

Minutes of Meeting of National Standing Committee for Operational Research (OR) under RNTCP held at Lala Ram Swarup Institute (LRSI) of Tuberculosis and Respiratory Diseases, New Delhi on 8th February 2012

Meeting of the National Standing Committee for Operational Research in RNTCP was held at LRS Institute, New Delhi on 8th February 2012 under the Chairmanship of Dr. S. K. Sharma, Prof & Head, Dept of Medicine, AIIMS, New Delhi. Agenda of the meeting and list of the participants are attached as Annexure.

Chairman welcomed all the Committee members and the Principal Investigators and briefed about the objectives of the meeting. Dr. D. Behera, Director, LRS hospital for TB and other Respiratory Diseases, Mehrauli welcomed the participants to the Institute.

It was suggested by the National Standing Committee for Operational Research to RNTCP that any Operational Research being conducted by other agencies under the aegis of RNTCP should be brought to the notice of National Standing Committee for Operational Research. Some of the members pointed out that they were not aware of GeneXpert related OR. However, from CTD it was clarified that it is a commissioned project by RNTCP and was not an Operational Research. Members of the Committee insisted that the latest development(s) and/or any change(s) made in the programme should be brought to the notice of the committee members from time to time in order to avoid duplication of efforts. This was accepted by the CTD Officials and Dr. Niraj Kulshrestha assured the Committee members that henceforth there will be a presentation by CTD in every OR Committee meeting on the latest events developments related to the national programme.

It was also decided that the stricter deadlines should be followed for submission of OR protocols to the Committee / CTD. CTD should try to get external review of OR proposals and members of the Committee should be informed about scores of OR proposals.

It was also proposed by the Committee to central TB Division to organize OR dissemination Workshop to a larger audience, so that the results of the studies conducted are shared by the scientific community who are expected to use these results. CTD agreed to support this initiative and such workshop is to be held at NTI, Bangalore before June 2012.

It was also proposed that since many of the Operational Research studies have actually concluded and these studies should be published and information should be disseminated in various ZTF meetings. It was accepted by CTD to arrange such review of articles for policy changes before April 2012.

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One new proposal and three revised research proposals were presented by the PIs. These proposals had been peer reviewed and Reviewers' comments were placed in the meeting for consideration. **Three resubmitted Proposals:**

1] Study Title: Initial default among TB patients diagnosed at Medical Colleges in India: Issues and Possible Interventions

PI: Dr. Anil J Purty, Puducherry Pondicherry Institute of Medical Sciences

Budget: Rs.1,34,52,550/-

Experts Panels reviewers' Score & recommendation:

Reviewer 1: 65/100. Recommended

Reviewer 2: review report not submitted

Reviewer 3: review report not submitted

Discussion, Comments and suggestions:

Initial default is an important public health related topic and more relevant to medical colleges which diagnose every fourth of the TB patient in the programme.

Comment: Though average Initial default percentage is taken as 10% for the purpose of sample size calculation, it is important to note that the range is wide (10-50%) e.g. in UP medical colleges. It is large therefore, this will have an impact on sample size for each site.

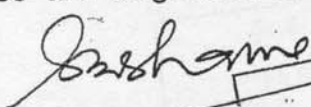
Comment: Dr. Purty replied that whichever site has more number of initial defaulters, sample will be taken through systematic random sampling. Also, lottery method will be used for selecting 25-30 patients for enrolment in the study.

Since, there is a lot of heterogeneity throughout the country for initial default rates, and the selection of the medical college is purposive, inferential ability to generalize the results is limited.

Comment : It is not clear whether DOTS-Plus patients will be enrolled in this study or not?

Response: Dr. Purty replied that currently as per protocol only new smear positive pulmonary TB patients will be included in the study, but expressed willingness to include any other type of patients if national OR Committee recommends so.

It was proposed by the committee that since many smear negative TB cases and extra-pulmonary cases are diagnosed in the medical colleges and currently there is no


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system to know how many such patients were actually diagnosed and out of them how many were put on treatment, so it would be of much value to inform the programme if smear negative TB patients are also included in the study and some tool can be developed to manage this information about quantum of problem of diagnosed smear negative patient and not put on treatment (initial default). Dr. Purty agreed to this suggestion. Operational definition for this OR study will include smear negative TB cases also.

Comment: Initial default reported by medical colleges need not be really initial default and actually patient might have actually been put on treatment in the periphery and such information / feedback is not given to the medical colleges. In such cases how the study will differentiate or actual label of initial default?.

Response: Dr. Purty described mechanisms to trace the patients in the study.

One of the concerns was the output of the study against the huge monetary investment. No computer system will be given. Only one field supervisor as against two will be permitted.

Getting 30 patients for the study at each site was raised as a concern by the Committee as training mechanism of patients by itself would reduce the initial default ('study effect'). Dr. Purty mentioned that intervention will be planned in the second stage of study.

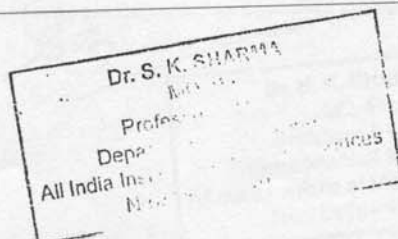
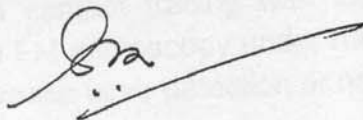
Salary of Rs.12,000/- for supervisors should be as per ICMR guidelines for various categories of research staff. Also Rs.3.5 lakhs per site for travel seems to be a huge budget for visits of just 30 patients.

TB Health Visitor (TBHV) supported to the medical colleges by the programme is also expected to visit the patients and alternative to appointment of additional supervisors under OR: Efforts to effectively utilize these TBHVs will be more practical and replicable by the programme later on.

It was made clear by the Committee that no extension will be considered for the study.

Decision of the Committee:

Resubmission of the protocol with suggested changes on inclusion of smear negative cases and revision of budget. The proposal has not been recommended so far. Next presentation will be on July 18th, 2012.



2] Study Title: ADA assay as a sensitive diagnostic tool in tubercular serosal effusions

PI: Dr.Pallavi Bhuyan, S.C.B. Medical College & Hospital, Cuttack

Budget: Rs.6,52,000/-

Experts Panels reviewers' Score & recommendation:

Reviewer 1: 21/100. Not recommended

Reviewer 2: 43/100. Not recommended

Reviewer 3: 73/100. Recommended

Decision of the Committee:

The proposal was not considered as the Principal Investigator was not present in the meeting for discussion.

3] Study Title: Assessment of effectiveness of intervention of using LED-FM and systematic contact investigation under routine programmatic conditions – a comparative study

PI: Dr. B.S. Ohri, Joint Director (TB), State TB Cell, Madhya Pradesh

Budget: Rs.52,98,005/-

Experts Panels reviewers' Score & recommendation:


Reviewer 1: 52/100 recommended

Reviewer 2: 60 / 100 recommended

Reviewer 3: review report not submitted

Discussion, Comments and suggestions:

It was not clear that why Dr. Ohri has not included medical college(s) in his proposal? Dr. Ohri mentioned that this proposal is for testing unique question whether 'intensified Case finding with contact tracing with increased workload on suspect examination supported by LED FM microscopy under routine programme conditions – is an effective intervention to increase case detection or not?'


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How LTs will be trained for LED FM Proposal? Dr. Ohri mentioned that LTs will be trained at three accredited C&DST laboratories in the state. Ethics Committee clearance has not yet been taken.

During discussion issues were raised by Committee members regarding use of LED Fluorescent Microscopy under the RNTCP. When and on whose advice RNTCP decided to use LED Fluorescent Microscopy in the programme? Has it been approved by Central TB Division and notified to stakeholders across the country? X

Without the knowledge of National OR Committee, how it was decided that The Union will be doing an Operational Research and giving 200 LED F Microscopes to the medical colleges and what for? Also, how the patients diagnosed on LED FM will be treated? Will the programme consider this diagnosis of TB using this tool which is not yet validated? If Union's project is validating LED FM, then proposal from STO, MP will have duplication. Clear guidelines on this issue need to be given by the programme. Chairman also mentioned that the decision to recommend this OR proposal by MP, STO will be considered only after the Programme clarifies these questions.

In response to these question, Dr. Sreenivas, NPO(TB) informed the house that, no policy decision is taken in RNTCP without approval of the concerned Technical Committees as well as technical approval from Directorate and administrative and financial approval of the Ministry of Health & Family Welfare, Govt of India. Secondly the union's initiative to provide 200 LED FM microscopes to the medical colleges is actually a project and not an Operational Research proposal. It is a project proposal submitted to the TB REACH for funding. Since this was not an OR proposal asking for funds from the programme, so it was not probably referred to National OR Committee. Moreover, he referred to the minutes of 19th National Laboratory Committee which clearly mentioned about the EQA for LED based fluorescent microscopy that the fluorescent microscopy is being carried out at IRL and tertiary hospitals and it was decided to use the results for patient management. And that it was recommended that the patients sputum examination results for FM under EQA are to be treated equally under the programme as a result from conventional ZN under EQA. He also referred to the minutes of 20th National Laboratory Committee that LED FM microscopes are user friendly, cheap, maintenance free, has long bulb hours, battery backup, increased sensitivity compared to conventional microscopy and extremely useful in settings where electricity is a concern and the programme's consideration of phasing in of LED based microscopes when they are to be replaced after condemnation of conventional binocular microscopes.

Decision of the Committee:

This OR proposal to be considered approved after CTD clarifies the issues raised by the Committee on decision of the Programme to use LED FM in the programme. It was



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again voice by committee members that National Standing Committee for Operational Research must be informed about all recent developments/policies.

One newly submitted proposal:

1] Study Title: Program for intensified case finding, diagnosis and treatment support for rural and remote communities through a social mobilization campaign using interpersonal communication and media materials as a catalyst

PI: V. Sasi Kumar, Australian International Health Institute

To know more about the OR background and the PI, qualification of the Pincipal investigator was asked by the Committee. MrSasi Kumar replied that he holds MBA degree with national and international experience in development sector with around seven years of experience of working closely with the community in north east region of India.

Mr. Sasikumar also mentioned that Main indicator of the proposal was increase in TB suspect and case detection rates. The difference between GFR-9 project and this proposal is that GFR-9 ACSM project is Top Down approach and this proposal is bottom up approach. This was further debated and Committee was also informed about the GFR-9 ACSM project strategies and activities.

Experts Panels reviewers' Score & recommendation:

Reviewer 1, 2 & 3: reviewer's comments not received.

Discussion, Comments and suggestions:

It is important to address the issue of ACSM and with the newer objectives of Universal access to TB Care, intensified case finding is important and this study is important for achieving 90% case detection targets.

This proposal is not really an Operational Research, but is an important programmatic intervention and may be considered for funding by Central TB Division.

The proposal addresses only Community and not the private sector or even public sector improvement. When only one of the three components are attacked success is less likely.

Duration of the Project is long. Only first phase will be considered for funding by the National OR Committee.



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Decision of the Committee:

Fresh proposal to be resubmitted after reducing the number of districts, including only stage one and reducing the budget with justifying the costing of activities.

Findings of the Two completed & Five ongoing Operational Research studies were presented to the Committee and discussed. Important Comments of the Committee are as below:

Two Completed Studies:

1] Study Title: Socioeconomic implications and incidence of default amongst patients on DOTS, Himachal Pradesh 2008-2010

PI: Dr. A. K. Bhardwaj, IGMC, Shimla

Comments:

Committee members felt that very low default of 1.5% could be because of the 'study effect' as overall default rates of HP are over 5%. It was conveyed to the PI that results under research conditions are different. And rather the question can be reframed as what was the reason of low default in the study sample as compared to the non study sample. In the delay in care, indicator only patient delay was measured and not the provider delay. Chairman of the committee did not agree with the results of the study and found that the results are paradoxical. Cost of the TB treatment was not understood to the committee members, which was explained by the presenter that it included indirect costs e.g. for travelling to the DOTS center and for travelling to the DMCs as patient has to give two samples, which required two visits and one more visit to receive the results, so for each of the follow-up examination three visits are need.



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2] Study Title: Treatment of Genital Tuberculosis: A Randomized controlled trial of either discontinuation at 6 months or continuation till 9 months after initial response to RNTCP Category I treatment.

PI: Dr. J. B. Sharma, Department of Obstetrics and Gynaecology, AIIMS, New Delhi

Comments:

Extension of 6 months was requested by the PI without asking for additional budget.

Analysis of the data after regrouping the patients based on microbiological diagnosis and clinical diagnosis was suggested. No follow-up was included in the study and also no safety data were presented. On this, PI informed that patients were being followed up at AIIMS only in the subsequent visits. Definition of outcome parameters was not clear. Sample size was found to be inadequate. It was not clear as to what was the basis / criteria of the decision of continuation or discontinuation of treatment after 6 months. PI was advised to have more discussion with Chairman in order to improve analysis of results.

Five ongoing Studies:

1] Study title: Evaluation of the efficacy of trice weekly DOTS regimen in TB Pleural effusion at 6 months

PI: Prof S. K. Sharma, AIIMS, New Delhi

Comments:

High default amongst the study subjects at the site of SMS, Jaipur was observed.

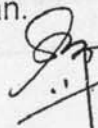
Although Cat III no longer exists in the programme, however, results of efficacy and safety with the use of three drugs (RHZ) are impressive. Efforts should be made to disseminate the results. Results should be published at an earliest.

2] Study Title: Assessment of RNTCP Strategy of FNAC diagnosis and duration of treatment for peripheral lymphadenitis

PI: Prof S. K. Jindal, PGI Chandigarh

Comments:

Since Dr. Jindal could not attend the meeting some of the important findings were communicated to the Committee by the Chairman.


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3] Study Title: Study on the treatment of abdominal tuberculosis: A randomized controlled trial to compare the 6 months of cat-I treatment with 9 months of Cat-I treatment (extension for 3 months) in abdominal TB under RNTCP

PI: Dr. Govind Makharia AIIMS, New Delhi

Comments:

As per the OR protocol one arm of the study need to be given 9 months of regimen, but there are difficulties as the local Medical Officer refuse to extend CP. This non-compliance by the programme staff must be addressed by the District TB Officers, State TB Officer & CTD. 170 out of the total 212 patients have been already enrolled. Only 133 enrolled patients will be able to complete treatment till July 12. PI has already requested for the extension of the study for one year. To consider that study is powered enough to complete the sample size as required, keeping in mind the tentative date of last patient enrollment, the treatment duration of 9 months for the last patient and one year follow-up – a detailed report of the study progress is required to be submitted to CTD for advocacy. Chairman of the OR Committee has already recommended extension of the study.

For greater utility of the study, OR committee suggested Dr. Makharia to publish the early results as an interim paper or a short communication to the reputed journals.

4] Study Title: ARTI Survey in urban slum of Delhi

PI: Dr. Rohit Sarin, LRS Institute, New Delhi

Comments:

ARTI of 2.3 – 3% was observed in the urban slum of Delhi, which is still high as expected.

It will be worthwhile to repeat the survey after 5 years in the same area with the same protocol. However, shifting population (migration) in these urban areas may make the interpretation of the trend.



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5] Study Title: Sputum smear conversion and treatment outcomes of New Smear Positive tuberculosis patients with co-existing diabetes mellitus put on Category I RNTCP treatment

PI: Dr. Jaishankar Additional Director of Health Services, Kerala

This study could not be discussed as the Principal Investigator could not attend the meeting due to prior commitments.

In addition, Dr. Niraj Kulshrestha informed that the OR proposal titled 'A Randomized control trial between 6 months short intermittent and 9 month short intermittent ATT Regimen in extraspinalosteoarticular tuberculosis: A non-inferiority trial' (with total budget of Rs.1,24,29,000/-) has been recommended by National Standing OR Committee and the pending Institutional Ethics committee clearance was submitted by the Principal Investigator, Dr. Dr. Chandrashekhar Yadav to CTD, which was submitted to higher officials for necessary administrative and financial approval for release of first installment. However, the file is lying with higher officials and the study could not be started yet. Study proposal titled, 'Multi-centric cohort study of recurrence of tuberculosis among newly diagnosed sputum positive pulmonary tuberculosis patients treated under RNTCP' was also approved and recommended by National Standing OR Committee two years before and now it has also been re-submitted with revised budget. Committee approved the re-submitted proposal with revised budget of Rs.8,11,00,650/-.

It was emphasized by members of the committee that results of all completed projects should be disseminated in ZTF and NTF meetings should be published in 2012.

Next meeting of National Standing Committee for Operational Research in RNTCP is scheduled on 18th July 2012.

It was suggested by members of the committee that all efforts should be directed to start the study at an earliest as it is most relevant to RNTCP. CTD should take appropriate steps in this direction.



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Agenda

Venue: Conference Hall, 2nd Floor, OPD Building, LRS Institute, New Delhi

Date: 8th February 2012

Objectives:

1. To review three revised OR proposals, resubmitted after revision
2. To review onenewOR proposal received
3. To review progress in five ongoing OR studies
4. To review the final results (and reports) of two completed OR studies

Time	Topic	Speaker
9:30 am – 9:45 am	Welcome address	Prof S. K. Sharma, Chairman
9:45 am – 10:00 am	Briefing about the days proceeding	DDG(TB)
10:00 am – 11:30 am	Presentation & discussions on three resubmitted proposals	Principal Investigators
11:30 am – 11:45 am	Tea Break	
11:45 am – 12:30 pm	Presentation & discussion on New proposal	Principal Investigators
12:30 pm – 1:30 pm	Presentation & review of results of two completed OR projects	Principal Investigators
1:30 pm – 2:30 pm	Lunch break	
2:30 pm – 4:00 pm	Presentation & review of progress of five ongoing OR projects (half hour each)	Principal Investigators
4:00 pm – 4:15 pm	Tea Break	
4:15 pm – 5:15 pm	Presentation & review of progress of five ongoing OR projects (half hour each)	Principal Investigators
5:15 pm – 5:30 pm	Final remarks	DDG(TB) & Chairman

OR Proposals for discussion / Ongoing OR Projects / Completed OR Projects

Sr No	PI	Institute	Title of the Study
Resubmitted three proposals			
1	Dr. Anil J Purty, Puducherry	Pondicherry Institute of Medical Sciences	Initial default among TB patients diagnosed at Medical Colleges in India: Issues and Possible Interventions
2	Dr. Pallavi Bhuyan	S.C.B. Medical College & Hospital, Cuttack	ADA assay as a sensitive diagnostic tool in tubercular serosal effusions
3	Dr. B.S. Ohri, Joint Director (TB)	State TB Cell, Madhya Pradesh	Increasing Case Detection Rate at an Early Stage by using Newer Diagnostic Tool- LED based Fluorescent Microscopy and Systemic Evaluation of Contacts of Sputum Positive Cases under Routine Programmatic Conditions
Newly submitted proposal			
1	V. Sasi Kumar	Australian International Health Institute	Program for intensified case finding, diagnosis and treatment support for rural and remote communities through a social mobilization campaign using interpersonal communication and media materials as a catalyst
Ongoing five OR projects			
1	Prof S. K. Sharma	AIIMS, New Delhi	Evaluation of the efficacy of trice weekly DOTS regimen in TB Pleural effusion at 6 months
2	Prof S. K. Jindal	PGI Chandigarh	Assessment of RNTCP Strategy of FNAC diagnosis and duration of treatment for peripheral Lymphadenitis
3	Dr. Govind Makharia	AIIMS, New Delhi	Study on the treatment of abdominal Tuberculosis: A randomized controlled trial to compare the 6 months of cat-I treatment with 9 months of Cat-I treatment (extension for 3 months) in abdominal TB under RNTCP
4	Dr. Rohit Sarin	LRS Institute, New Delhi	ARTI Survey in urban slum of Delhi
5	Dr. Jaishankar	Additional Director of Health Services	Sputum smear conversion and treatment outcomes of New Smear Positive tuberculosis patients with co-existing diabetes mellitus put on Category I RNTCP treatment
Completed five OR projects			
1	Dr. A. K. Bhardwaj	IGMC, Shimla	Socioeconomic implications and incidence of default amongst patients on DOTS, Himachal Pradesh 2008-2010
2	Dr. J. B. Sharma	AIIMS, New Delhi	Treatment of Genital Tuberculosis: A Randomized controlled trial of either Discontinuation at 6 months or continuation till 9 months after initial response to RNTCP Category I treatment.

List of participants

Sr No	Name	Designation	
1	Dr. S.K.Sharma	Head, Deptt. Of Medicine, AIIMS (Chairman)	Chairman
2	Dr. D. Behra	Director, LRS, Delhi.	Member
3	Dr. Aleyama Thomas	Director, TRC, Chennai.	Member
4	Dr. P. Kumar	Director, NTI, Bangalore.	Member
5	Dr. S.Radhakrishna,	Bio-statistician, Hyderabad.	Member
6	Dr. Rajendra Prasad	Zonal OR Committee Chairman, North Zone	Member
7	Dr. Sreenivas	NPO-TB, WHO	Member
8	Dr. Niraj Kulshrestha	Addl DDG (EHR)	Member
9	Dr. Anil J Purty, Puducherry	STF Chairman, Puducherry, Pondicherry Institute of Medical Sciences	PI
10	Dr. B.S. Ohri,	Joint Director (TB), STO, MP	PI
11	V. Sasi Kumar	Australian International Health Institute	PI
12	Dr. Govind Makharia	AIIMS, New Delhi	PI
13	Dr. Rohit Sarin	LRS Institute, New Delhi	PI
14	Dr. A. K. Bhardwaj	IGMC, Shimla	PI
15	Dr. J. B. Sharma	AIIMS, New Delhi	PI
16	Dr. Kiran Rade	CTD Consultant, Epidemiologist	