RNTCP RESEARCH PRIORITIES

Research priorities for TB control in India are listed under the following sub-themes:

1. **Strengthening surveillance and tuberculosis notifications**
   - To identify and test various interventions to strengthen the case based electronic TB notification system (Nikshay) across the country
     - The studies include assessing provider related challenges, novel demand generation efforts targeted at patients – so they demand notification from their providers, assessment of penalties for under notification, evaluation of new tools or technologies that will help in improving notification by private sector and public health action.
   - Identification of sources of under-notification of TB cases through inventory studies (capture/ recapture), Sentinel sites or through ‘onion model’ approach
   - Integration of routine laboratory screening for TB & DR-TB from public and private sector laboratories into a unified TB and DR-TB reporting and surveillance systems.
     - This effort, in the context of universal DST efforts, can replace large scale surveys if effectively implemented. Success will require improving testing for drug resistant TB and reporting of it across the country in both public and private sector. The systems of data integration, analysis, validation, and dissemination, can be regardless immediately developed.
   - Evaluate the quality of data that’s collected through the routine notification system
   - Validation and strengthening of routine medical certification of the cause of death
   - Establishment of a registry for documenting TB among health care workers

2. **Improvement of TB disease burden estimation**
   - A series of state-representative prevalence survey that will allow estimation of TB prevalence at the national and state levels
     - This study can also provide information on the distribution of various genotypes/strains in India, strains/mutations associated with drug resistance etc., and also the prevalence of mixed infections with various strains.
   - Studies to identify determinants of adverse TB treatment outcomes (including those for drug resistant TB) through longitudinal cohort surveys and interventions to address these determinants.
     - A PROSPECTIVE COHORT study for TB patients treated with daily FDCs, with isolates and genotyped, powered for relapse among subgroups (e.g. non-RIF DR-TB, HIV, diabetics), also with genotyping.
   - Repeat prevalence surveys, verbal autopsy surveys, DRS surveys after 5 years
     - If the notification system is strengthened and if universal DST is offered by the programme then, these surveys may not be necessary.
   - Relapse/re-infection (a is study under progress)
   - Interventions to improve Medical Certification of Cause of Death in Partnership with Registrar General of India

3. **Understanding TB transmission and how best to interrupt it**
   - Use of molecular methods to understand TB disease dynamics/transmission in various settings
     - Identify hot spots for TB transmission– Using molecular epidemiological methods
• Evaluate interventions to reduce transmission at households and at the community level especially in urban slums and congregate settings.
• Assess the compliance to airborne infection control guidelines at health facilities and interventions aimed at improving compliance

4. **Demand generation, Prevention, systematic screening of high-risk groups, and early case finding.**
• To find the optimum combination of interventions for early case detection and improving treatment outcomes both in public and private sector
• Assessing the effectiveness of various models to engage private sector health care providers in India for diagnosis and treatment of patients.
• Studies to assess the feasibility, acceptability, operational challenges, predictability, effectiveness in reducing diagnostic delays etc., of the various diagnostic algorithms in the new technical and operational guidelines
• Smear negative TB
  o Studies to assess accuracy of diagnosis at various levels of health system in detecting smear negative, culture or CB-NAAT positive TB.
  o Studies that assess the effect of capacity building (for MO-PHIs) on reading chest radiographs in diagnosis of pulmonary TB
  o Diagnostic algorithm using Xpert / smear needs a relook as dead bacilli may persist for variable periods of time and there are instances (case reports) where Xpert positive previously treated patients became asymptomatic after a course of broad spectrum antibiotics and did not require ATT
• Childhood TB and extra-pulmonary TB
  o Accuracy and challenges for diagnosis at various levels of the health system
  o Effect of capacity building for obtaining appropriate biological specimens on the diagnosis of pediatric TB
• Intensified case finding
  o Diagnosis of TB in High risk individuals at health facilities/institutions- development of algorithms/ assessing the appropriateness of the existing algorithms.
  o Active case finding in High risk populations (close contacts/slums/tribal populations/occupational risk groups/closed institutions)—Assessment/development of effective algorithms
• Drug resistant TB
  o Developing guidelines to address/deal with discordance in drug resistance patterns between different diagnostic tools/tests.
  o Adequacy of follow-up sputum smears examination at 2-months and 6 months among patients on TB treatment in timely diagnosis of MDR-TB. A previous study had shown that mid-CP sputum examination does not add much value in early diagnosis of MDR-TB, however, this study was based on reviewing routine programmatic data [26]and there is a need for re-examining this issue using more rigorous culture based methods.
• Use of Information Communication Technology for lab information systems and its effect on patient tracking and preventing pre-treatment loss to follow-up.
• Studies to evaluate / modify lab quality assurance protocols
• Studies to identify context specific communication strategies for early and complete detection of TB cases.
• Innovative strategies using CBOs and NGOs to spread TB awareness in the community and its effect on controlling TB in the communities.
• Call for more research on community engagement/community ownership activities as part of ACSM
• Community driven models to evaluate the quality of RNTCP services using grass root level workers and community representatives for timely intervention
• Studies on care seeking behaviour studies among migrants and hard to reach groups in terms of reaching care in the RNTCP
• Larger scale innovative intervention studies to improve TB services among tribal populations
• Screening strategies to improve case finding among the corporate sectors, other occupations such as drivers (public and private)
• Evaluate interventions to reduce transmission in urban slums and congregate settings.
  o E.g., Effectiveness of various interventions to promote cough hygiene at the community level.
• Studies to explore vulnerable groups for TB to facilitate targeted interventions (Drivers, migrants, miners etc)
• Implementation research on various providers of treatment support at the community level to be included in the programme.

5. **Improving the cascade of care in public and private sector care**
• Interventions to prevent pre-treatment loss to follow-up (~5-20% of the patients diagnosed at various levels of the health care system are estimated to be lost to follow-up prior treatment)
• Treatment support systems
  o Demonstration studies using new tools to improve adherence (e.g., medication monitors[27])
  o Demonstration of models to link patients to various welfare schemes and its effect on patient welfare and TB treatment outcomes
  o Studies evaluating the effect of providing financial incentives to patients and providers of treatment support in promoting adherence to treatment and treatment outcomes(e.g., cash transfer, microfinance interventions[28])
• Monitoring response to treatment
  o Studies assessing compliance/feasibility of monthly clinical monitoring of patients (including children) on TB treatment (as outlined in the new technical and operational guidelines)
  o Identify barriers to culture based declaration of treatment outcomes(as outlined in the new technical and operational guidelines) and how to address them
  o Death audit - development of tools and demonstrating its feasibility under various programmatic conditions
• Monitoring and managing the side effects/ adverse events of anti-TB drugs
  o Timely identification, reporting and effective management
  o Role of health staff at different levels and effect of training various health staff on timely management of these adverse events
• Drug resistant TB MDR/pre-XDR-TB/ XDR-TB
  o Studies for streamlining the management of Mono-Poly drug resistant TB/MDR-TB with mixed patterns of resistance
• Use/efficiency of ICT (eg., NIKSHAY) in tracking patients who migrate during TB treatment
• Post treatment follow-up
  o Assessing feasibility and addressing barriers for implementing the current RNTCP guideline of 2 years post treatment follow-up of TB patients to identify relapse early.
Preventive therapy
- Identifying individuals/groups (other than HIV, child contacts) who are likely to benefit from treatment of latent TB infection
- Effectiveness and feasibility of shorter preventive treatment regimens

Non-Tuberculous mycobacteria:
- Proportion of NTM disease among treatment non-responders
- Studies that assess the diagnostic algorithms and treatment regimens for NTM

Pharmacokinetic and pharmacodynamics studies in the light of issues of daily FDC introduction (under dosing of INH in 25-39 weight band, overdoing of Rifampicin in >70kg and overall HIV and pediatric group for Indian population)

Multi centre RCT studies of counselling interventions to address alcohol use disorder, smoking, and malnutrition, to promote better TB medication adherence and treatment outcomes.

It is also important that programme and policy makers take cognisance of the evidence that is available (as in alcohol intervention and smoking cessation) and include these as priority areas in RNTCP for implementation research.

Experimental studies using the RCT design to evaluate the impact of trained counsellors in dealing with TB-related stigma, to see if these counselling interventions improve treatment adherence and treatment outcomes especially among MDR-TB patients

Studies on interventions to reduce stigma and discrimination in families and communities

Determining the direct and indirect costs (out of pocket expenditure) incurred by TB patients during diagnosis and treatment in various contexts and identifying interventions to reduce them.

Impact of social interventions on psycho-social condition of drug susceptible and drug resistance TB patients

Developing interventions for sustainable disease free environment for migrant labourers in industry

6. Socio-economic impact and poverty alleviation
- Estimating cost effectiveness (cost per life saved) of specific new initiatives, such as daily regimens and free drugs in the private sector
- To find the optimum combination of interventions for early case detection and improving treatment outcomes using mathematical models.
- Research to evaluate these direct and indirect costs due to TB
- Evaluation of the access of TB patients to government welfare schemes
- Demonstration of models to link patients to various welfare schemes and its effect on treatment outcomes
- Studies evaluating the effect of financial incentives to patients and providers of treatment support in promoting adherence to treatment and treatment outcomes (e.g., cash transfer, microfinance interventions[28])

7. Strengthening RNTCP management
- Addressing managerial, infrastructure and administrative constraints in implementing RNTCP
  - Studies related to identification and addressing challenges in human resource management[29], financial management, integration into general health services, procurement and logistics management
  - Barriers to utilization of RNTCP services in high risk populations - urban slums, tribal areas, migrants, prisoners, elderly, diabetics, PLHIVs, high risk occupational groups.
  - Studies on incorporating newer training tools/techniques and its efficacy
  - Time motion analysis of program staff and how to optimize efficiency, on performance improvement programs to deal with their real issues.
• Quality of care-surveys within public health facilities (for example by using Standardized patients[30] or by prescription audits);
• Patient satisfaction surveys
• Improving routine data usage at district and state levels to improve programme performance (MIFA)
• Locating correlates of health system resilience at district level in dealing with challenging situations (such as high TB-HIV burden, high MDR-TB burden etc.,) and developing interventions to cope with these challenging situations
• Issues with relation to effective infection control measures thereby recommending model RNTCP clinics to curb TB transmission in clinics/tertiary care centres
• Innovative strategies to strengthen health system towards TB notification both at the private and public level.

8. **Integration with State Insurance and UHC initiatives**

**Research Priorities**

• Evaluation of the access of TB services under various public and private health insurance scheme.
• Demonstration of models to link patients to various insurance schemes and its effect on treatment outcomes