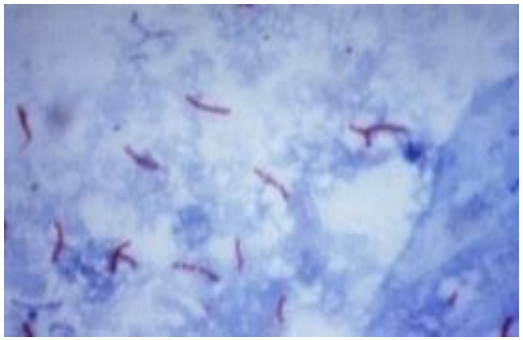
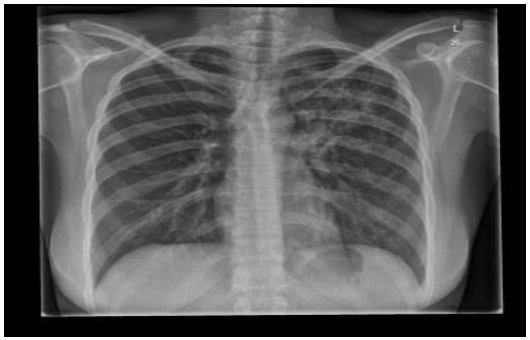
Managing Tuberculosis Today





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Managing Tuberculosis Today - Outline:

- **Tuberculosis (TB): Active and Latent**
- **TB Screening:**
  - ***Why Screen for TB***
  - ***Contact Tracing***
- **TB Incident Management**
- **Case Management**
- **New / Updated NICE TB Guidelines - 2016**
- **Update on The Collaborative TB Strategy: - PHE and NHS England 2015**
- **TB Awareness – Myths and Stigma**
- **Questions**

Acknowledgements

- **Public Health England (Data and Slides)**
- **Paediatric TB Network Group / NIKS Study**
- **Dr Martin Dedicoat (Local Data)**

Tuberculosis (Active):

Tuberculosis, or TB, is an Infectious Bacterial Disease caused by *Mycobacterium Tuberculosis (MTB)*, which most commonly affects the Lungs, but can affect Any Part of the Body.

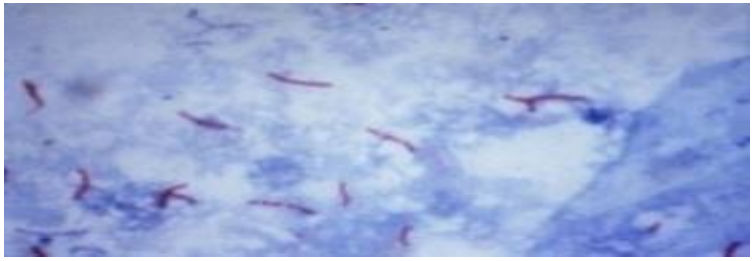
It is Transmitted from Person to Person via Droplets from the Throat and Lungs of People with the Active Pulmonary Disease.

http://www.who.int/topics/tuberculosis/en/

Sites of Disease:

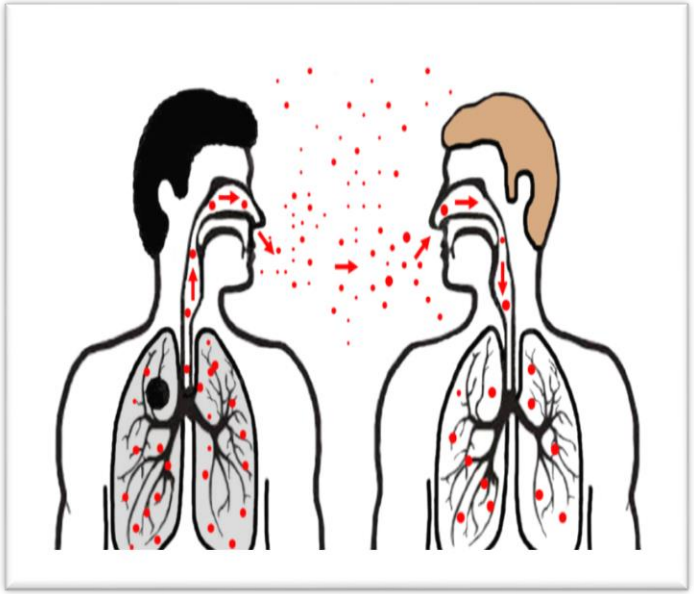
- Lungs (common and usually infectious)
- Central Nervous System: usually occurs as Meningitis, but can occur in Brain or Spine
- Miliary: occurs when Bacilli spread to all parts of the body; rare, but fatal if untreated
- Lymph Nodes (Neck and Axilla)

Pathogenesis



A small number of tubercle bacilli enter the bloodstream and spread throughout the body. The tubercle bacilli may reach any part of the body, including areas where TB disease is more likely to develop (such as the brain, larynx, lymph node, lung, spine, bone, or kidney).

Probability TB Will Be Transmitted:



- **Susceptibility of the exposed person**
- **Infectiousness of person with TB (i.e., number of bacilli TB patient expels into the air)**
- **Environmental factors that affect the concentration of *MTB* organisms**
- **Proximity, frequency, and duration of exposure (e.g., close contacts)**
- **Can be transmitted from Children, though less likely**

TB Signs and Symptoms:

Pulmonary:

- Cough – more than 3 weeks
- Loss of Appetite / Weight Loss
- Fever – more than 3 weeks
- Night sweats

Extra-Pulmonary:

?Site

Lymph Nodes: Swelling

Brain / CNS: Headache / Confusion

Spine: Pain / deformity / disability

Diagnosis of Tuberculosis

- **Microbiology of pathological samples - discharged pus or biopsy material**
  - **direct staining, culture**
  - **other methods e.g. PCR**
- **Histopathological pattern of Inflammation**
- **Tuberculin Skin Testing (TST) / Interferon-gamma release assay (IGRA)**
- **Radiographic Image**
- **Clinical Diagnosis**

Latent TB:

Latent tuberculosis infection (LTBI), defined as a state of persistent immune response to prior-acquired Mycobacterium tuberculosis antigens without evidence of clinically manifested active TB.

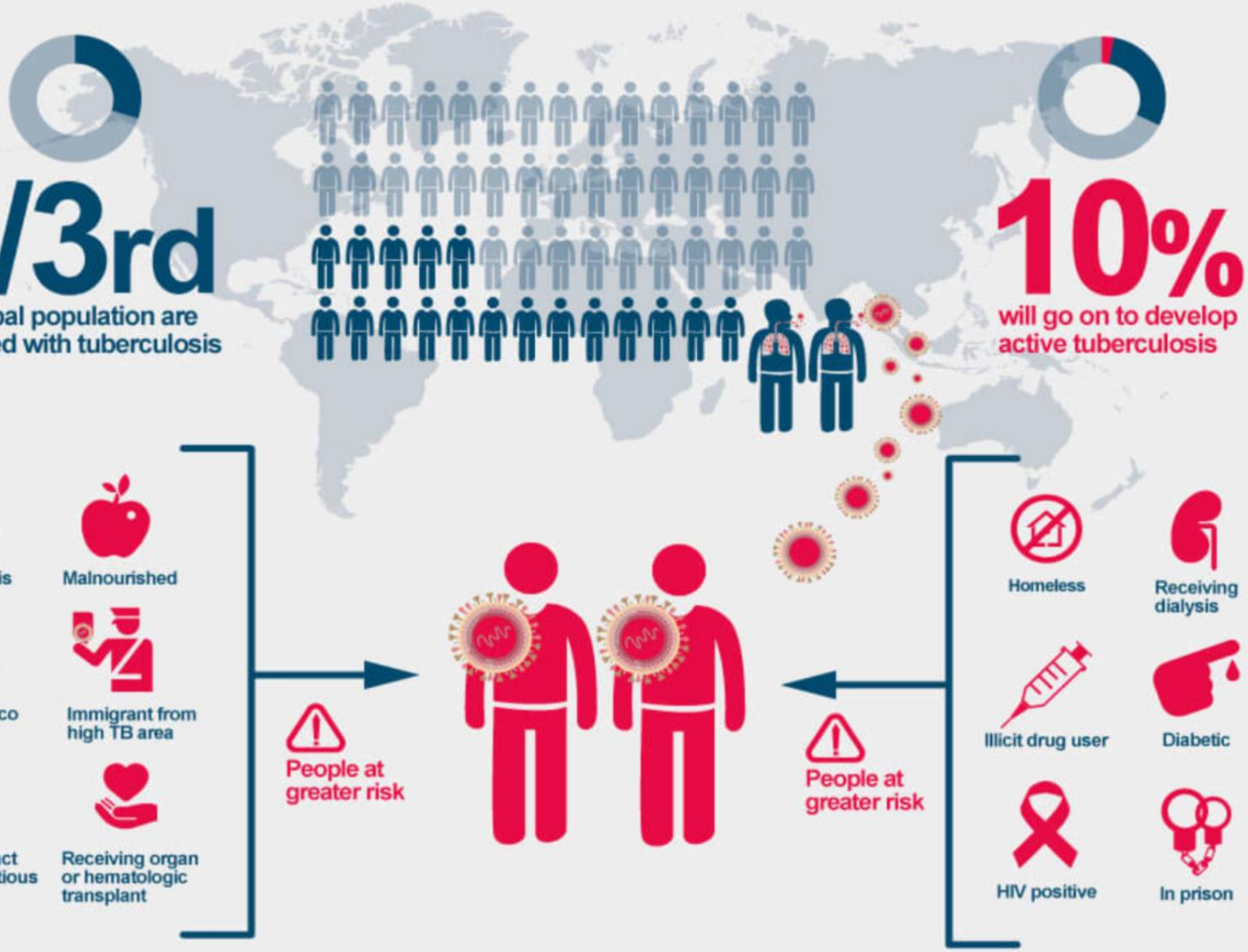
It affects about one-third of the world's population. Approximately 10% of people with LTBI will develop active TB disease in their lifetime.

The majority develop the disease within the first five years after initial infection.

Currently available treatments have an efficacy ranging from 60% to 90%.

Guidelines on the Management of Latent Tuberculosis Infection , World Health Organisation, 2015.

Risk of infection with tuberculosis



Source: World Health Organisation
Credit: Rebeccah Robinson

Persons with weak immunity at increased risk of progressing to TB disease:

- Untreated HIV infection highest risk factor: risk of developing TB disease is 7%–10% *each year*;
- Children <5 years of age are at increased risk
- Aim of LTBI Screening / Treatment is to prevent progression to TB Disease

LTBI vs. TB Disease

Person with LTBI (Infected, but not Infectious)

- Has a small amount of TB bacteria in his/her body that are alive, but inactive
- Cannot spread TB bacteria to others
- Does not feel sick, but may become sick if the bacteria become active in his/her body
- Usually has a TB skin test or TB blood test reaction indicating TB infection
- Chest X-ray is Normal
- Sputum smears and cultures are negative
- Will be offered Treatment for LTBI to prevent TB disease
- Does not require respiratory isolation
- Not a TB case – Latent Cases Not Notified – but Recorded Locally

Person with TB Disease (Infectious – if in the Lungs)

- Has a large amount of active TB bacteria in his/her body
- May spread TB bacteria to others
- May feel sick and may have symptoms such as a cough, fever, and/or weight loss
- Usually has a TB skin test or TB blood test reaction indicating TB infection
- Chest X-ray may be Abnormal, or other Scan
- Sputum smears and cultures may be positive
- Needs treatment for Active TB disease
- May require respiratory isolation
- A TB case – for Notification

Treatment – Active TB:

6 months oral antibiotic treatment:

- First 2 months, 4 antibiotic drugs are used Isoniazid, Rifampicin, Pyrazinamide (Rifater) & Ethambutol
- Then 2 antibiotics for 4 months - Isoniazid, Rifampicin
- Treatment 12-18 months if TB is in the Bone or Brain

Drugs Side-effects:

Common side effects:

- Nausia / Vomiting / Pruritus / Rash / Tiredness / Joint Pains

Less Common

- Peripheral Neuropathy / Gout / Drug induced hepatitis / Acne / Menstruation

Rare

- Vision Problems / Hearing Loss / Psychosis

MDR /XDR TB:

- TWO Years if it is Drug Resistant TB
- Treated with 6 drugs one of which should be injectable for 6 months
- Amikacin/ Capreomycin/ Streptomycin
- Prothionamide, Cycloserine, PAS, Moxifloxacin, Clarithromycin,

Latent TB Treatment:

Treatment as Local / Nice Guidelines:

3 months of Rifinah (Rifampicin and Isoniazid) or 6 months of Isoniazid with Pyridoxine

Treatment for Latent TB:

- **All Children younger than 2 years of age – close contact with PTB – Referred to Specialist Pediatrician for Prophylaxis, following screening- risk of developing Active TB**

- **Asymptomatic, Positive TST (5mm or larger is +ve – regardless of BCG history) and or IGRA**

- **HIV Testing (New Guidelines)**

Treatment as per Local / Nice Guidelines:

- **3 months of Rifinah (Rifampicin and Isoniazid) or 6 months of Isoniazid with Pyridoxine**

What is Case Management?

Case management is described as 'the process of planning, co-ordinating and reviewing the care of an individual'.

It as 'a collaborative process of assessment, planning, facilitation, care coordination, evaluation, and advocacy for options and services to meet an individual's and family's comprehensive health needs through communication and available resources to promote quality cost-effective outcomes'.

Kings Fund 2011

…cont…Case Management

- **Case Management Tool – being updated:**

Case Management & COHORT Review: Guidance for Health professionals. 2011. British Thoracic Society, Health Protection Agency and National treatment for Substance Misuse. Royal College of Nursing

- **Caseload……..? 1: 40….excluded by NICE**

Direct Observed Therapy (DOT):

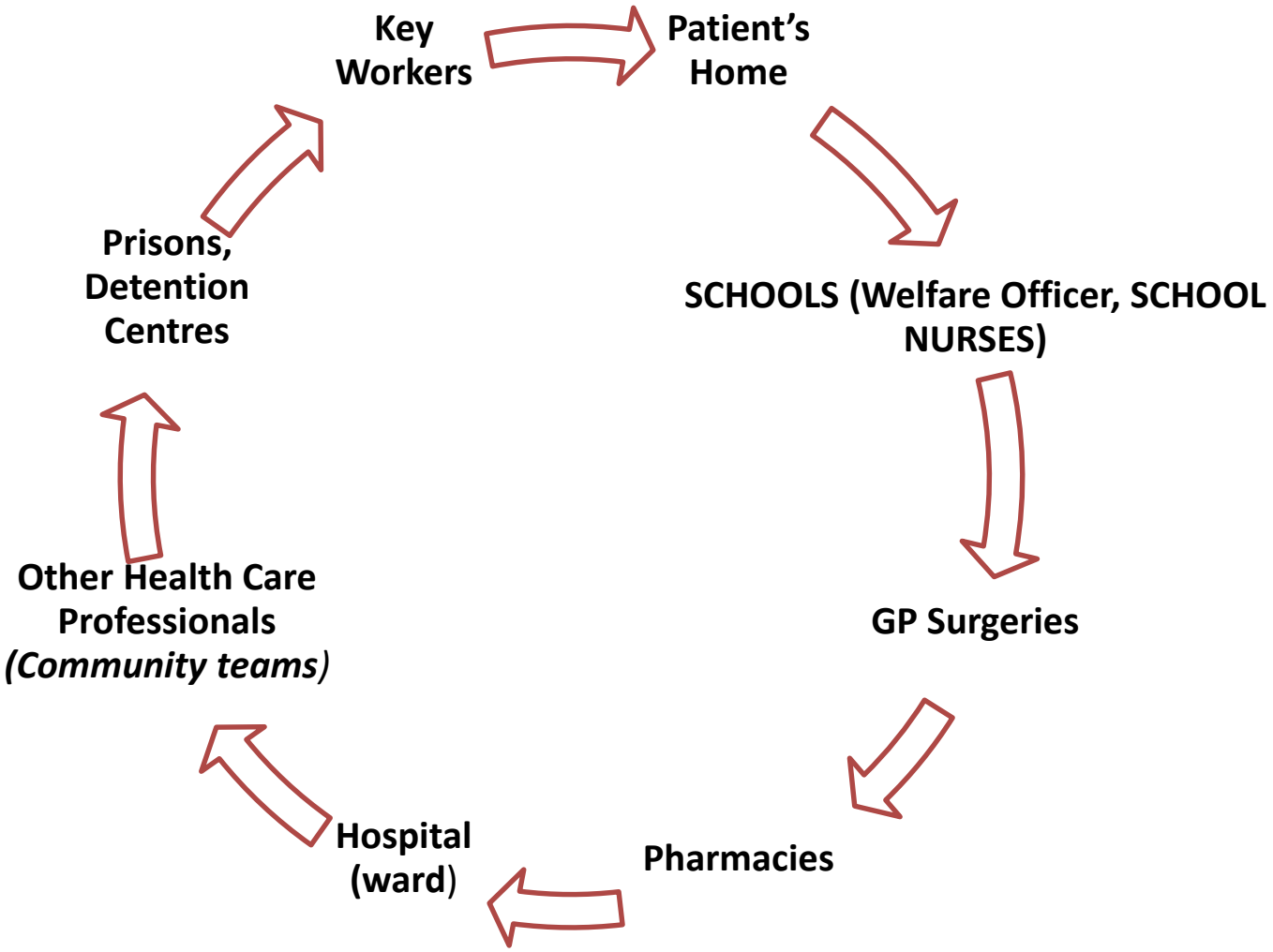
Witnessing of The Correct Dosage of TB Medicines Taken By The Patient.

Risk Assessment for Adherence / Compliance.

- Social Risk Factors (homelessness, substance and alcohol misuse
- MDR, History of Previous TB
- Safeguarding Concerns
- Other Siblings in the Household on Treatment
- Parents – History of Non-Compliance
- Previous History of LTBI
- Housing Issues

Virtual Observed Therapy (Adults only): Research TB Reach (University College of London)

Who Can DOT:


Key Workers
Patient's Home
SCHOOLS (Welfare Officer, SCHOOL NURSES)
GP Surgeries
Pharmacies
Hospital (ward)
Other Health Care Professionals (Community teams)
Prisons, Detention Centres

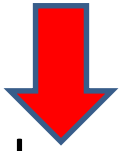
TB Screening:

- **Contact Screening – Contacts**
- **Opportunistic Case Finding – New Entrants From High Incidence Countries**
- **Health Assessments – Vulnerable persons**
- **Pre-employment – Healthcare Workers**
- **Incidents / Outbreaks – Response**
- **BCG Vaccination – Risk Assessment for 6 and under years of age (Green Book, 2006)**
- **Differential Diagnosis, Anti-TNF / Biological Agents**

Nice Institute for Health and Care Excellence, (NICE) 2016, and WHO Guidelines for LTBI,2015

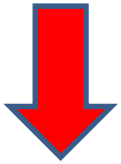
Why Contact Screen?

Infectious Person (coughing)



Infects 10 People with TB Bacilli

10 People have LTBI



1 Person develops Active TB – That 1 Person becomes Infectious

FIVE Contacts for PTB Cases

Health Protection Agency, 2008

Why Screen for Latent TB?

Systematic testing and treatment of LTBI in at-risk populations is a critical component of WHO's eight-point framework adapted from the End TB Strategy to target pre-elimination and, ultimately, elimination in low incidence countries.

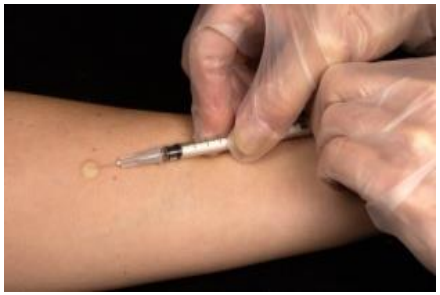
Guidelines on the Management of Latent Tuberculosis Infection , World Health Organisation, 2015

Screening for Latent TB /Contact Tracing Involve:

- **Symptom Check – Exclude Active TB (Questionnaire)**
- **Tuberculin Skin Test (TST)**
- **Interferon Gamma Release Assays (IGRA)**
- **2 to 8 weeks after infection, LTBI can be detected via TST or interferon-gamma release assay (IGRA)**
- **CXR (over 65)**

Diagnostic Tests for TB Screening:

Tuberculin Skin Test (TST): purified protein derivative; PPD) – Mantoux



New NICE Guidance:

5mm and above +ve,

Regardless of BCG

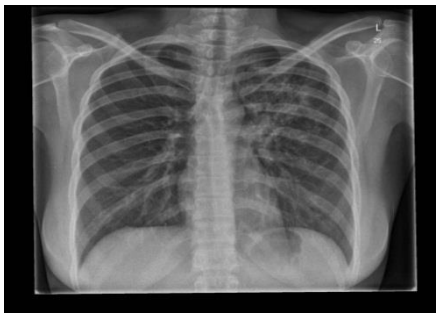
History

Blood Tests (IGRA)

Results: +ve or –ve,

Repeat if Indeterminate

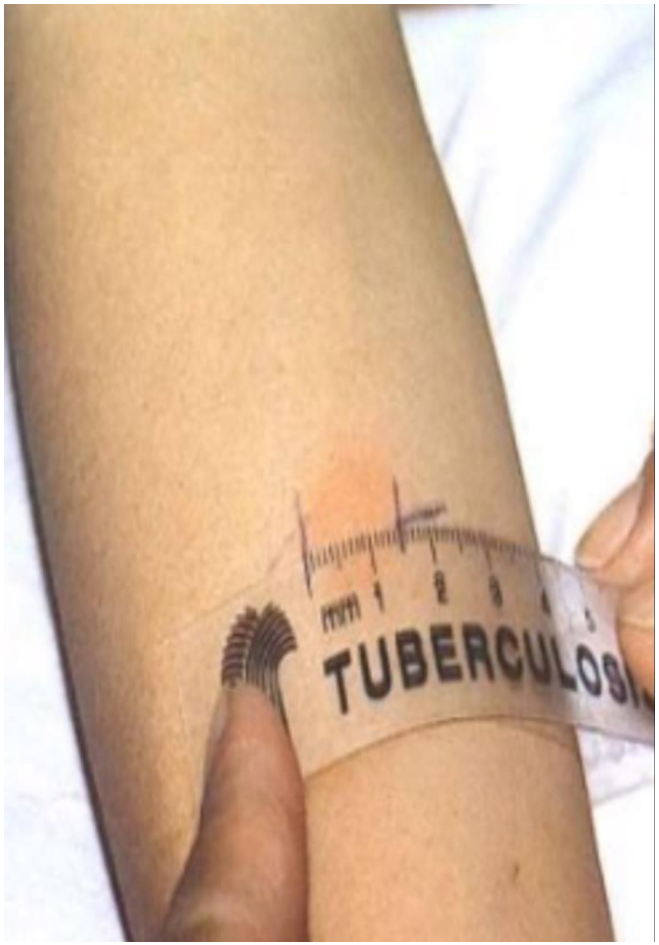
CXR: over 65's



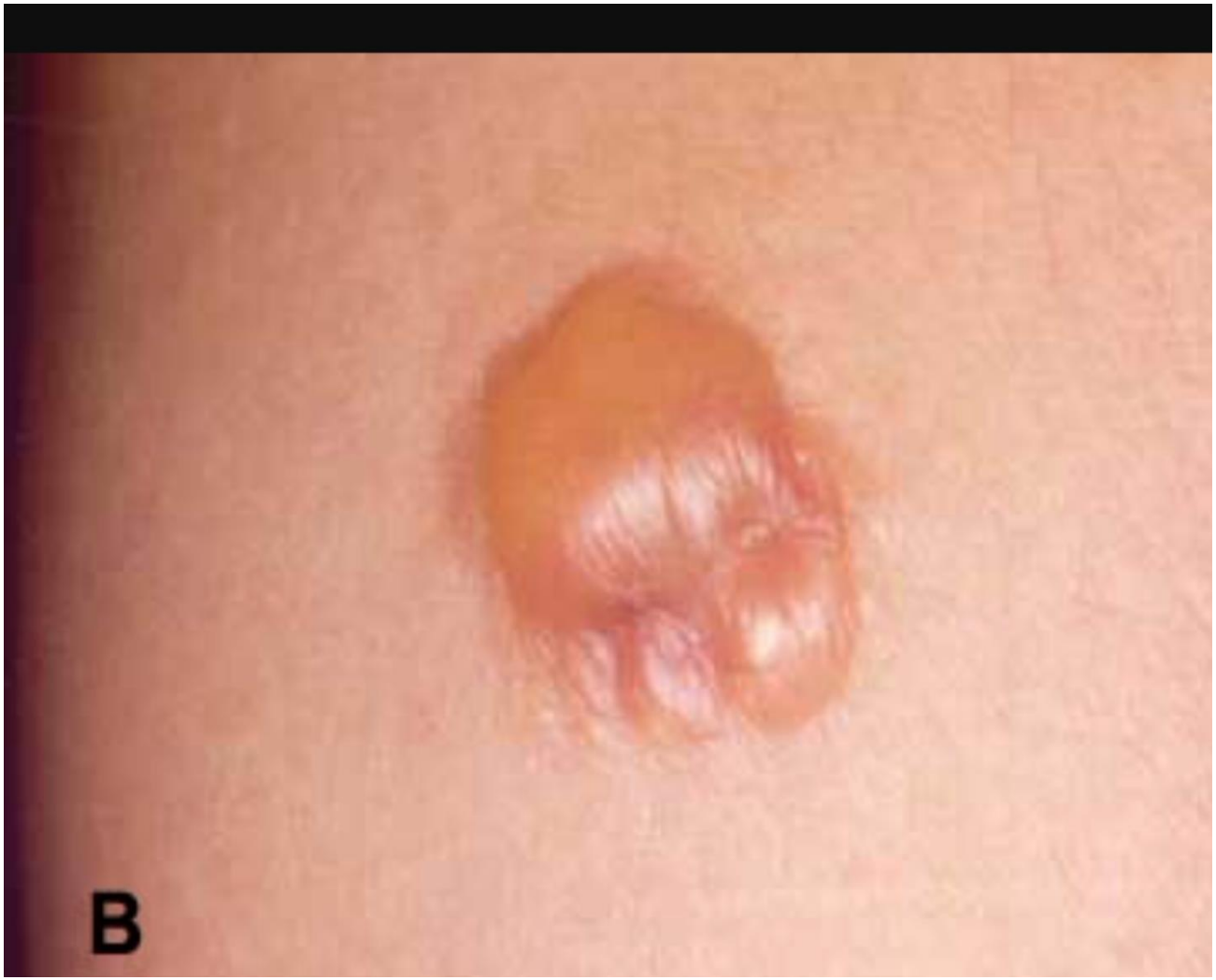
Tuberculin Skin Test

Reading: after 48-72 hours Of Injection

≥5mm is now Considered +ve, regardless of BCG Vaccination History:



(NICE Guidelines, 2016)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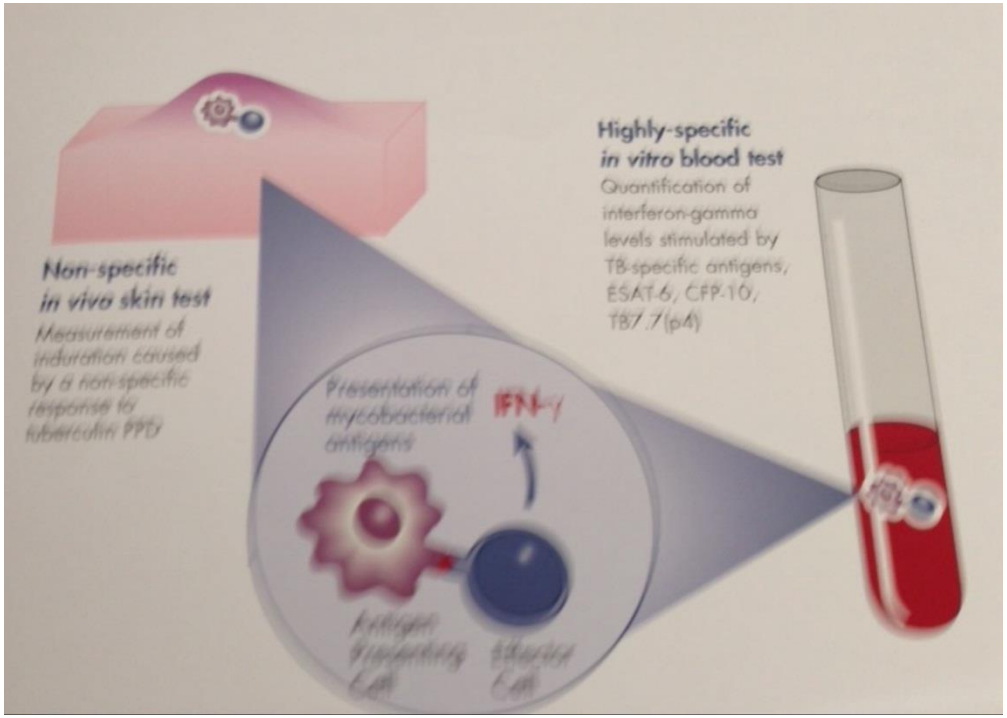
Interferon-gamma release assay (IGRA)

Measures an immune response that reflects contact to MTB



Interferon-gamma release assay (IGRA):

QuantiFERON (QFT) – measures interferon gamma produced by sensitised T Cells stimulated by TB antigens

T. SPOT – counts the number of anti-mycobacterial effector T Cells, White Blood Cells, that produce interferon-gamma, in a sample of blood

Incident – TB?

A TB Incident is a Situation that requires or warrants Public Health Investigation & Management, due to an Infectious TB Case (or potentially) has had significant contact with Individuals other than household members / relatives / friends. Establishments may include: Educational, Healthcare, Prisons, Workplaces etc..

Outbreak – TB?

A TB Outbreak is an Incident where there are two or more epidemiologically linked cases with the same strain of TB.

An epidemiological link is established when known contact has occurred between cases, or where contact is *possible* or *likely* because they belong to a defined cohort of individuals.

Even if microbiological confirmation is absent or results pending – an outbreak might be suspected – if there are strong epidemiological links between the cases.

RISK ASSESSMENT:

Infectiousness	Exposure	Susceptibility/Vulnerable
Sputum smear +ve	Duration	Age (small child)
Sputum vs BAL	Ventilated environment	Immunocompromise
Cough	Closed vs spacious setting	BCG
Lung cavitation		Severe/ Chronic illness
Adult >> Child		

Incident Management - Key Members/ Organisations:

- TB Case Manager / Specialist Nurse
- Public Health England (PHE), Consultant in Communicable Disease Control (CCDC)
- TB Physician / Paediatrician
- Microbiologist
- Place of Incident – Manager, Head Teacher, Infection Control & Prevention Team/Director etc.
- Communication: Press / Media Team

Case Study / Scanario:

- **A 22 year old female, diagnosed with (AFB+ve) Fully Sensitive Cavitory Pulmonary TB: 2013.**
- **Presented via A&E due to SOB. Was admitted (side-room).**
- **Symptomatic for 6 months (cough, fever, weight loss and malaise).**
- **Born in the Philippine's, came to UK 2005. Had BCG Vaccination.**
- **Completed 2 Courses of ABX from GP – no effect.**
- **Home Situation: shared house with friend's family (husband & 2 young children at the age of 1 and 6yrs).**
- **She was a Nursing Student – recently completed a 6 week Placement in ICU.**
- **She recently attended Lectures at University.**

…cont…Case Study (Case & Incident Management):

- She tolerated ATT well, although initially suffered rash and nausea – both relieved by anti-histamine and anti-metic.
- Assess for Compliance & Adherence.
- Notify Patient.
- Report TB Incident to PHE (ICU & University).
- Screen household contacts as Local and NICE Guidelines (refer 1yr old to Paediatrician for Chemo).
- Support Patient – as per Local Pathway – throughout Treatment.
- Repeat Sputums – Returning to School / Work / Placement.
- In addition to the 1 year old, one adult had +ve TST, Completed LTBI Rx.
- Work in Partnership with PHE , Hospital, University – (Risk Assessment).
- Incident Meeting (One arranged at Hospital).

…cont…Case Study (Case & Incident Management):

- University: 62 identifies as contacts (1 lady pregnant, no individuals immunosuppressed). **(all under 35)**
- 45 screened (17 DNA's – re-appointed, repeat DNA's, D/C), 2 Positives: offered LTBI Rx.
- Hospital / ICU – all patients and staff whom the TB Case had contact with were screened: 5 Patients and 6 Staff. (ICU – patients are Vulnerable). All NAD.

- Case Manage those receiving treatment for LTBI or chemoprophylaxis.
- Close Incident once, all screening, follow-up etc.. completed, report to PHE of outcome.
- Continue supporting patient/source till ATT completed.
- Up-date databases, and present Case at COHORT REVIEW.

CLOSE Incident, Patient Completed Rx, Present at COHORT REVIEW

So What ‘s New / Up-dated in The Guidance:

NICE
National Institute for
Health and Care Excellence

- **Diagnosing Active TB / Treatment – in-terruptions**
- **Diagnosing / Screening for Latent TB Infection**

Diagnosing Active TB / Treatment – Up-dated:

- **Request Rapid Diagnostic Nucleic Acid Amplification Tests (NAATs) for M.TB**

- **How To Re-establish Treatment for Active or Latent TB after Interruptions following adverse reactions form drugs / medication**

Diagnosing / Screening for Latent TB Infection:

1) Offer TB Screening to Close Contacts of

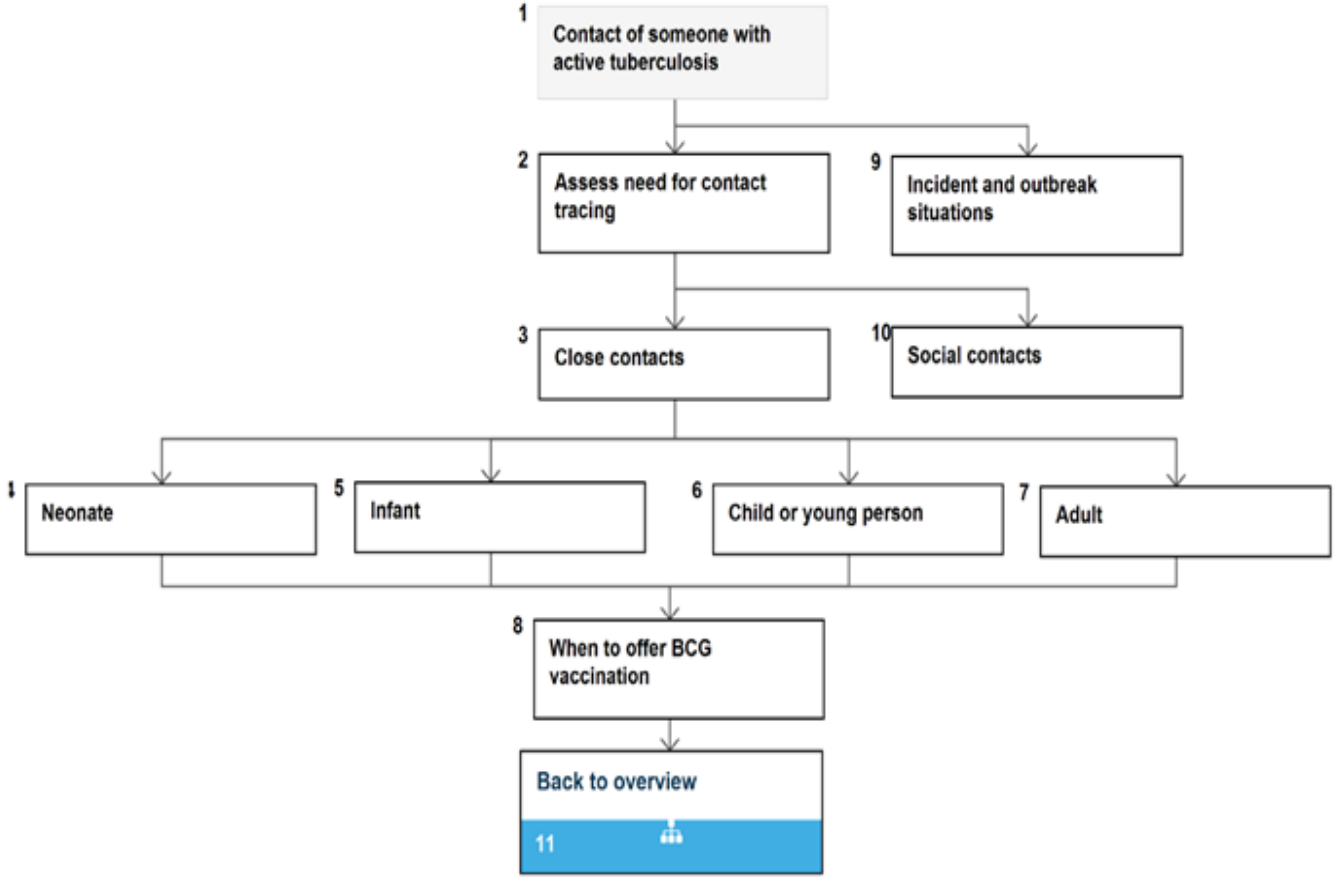
- People with Pulmonary or Laryngeal TB..? Non-Pulmonary?

2) Induration of ≥5mm of Tuberculin Skin Test (TST) is Considered Positive Regardless of BCG History

3) Increase In Upper Age Limit For Testing And Treatment For Latent TB from 35 years to 65 years

Tuberculosis: contact tracing and testing

NICE Pathways



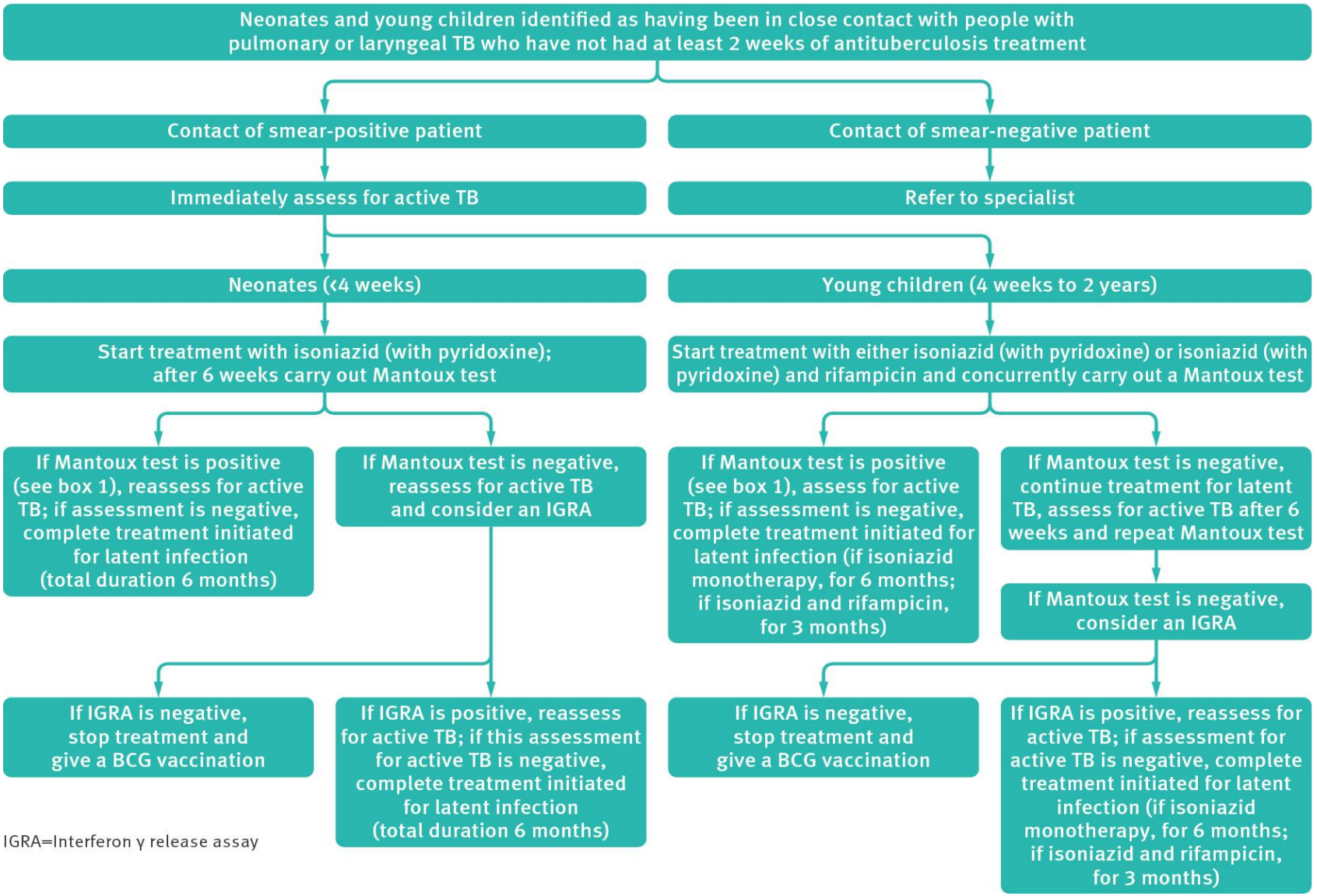


Fig 1 Pathways for diagnosing latent TB infection in neonates and young children *[Updated recommendation 2016]*

Offer TB Screening to Close Contacts of:

- *People with Pulmonary or Laryngeal TB*

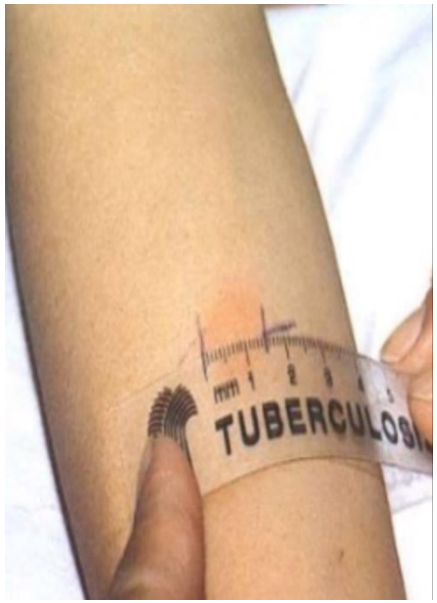
??? Non-Pulmonary TB Contacts:

- **Between 2013 - 2015 we saw 1359 Contacts of Extra-pulmonary TB patients**
- **SIX were found to have Active TB**
- **62 were treated for latent TB**
- ***Please Note this is prior to the New Age Guidelines as were only screening for Latent TB in under 35's it is likely we will pick up much more latent TB***

Data / Source: Birmingham & Solihull TB Service, Dendrite Database May 2016

Induration of ≥5mm of Tuberculin Skin Test (TST) is Considered Positive Regardless of BCG History:

- Paediatric TB Group…..**update**
- Simpler Algorithm



NIKS
NIHR IGRA Kids Study

OPEN ACCESS

ORIGINAL ARTICLE

The impact of BCG vaccination on tuberculin skin test responses in children is age dependent: evidence to be considered when screening children for tuberculosis infection

James Seddon, James Paton, Zohreh Nademi, Denis Keane, Bhanu Williams, Amanda, Steven Welch, Sue Liebeschutz, Anna Riddell, Jolanta Bernatoniene, Sanjay Patel, Nuria Martinez-Alier, Paddy McMaster, Beate Kampmann

Thorax 2016 (in press)

Interpretation of NIKS data in the context of "New Nice"

	"Old NICE"	"New NICE"
TST+ve	27.9%	41.8%
IGRA+ve	24.4%	

Use of "new NICE" TST cut off's would have resulted in almost 50%
more children receiving Isoniazid / Rifampicin

Conclusion – NIKS STUDY:

- **Impact of infant BCG on TST response wanes with age**
- **5mm cut off associated with low sensitivity in young BCG-vaccinated children**

PLAN:

- **Follow NICE – Monitor and Record Data for Analysis**

Increase In Upper Age Limit For Testing And Treatment For Latent TB from 35 years to 65 years:

Latent TB Completion Rates - Birmingham & Solihull TB Service – 2014 - 15:

Latent TB - Treatment Completion Rates ≥90%; 65-89%; <65%)	Target: 90%	92%	86%	90%	92%

NEW TB Guidance - Impact on TB Services:

- **Increase Number of Latent Cases** ***(5mm TST and age increase to 65.***
- **Increase Workload**
- **Case Management for Latent Cases**
- **Older Patients…?adverse reactions**
- **Support / DOT…….ECM – (Active and Latent)**
- **Data Monitoring**

TB Strategy:

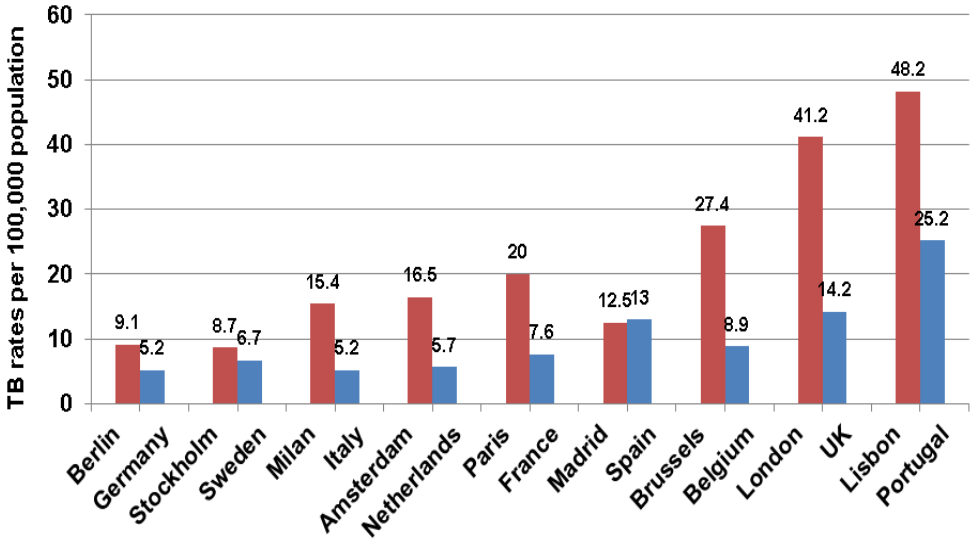
- The Collaborative TB Strategy for England 2015 to 2020 - A Joint PHE / NHS England (NHSE) Document.
- NHSE have invested 10 million pounds for screening **(Latent TB: 16 – 35years).**
- PHE have put Regional Control Boards together (Nationally: 9)
- Aim is to achieve a year-on-year Decrease in TB Incidence.

https://www.gov.uk/government/publications/collaborative-tuberculosis-strategy-for-england

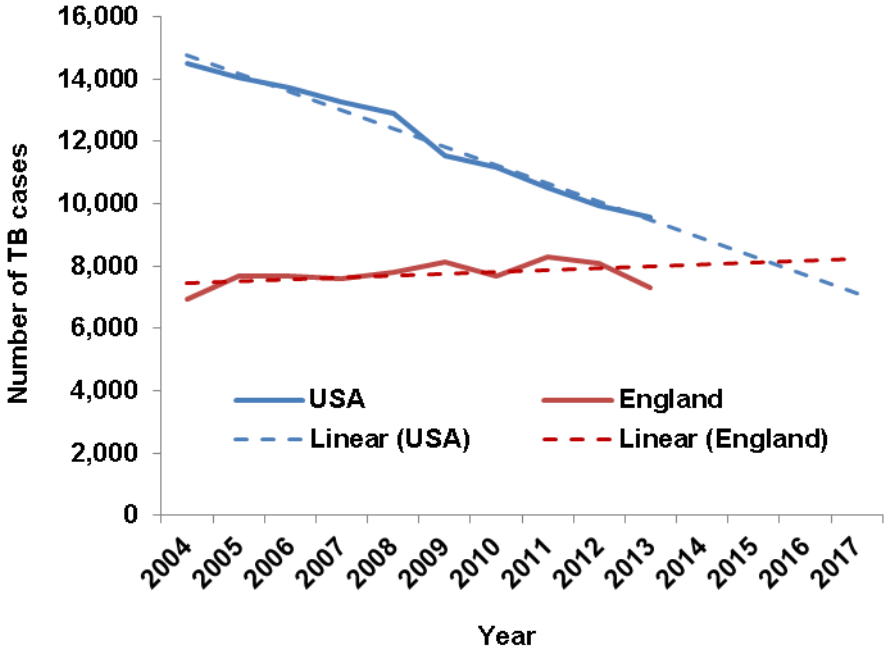
Background to Strategy:

- **England - one of the highest TB rates in Western Europe**
- **Rates of TB in England >4x higher than USA**

Comparison of TB rates per 100,000 pop. in W. European countries and cities (2012)

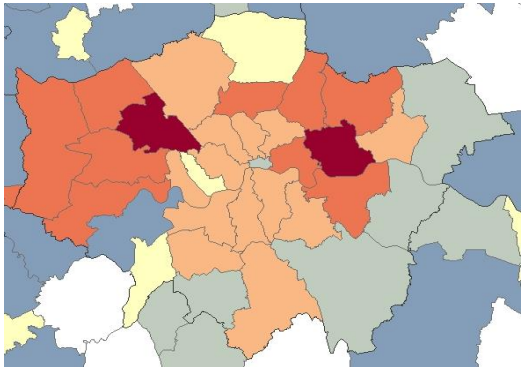


No. of TB cases in England versus the US



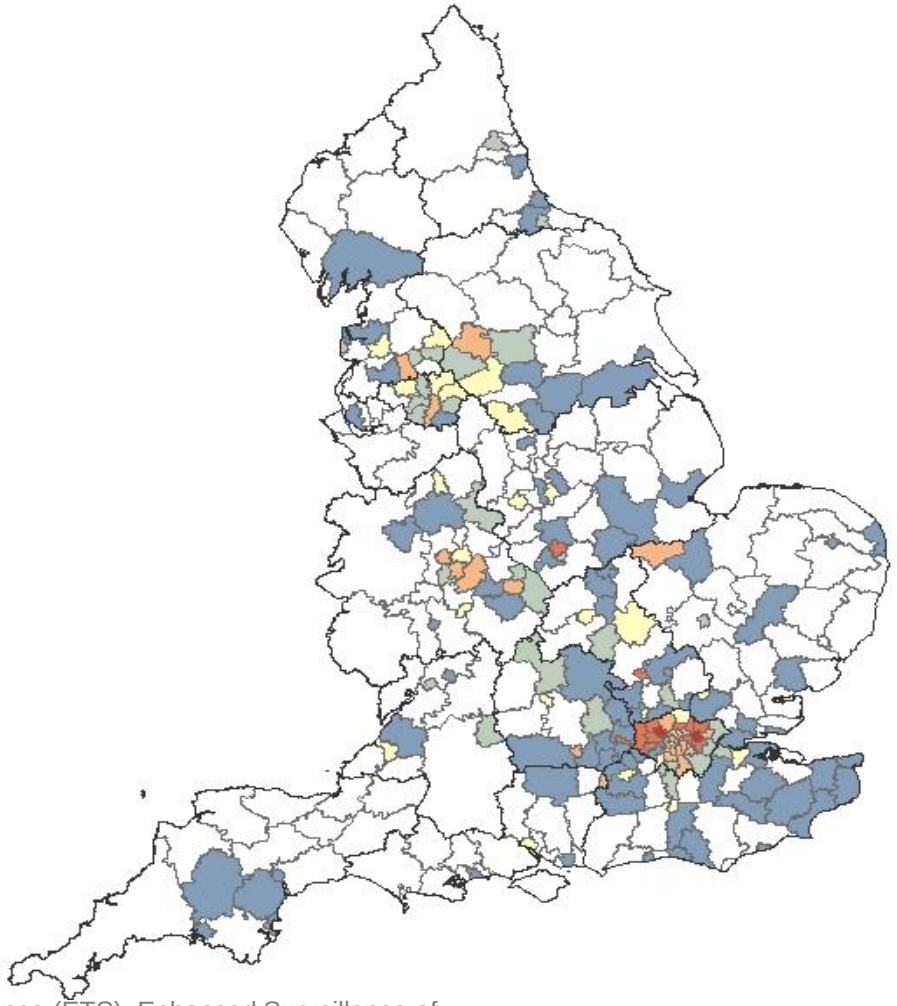
Three-year average TB case rates by local area, 2012-2015

London



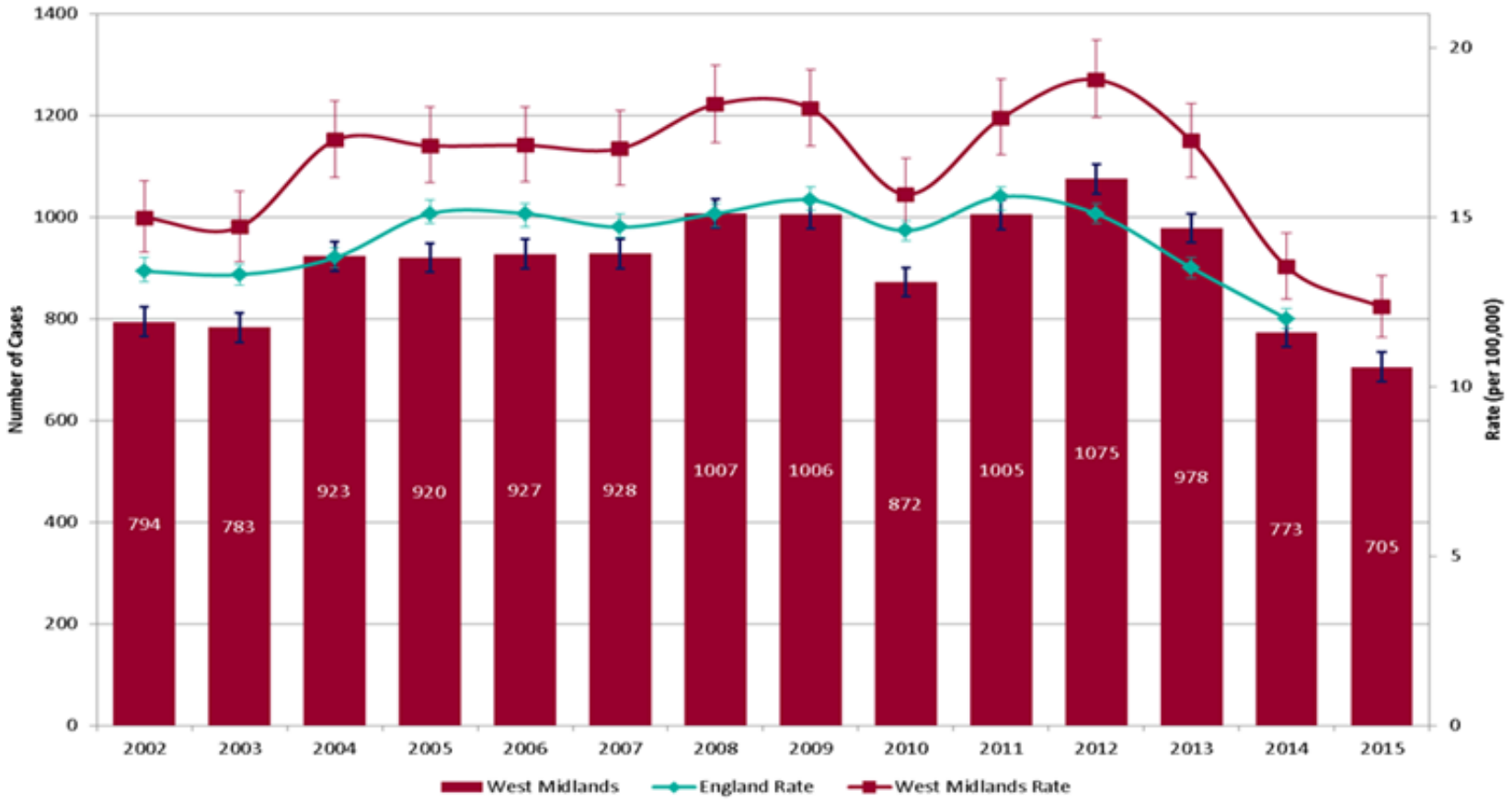
Tuberculosis rate (per 100,000)

- 0.0- 4.9
- 5.0 - 9.9
- 10.0 - 14.9
- 15.0 - 24.9
- 25.0 - 39.9
- 40.0 - 69.9
- >70.0



Source: Enhance Tuberculosis Surveillance (ETS), Enhanced Surveillance of Mycobacterial Infections (ESMI), Office for National Statistics (ONS)
Data as at: May 2014. Prepared by: TB Section, Centre for Infectious Disease Surveillance and Control, Public Health England

Figure 1. Tuberculosis cases and rates in the West Midlands and England, 2002 to 2015 (with 95% CIs)*



*Data for 2015 for England is not yet available and data for the West Midlands is provisional.

Note: 2013 mid-year population estimates from the Office of National Statistics (ONS) were used to calculate rates.

Data sources: Enhanced Tuberculosis Surveillance (ETS) downloaded on 12 March 2016.

Prepared by: chanice.taylor@phe.gov.uk Field Epidemiology Service (Birmingham), Public Health England

Key Priorities – TB Strategy:

1) Improve access and early diagnosis

2) Provide universal high quality diagnosis

3) Improve treatment and care services

4) Ensure comprehensive contact tracing

5) Improve BCG vaccination uptake

6) Reduce Drug Resistant TB (INH / MDR / XDR)

7) Tackle Underserved Populations – **TASK & FINISH GROUP**

8) Implement New Entrant LTBI Screening / Primary Care – **LTBI Group**

9) Strengthen Surveillance and Monitoring

10) Ensure an appropriate Workforce - **REVIEW**

Case Scenario – in brief:

- 44 year old gentleman diagnosed with AFB+ve TB
- NRPF / No Income
- Non-compliance to treatment / DOT
- Very poor Housing Conditions
- Housing – Too late!
- ?Underserved – Task & Finish Group: Housing SLA – TOOL KIT

Challenges in TB:

STIGMA

Delayed Presentation

Duration of Treatment

Patients with Complex Needs

Increasing Incidence

Under Resourced Services

UNDERSERVED POPULATION

Delayed Diagnosis

Multi-Drug Resistance

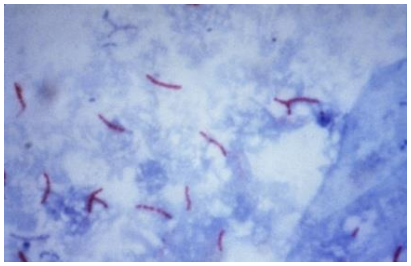
STIGMA – MYTHS:

- Disease associated with Poverty, Homelessness, Drug & Alcoholic Misuse
- Some cultures – associate to blame: women can get divorced
- Other cultures relate it to witchcraft
- Stigma may prevent people accessing health care
- Denial can lead to denial of TB Diagnosis - ?Compliance
- Work / Study establishments : Discrimination Concerns

What May Help:

- Patient Advocacy – **Peer Support**
- Raising Awareness
- Ensure patient doesn't feel Discriminated

Prevention:



- Awareness & Education
- Early Diagnosis & Treatment – Supervision / **DOT**
- BCG Vaccination
- Contact Screening / LTBI Screening
- Active Case Finding

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Thanks!

Questions ?