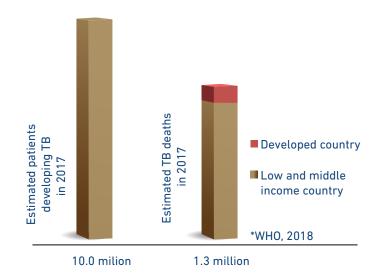


# **Tuberculosis: A deep-rooted problem**

According to WHO, in 2017, an estimated 10.0 million people developed tuberculosis (TB) and 1.3 million died from the disease, globally<sup>1</sup>



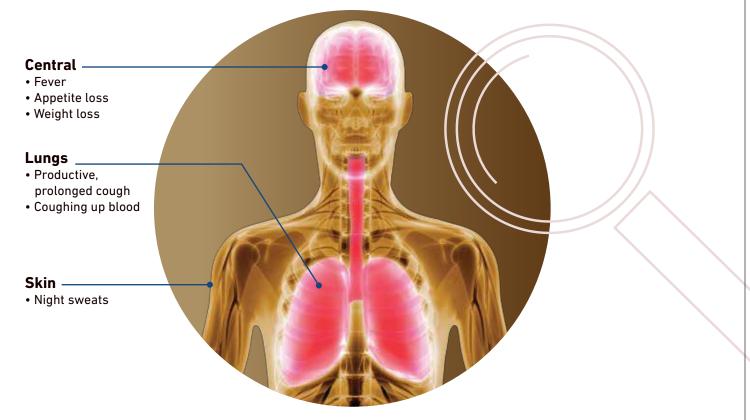
→ More than 1/4th of these TB cases were reported from India²



1 person dies of tuberculosis every minute<sup>3</sup>

# The first step in diagnosis is to suspect tuberculosis

• Pulmonary TB (PTB) is characterized by persistent cough for ≥2 weeks with fever, loss of weight and appetite<sup>4</sup>

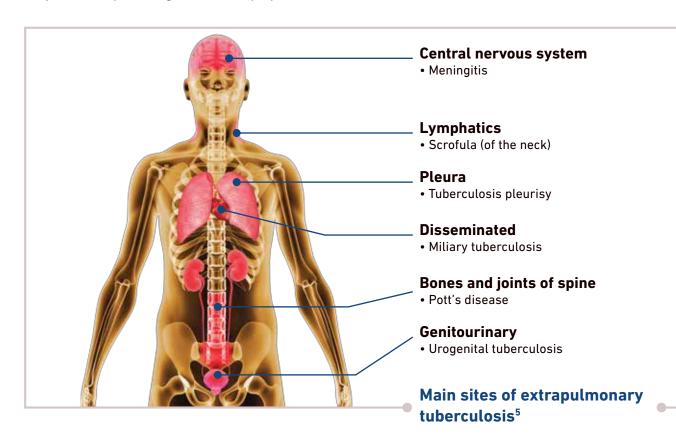


Main symptoms of pulmonary tuberculosis<sup>5</sup>

Complaints of prolonged fever can be a sign of TB, and a chest x-ray must be suggested. Many TB patients seek care for fever, but may not complain about prolonged cough and weight loss.

# Tuberculosis can affect any organ in the body

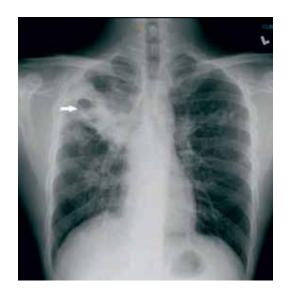
 Extrapulmonary TB (EPTB) affects the central nervous system, lymphatic system, bones and joints of spine or genitourinary system<sup>6</sup>



- Underlying conditions like HIV, diabetes, chronic renal disease, cancer are known to weaken the immune system and put patients at a higher risk of TB<sup>7</sup>
- Patients residing in overcrowded localities with unsanitary conditions and poor ventilation are more prone to TB complications<sup>8</sup>

# Chest x-ray is only a screening test

# It is a screening test but not a confirmatory test





Classical picture of active pulmonary TB<sup>9</sup>

Presumptive TB patient9



Chest x-rays: Provide supportive evidence for pulmonary TB<sup>10,11</sup>



Chest x-rays: Neither specific nor sensitive<sup>10,11</sup>



Other diseases may mimic TB on chest x-rays<sup>10,11</sup>



Supplement to microscopy, NAAT+ and culture<sup>10,11</sup>

Treatment of TB purely on the basis of x-rays can result in significant unnecessary overtreatment with adverse consequences for non-TB patients'

#### CBNAAT 12



99% specificity and 94% sensitivity when compared to culture

#### LPA (Line Probe Assay)<sup>13</sup>



99% specificity and 98% sensitivity for RIF resistance

First-line LPA is only

for smear

99% specificity and 84% sensitivity for INH resistance

#### Serological tests

In 2012, government of India had banned the use of these tests for diagnosis of PTB &

#### **Sputum** microscopy

Sputum - Right clinical specimen for detecting PTB

#### **IGRAs** and TST

As per WHO recommendation, should not be used for diagnostic work-up of active TB in adults

WHO-endorsed Tests

LED

microscopy<sup>14</sup>

Culture (Liquid and solid)<sup>15</sup>



10%-20% more sensitive than conventional microscopy

Liquid culture is the gold standard for diagnosis

Can assay all anti-TB drugs

Ideal test for EPTB and smear-negative PTB

positive its sensitivity and specificity\*

the sensitivity and specimenty								
Test type	CBNAAT**12	Liquid Culture <sup>14</sup>	Line Probe Assay <sup>13</sup>					
Specificity	99%	99% Gold 99% Standard (RIF & I						
Sensitivity	94%	Gold Standard	98% - RIF & 84% - INH					
MDR resistance	Yes (Only RIF resistance)	Yes (For majority)	Yes (INH & RIF resistance)					
Turnaround time	Within 1 day	Within 15-42 days	Within <b>2-3 days</b>					

WHO assesses the quality of a diagnostic test based on

\*Provided sensitivity and specificity is for PTB sample \*\*GeneXpert

CBNAAT: Cartridge-based nucleic acid amplification test

# **CBNAAT** test

- CBNAAT (Cartridge-based nucleic acid amplification test) is a fast, automated and qualitative real-time PCR test that analyzes the sputum specimens for identification of:<sup>14,15</sup>
  - Mycobacterium Tuberculosis Complex (MTB) DNA
  - Resistance to rifampicin (RIF)

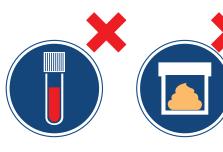
Recommended by WHO for detection of pulmonary and extrapulmonary TB in adults as well as children<sup>14,15</sup>

Turnaround time only 2 hours 14,15





Sample for PTB - 5 ml mucopurulent sputum without saliva or blood



Blood and faeces are not samples for TB diagnosis

# Sensitivity & specificity of CBNAAT\* for EPTB

Sample	Sensitivity#	Specificity#		
Lymph nodes	83%	94%		
CSF	81%	98%		
Pleural fluid	46%	99%		

#Compared to culture as the reference standard

## Extrapulmonary TB<sup>16</sup>



TB lymphadenitis

Lymph node aspirate or biopsy



Ascites (Abdominal TB)
Ascites fluid and peritoneal biopsy



**TB meningitis**Cerebrospinal Fluid (CSF)



Urinary tract and kidneys TB
Urine and tissue via biopsy



Pleural effusion (TB pleuritis)
Pleural fluid and pleural biopsy



Bone and joint TB

Bone/synovial tissue via biopsy



Genitourinary tract TB

Tissue via biopsy (Endometrial tissue in women)

\*GeneExpert

# **FDC** - The advantages

### Simplicity of treatment

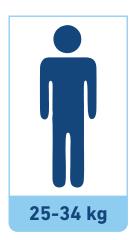
Increased patient acceptance



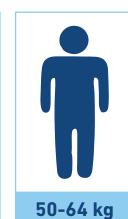


Prevents 'concealed' irregularity.
Many a time patients will consume
a few drugs and leave out some;
this gets mitigated when
FDCs are used.

- Lower risk of emergence of drug resistance
- Easier-to-adjust dosages by body weight (There are 5 adult weight bands and 6 pediatric weight bands classified by RNTCP)











FDC - Fixed dose combination

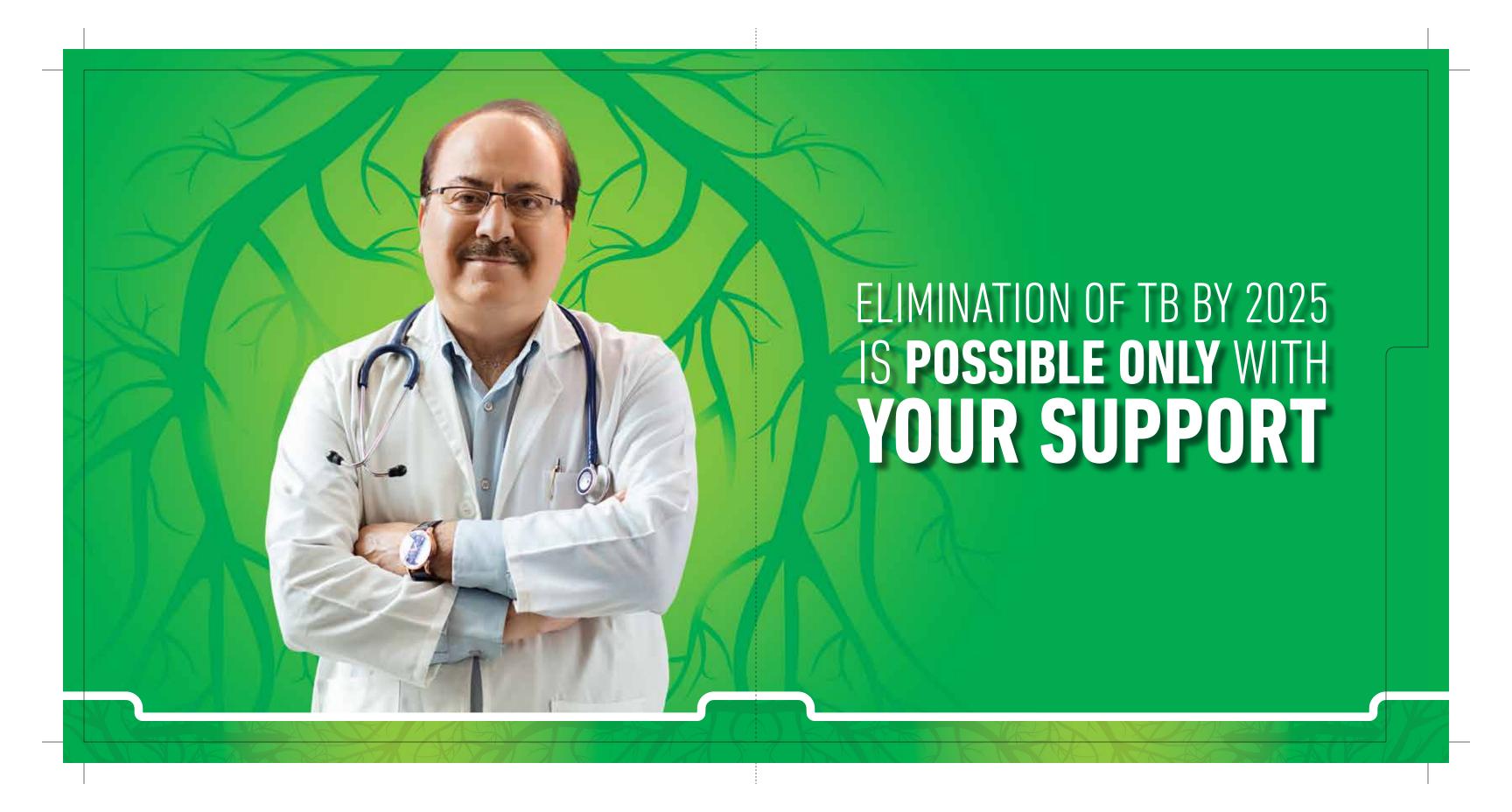
# Daily FDC regimen schedule for adults

		Number of tablets to be consumed			Number of tablets to be consumed			
	Type of	Intensive phase	Dose in IP	No. of strips	Continuation phase	Dose in IP	No. of strips in CP	
category	ory case	HRZE (4 FDC)			HRE (3 FDC)			
		75/150/400/ 275 mg per tab		Each strip contains 28 tablets	75/150/275 mg per tab		Each strip contains 28 tablets	
25-34 kg		2	56 doses	4 strips	2	112 doses	8 strips	
35-49 kg		3	56 doses	6 strips	3	112 doses	12 strips	
50-64 kg	New and previously treated	4	56 doses	8 strips	4	112 doses	16 strips	
65-75 kg		5	56 doses	10 strips	5	112 doses	20 strips	
>75 kg*		6	56 doses	12 strips	6	112 doses	24 strips	

# Daily FDC regimen schedule for pediatric (<18 yrs)

		Number of tablets to be consumed			Number of tables to be consumed				
Weight Type of case	Intensive pl	ohase			Continuation phase				
	HRZ (3 FDC-P) 50/75/150 mg	E* 100 mg	Dose in IP	3 FDC No. of Strips & Tabs in IP	HR (2 FDC-P) 50/75/150 mg	E* 100 mg	Dose in IP	3 FDC No. of strips & tabs in IP	
4-7 kg		1	1	56	2 x 28s E-56	1	1	112	4 x 28 E-112
8-11 kg		2	2	56	4 x 28s E-112	2	2	112	8 x 28 E- 224
12-15 kg		3	3	56	6 x 28s E-168	3	3	112	12 x 28 E-336
16-24 kg		4	4	56	8 x 28s E-224	4	4	112	16 x 28 E-448
25-29 kg		3+1 A*	3	56	6 x 28s E-168 A-56	3+1 A*	3	112	12 x 28 E-336 A-112
30-39 kg		2+2 A*	2	56	4 x 28s E-112 A-112	2+2 A*	2	112	8 x 28 E- 224 A-224

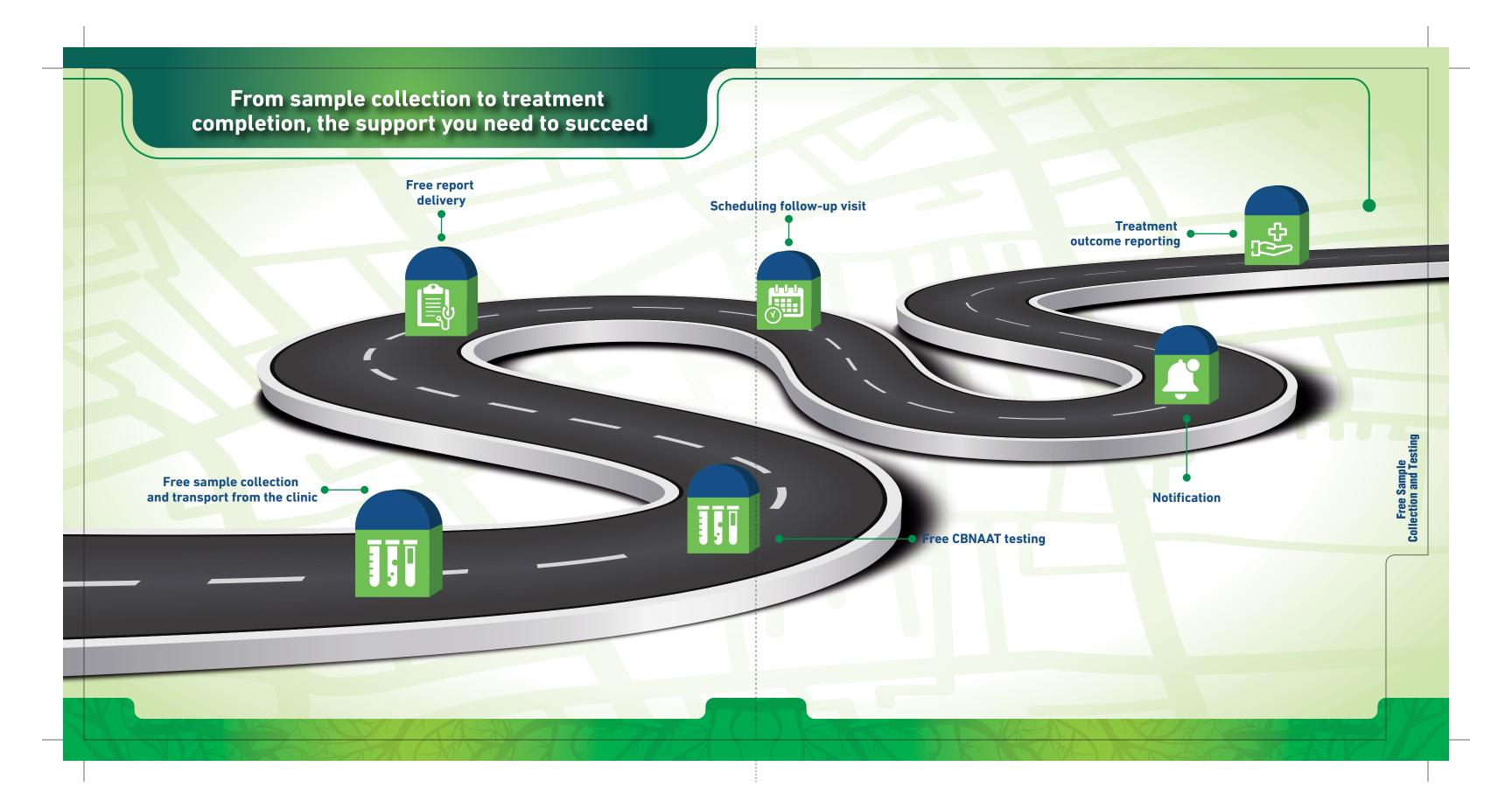
\*Patient >75kg may receive 5 tablets/day if they do not tolerate. Dose to be adjusted by treating physician in individual cases if required
\*E-Ethambutol \*A-Adult FDC Tab

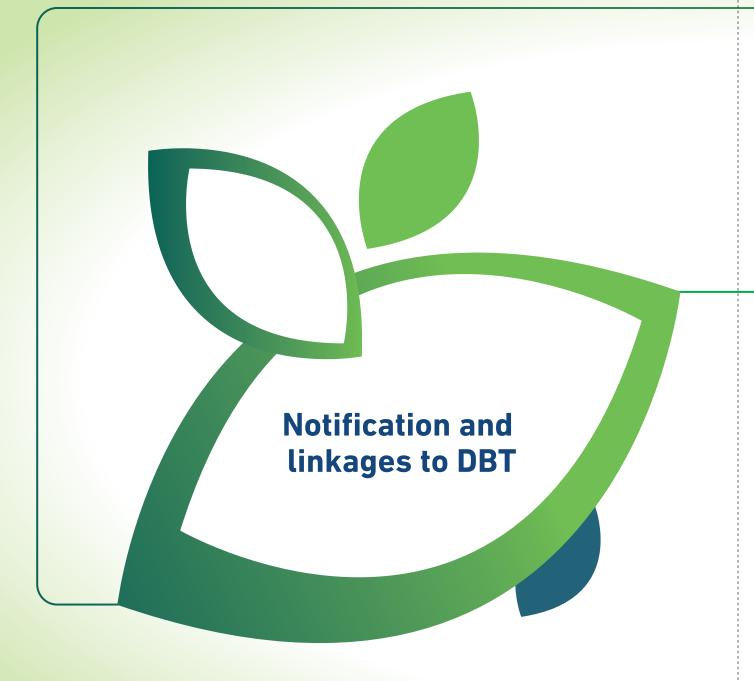


# TEGETHER WE STAND AGAINST TB









From notification to treatment completion, the support patients need to succeed



Government of India offers all notified patients •

Financial assistance of Rs. 500/- per month

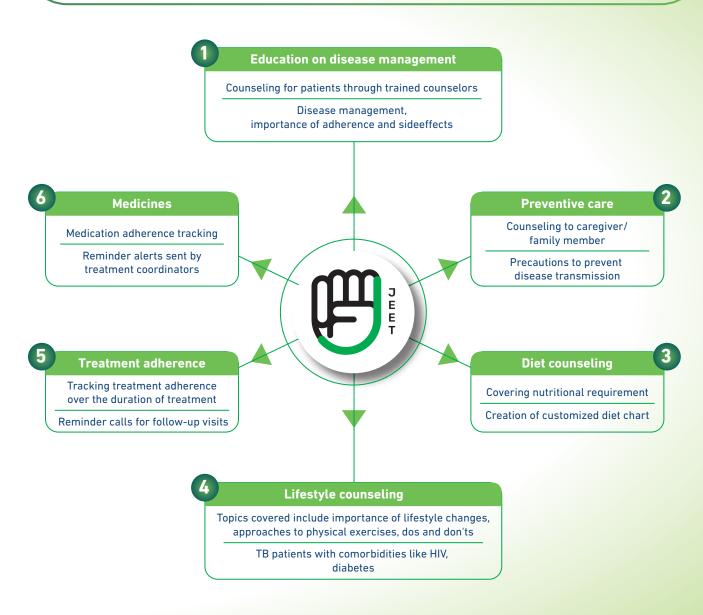
Until treatment completion to support their nutritional needs and fast recovery

JEET team will also support patients until treatment completion

Notification & DBT



# From treatment initiation to completion, the support your patients need to fight TB



#### **REFERENCES**

- Global Tuberculosis Report 2018. From the website of the World Health Organization.
   Available at: ttps://www.who.int/tb/publications/global\_report/en/; Accessed on: Oct. 15, 2018.
- Central TB Division, Ministry of Health and Family Welfare. (2014). TB India 2014 Annual Status Report. Available at: https://tbcindia.gov.in/showfile.php?lid=3314 [Accessed 06 Sept. 2019.
- 3. World TB Day: A Conversation with a TB Warrior from India.

  Available at: https://longitudeprize.org/blog-post/world-tb-day- conversation-tb-warrior-india; Accessed on: Sep. 11, 2018.
- 4. Mainous A, Pomeroy C. Management of antimicrobials in infectious diseases. 1st ed. Totowa, N.J.: Humana Press; 2010.
- 5. Bennett J, Dolin R, Mandell G. Mandell, Douglas, and Bennett's Principles and practice of infectious diseases. 1st ed. Philadelphia: Churchill Livingstone Elsevier; 2010, Chapter 250.
- 6. Golden M, Vikram H. Extrapulmonary tuberculosis: an overview. Amer Fam Phys. 2005;72(9):1761-1768.
- 7. Gibson P, Abramson M. Evidence-based respiratory medicine. 1st ed. Malden, Mass.: BMJ Books/Blackwell Pub.; 2005.
- World Health Organization. Global Tuberculosis Report 2013 [Internet]. 2013.
   Available from: http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656\_eng.pdf
- 9. Interpretation of chest X-rays in Tuberculosis. GP Clinics. Let's Talk TB (supplement). First Edition, 2014.
- 10. Pai M. Diagnosis of pulmonary tuberculosis: what every GP should know. GP Clinics 2013;3:22-28.
- 11. Hopewell PC, Pai M, Maher D, et al. International standards for tuberculosis care. Lancet Infect Dis 2006;6:710-725.
- 12. Cepheid Xpert MTB/ RIF (GXMTB/ RIF-US-10) Package Insert, 301-1404, Rev. B
- 13. Ling DI, Zwerling AA, Pai M. GenoType MTBDR assays for the diagnosis ofmultidrug-resistant tuberculosis: a metaanalysis. Eur Respir J. 2008Nov;32(5):1165-74.
- 14. Who.int, (2014). WHO. Global Tuberculosis Report 2013. [online]
  Available at: http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656\_eng.pdf [Accessed 1 Aug. 2014].
- 15. Boehme, C., Nicol, M., Nabeta, P., Michael, J., Gotuzzo, E., Tahirli, R et al (2011). Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study. The Lancet, 377(9776), pp.1495-1505 PCR: Polymerase Chain Reaction.
- 16. Diagnosis of Tuberculosis: Importance of appropriate specimen collection. GP clinics, Let's talk TB (supplement) First edition 2014.



