBT was reported at 9.75 and 23 hours in two studies. Volume of saline filled in Bakri UBT was reported to be 363 and 465 ml in two studies. One case of maternal death was reported in Bakri UBT studies and was associated with coagulopathy before initiating surgical treatment. One study points out possibility of suboptimal filling of Bakri balloon leading to reduced efficiency of the device. Higher amount of blood loss and coagulopathy have been identified as factors associated with failure of Bakri UBT in these studies. The review suggests Bakri UBTs to have been successful in achieving haemostasis for atonic PPH cases and thus acting as a measure to avoid further surgeries in these cases. Table 5 highlights a comparison of findings of condom UBT and Bakri UBT in terms of their clinical effectiveness reported in the studies included in the review.

Table 5: Comparison of Condom and Bakri Balloon from the targeted review

PARAMETER	CONDOM CATHETER – UBT		BAKRI BALLOON UBT	
	Range (Avg.)	Sources	Range (Avg.)	Sources
Success rate (%)	84.84 to 98.33 (93.44)	1,3,4,5,6,7,8,9	69 to 95 (86.43)	10,11,13,14
Caesarean Section before PPH (%)	6.5 to 64 (26.1)	1,3,5,8,9	22.2 to 24.3 (23.26)	11,14
Need for further intervention/Surgery (%)	0 to 15.2 (6.27)	1,3,4,5,6,7,8,9	5.4 to 31 (17.75)	10,11,13,14
Hysterectomy (%)	0 to 7.14 (3.12)	1,3,4,5,6,7,8	0 to 5.55 (2.95)	10,11,13,14
Mean time for controlling bleed (minutes)	8.75 to 15 (11.74)	1,4,5,6,7,8	2	11
Average blood loss (ml)	800 to 2200 (1475)	2,3,4,5,8,9	1130 to 1385 (1257)	11,13
Average time taken for assembly of device (minutes)	5 to 7 (6.06)	2,5	-	-
Mean time for which device was retained (hours)	9.11 to 27.5 (17.81)	1,2,3,4,5,8,9	9.75 to 23 (16.37)	11,13
Average volume for balloon inflation (ml)	222 to 443 (340.6)	2,3,4,5,8,9	363 to 465 (414)	11,14

Please note: Bakri Balloon, not all 28 studies are presented in this table. (But the average taken in the model is of all relevant studies).

CONDOM UBT references

- 1 – *Santhanam R. et al: Prospective study, Sample size: 61*
- *2 – Tort J et al: RCT, 5 cases/ 5 control*
- *3 – Rathore A. et al: Prospective study, Sample size: 18*
- *4 – AK Aderoba et al: Prospecive observational study, Sample size: 229*
- *5 – Mishra N. : Case report, Sample size: 13*
- *6 – Darwish , RCT, 33 Condom vs 33 Bakri balloon cases*
- *7 – K Tindell, Systematic review, 13 studies*
- *8 – Nalini mishra, Sample size:60*
- *9 – Kandeel 2016, Peospective observational, Sample size:50*

BAKRI UBT references

- *10 - Anderson Lo : Retrospective cohort study, Sample size: 43*
- *11 - Emanuelle Vintejoux: Retrospective cohort, Sample size: 36*
- *13 - Brown H. : Prospective observational intervention study, Sample Size: 55*
- *14 - M Revert: Prospective cohort study, Sample size: 226*

Qualitative aspects of the three UBTs (Based on interviews with experts and health care providers)

On interviewing experts and health care providers, it was gathered that Bakri UBT was easy to use as there was no need of tying of thread. Bakri was reported to be less cumbersome in removal and controlled deflation was possible. The disadvantages of Bakri was that it was not available everywhere and was expensive. Condom UBT was easily available and very cheap, assembled using materials available in the health facility. But providers reported that there was a fear of the condom bursting or bulging and getting displaced from the intended site. Also, it was cumbersome to deflate slowly or in a controlled manner. ESM UBT user experience in our country is limited to a few centers and through informal discussion with the users, they seem to be satisfied with the device

Targeted review on cost-effectiveness of UBT:

Databases were searched for studies which evaluated costs and cost- effectiveness of any uterine balloon tamponade, alone or in combination, in comparison such as Bakri Balloon, Condom catheter, ESM-UBT used for the management of PPH due to uterine atony in women in any setting. Only one study related to cost-effectiveness of ESM UBT was found. It compared scenarios where no other UBT were used as standard of care. Mvundura et al. conducted cost effectiveness of condom uterine balloon tamponade in Western Kenya in 2015. The study used the decision tree model to analyze three different scenarios for the treatment of PPH including,

i) Standard of care without either uterine packing or uterine balloon tamponade.
ii) Standard of care with uterine packing but without uterine balloon tamponade.
iii) Addition of the ESM-UBT device to standard care for the treatment of PPH.

Effectiveness outcomes measured included numbers of hospital transfers, hysterectomies, deaths, and disability-adjusted life years (DALYs) and incremental cost-effectiveness ratios (ICERs) obtained by calculating the difference between costs for controlling PPH with ESM-UBT versus standard care. It was estimated that 1.5 million deliveries occurred in Kenya in 2015 with about 110000 experiencing atonic PPH. 10 % or 10,230 case would be severe. With no uterine packing scenario, an estimated 1390 transfers from health centers to hospitals, 462 hysterectomies to treat severe PPH and 412 deaths would have resulted with approximately 80% of deaths occurring after home births. Use of ESM-UBT would have averted 430 hysterectomies and 44 deaths. The estimated costs for scenario 1 were $453 884, price of $5 per ESM-UBT device, the estimated costs were $518 225 and the incremental cost per DALY averted was $26. If the ESM-UBT device was priced at $15, the incremental cost per DALY averted was estimated at $40.With second scenario where standard of care plus uterine packing would be 60% effective at stopping uncontrolled PPH, the use of ESM-UBT would have averted 116 hysterectomies and 18 deaths. The incremental cost per DALY averted was estimated be $164 or $199 if the price per ESM-UBT device was $5 or $15, respectively.

This study showed that use of ESM-UBT represented an effective and affordable measure to manage PPH even at the low level of health system.

Estimation of costs -Micro Costing Primary Study

To populate the model, a primary micro costing study was undertaken to estimate costs required for the decision analytic model. Written permissions were obtained from all relevant officials prior to conducting the study.

Study Setting:

The study was done in Indian context from health system as well as societal approach. The primary data collection was done in Maharashtra state, in one teaching tertiary hospital in Mumbai, one district hospital, one SDH, and one PHC. These centers were chosen based on convenience of the researchers. The SDH was located about 120 Km from the state capital. The PHC was in the same area as the SDH, maintaining the referral chain. The district hospital was located in a sub-urban area, close to the state capital.

Data collection

A bottom-up approach of costing was used, which meant that prices of various components like equipment, consumables, vehicles, capital, electricity, water, telephone bills, staff salaries, incentives etc. were collected. Data was collected in January to June 2019 by the HTA research team. Sources of data for the above mentioned categories were as follows:

a) Facility registers

b) Computer data

c) Health Management information system: HMIS

d) Blueprints of the health facility etc. maintained by the health facilities.

Apart from this, staff interviews were conducted to assess the time spent by the staff doing different activities. Activities were classified as routine/ fixed and their frequency was noted. Time spent on each patient in OT, IPD, time taken to do a surgery was asked, to the senior-most specialist/ doctor. Apportioning of time spent by human resources in PPH management has been based on expert opinions. Also, a survey of the health facility was done to measure area, observe and count medical and non-medical equipment. This was double checked with the records provided by the facility. The number of patients who received various services like inpatient admissions, vaginal and caesarean deliveries and related statistics in the financial year 2017-18 was collected from the HMIS in each facility. Total numbers and break-up of the above were collected.

Data analysis for the micro-costing study:

Economic costing was adopted.

1) For each of the facilities, annualization of capital costs was done. Annual factor was calculated using a discount factor of 3% and the life of the item. A maintenance rate of 10% was applied.
2) Apportioning of joint costs (Personnel, Space or equipment that are being used for more than one activity) was done for each of the health facilities. For example, if an OBGYN doctor worked in IPD, OT and outreach, his/her salary would be apportioned taking into account the time he/she spent in those activities. If a OT was being used for conducting Orthopedic, Ophthalmic, OBGYn surgeries, then the space, equipment, staff and capital

would be apportioned based on number of surgeries and time taken of OBGYN as a proportion of the rest. Total working days in a year were considered after deducting Sundays, public holidays and leave.

3) For each health facility a unit cost was derived for IPD, ICU admission cost per day and OT per day by using PPH beneficiaries as denominator.
4) For the decision tree model, PHC as primary, SDH as secondary, DH and medical college as tertiary level respectively were combined wherever applicable to derive health system costs.
5) Using these combined health system costs for IPD, ICU and OT; conducting devascularization and hysterectomy surgeries for Post-partum haemorrhage was derived.
6) Out-of-pocket expenditure was added to the above costs to derive societal perspective costs(46)

Table 6 shows the costs that were used to populate the model.

Price of the three UBT devices was estimated as follows:

1) Condom UBT: INR 128
   (Included price of condoms, Foley's catheter, ties, IV set and syringes)
2) ESM UBT: INR 397
   (Price of device from unpublished literature to which IV fluids was added)
3) Bakri UBT: INR 9554
   (Price of device from an online vendor to which price of consumables was added)

Table 6: Costs derived for the model

Cost component	Primary level (INR)	Secondary level (INR)	Tertiary level (INR)	Source
Cost of insertion of Condom-UBT	163	245	526	Primary micro costing study
Cost of insertion of ESM-UBT	432	515	796	
Cost of insertion of Bakri-UBT	9589	9687	9952	
Cost of devascularization surgery	NA	4396	4024	
Cost of hysterectomy surgery	NA	5873	5400	
Cost of ICU admission	NA	NA	3454	
Cost of inpatient admission in OBGYN department	NA	2026	2127	
Cost of referral per patient	1001	1001	NA	(38)
Out of pocket expenditure per delivery	3197	3197	3197	(47)

III) **Addressing uncertainty in the model:** The structural uncertainty in the model was addressed by consulting clinical experts and by reviewing literature on decision analytical models constructed for PPH management. The AdViSHE checklist was used to address uncertainty in the model(48). Parameter uncertainty was addressed by considering the upper and lower bound limits from literature, where available.

IV) **Data Analysis**

Data analysis was done using Microsoft Excel. The model was built mathematically and logically in an excel workbook. The primary outcomes of interest, for this HTA were cost per QALY gained and cost per DALY averted for the following two comparisons:

1) ESM UBT Vs. Condom UBT and
2) Bakri UBT Vs. Condom UBT

For this, ICUR (Cost per QALY) and ICUR (cost per DALY) values were derived from the model. The analysis was conducted using Microsoft excel in the following steps:

a) At each node, the branch probabilities were noted in Microsoft Excel. At every endpoint of the branches of the decision tree, total costs, QALYs and DALYs of that particular branch was calculated.

b) QALYs were calculated by using life tables for women from Sample registration system of India. The average life expectancy for Indian women was taken as 70 (49). The average age at PPH and related events was taken to be 25 years based on Age-specific fertility rates from NFHS-4 (50). The disability weight for post-hysterectomy condition was taken from Global burden of disease loss of function weights (51).

c) 'N' was the number of women at every endpoint, calculated by multiplying the branch probabilities from the start of the tree, leading up to that endpoint.

d) 'N' of each endpoint was then multiplied with the respective costs, QALYs and DALYs.

e) A sum of all these costs, QALYs and DALYs were then calculated for every decision tree.

f) All these totals for each of the trees was divided by the cohort size (to estimate per capita values)

g) For each of the two comparisons, Incremental costs, QALYs, DALYs were computed and using these, ICUR were calculated as follows

$$\text{ICUR} = \frac{Cost\ of\ Condom\ UBT - Cost\ of\ ESM\ or\ Bakri\ UBT}{Outcome\ of\ Condom\ UBT - Outcome\ of\ ESM\ or\ Bakri\ UBT}$$

h) Maternal deaths averted were calculated for each device. The deaths in current scenario were derived from the maternal mortality rate. To this, appropriate percentages were applied to derive deaths due to atonic PPH (52). A difference between the current scenario deaths and the deaths in each decision tree derived from the model was reported as maternal deaths averted. The limitation here is that different UBT types are already being used in current Indian settings

i) Net health benefits (NHB) and net monetary benefits (NMB) were calculated, as there were three alternatives. The formulae used were as follows(53):

$$\text{NHB} = (\text{QALYs in UBT}) - \left(\frac{Cost\ of\ that\ UBT}{WTP\ threshold}\right)$$

NMB= (QALYs of UBT* WTP threshold) - (Cost of that UBT)

Where WTP threshold is one times GDP per capita (INR 1,38,468.7)

j) One-way sensitivity analysis was done by varying individual input parameters by 20% (for those parameters, which did not have upper and lower bound limits from literature). A tornado diagram was constructed to show the parameter which affected the ICUR value the most.

k) Probabilistic sensitivity analysis was done by choosing appropriate distributions for each input parameter and running 1000 Monte Carlo simulations. Cost-effectiveness acceptability curve was constructed to show change in proportion of simulations that are cost-effective with varying WTP thresholds.

l) Budget impact analysis was done to show implications of introducing ESM UBT into the public health system of India.

CHAPTER 3: RESULTS

There were a total of 2,07,85,669 births in India in the year 2017-18. Applying the incidence of PPH and the effectiveness of medical management to this, we estimated that 59,862 women will require UBT. In this cohort, our model estimates the total costs, deaths, QALYs, DALYs and surgeries of each of the three decision trees as presented in Table 7. These have been derived by summing up components at each node and then dividing the totals by the cohort size.

Table 7: Results of the three decision trees in terms of costs and outcomes per woman

	Condom UBT	ESM UBT	Bakri UBT
Total costs in INR (Health system perspective)	₹ 3,858.54	₹ 3,786.29	₹ 13,635.45
Total costs in INR (Societal perspective)	₹ 13,671.77	₹ 12,096.06	₹ 22,300.75
Total QALYs	23.77	23.77	23.76
Total DALYs	0.22082	0.20291	0.28829

Health system cost per woman:

ESM UBT < Condom UBT < Bakri UBT (ESM is least expensive)

Societal system cost per woman:

ESM UBT < Condom UBT < Bakri UBT (ESM is least expensive)

QALYs gained per woman:

ESM UBT > Condom UBT > Bakri UBT (ESM has most QALYs gained)

DALYs per woman:

ESM UBT < Condom UBT < Bakri UBT (ESM is better, as least DALYs)

Table 8 shows the incremental costs and outcomes, for the two comparisons i.e. ESM UBT vs. Condom UBT and Bakri UBT vs. Condom Balloon. These are derived by subtracting the respective costs and outcomes from preceding Table number 7.

The difference in QALYs is very minimal between the three alternatives.

Table 8: Incremental costs and outcomes of the two comparisons in UBT per woman in the cohort

	ESM UBT Vs. Condom UBT	Bakri UBT Vs. Condom UBT
Incremental costs (Health system)	-₹ 72.25**	₹ 9,776.91
Incremental costs (Societal perspective)	-₹ 1,575.71**	₹ 8,628.98
Incremental QALYs	0.00131	-0.004926
Incremental DALYs	-0.0179	0.0675

** Negative sign implies that the value of first comparator is lesser than the second one

Incremental QALYs is very negligible in both the comparisons. Cost difference is very minimal for ESM vs. condom UBT.

The primary and secondary outcomes are presented in Table 9, using societal perspective costs.

Table 9: ICURs of the two comparisons of UBT (Societal perspective)

	ESM UBT Vs. Condom UBT	Bakri UBT Vs. Condom UBT
ICUR (QALYs)	**-12,05,590**	**-17,51,769.25****
ICUR (DALYs)	**88,009.28##**	**1,27,880.92**

** Negative values indicate that either the numerator or denominator is negative (derived from table 9)

These values are positive because both numerator (Incremental costs) as well as denominator (Incremental outcomes) are negative

Interpretation of Table 9:

A) Comparing ESM UBT and Condom UBT

- Incremental cost is very minimal and incremental QALY is very low, indicating an insignificant difference between ESM and Condom UBT. Hence ICUR (QALYs) of -12, 05,590 indicating that there will be a saving of INR 12,05,590 if ESM UBT is used instead of Condom UBT; to gain one QALY. Hence ESM UBT is cost-effective in terms of ICUR. ICUR (DALYs) of 88,009 indicates that there will be saving of expenditure of INR 88,009 if ESM UBT is used instead of Condom UBT; to avert one DALY

Conclusions:

HTAIn reference case recommends use of QALYs as primary outcome measure. Hence we conclude based on ICUR that ESM UBT is cost effective than Condom UBT, also noting that the two aren't significantly different in terms on incremental costs and QALYs

B) Comparing Bakri UBT and Condom UBT

- ICUR (QALYs) of -17,51,769.25indicates that expenditure of INR 17,51,769.25will be incurred if Bakri UBT is used instead of Condom UBT; to gain one QALY. (Condom UBT is less expensive and there is a gain in QALYs with condom UBT. Hence Bakri is not cost-effective. ICUR (DALYs) of 1,27,881 indicates that an expenditure of INR 1,27,881 will occur along with one DALY being gained if Bakri UBT is used instead of Condom UBT. Hence Condom UBT is cost-effective (DALY gain is unfavorable).

Conclusions:

We conclude based on the ICUR value of -17, 51,769.25 INR /QALY that Bakri UBT is not cost-effective.

Incremental cost utility planes

The ICUR values have been plotted on planes. The figures below depict the cost utility planes where X axis is incremental outcomes and Y axis is incremental costs.

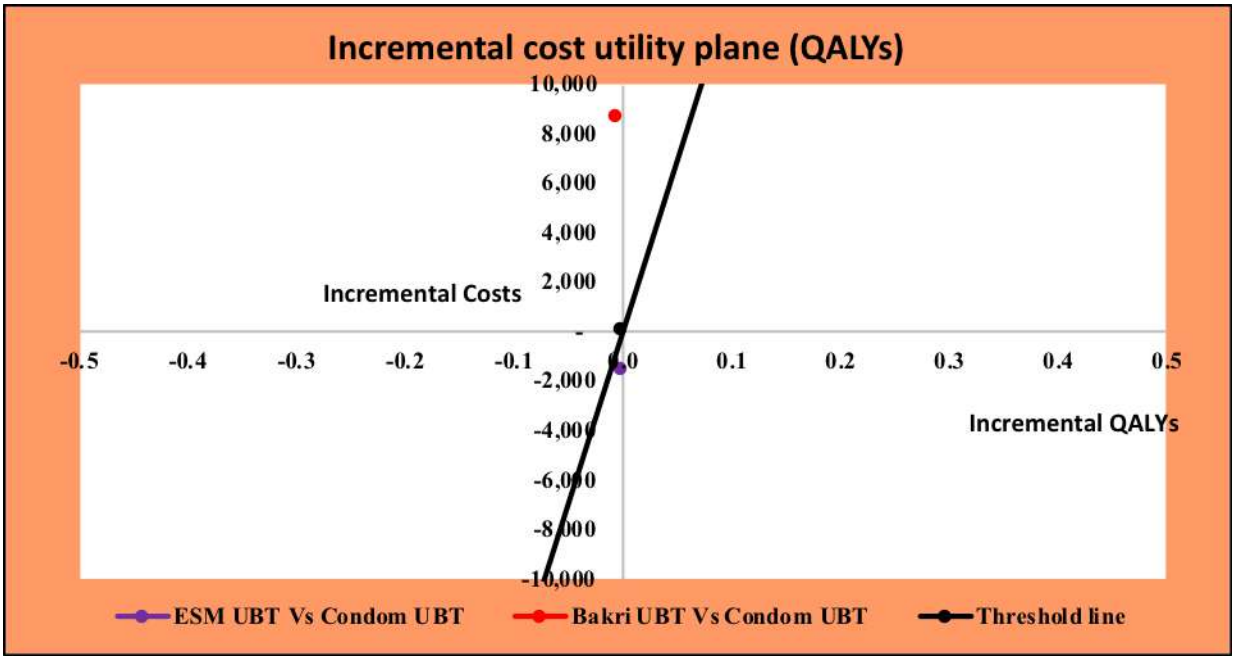


Figure 7: Incremental cost utility plane (QALYs)

Interpretation: ESM UBT ICUR (purple dot) lies in lower right quadrant. Hence ESM UBT is more cost-effective than Condom UBT. But the purple dot is close to 'zero' for incremental QALYs; indicating the minimal gain in QALYs of ESM UBT over condom UBT. The red dot indicates that Bakri UBT is more expensive and also a loss in QALYs as compared to Condom UBT thus demonstrating that it is not cost effective

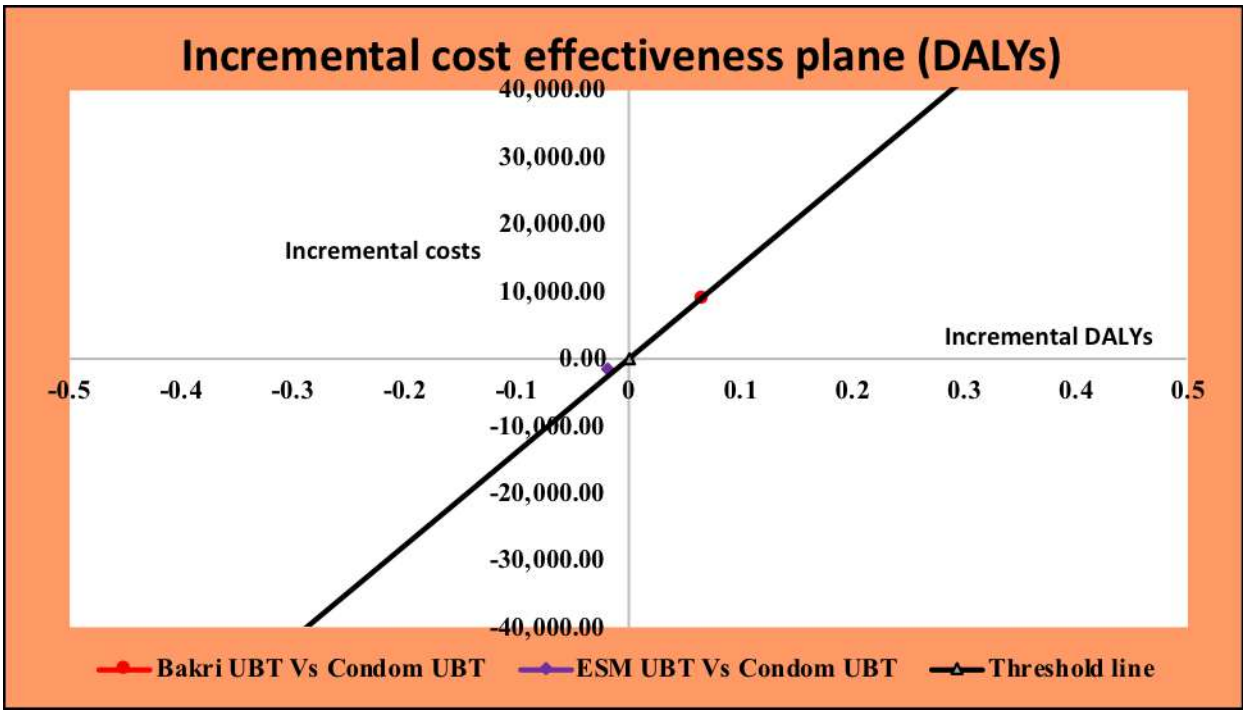


Figure 8: Incremental cost utility plane (DALYs) for the three UBTs

Interpretation: For DALYs, the interpretation has to be made in a reverse manner. If incremental DALYs are positive, the outcome is unfavorable. The purple dot shows that at a cost lower than the CE threshold, ESM has lower DALYs than Condom UBT. Hence ESM UBT is more cost effective than condom in terms of DALYs averted. But the purple dot is close to 'zero' for incremental DALYs; indicating the minimal aversion in DALYs of ESM UBT over condom UBT. The red dot indicates that costs and DALYs in Condom UBT are lesser than that in Bakri UBT. Hence Condom UBT is cost effective as compared to Bakri UBT.

Maternal deaths averted

The maternal deaths averted are presented in Table 10.

Table 10: Maternal deaths averted as compared to current scenario (cause specific MMR)

	Total Deaths as per model	Deaths averted (compared to current scenario**)
Condom UBT	283.00	10038.16
ESM UBT	280.03	10041.13
Bakri UBT	294.19	10026.97

** Current scenario specifies deaths due to current cause specific mortality in India ie PPH. The current scenario can have situations with varying use of different UBTs as no such specific information is currently available

Deaths as per model assume that all women experiencing atonic PPH are administered either one of the three devices. The limitation here is that different UBTs are already being used in current Indian scenario. Table 10 shows that deaths averted by ESM UBT > Condom UBT> Bakri UBT.

Surgeries

The decision tree model revealed that the least surgeries occurred in the ESM-UBT alternative, followed by Condom UBT and Bakri UBT. In the three decision trees of ESM UBT, Condom UBT and Bakri UBT, the respective number of surgeries from the model were 2,808; 3,919 and 8,107.

Table 11: Total number of surgeries in the three UBT alternatives of the model

	Total number of Surgeries
Condom UBT	3919
ESM UBT	2808
Bakri UBT	8107

Net health benefits and Net monetary benefits

Expressing cost-effectiveness in terms of net benefit is particularly useful when there are multiple alternatives. Net health benefit (NHB) and net monetary benefit (NMB) have been calculated and presented in Table 11.

Table 12: ICURs (QALYs) and Net Benefit with UBT alternatives

	Societal Costs	QALYs	Net Health Benefit (QALYs)	Net Monetary Benefit (INR)
Condom UBT	₹ 13,671.77	23.767	23.67	₹ 32,77,376.36
ESM UBT	₹ 12,096.06	23.769	23.68	₹ 32,79,133.05
Bakri UBT	₹ 22,300.75	23.763	23.60	₹ 32,68,065.30

Interpretation:

- All three UBTs have NHB>0, hence they are all cost effective(54). The incremental NHB between condom UBT and ESM UBT is negligible (0.002). Similarly the incremental NHB between condom UBT and Bakri UBT is minimal.
- At the WTP threshold of ₹ 1,38,468.76, ESM UBT, Condom UBT and Bakri UBT provide NMB of ₹ 32,79,133.05, ₹ 32,77,376.36and ₹ 32,68,065.30 respectively.

One way Sensitivity analysis:

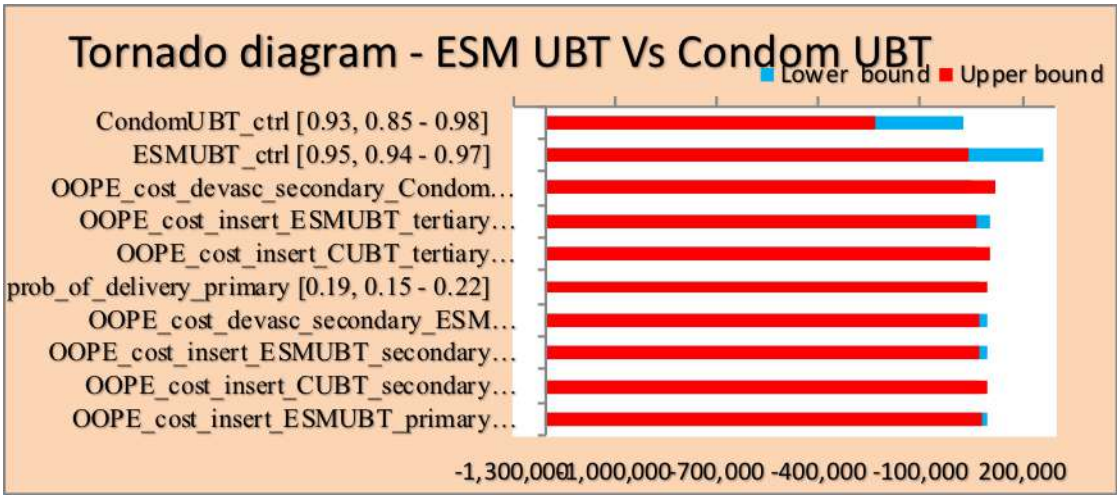


Figure 9: Tornado diagram depicting one way sensitivity analysis for ESM UBT vs. Condom UBT

Abbreviations in the chart

CondomUBT_ctrl: Effectiveness of condom UBT in controlling bleeding
ESMUBT_ctrl: Effectiveness of ESM UBT in controlling bleeding
OOPE_cost_devasc_secondary_Condom: Societal cost of devascularization surgery after Condom UBT at secondary facility
OOPE_cost_insert_ESMUBT_tertiary: Societal cost of insertion of ESM UBT at tertiary facility
OOPE_cost_insert_CUBT_tertiary: Societal cost of insertion of condom UBT at tertiary facility
prob_of_delivery_primary: Probability of women seeking delivery care at primary level of healthcare
OOPE_cost_devasc_secondary_ESM: Societal cost of devascularization surgery after ESM UBT at secondary facility
OOPE_cost_insert_ESMUBT_secondary: Societal cost of insertion of ESM UBT at secondary facility
OOPE_cost_insert_CUBT_secondary: Societal cost insertion of condom UBT at secondary facility
OOPE_cost_insert_ESMUBT_primary: Societal cost of insertion of ESM UBT at primary facility

Interpretation: The tornado diagram indicates the ten parameters that affect the ICUR value (of condom UBT vs. ESM UBT) the most. The effectiveness of condom UBT and ESM UBT are the parameters that affect the ICUR the most.

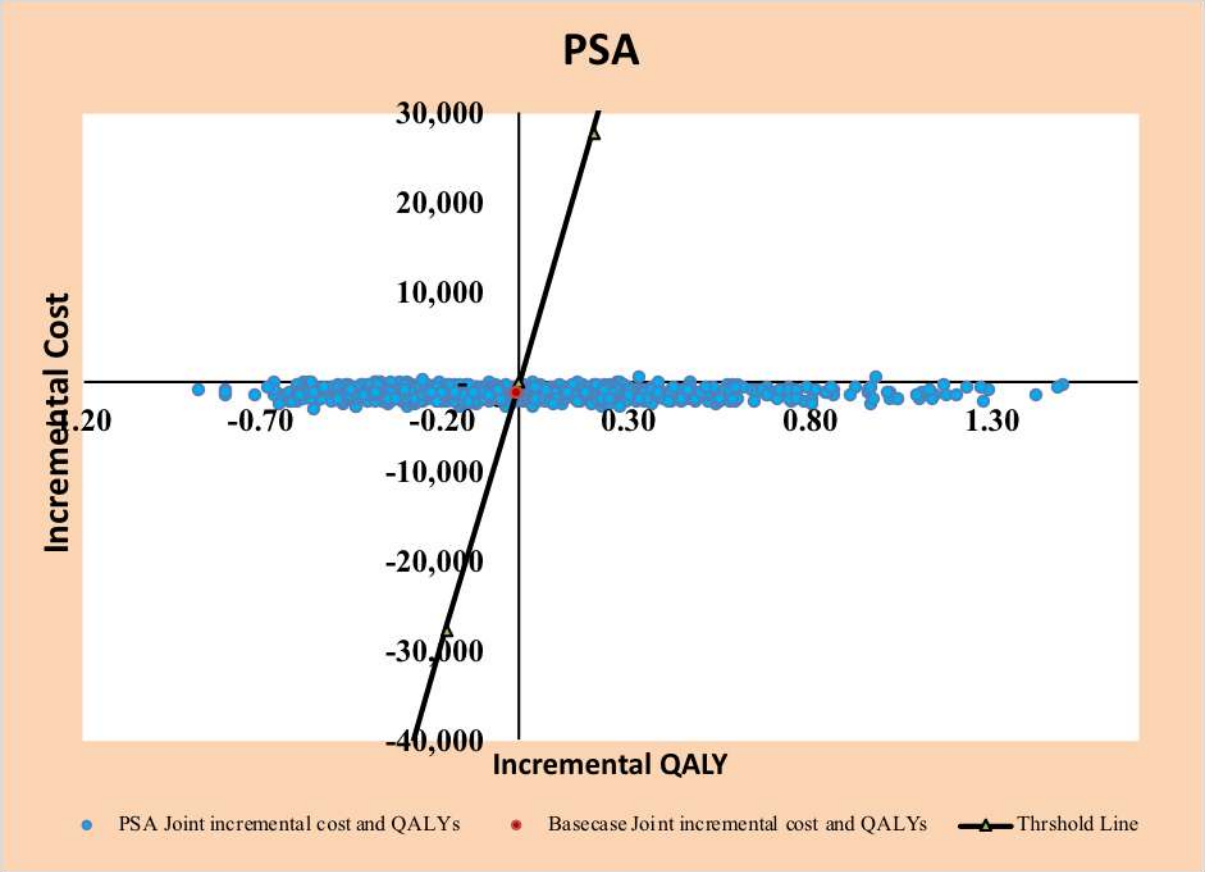
The red bars indicate that the parameter has been varied to the upper bound value of that parameter and the blue bars indicates that the parameter has been varied to the lower bound value of that parameter. Once the parameter is varied in either direction, the effect on ICUR is determined based on whether the bar is to the right of the base-case ICUR value or the left. The base-case ICUR value in this graph, is at -12,05,590. The red and blue bars are all on the right of the base-case indicating that none of the variations in the input parameters gets an ICUR < than the current base-case.

Main findings: If efficacy of ESM-UBT decreases (blue bar, lower bound); ESM-UBT ceases to be cost-effective

If efficacy of condom UBT increases, there continues to be a minimal difference between the two in terms of QALYs and costs.

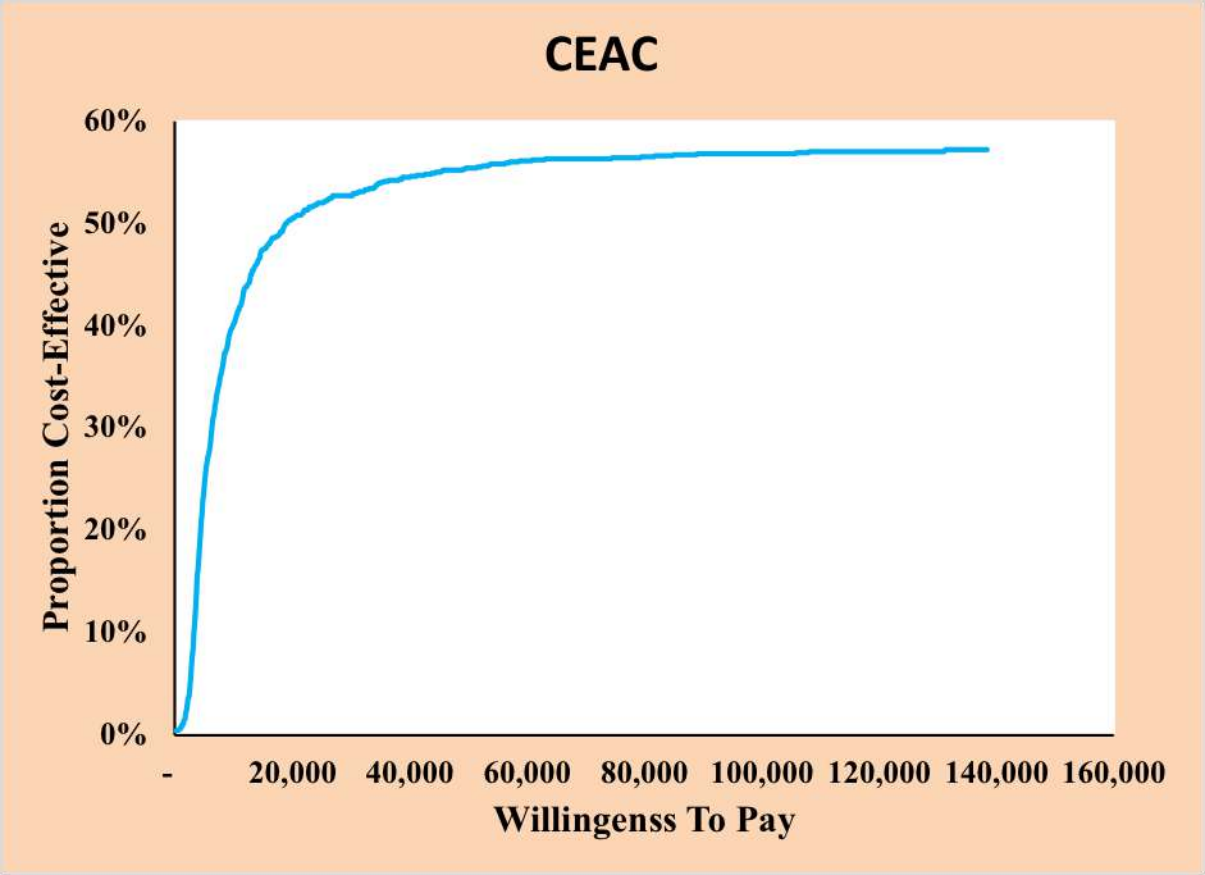
Probabilistic sensitivity analysis

Figure 10: Cost-effectiveness plane showing 1000 Monte Carlo simulations of Probabilistic sensitivity analysis



Interpretation of figure 10: Of the 1000 simulations,57.2%, a majority show that ESM UBT is not cost-effective. 41.7 % are in right lower quadrant (cost-effective); 0.2% and 0.9% in right upper quadrant and left lower quadrant below the WTP threshold line respectively. Hence about 42.8% of the the 1000 simulations are cost-effective. Each blue dot is an ICUR value derived from the Monte carlo simulations. The red dot is the base-case ICUR result.

Figure 11: Cost-effectiveness acceptability curve



Interpretation: This curve shows that as willingness to pay increases, the proportion of simulations that shows ESM UBT is cost-effective increases. The curve plateaus at about 50%, the maximum proportion of simulations that can be cost-effective in this model.

CHAPTER 4: EQUITY ISSUES

Table 12 lists a few key studies that highlight equity issues in the context of institutional delivery. We have used the equity issues associated with institutional deliveries as uterine balloon tamponade is a component of care given during institutional delivery. Studies from India have been considered.

Table 13: Studies assessing equity issues in healthcare during institutional delivery

Equity issue	*Brief excerpt*	*Source*
Education	Higher education levels affect the use of health services in several ways such as antenatal check-up, institutional deliveries, consulting the doctors, contraceptive use and sexual health care. The likelihood of practicing contraception, receiving antenatal check-up and institutional deliveries rise sharply with educational attainment.	(55)
Socioeconomic status	It has been observed that women of lower socioeconomic status often do not avail the existing reproductive health care services, particularly delivery care services.	(56)
	In rural India, economic status emerges as a more crucial determinant than access. Economic status strongly determines the choice between a private-for-profit or public facility amongst institutional births.	(57)
	In India studies show a very high out of pocket expenditure on delivery care, and, although the private sector is more expensive, the cost of public sector inpatient care services has increased since the 1990s. Hence, income is a major determinant of care seeking.	(58,59)

High delivery costs and distance	The impact of high delivery costs and distance to services as barriers to care seeking was highlighted in the 2006 Lancet Maternal Survival Series.	(60,61)
Parity	The likelihood of receiving antenatal check-up and institutional deliveries decline with parity unlike ccontraceptive use that displays a positive linear relationship with parity.	(55)
Awareness among pregnant women and family members	The most commonly reported enabling factor in the decision to use an institutional delivery care facility is awareness among pregnant women and family members about the value of institutional delivery care facilities for safe childbirth. The ability to pay for healthcare also positively affects the decision to use an institutional delivery care facility.	(62)
Previous experience with the health system	The health behavior of the population is impacted by previous interactions with healthcare settings. This may include not only women's own previous experiences directly related to delivery care (e.g., during ante-natal care checkups), but also experiences with non-obstetric services by the expectant mother, as well as healthcare experiences of other family members. Likewise, perceived and/or experienced safe childbirth at institutional delivery care facilities also acts as an additional enabling factor. Participants also commonly highlighted the availability of good quality institutional delivery care and support from nurses and doctors, and fully or partially subsidized institutional delivery care facilities including doctor and nurse	(62)

	services, medicines and diagnostic services as enabling factors.	
Government schemes to support institutional delivery	Several JSY-related factors served as important enabling factors for pregnant women and their families on switching their preferences from home to institutional delivery care facilities. They found ASHAs' support services and the cash incentive as two often mentioned JSY-related factors.	(62)
Social and religious factors	Social factors (respondent's religion, respondent's age at marriage, Respondent's Husband's Occupation play a major role for institutional and non-institutional deliveries practices.	(63)
Fertility and demand for male child	Fertility and demand for male child has emerged as a notable factor accounting for 33.13% of institutional deliveries and 37.28% of non-institutional deliveries.	(63)

Institutional deliveries have a wide spectrum of socio-economic and cultural factors linked to equity. As seen in our review, education, knowledge/awareness, access and income are the key areas where inequitable distribution of healthcare resources is occurring. Other factors like parity and demand for male child affects healthcare seeking for Institutional deliveries. As PPH is an event that occurs during delivery, these equity issues are applicable to women experiencing PPH.

CHAPTER 5: BUDGET IMPACT ANALYSIS

We conducted a budget impact analysis to ascertain how the budget would be impacted if ESM-UBT is introduced into the public health system of India.

Methods: Steps followed

1) Estimated requirement of UBT per year (atonic PPH cases which did not respond to medical management). Assumption was that ESM UBT will be provided and used in all these cases. A weighted average of incidence of PPH was used (vaginal and caesarean delivery)

2) Estimated deaths and surgeries averted in a year (If ESM is provided to all who require it, how many deaths and surgeries can be averted)

3) Estimated costs of providing the UBT to the user group

- Price of ESM UBT taken as 397 INR
- Training, refresher for 1/2 day to all MOs and ANMs
- Cost of surgery

4) Estimated the proportion of the budget that will have to be allocated to this technology (additional cost to introduce ESM: what percentage of the total health budget was spent)

5) Cost savings were calculated based on potential surgeries averted

Findings:

Annual additional budget for ESM UBT introduction into India's public health system is estimated to be 0.004 % of the total health budget and 0.005% of the total maternal and child health budget if ESM-UBT is available to 100% of women who require it.

Table 14: Annual Deaths and surgeries averted, monetary savings in different coverage scenarios as per the model

	ESM UBT Deaths	Condom UBT Deaths	Deaths averted by ESM UBT	ESM UBT surgeries	Condom UBT surgeries	Surgeries averted by ESM UBT	Costs saved due to reduced surgeries
100% Coverage	280	283	3	2808	3919	1111	₹ 85,61,377
50% coverage	656	658	2	31335	31891	556	₹ 42,84,542
20% coverage	882	883	1	48452	48674	222	₹ 17,10,734

If the coverage of ESM-UBT is 50%, the percentages increase to 0.02% and 0.03% of the total health budget and the total maternal and child health budget respectively.

CHAPTER 6: DISCUSSION

To our knowledge, this is the first study comparing three different types of UBT through an HTA perspective. Our study shows that ESM UBT is most cost-effective in comparison to Condom and Bakri considering the ICUR values. When ICER (DALYs) is considered, ESM UBT is more cost-effective than condom UBT. Again the difference is very marginal.

These are the base case results of the decision analytical model. A few key parameters that influence this base-case result are: the efficacy of the ESM-UBT and Condom-UBT. The efficacy of ESM-UBT is derived from the systematic review that was conducted as a part of this HTA. The review showed that there were only three case-series available. No RCTs were available. The critical appraisal of the three case-series showed that they were of poor to fair quality. Also, the probabilistic sensitivity analysis indicates that less than 50% of the 1000 Monte Carlo simulations showed ESM-UBT to be cost-effective.

The model shows that all three UBTs avert similar number of maternal deaths. ESM-UBT averts most surgeries, and all three have similar net monetary benefit. These benefits are estimated are assuming there is universal coverage of any one type of UBT in the respective situations.

The three UBTs under consideration have their own advantages and disadvantage in terms of cost, the device structures, the ease of use, the confidence it gives to the provider in terms of monitoring the blood loss and the chance of its retention in the uterus after insertion. In Condom UBT all available items are assembled and used while in ESM this assembly comes in a ready to use pack with high quality condom and better modalities to secure the condom in place. However, ESM UBT lacks the component of assessment of blood loss. This aspect is taken of if the existing Condom UBT is modified as per the Chhattisgarh UBT. While Bakri Balloon has set high standards to outweigh these disadvantages in terms of ready to use balloon (with no need to tie the condom to the catheter), a port to check the blood loss the effectiveness shown is lesser in comparison to other two UBTs and is also expensive.

Also, the ready to use sterile pack has not been studied in terms of its effectiveness in reducing infections. Studies on ESM UBT are not published in Indian settings and the experience of its use is limited to certain settings.

In a scenario where Condom UBT is already in our guideline and providers are trained there is a definite advantage of efficiently using condom UBT. Modifications to the condom UBT like the one made in the Chhattisgarh balloon would improve the qualitative aspect of using the UBT from a health providers' perspective as it gives better judgment to measure the blood loss which is found in Bakri Balloon and not reported in ESM UBT. In an informal discussion with experts it has been observed that some complain about the condom protruding out of cervix once inserted.

Our literature search showed that there was only one cost-effectiveness study done in Kenya using ESM UBT in which the comparator was not another UBT but standard of care without uterine packing. The study demonstrated that ESM UBT was cost-effective. The Kenya study ESM UBT cost-effectiveness model uses a scenario of home deliveries and also accounts for situations where uterotonic drugs are available and accessible. However, in our model we presumed the cohort of all births as institutional deliveries given that it's the scenario we have all aimed to achieve with a number of government schemes to support institutional deliveries. Although we are cognizant of the fact that such situations may prevail in some pockets, we have not considered it in our model.

Our model has considered ICU admission too which is lacking in the Kenya study. The UBT insertion in our model considers medical officers being trained and skilled to insert UBTs. However, there is a need to conduct the feasibility of assessing if ANMs who are the ones performing deliveries be trained to insert UBTs that can make a lot of difference and save lives of women during referrals.

It is imperative to consider equity issues in making UBT accessible to women irrespective of the many sociocultural, geographic and health system barriers. This is possible when the lowest cadre of health personnel i.e. ANM in the village is trained. This has to be supported by a strong referral network especially in the hard to reach geographic areas such as hilly terrains or forest areas where mobile and road connectivity is very poor.

Equity issues about institutional delivery are highly prevalent in Indian settings. Number of socioeconomic, cultural and demographic barriers influence access to services. As for institutional delivery, the following issues need to be considered for Universal access:

- Preconception care for educating young couples about pregnancy and related risk
- Early ANC enrollment
- Adequate spacing between pregnancies and delaying age of first pregnancy after 21 years of age for women
- Access to all government schemes related to pregnancy care
- Women empowerment through social interventions such as education, employment and decision making
- Male involvement and support during pregnancy and care of the newborn
- Improving health workers' support services focused on marginalized populations along with better public healthcare facilities are likely to promote the uptake of institutional delivery care in resource-poor settings.
- Availability of referral services and access to quality care
- Skilled manpower to manage PPH
- Availability of drugs, blood and blood products

Given all these intervention discussions, the bottom line remains early ANC registrations; complete ANC checkups, identifying all high risk pregnancies and ensuring that they deliver at facilities with comprehensive obstetric care services are available and universal coverage of life saving interventions such as the UBT. Life of every woman is very precious and it has to be saved by improving quality care by skilled providers using clinically effective evidence-based interventions. Uterine Balloon Tamponade intervention can make a difference to both the health system and families at large especially the pregnant woman and her newborn.

CHAPTER 7: LIMITATIONS OF THE STUDY

- The efficacy value of ESM UBT that has been used in the model was derived by taking averages of values from three case series of fair quality, due to lack of any robust meta-analysis/ randomized control trials. The efficacy of ESM-UBT needs to be established with RCTs. Better quality evidence in Indian setting is required, as the current evidence for ESM is limited.

- The cost of ESM-UBT has been taken as INR 397 in the model. The exact price of the product if introduced into the system needs to be estimated.

- The coverage of ESM-UBT in the model has been assumed to be 100%. This needs to be looked at with a pragmatic lens.

- Preventing maternal deaths has numerous consequences, and not all can be quantified based on monetary terms. Beyond the obvious benefit of DALYs saved for mothers, the other benefits include the fact that reducing maternal deaths ensures that more children grow up with their mother's care improving their health and education. Our model accounts for only a few benefits of the intervention and comparators; and not all the above mentioned benefits. Hence a complete valuation of costs has been done, but a complete valuation of benefits, underestimating the benefits of the interventions.

- Utility weights used in our model are from studies done in western settings. Indian utility weights would have been more appropriate. Specific utility scores for the use of individual devices are not available.

- Primary health system costing study was done in a few public health centers in the state of Maharashtra. The costs may not be applicable across the different states of India (This was addressed in the sensitivity analysis).

- The group of surgeries that we have included in our model under the heading of "devascularization surgeries" includes uterine artery/iliac artery ligation and B-Lynch suturing. It does not include embolization of arteries. Hence cost of devascularization group of surgeries excludes cost of embolization

CHAPTER 8: RECOMMENDATIONS

- QALY gain in ESM UBT and condom UBT are very similar. ICUR value of ESM UBT against Condom UBT shows that ESM UBT is cost-effective, but the probabilistic analysis shows that a majority of 57.2% of the simulations show that ESM-UBT is not cost-effective; while only 42.8% of the simulations show that ESM-UBT is cost-effective. We recommend that good quality efficacy data on ESM-UBT should be generated by doing RCTs in Indian settings, before any decision regarding the same is undertaken

- There is less than 0.1 difference in the net health benefits between the three alternatives; indicating the similarity in health benefits of the three UBTs.

- Considering the above statements, decision-making regarding ESM UBT's introduction into the public health system must be made with caution. Also, studies on ease of use by Indian healthcare providers and qualitative aspects need to be conducted and its actual costs for use in public health system need to be derived.

- If ESM-UBT is considered for introduction, it should be noted that to gain the benefits estimated by the model, a universal coverage needs to be attained (100%) which currently seems to be very challenging given the current poor use of condom UBT in spite of being recommended in the Govt. of India Guidelines .

CONCLUSIONS:

We have considered the effectiveness of condom UBT, ESM UBT and Bakri UBT to be 93%, 95% and 86% respectively, from available literature. The price of condom UBT, ESM UBT and Bakri UBT were taken to be INR 128, INR 397 and INR 9554 respectively. The total costs from the model from societal perspective for one woman using condom UBT, ESM UBT and Bakri UBT were INR 13,672, INR 12,096 and INR 22,301. The QALYs per woman in condom UBT, ESM UBT and Bakri UBT were 23.767, 23.769 and 23.763 respectively; showing a very minute difference in QALYs.

For ESM UBT vs. Condom UBT, the ICUR is -12,05,590 INR /QALY and hence ESM UBT is more cost-effective than Condom UBT, but PSA shows that ESM UBT is not cost-effective, 57.2% (majority) of the times and is cost-effective in only 42.8% of the 1000 Monte Carlo simulations. ICUR of Bakri UBT vs. Condom UBT is -17,51,769 indicating that Bakri UBT is not cost-effective as compared to condom UBT. Maternal deaths that occurred as per the model in each of the three alternatives were compared with the maternal deaths of current scenario (MMR). Condom UBT, ESM UBT and Bakri UBT were found to avert 10,038, 10,041 and 10,026 maternal deaths respectively. Surgeries in ESM UBT, Condom UBT and Bakri Balloon UBT were 2808, 3919 and 8107 respectively.

- As there were multiple mutually exclusive UBT alternatives, net health benefits (NHB) and net monetary benefits (NMB) were calculated. All three UBTs have NHB>0, hence they are all cost effective. The incremental NHB between condom UBT, ESM UBT and Bakri UBT was very minimal.
- At the WTP threshold of ₹ 1,38,468.76, ESM UBT, Condom UBT and Bakri UBT provide NMB of ₹ 32,79,133, ₹ 32,77,376 and ₹ 32.68.065 respectively.
- Budget impact analysis shows that annual additional budget required for introduction of ESM UBT into India's public health system is estimated to be 0.004 % of the total health budget and 0.005% of the total maternal and child health budget

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ACKNOWLEDGEMENTS

- We thank Secretary DHR Dr. Balram Bhargava and Joint Secretary Smt. Anu Nagar for providing us the opportunity and support to conduct this study.
- We thank Dr. Dinesh Baswal , Deputy Commissioner, Maternal health, Ministry of Health and Family Welfare, India for his guidance
- We thank Dr. Kavitha Rajashekar, Scientist E, Department of Health Research, MoHFW and her team for their support
- We thank Dr. Smita Mahale, Scientist G, Director, NIRRH for her encouragement.
- Dr. Anushree Patil (Scientist E, ICMR-NIRRH) and Dr. Niranjan Maydeo (Head, OBGYN, KEM hospital Mumbai) for giving clinical expert Guidance on PPH management
- Ms. Maria De Francesco for her invaluable inputs
- Dr. Malkeet Singh, Junior Health Economist, HTAIn, DHR, Ministry of Health and Family Welfare, India for assisting during proposal writing
- Dr. Amita Pandey for sharing data on PPH management by Bakri Balloon Tamponade
- Dr. Amit Patel from Jivdaya Foundation who agreed to share data on Bakri Balloon
- Dr. Archana Patil (Director,State Health Dept Pune) and the nodal officer for HTA from Maharashtra, Dr. Anirudha Deshpande (Asst. Director HFWB Pune) for facilitating data compilation of 108 ambulance service in Maharashtra
- Dr. Dynaneshwar Shelke from BVG for compiling 108 Ambulance data
- All hospital authorities and staff who helped in data collection for costing

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