Record of discussion of the Technical Appraisal Committee meeting held on 26th and 27th August, 2019, 10.00 AM in the Department of Health Research (DHR), MohFW, New Delhi under the Chairmanship of Prof. T. Sundararaman, Former ED, NHSRC to discuss HTA study proposals and outcome reports.

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1. The 15th TAC meeting was held on 26th and 27th August, 2019, 10.00 AM in the Conference Room, DHR, MoHFW, 1st Floor, IRCS Building, New Delhi, under the Chairmanship of Prof. T. Sundararaman, Former ED, NHSRC in presence of Smt. Anu Nagar, Joint Secretary, DHR, MoHFW.
2. The purpose of the meeting was to discuss the following:

   Outcome reports of

   i. HTA on Pulse Oximeter
   ii. HTA on Uterine Ballooon Tamponade
   iii. HTA on Sohum - A Neonatal Hearing device
   iv. Revised HTA on Bempu Hypothermic Device
   v. HTA of TrueNAT - TB Diagnostic Device

   Proposals on

   i. Proposal on ENTRaview
   ii. Revised HTA Proposal on Iron sucrose substitute for Anaemia patients
   iii. Proposal on Cardiac Topics (CAD and Related Disease)
3. HTAIn Secretariat briefed TAC on the action taken on the decisions of the previous TAC and revision of proposals/reports done accordingly, and the agenda of current meeting.
4. The chair instructed that one of the TAC members, who is assigned this task should lead the discussion of the proposal or report as the lead discussant in those proposals. This ensures closer scrutiny by some members because the number of proposals are becoming too many for everyone to study all of them with equal rigor.
5. The session was opened to discuss the HTA proposals and outcomes.

I. Outcome report on HTA of Pulse Oximeter by SCTIMST, Kerala

1. The rationale, objective, methodology and summary of finding were presented.
2. The comparison was between IMCI+PO (intervention) vs. IMCI (comparator). Integrated Management of Childhood Illness (IMCI) guidelines are already there in the health system but Pulse Oxymeter (PO) detects oxygen saturation levels which in turn identifies both severe and moderate pneumonia and helps in its management and early referral of severe cases.
3. The ICER was found to be negative and sensitivity analysis confirmed that it was a cost saving intervention.

4. TAC commented at what threshold of oxygen saturation the cases may be referred would be useful. It was also suggested that it may be clubbed with the Standard Treatment Guidelines.
5. TAC suggested that the recommendations should address: How it improved referral? How much mortality was reduced? At what levels should PO be introduced and in which of these the output would be referral as different from in-house management of severe pneumonia? What training was required in its handling (User friendly)? What are the Budgetary implications?
6. The cost of oxygen supply in PHCs/ CHCs needs to be included.
7. Final recommendations should include that appropriate training and referral mechanisms should be in place. The effectiveness of this technology would be very much dependent on this.
8. Comments of the TAC were well addressed and the Outcome report was approved.
9. The resource hub informed that they met with the Mission Director of NHM, Kerala who has appointed a Nodal Officer for the resource hub by the Govt. of Kerala. They will send a list of topics for HTA to DHR soon.
10. Sensitization initiatives plans of the SCTIMST for NHM district program managers, district medical officers and nodal officers were presented intended to familiarize them with the concept of HTA and how it will be beneficial for Kerala State.
11. A workshop plan for the resource team was also presented with an intent to bring up research questions relevant to the HTA context and also help them better analyses the wealth of data the health system already possesses.

II. <u>Intrauterine Balloon Tamponade, NIRRH-Mumbai</u>

1. The background, research question, aim, objectives, methodology and results were presented…ESM and Bakri Balloon were compared with standard care i.e Condom UBT.

2. ICERs indicated that Condom UBT was more cost-effective than ESM though the difference was not much. Qualitative issues such as ease of use that makes ESM more user friendly needed to be confirmed. Even though health Utility Score of Bakri Balloon was found to be better it was not cost-effective when compared against condom and ESM UBT. By threshold analysis if the cost of Bakri Balloon is reduced to Rs. 5000 it becomes cost effective. Based upon net health benefit Condom UBT was found to be most cost-effective among the three interventions.

3. The User Department representative stated that HLL Lifecare made a kit where they assembled the condom UBT using silicon catheter, and this was already sanctioned and in use, but the HLL product had not been used as a comparator.The NIRRH team responded that the team had contacted HLL UBT and was not aware of their certification of bioequivalence with ESM UBT and no study with the product was reported.

4. TAC asked if it was a bridge-therapy or definite therapy because it mentioned averting more surgeries instead of averting Maternal Mortality Rate (MMR). Ideally, MMR averted and surgeries averted should go in the same direction. TAC suggested the team to re-check the number of maternal death and number of surgeries averted- and to use the latter as the main outcome indicator. The time taken after delivery and before introducing UBT was also an important determinant of outcomes..
5. TAC asked if private sector cost was factored in the study to which the team responded that since the request was for public sector implementation therefore private sector cost was not taken. Another member suggested that in private sectors also, cost may vary but the conclusions will remain the same.
6. A co-opted expert commented that both Condom UBT and ESM UBT appear to be useful in field setting. However, the time taken and manpower engaged to assemble the Condom UBT vs. ESM UBT was not assessed (lack of data??). ESM UBT can be EtO sterilized if the Govt. choose to approve it.
7. One of the TAC members commented that Bakri is too expensive (about 25 times than ESM and even more for condom catheter) then it doesn't make sense to include it in the comparison. ESM and Condom catheter seems more comparable devices-wise the only difference being ESM does not measure blood loss though it comes in ready to use assembled form. Thus, a comparison between these two would have been sufficient. The question is whether ESM and condom UBT yield more or less similar results or are the two differences mentioned above major enough to yield different outcomes and benefits. The team responded that Bakri balloon was a ready to use device and measures blood loss, and since this device is currently in practice at many places, that's why it was also considered in the assessment.
8. The TAC asked whether there are equity issues such as problem in poorer and marginalized community? In equipment, set up, trained manpower etc. The team responded that trained manpower is required in all of them. So, challenges lie ahead getting an ANM trained.
9. The TAC concluded that earlier meeting's comments were well addressed and the Outcome Report was approved by the TAC.
10. The resource hub team of NIRRH informed that they have received 10 more topics from Maharashtra Govt. that may be taken for HTA study.

III. <u>Sohum Hearing device, RMRC Bhubaneswar</u>

1. The background, methods overview, perspective, PICO and results were presented.
2. Sohum and OAE were compared with Gold Standard BERA.
3. Out 198 participants, all those detected positive for hearing loss by either device were not confirmed with BERA. Rather, a sub-sample of 27 participants were tested by BERA.

4. TAC raised this concern that the generated values for sensitivity and specificity was representative of the subsample (27) rather than the total sample.
5. Another concern raised was the inconsistency in the unit used for calculations – some were done for the total number of patients tested while some were done for the total number of ears tested. This should be consistent throughout the report either ear or the no. of patients.
6. The TAC pointed out that the study sample was from only one level of health facility and not representative of the general population. It was recommended that samples from different level of facilities should have been incorporated.
7. A co-opted domain expert pointed out that the duration of testing with BERA in practice is generally around 30-45 min while the study showed 90 minutes which is high. Please look into it.
8. Another expert suggested that ideally the newborns should be screened for deafness before discharging from the hospital so that out-of-pocket expenditure on travel will be reduced to zero.
9. It was suggested to mention the costing and model assumptions clearly. TAC also suggested to compute cost for universal screening and high risk population screening. If cochlear implant was required, then operation cost should also be included. Cost of hearing aid should also be included as it may get replaced periodically during the lifetime.
10. Diagnostic accuracy of Sohum was better (Sensitivity-90-95%, specificity-94-95%) than OAE (Sensitivity – 75%, specificity -68%)
11. One of the experts informed that a validation study was ongoing in Maulana Azad Medical Coleege and the sensitivity and specificity of Sohum has been reported 100% and 97% respectively while OAE showed 75% and 74%. All the three devices were tested on the same infant and not randomly. One of the TAC member suggested to take the results of MAMC study as it was on a larger scale and more robust study design.
12. TAC also suggested to use the generic name because the principle of the device is what is being considered so better call the device as Portable Automated ABR rather than Sohum. Also, to look if ABR is included in the guidelines of other countries?
13. Finally, TAC recommended that the final report require some improvements,. These would include factoring in the rehabilitation cost, and hearing aid cost in cochlear implant contexts also. Also to base it on the validation data from MAMC. Go through the guidelines regarding hearing and re-check the computation after incorporating above points.
14. TAC suggested that this final report and recommendations may be Peer reviewed by Prof. Siddharth Ramji and Prof. Sundararaman.

IV. Revised HTA Outcome on Bempu, RMEC – IIPH, Shillong

1. Previous comments and recommendations by the TAC were presented and also how they were incorporated in the revised outcome.

2. The TAC accepted the recommendations of the study that Bempu was not a cost-effective intervention.
3. In principle, the study was approved with the recommendation to see at what cost it will become cost effective through the threshold analysis.
4. TAC also recommended that some operational research and validation may be suggested to generate data such as is it adding benefits for high risk babies, at a community setting. Due to the lack of data, this device has not been assessed for use in high risk babies in a community setting.

V. HTA proposal on ENTRaview, HTAIn Secretariat, New Delhi

1. A product of Bangaluru based startup company – Icarus Nova
2. The background of about SHRUTI Program was discussed on a ppt. presentation
3. Policy Question: Research question, Aims and PICO were discussed.
4. TAC asked about the prevalence of the ear infection that require autoscopy and when it is mandatory? What is it being used for?
5. The team responded that it is used for both acute and chronic hearing loss, require less manpower capacity and help in referral.
6. TAC was informed that the device is being used in Shroff's hospital, Delhi and AIIMS, Jodhpur and many other centers for screening.
7. TAC suggested that in view of the lack of data of use in a community/primary healthcare setting, for which it is being considered, it may go to the Project Appraisal Committee and asked to develop an operational research proposal.

VI. HTA proposal on Iron Sucrose and Ferrous Carboxyl Maltose for first line management of iron deficiency anemia among pregnant women, Indian Institute of Public Health Gandhinagar

1. The background – research question, aims, objectives were presented through a ppt. presentation.
2. The team informed that FCM Is already in practice in some districts of Gujarat
3. One of the TAC member who had joined through skype call commented that moderate and severe case detection is established, moderate we need to see, mild was not proposed.
4. NIRRH, Mumbai team informed that FCM is under study in Maharashtra.
5. The TAC recommended:
    - to develop an Operational Research proposal (analyze the sample size, study design) and send it to the PAC.
    - that NIRRH, Mumbai may help in the peer review of the study.
    - to look whether the DGCI approval is there and consult the i-NIPPI guidelines while preparing the proposal.

VII. HTA outcome report on TrueNAT, HTAIn Secretariat, New Delhi

1. TrueNat is a molecular test that can diagnosis TB in one to three hours and it is advantageous in field settings. Sufficient data was available in the literature but feasibility data (people who are actually using it) not available. TAC suggested for operational research for feasibility data, if required. Feasibility may also be seen from the existing guidelines.
2. The background, research question, methodology and results were shown through a ppt. presentation. TrueNAT was compared with Gene Expert.
3. TAC asked about the requirement of training to operate TrueNAT, the team responded that minimum expertise (simple lab techniques/ knowledge of pipetting) is required.
4. TAC raised concerns that TrueNAT may detect many false positive to which team responded that detected cases are sent for culture/ nested PCR and 78% cases were concordant with TrueNAT.
5. The results showed that TrueNAT was better but the TAC pointed out the following areas that required clarification and/or re-working:
    - In the absence of a single to gold standard findings of the tests should be compared against a composite clinical gold standard i.e. diagnostics available such as culture or histopathology. The current presentation shows only relative sensitivity. It was mentioned that an ICMR study compared Smear and Culture, it may be referred.
    - In addition to that, concordance between gene expert and trueNAT may be presented.
    - TrueNat may have false positives- and therefore one should explore results in two scenarios- one where this is the only test and another where this is one test in a larger set of diagnostics- and the degree of confidence in each should be shown.
    - consumable, shelf life (if applicable) and treatment cost should also be included and assumptions in the model should be clear.
    - costing of the number of samples per test should be considered and not only unit cost let's say, TrueNAT can detect 4 sample per experiment and gene expert 8 samples per experiment so costing per sample will vary when used for single sample per experiment and 4 or 8 samples per experiment. In the periphery/ remote areas it may not matter (due to less number of cases) but in district hospitals it will matters so it may be looked carefully while doing the costing.
    - Details of cost effectiveness and cost should be given.
    - For Budget Impact Analysis financial cost and not economic cost should be preferred and it should be more realistic i.e. impact should be seen during a span of let's say 5 years or more and not just one year.

- Can discuss with ministry the level of introduction- may not be suitable for HWCs, but there is a case for PHCs and this has implications for the final report.

6. TAC took this as a preliminary presentation and would look forward to the final report and recommendations.

VIII. HTA Proposals for Cardiac Topics (CAD and Related Diseases), HTAIn Secretariat

1. Background, research question and methodology were presented through a ppt. presentation.
2. TAC suggested to look at TVD (triple Vessel Disease) and Stable Left Main CAD (Coronary Artery Disease) separately with their respective treatment modalities.
3. Similarly, the topic for MVD (Multi-Vessel Disease) was changed to 1 and 2 vessel disease without the involvement of stable Left Main CAD and correspondingly look at its treatment modalities.
4. TAC discussed and recommended that for the required QoL data, primary data collection need not be done.; suggested to use the secondary data sources available.
5. TAC also required disease complications and its prevention to be incorporated into the model.
6. In principle, the study proposal was approved.

After Detailed Deliberations following Action Point Emerged

1. **Pulse oximeter Outcome**
   - Recommendations should address: How it improved referral? How much mortality was reduced? At what level of health setting should it be introduced? What training was required in its handling (User friendly)? Cost and Budget implications should also.
   - The recommendations were approved but a revised outcome report to be circulated after incorporating the comments of the TAC.
2. **Intra-uterine Balloon Tamponade Outcome**
   - Re-check the number of maternal deaths and surgeries averted.
   - Conduct a Budget Impact Analysis.
   - The recommendations were approved but a revised outcome report to be circulated after incorporating the comments of the TAC.
   - On the HLL Lifecare device, data and studies are awaited and these could be incorporated later. If there is a certificate that it is the same working design as the ESM then the findings of these would tentatively apply.
3. **Sohum Hearing Device Outcome**
   - Suggestion were made to do calculations based upon for total number of patients tested instead of total number of ears to avoid the discrepancy.
   - Cross-check the duration of testing with BERA.
   - Mention the assumptions clearly and relook into the costing keeping in mind following points:
     - Testing the neonates delivered in the hospital before discharging them may save the transportation cost.
     - Compare the cost for universal screening and high risk population screening.
     - If cochlear implant was required, then operation costs plus. cost of hearing aid should also be included as it may get replaced periodically during the lifetime.
   - The team may consider using data from the MAMC study as it is a bigger study with more samples.
   - Use the generic name of any product based upon its principle such as Portable Automated ABR for Sohum.
   - Outcome report may be revised and circulated among the TAC members. It will be peer reviewed by Prof. Siddharth Ramji and Prof. Sundararaman.
4. **Bempu, Hypothermic Device Revised Outcome**
   - The revised outcome was approved with the recommendation to see at what cost Bempu will become cost effective through the threshold analysis.

5. **ENTRaview Proposal**
    - The proposal may go to the Project Appraisal Committee (PAC) and the team was asked to develop an operational research proposal.
6. **Iron Sucrose and FCM Proposal**
    - TAC recommended to develop an Operational Research proposal (analyze the sample size, study design) and send it to the PAC.
    - NIRRH, Mumbai may help in the peer review of the study.
    - Team may look whether the DGCI approval is there and consult the i-NIPPI guidelines while preparing the proposal.
7. **TrueNAT Outcome**
    - The study may proceed and come up with a detailed report- taking into consideration all the points raised in the discussion (see earlier section):
    - The outcome report may be finalized and circulated to the members after incorporating above comments.
8. **CAD and Related Disease Proposals**
    - Study TVD (triple Vessel Disease) and Stable Left Main CAD (Coronary Artery Disease) separately with their respective treatment modalities.
    - MVD (Multi-Vessel Disease) was changed to 1 and 2 vessel disease without the involvement of stable Left Main CAD and correspondingly look at its treatment modalities.
    - Primary data collection for QoL need not be done, use the secondary data for now.
    - Disease complications may be incorporated into the model.
    - It was recommended to revise the proposal incorporating the above mentioned points, and proceed with the study

The meeting ended with a vote of thanks to the chair and all the participants.

T. Sundararaman, Chairperson, TAC, HTAIn

Annexure-I

List of Participants

A. TAC Members

1. Prof. T. Sundararaman, Former ED, NHSRC – Chairman
2. Prof. J.V. Peter, Director, CMC, Vellore.
3. Prof. V.R. Muraleedharan, IIT, Chennai – Member (On skype)
4. Prof. Shankar Prinja, School of Public Health, PGIMER, Chandigarh
5. Dr. Sudha Chandrashekhar, World Bank – Member

B. DHR Officials

1. Smt. Anu Nagar, Joint Secretary, DHR, New Delhi.
2. Shri Daulat Ram Meena, Deputy Secretary, DHR, New Delhi

C. Co-Opted Members

1. Dr. Dinesh Baswal, Deputy Commissioner (MH) MoHFW, New Delhi
2. Dr. Sangeeta Abrol, DDG (MoHFW), Eye Safdurjang, New Delhi
3. Dr. Renu Shrivastava, CH Div., MoHFW, New Delhi
4. Dr. S. Ramji, Professor, Department of Pediatrics, MAMC, New Delhi.
5. Dr. Ashish Jain, Neonatology, MAMC, Delhi
6. Dr. N. N. Mathur, Principal and Director (ENT), VMMC and Safdurjang Hospital, New Delhi
7. Dr. Rakshita, Consultant, MoHFW

D. ICMR Hq. - Scientists

1. Dr. Ashoo Grover, ICMR Hq., New Delhi
2. Dr. Reeta Rasaily, Scientist G, ICMR Hq., New Delhi

E. Resource Centre/ Technical Partner Representatives

1. Dr. Beena Joshi, Scientist E, NIRRH, Mumbai
2. Dr. Kusum Moray, Scientist C, NIRRH, Mumbai
3. Dr. Siddesh Shetty, NIRRH, Mumbai
4. Dr. Sandra Albert, Director, IIPH, Shillong
5. Dr. Rituparna Ghosh, Research Feloow, IIPH, Shillong
6. Dr. Sanghmitra Pati. Director, RMRC Bhubaneswar
7. Dr. Debdutta Bhattacharya, Scientist-C, RMRC, Bhubaneswar
8. Dr. RInshu Dwivedi, Senior Research Officer, RMRC, Bhubaneswar
9. Dr. Krushna Sahoo, Public Health Specialist, RMRC, Bhubaneswar
10. Dr. Komal Shah, Economic Evaluation Specialist, IIPH, Gandhinagar
11. Mohammad Ameel, NHSRC, New Delhi
12. Dr. Rituparna Ghosh, IIPH, Shillong
13. Dr. Ibaplielad Jana, IIPH, Shillong.
14. Dr. Hisham Moosan, Technical Expert (Epidemiology) & Project lead, RTRC-HTA, SCTIMST, Trivandrum.
15. Dr. Antony Stanley, Research Associate, RTRC, SCTIMST, Trivandrum.
16. Dr. Maninder Pal Singh, Research Officer, PGIMER, Chandigarh

F. HTAIn. Sec., DHR

1. Dr. Kavitha Rajshekar, Scientist-D, DHR, MoHFW, New Delhi
2. Dr. Nidhi Singh, Scientist-C, DHR, MoHFW, New Delhi - Participant
3. Dr. Oshima Sachin, Scientist-D, HTAIn Sec., DHR, MoHFW, New Delhi
4. Dr. Aamir Sohail, Health Policy Analyst, HTAIn Sec, DHR, MoHFW, New Delhi
5. Mr Arvind Bhushan, Scientist-C, HTAIn Sec, DHR, MoHFW, New Delhi

6. Dr. Shalu Jain, Scientist-C, HTAIn Sec, DHR, MoHFW, New Delhi
7. Miss Jyotsna Naik, Scientist-C, HTAIn Sec, DHR, MoHFW, New Delhi
8. Dr. Malkeet Singh, Junior Health Economist, HTAIn Sec, DHR, MoHFW, New Delhi
9. Dr. Akshay Chauhan, Junior Health Economist, HTAIn Sec, DHR, MoHFW, New Delhi
10. Dr. K.V. Jagadeesh, Scientist B, HTAIn Sec, DHR, MoHFW, New Delhi
11. Dr. Shivangi Khanna, Scientist B, HTAIn Sec., DHR, MoHFW, New Delhi
12. Mrs. Safia Zaidi, Programme Manager, HTAIn Sec, DHR, MoHFW, New Delhi
13. Mrs. Kirti Tyagi, Scientist-C, HTAIn Sec, DHR, MoHFW, New Delhi
14. Miss Anjana Aggarwal, Scientific Consultant, HTAIn Sec., DHR, New Delhi
15. Miss Himanshi Tomar, Scientific Consultant, HTAIn Sec., DHR, New Delhi
16. Mr. Vipin Kumar, Personal Assistant, HTAIn Sec., DHR, New Delhi