

HIV-associated tuberculosis: new guidelines for the UK

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BHIVA TB/HIV Guidelines Writing Group

NW TB conference, 2018

HIV-associated TB: global

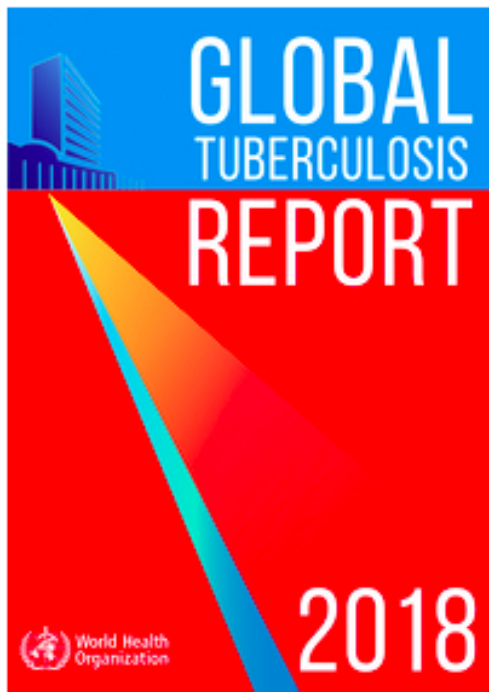
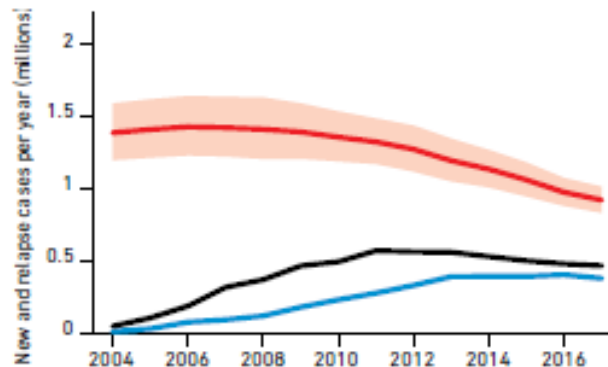


FIG. 4.9

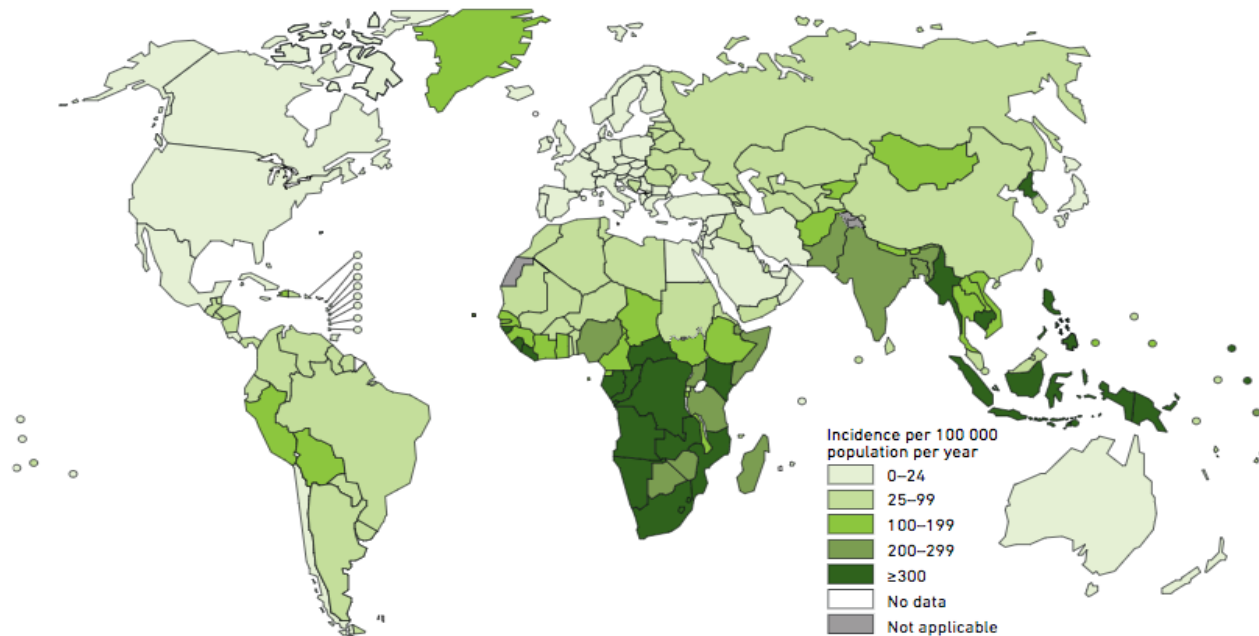
Global numbers of notified new and relapse cases^a known to be HIV-positive (black), number started on antiretroviral therapy (blue) and estimated number of incident HIV-positive TB cases (red), 2004–2017. Shaded areas represent uncertainty bands.



^a The calculation is for all cases in years prior to 2015.

TB: global

Estimated TB incidence rates, 2017



Lesotho	665
S Africa	567
Philippines	554
DPR Korea	513



High TB incidence: $\geq 151/100,000$ person years*

Medium TB incidence: $40\text{--}150/100,000$ person years*

HIV-associated TB: global and national

- What proportion of individuals with TB globally are HIV+?
- In the UK, what proportion of individuals with TB are HIV+?
- In the UK, what is the incidence of TB among HIV+ individuals, compared with general population?

HIV-associated TB: global and national

- What proportion of individuals with TB globally are HIV+?

12% (estimate from WHO TB report, 2018; of the 60% tested)

- In the UK, what proportion of individuals with TB are HIV+?

2.8% (PHE TB report, 2018; 93% adults are tested; peak 8.4% in 2004)

- In the UK, what is the incidence of TB among HIV+ individuals, compared with general population?

Gen pop: **9.2** per 100,000 in 2017 (15.6/100,000 in 2011)

HIV+: **328** per 100,000 in UK CHIC data published 2009

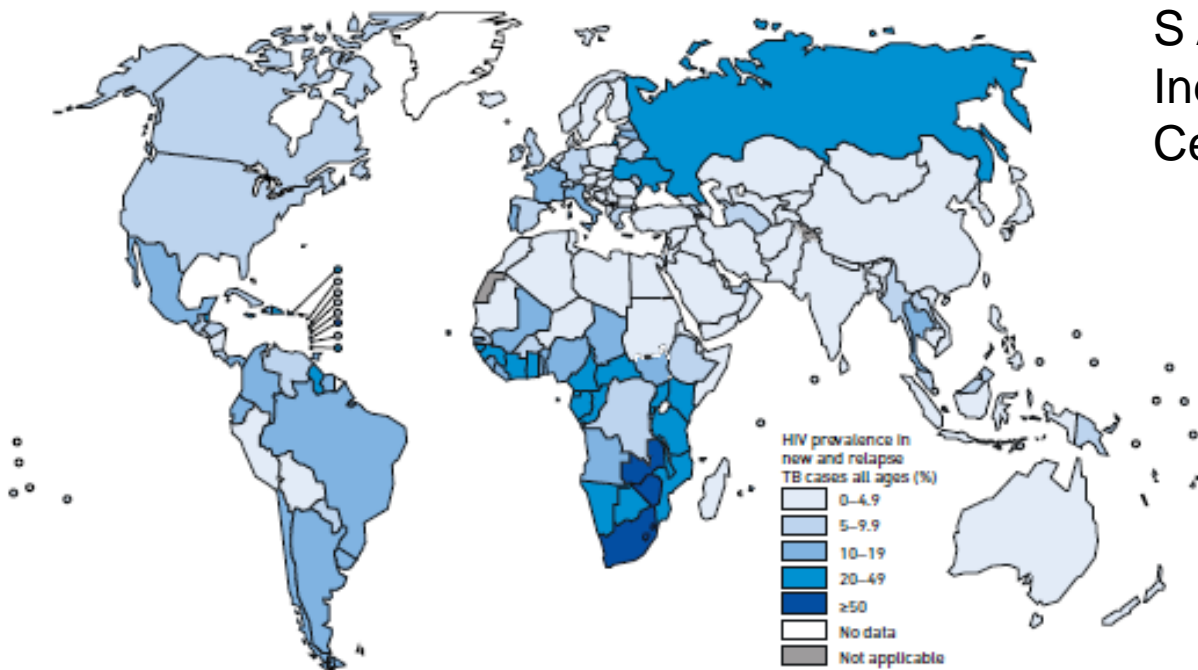
(845/100,000 Black Africans, 189/100,000 white, 375/100,000 other ethnicity)

Incidence reducing: more PLWH, fewer new TB cases in Black Africans

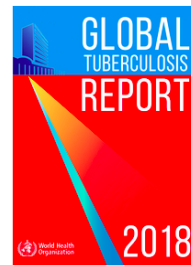
HIV prevalence among individuals with TB

FIG. 3.5

Estimated HIV prevalence in new and relapse TB cases, 2017



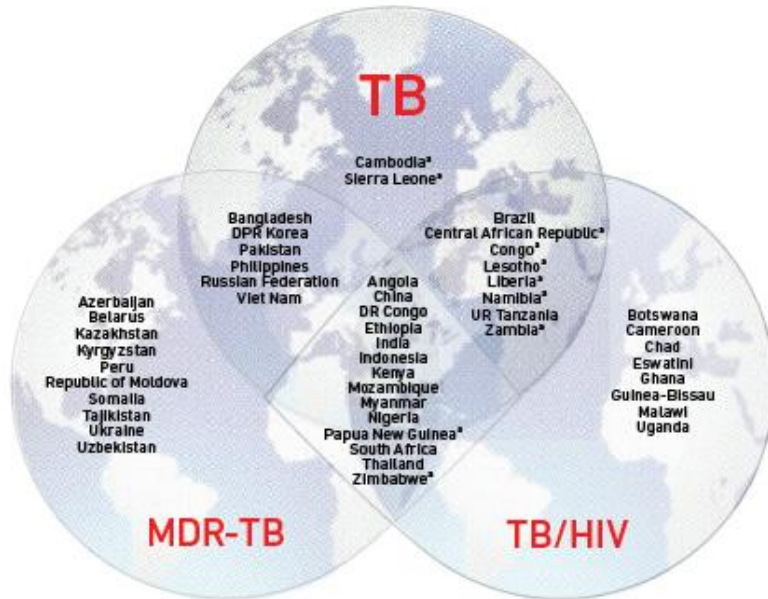
Lesotho	71%
S Africa	60%
India	3%
Central African Republic	32%



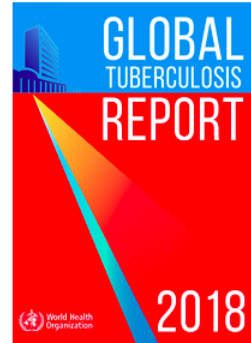
“High burden countries”

FIG. 2.5

Countries in the three high-burden country lists for TB, TB/HIV and MDR-TB being used by WHO during the period 2016–2020, and their areas of overlap



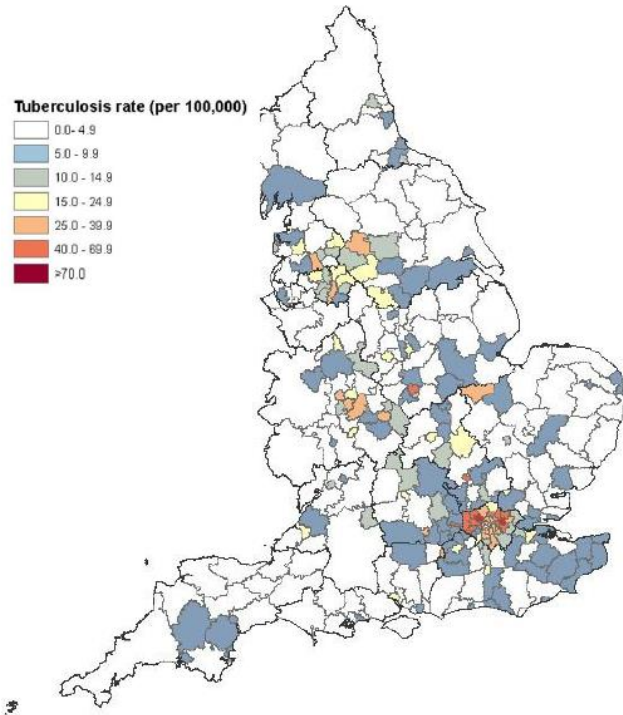
* Indicates countries that are included in the list of 30 high TB burden countries on the basis of the severity of their TB burden (i.e. TB incident cases per 100 000 population per year), as opposed to the top 20, which are included on the basis of their absolute number of incident cases per year. Also see Table 2.4.



- 10 million people fell ill with TB in 2017
- 9% were people living with HIV
- 72% of HIV-associated TB is in Africa

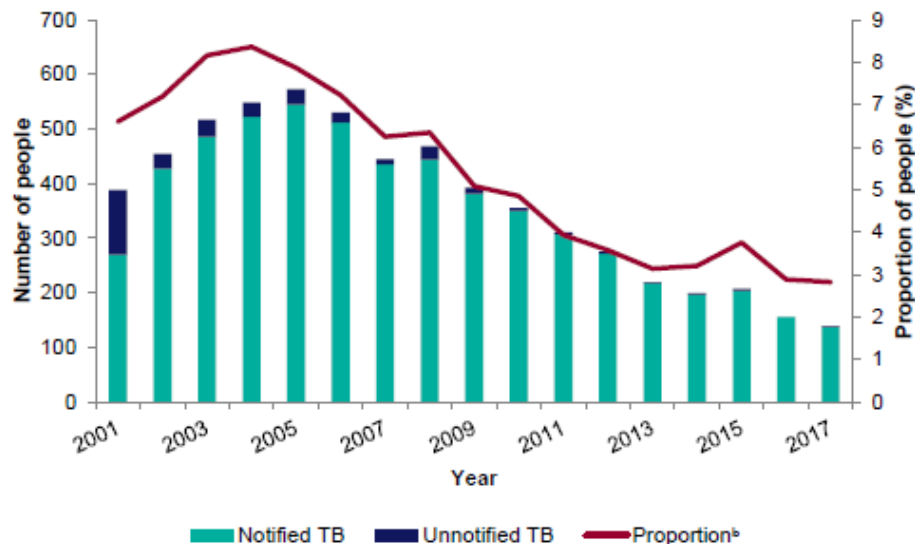
HIV-associated TB: national

Figure 2: TB rate per 100,000 by local authority and PHE centre, England 2011–2013



HIV-associated TB: national

Figure 8.1: Number and proportion of people with TB who have HIV co-infection^a, England, 2001-2017



All TB

5102 TB cases notified in 2017
(peak 8280 in 2011)

HIV-associated TB

109/136 (80%) of those with HIV-associated TB born outside the UK.

Of those, 70% born in sub-Saharan Africa.

In HIV clinic, who is at risk?

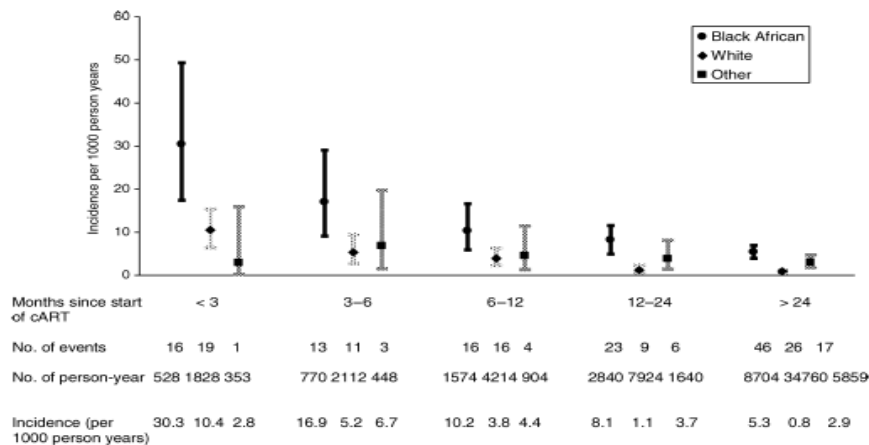
Tuberculosis among people with HIV infection in the United Kingdom: opportunities for prevention?

United Kingdom Collaborative HIV Cohort Study Group

AIDS 2009, 23:2507–2515



The UK Collaborative HIV Cohort
(UK CHIC) Study



Bars represent 95% confidence intervals around the point estimate of the incidence rate

Fig. 3. Incidence of tuberculosis after starting combination antiretroviral therapy, stratified by time after starting antiretroviral therapy and ethnic group ($N = 7181$).

Incidence: after >24 months on ART

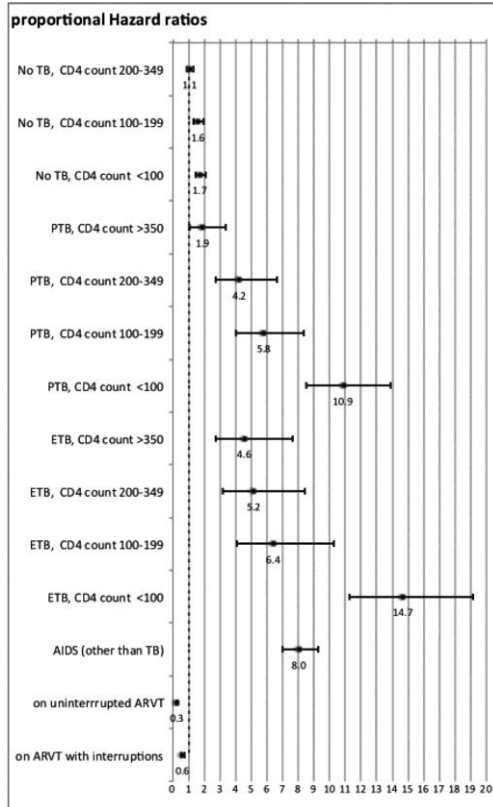
Black African: 530/100,000

White: 80/100,000

Other: 290/100,000

UK incidence at that time: 15/100,000

Mortality associated with TB-HIV coinfection



Impact of TB on the survival of people living with HIV infection in England, Wales and Northern Ireland

Dominik Zenner,^{1,2} Ibrahim Abubakar,^{1,2} Stefano Conti,¹ Rishi K Gupta,³ Zheng Yin,¹ Meaghan Kall,¹ Michelle Kruijshaar,⁴ Brian Rice,¹ H Lucy Thomas,¹ Anton Pozniak,⁵ Marc Lipman,³ Valerie Delpach¹

All-cause mortality for HIV-positive individuals in the UK 2000-2009. Hazard ratios for all-cause mortality (baseline, HR = 1, for 25-34 y/o MSM, never on ART, not TB infected, CD4 > 350).

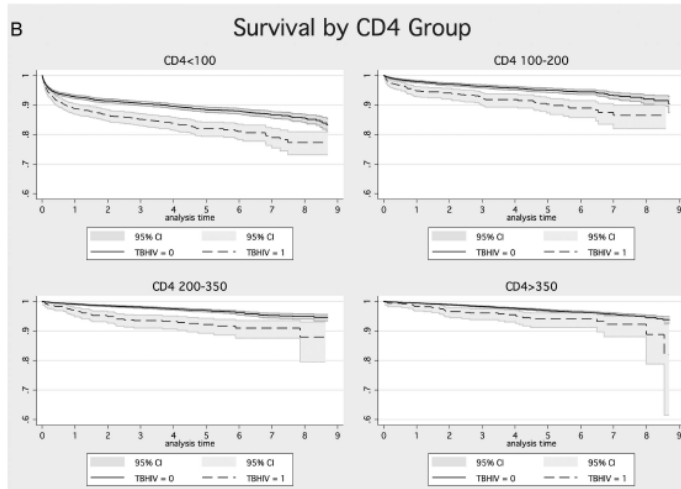


Figure 2 All-cause survival in a national HIV cohort (n=44 050) diagnosed between 2000 and 2008 in England, Wales and Northern Ireland stratified by TB-HIV coinfection status (A) and by CD4 count at diagnosis (B).

Guidelines and GRADE (-ing evidence)

BHIVA guidelines are NICE-approved and use GRADE methodology.

GRADE: gradings of recommendations
assessment, development and evaluation

Strength of recommendation: 1-2

1: “we recommend”

2: “we suggest”

Quality of evidence: A - D

Strong – weak (for a particular outcome)

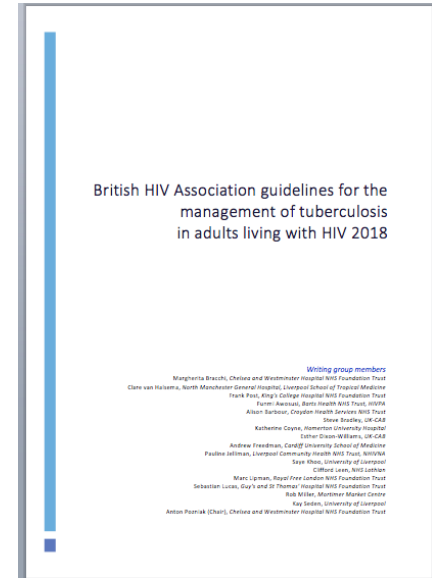
Good practice points (GPPs) outside of GRADE



These guidelines update the previously published BHIVA guidelines on the treatment of TB/HIV co-infection from 2011¹

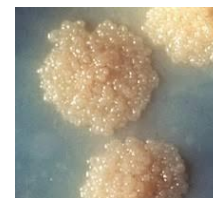
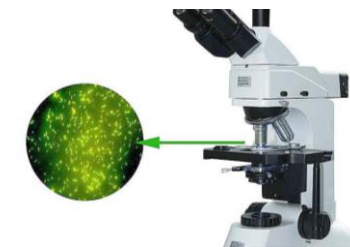
Should be used in conjunction with

- NICE: Tuberculosis guidance
- BHIVA guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy;
- Current WHO guidelines for the treatment of drug-resistant tuberculosis (including INH monoresistance);



Diagnosis of active pulmonary TB

- Microscopy for acid-fast bacilli, culture and drug-sensitivity testing should be performed on respiratory samples
- If smear-positive: **molecular testing** (eg. Xpert MTB/RIF Ultra) (GRADE 1B)
- All pulmonary smear-negative samples should be processed for culture and drug-sensitivity testing; molecular tests only if high suspicion for TB (GRADE 1B)



IGRAs should not be used to diagnose or exclude active TB

IGRA = interferon gamma release assay, eg Quantiferon, T-spot

Diagnosis of pleural TB



Pleural fluid +/-
tissue analysis (pleural biopsy)

Microscopy for acid-fast bacilli, culture
and drug-sensitivity testing

Even in the absence of obvious lung parenchymal involvement:



Induced sputum

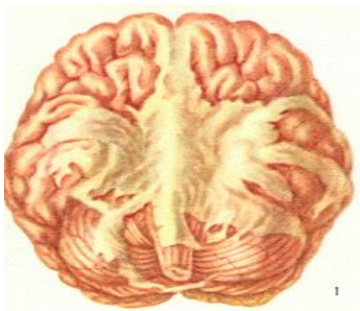


BAL

Microscopy and cultures on respiratory
samples should be performed (GRADE 1B)

Diagnosis of active extra-pulmonary TB

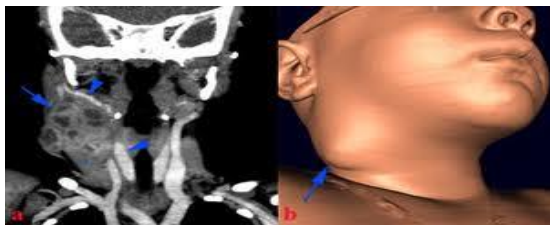
TB meningitis



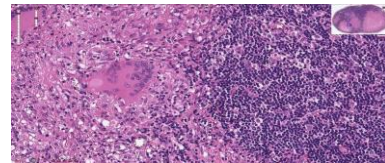
MOLECULAR TESTS on
CSF samples (RULE IN not
RULE OUT)



Other organs



- ✓ microscopy and culture for AFB
- ✓ histology
- ✓ molecular testing



Diagnosis of multidrug-resistant TB infection

Molecular techniques:

Eg Xpert, WHOLE GENOME SEQUENCING, in addition to phenotypic drug susceptibilities

Whole Genome Sequencing to diagnose TB

Posted on March 29, 2017 at 12:46 pm

Public Health England has announced that Whole Genome Sequencing (WGS) is now being used to identify different strains of tuberculosis (TB).

This is the first time that WGS has been used as a diagnostic solution for managing a disease on this scale anywhere in the world. The technique, developed in conjunction with the University of Oxford, allows faster and more accurate diagnoses, meaning patients can be treated with precisely the right medication more quickly. Where previously it could take up to a month to confirm a diagnosis of TB, confirm the treatment choices and to detect spread between cases, this can now be done in just over a week by Public Health England's Birmingham laboratory. This slows the spread of the disease and boosts the fight against anti-microbial resistance.



Public Health
England

This world first service has been developed in partnership with Genomics England, National Institute for Health Research (NIHR) and Wellcome Trust. The implementation of this technology will contribute to achieving the aims of the 100,000 Genomes Project.

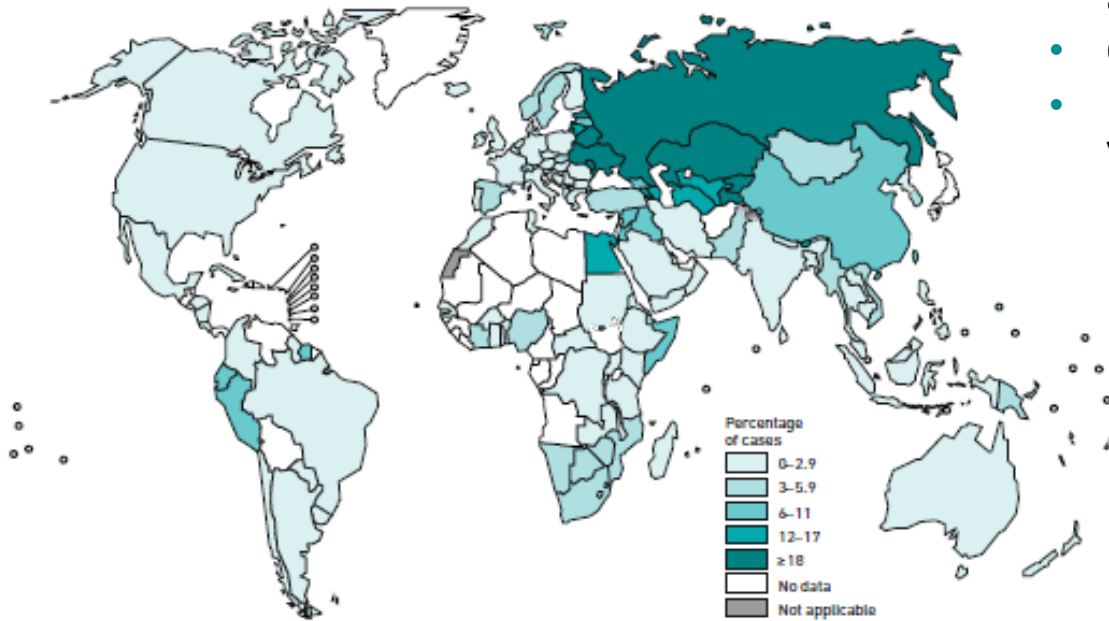
If rifampicin resistance: treat as MDR TB* and manage in conjunction with expert centre

*MDRTB definition**: resistance to at least isoniazid and rifampicin

Risk factors for possible drug-resistant TB

FIG. 3.20

Percentage of new TB cases with MDR/RR-TB^a



^a Figures are based on the most recent year for which data have been reported, which varies among countries. Data cover the period 2002–2018.

- Previous TB treatment (+/- poor adherence/prescribing)
- Contact with person with MDRTB
- Birth, travel or work in settings with very high RR/MDR prevalence

Diagnosing and treating latent TB infection (LTBI)

Active TB disease: 8 million
new cases per year

TB DISEASE

LATENT TB
INFECTION

– the “hidden epidemic”
– 2 billion people infected

Table 1 Risk factors for TB activation

Risk factor	TB risk ^a	Reference(s)	WHO's recommendation for screening and treatment for LTBI ^{d1}	
			Country A ^b	Country B ^c
High-risk factors				
HIV/AIDS	10–100	Landry <i>et al.</i> , ⁴ Hourburgh <i>et al.</i> ⁹ and WHO ¹⁴	Required	Required
Close contacts	15	Landry <i>et al.</i> ⁴ and Sutherland <i>et al.</i> ¹⁵	Required	Required for close contacts (<five years old)
Organ-transplantation recipients	20–70	Aguado <i>et al.</i> ¹⁶ and Sakhuja <i>et al.</i> ¹⁷	Required	Not mentioned
Chronic renal failure requiring dialysis	6.9–52.5	Andrew <i>et al.</i> , ¹⁸ Lundin <i>et al.</i> , ¹⁹ Belcon <i>et al.</i> ²⁰ and Hussein <i>et al.</i> ²¹	Required	Not mentioned
TNF-alpha blockers	1.6–25.1	Solovic <i>et al.</i> ²²	Required	Not mentioned
Silicosis	2.8	Cowie <i>et al.</i> ²³	Required	Not mentioned
Moderate-risk factors				
Fibronodular disease on chest x-ray	6–19	Grzybowski <i>et al.</i> ²⁴	Not mentioned	Not mentioned
Immigrants from high-TB-prevalence countries	2.9–5.3	Baumann <i>et al.</i> ²⁵	Options to be considered	Not mentioned
Health-care workers	2.55	Chu <i>et al.</i> ²⁶	Options to be considered	Not mentioned
Prisoners, homeless persons, illicit drug users	–	–	Options to be considered	Not mentioned
Low-risk factors				
Diabetes mellitus	1.6–7.83	Harries <i>et al.</i> , ²⁷ Dobler <i>et al.</i> , ²⁸ Jeon <i>et al.</i> , ²⁹ Boucot <i>et al.</i> , ³⁰ Kim <i>et al.</i> ³¹ and Baker <i>et al.</i> ³²	Not recommended	Not mentioned
Smoking	2–3.4	Altet <i>et al.</i> , ³³ Slama <i>et al.</i> ³⁴ and Maurya <i>et al.</i> ³⁵	Not recommended	Not mentioned
Use of corticosteroids	2.8–7.7	Jick <i>et al.</i> ³⁶	Not recommended	Not mentioned
Underweight	2–3	Palmer <i>et al.</i> ³⁷ and Comstock <i>et al.</i> ³⁸	Not recommended	Not mentioned

^aRelative risk of TB compared to the general population.

^bIn high- and upper-middle-income countries with an estimated TB incidence less than 100/100,000 population.

^cFor resource-limited countries and other middle-income countries that do not belong to country A.

TB in HIV: Where is the problem?

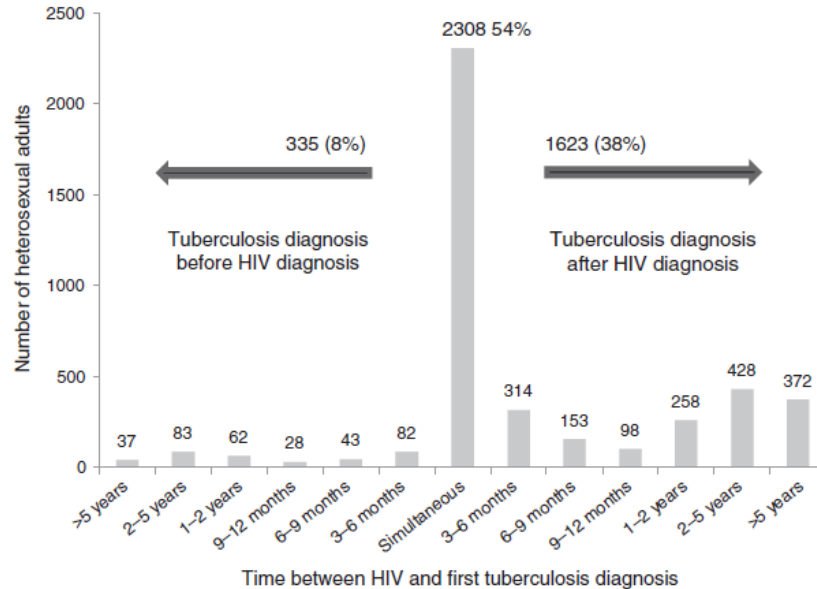


Fig. 1. Time interval between HIV and tuberculosis diagnosis among heterosexual adults living with diagnosed HIV in England and Wales, 2002–2010.

TB in HIV: Where is the problem?

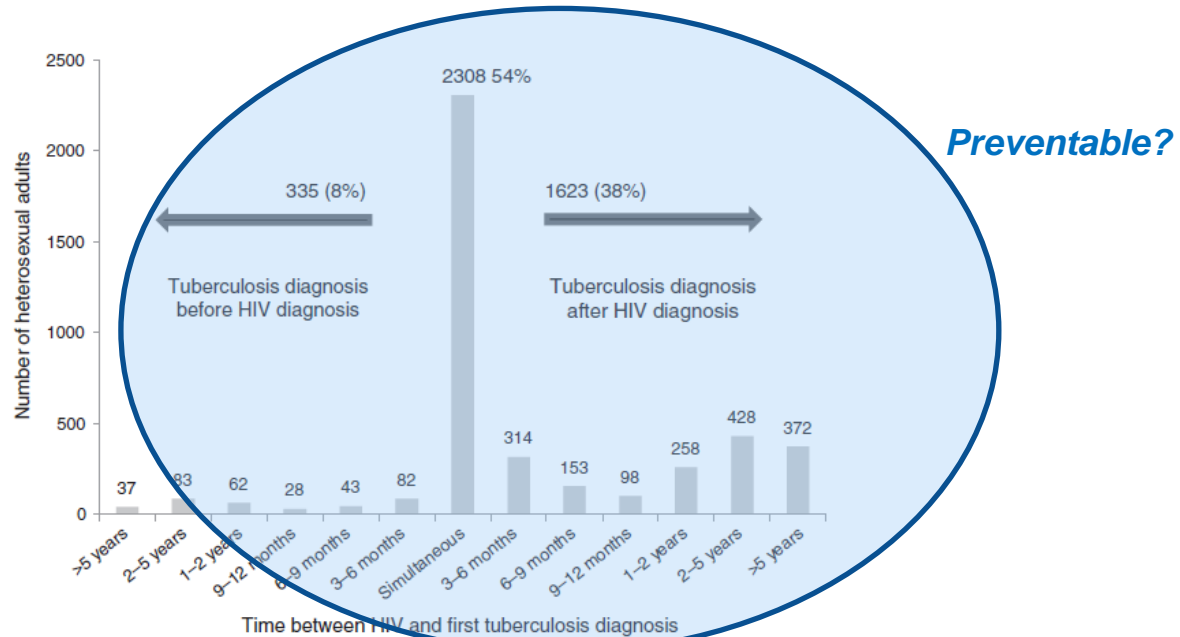
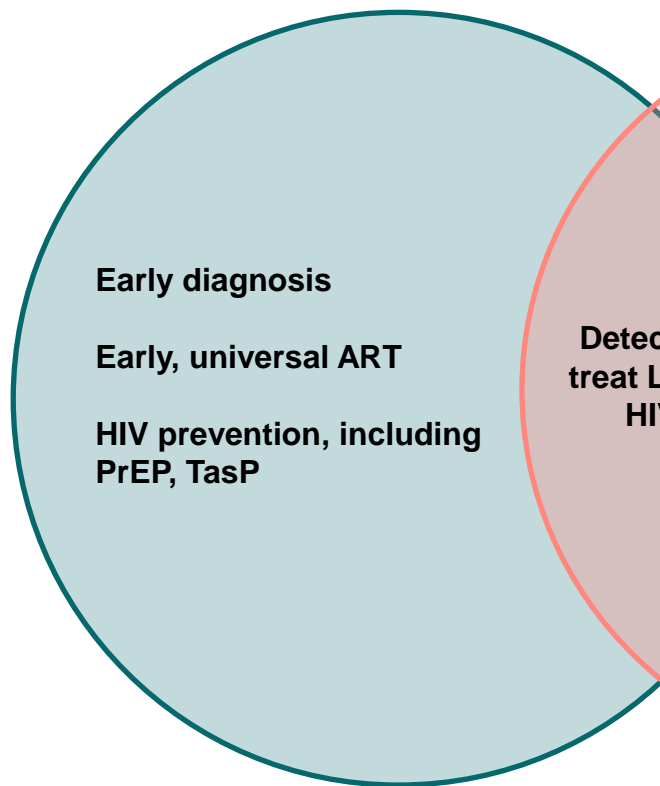


Fig. 1. Time interval between HIV and tuberculosis diagnosis among heterosexual adults living with diagnosed HIV in England and Wales, 2002–2010.

Prevention – potential targets

HIV



Early diagnosis

Early, universal ART

**HIV prevention, including
PrEP, TasP**

**Detect and
treat LTBI in
HIV+**

TB

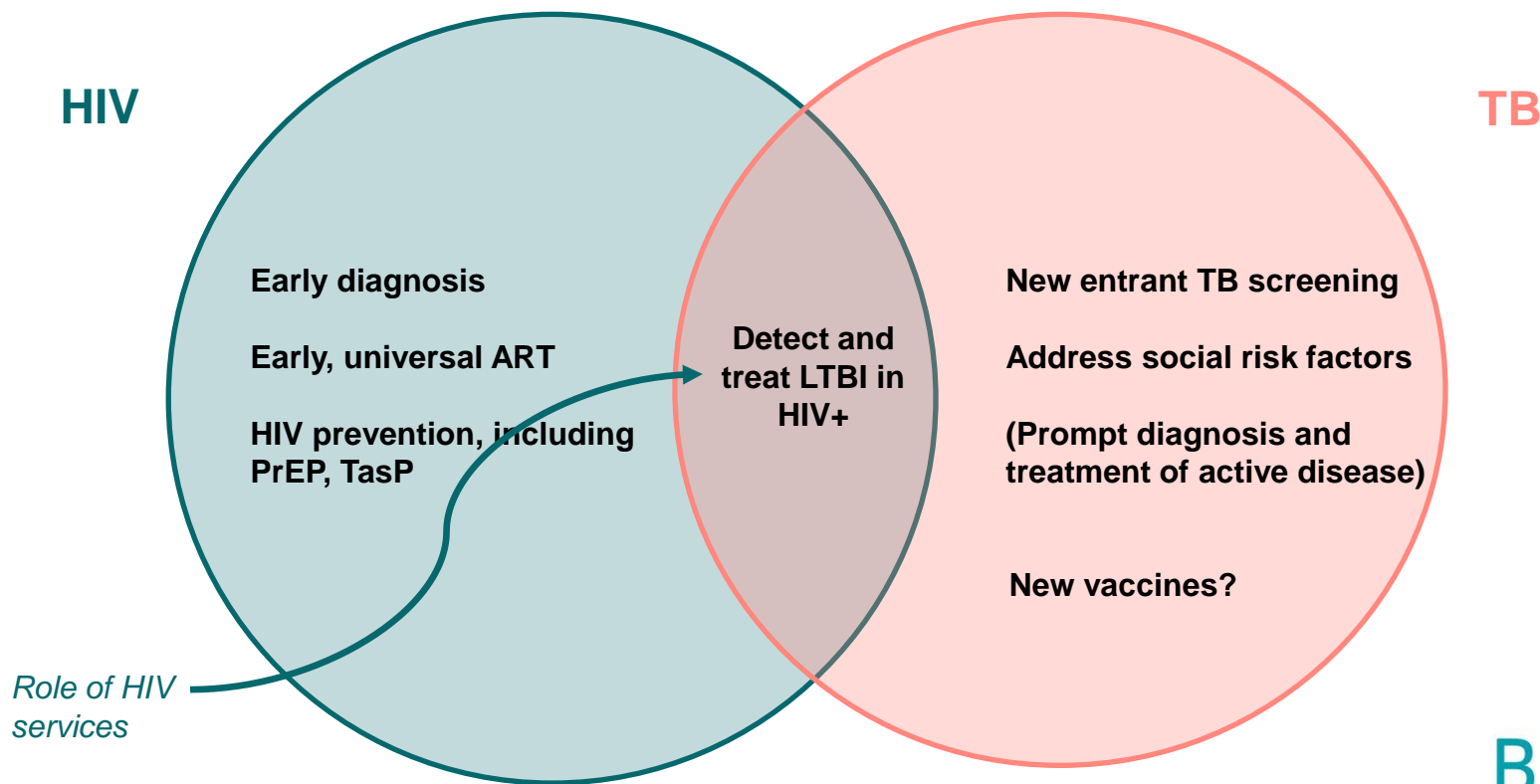
New entrant TB screening

Address social risk factors

**(Prompt diagnosis and
treatment of active disease)**

New vaccines?

Prevention – potential targets



NICE guidelines (TB: 2016) latent TB infection

1.2.1.3 For adults who are severely immunocompromised, such as those with HIV and CD4 counts of fewer than 200 cells/mm³ offer an interferon-gamma release assay and a concurrent Mantoux test.

- ❖ If either test is positive (for Mantoux, this is an induration of 5 mm or larger, regardless of BCG history), assess for active TB.
- ❖ If this assessment is negative, offer them treatment for latent TB infection. **[new 2016]**

1.2.1.4 For other adults who are immunocompromised, consider an interferon-gamma release assay alone or an interferon-gamma release assay with a concurrent Mantoux test.

- ❖ If either test is positive (for Mantoux, this is an induration of 5 mm or larger, regardless of BCG history), assess for active TB.
- ❖ If this assessment is negative, offer them treatment for latent TB infection. **[new 2016]**

BHIVA guidelines 2011 vs. 2018: Latent TB infection

2011	2018
IGRA rather than TST	IGRA rather than TST
Sub-Saharan Africa, ART < 2 years	All from medium or high incidence countries
Medium TB incidence countries, ART < 2 years, CD4 < 500	Low incidence countries, those with specific (social or medical) risk factors
Low-incidence countries, ART<6 months, CD4 <350	

2011: Although physicians can perform both tests in severely immunosuppressed patients, we believe that there are few data to support this strategy and doing this would add complexity, cost and difficulties in interpretation.

The majority of the Committee believe that an IGRA test alone would be sufficient.

New data would be welcome in guiding physicians in this difficult area.

2018 BHIVA TB guidelines

- ❖ We suggest that IGRA rather than TST be used when testing HIV-positive individuals for LTBI (2C)
- ❖ We recommend “test and treat” LTBI for all HIV-positive close contacts of people with infectious TB (1B)
- (unchanged)
- ❖ We recommend testing HIV-positive individuals from high and medium incidence countries for LTBI, regardless of CD4 count and antiretroviral therapy, with particular attention to those newly diagnosed with HIV. (1C)
- ❖ We recommend testing HIV-positive individuals from low-incidence countries for LTBI if they have additional TB risk factors. (1C)
- (new)

High incidence $\geq 151/100,000$ person years and medium incidence 40 – 150/100,000 person years. WHO TB report or PHE website for updated incidence figures. www.gov.uk/government/publications/tuberculosis-tb-by-country-rates-per-100000-people

IGRA: interferon gamma release assay

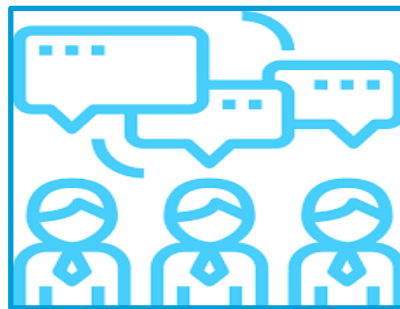
Diagnosing and treating latent TB infection (LTBI)

HIV-positive individuals from **low-incidence** countries should be **tested for LTBI** if additional TB risk factors are present (GRADE 1B)

- ✓ Exposure to a known TB case;
- ✓ Travel to or periods of time spent consecutively in higher-incidence countries
- ✓ Diabetes
- ✓ Stage 4/5 chronic kidney disease
- ✓ Chemotherapy for malignancy
- ✓ Immunosuppression (organ transplantation)
- ✓ Biological disease modifiers
- ✓ Prolonged use of corticosteroids
- ✓ Injecting drug use

Diagnosing and treating latent TB infection (LTBI)

Services should make local arrangements for managing the increase in numbers requiring testing (and treating) for LTBI



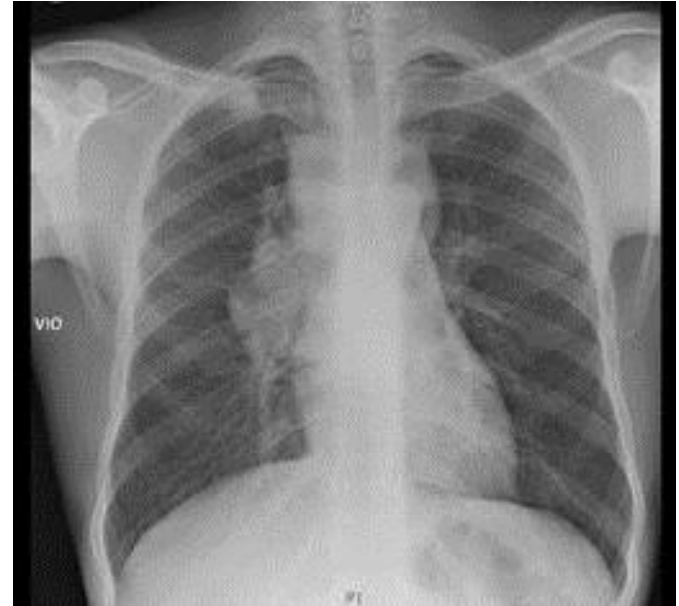
It is acceptable to discuss and offer testing to those at risk at their routine follow-up appointments

Diagnosing and treating latent TB infection (LTBI)

Small print...

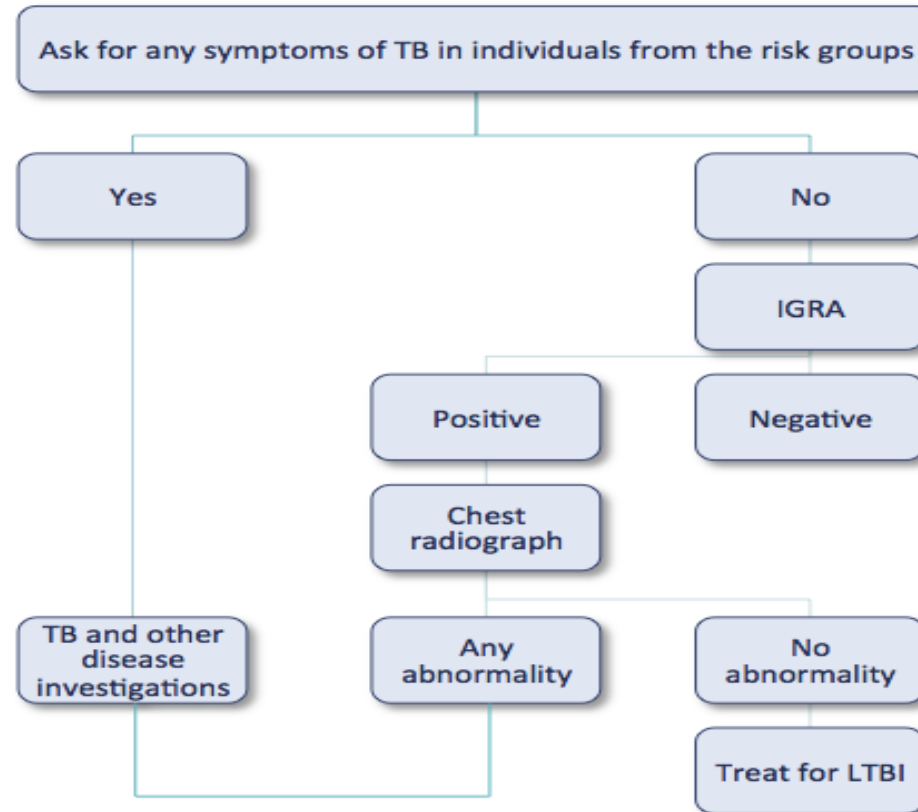
- If result is indeterminate or borderline
→ repeat IGRA within 4 weeks
- No testing for LTBI in individuals who have been previously treated for active tuberculosis

(GPP)



Diagnosing and treating latent TB infection (LTBI)

Exclude active TB



Diagnosing and treating latent TB infection (LTBI)

Recommended regimens (GRADE 1A):

- 6 months of isoniazid plus pyridoxine;
- 3 months of isoniazid plus rifampicin plus pyridoxine;



Rifapentine not yet available in UK – not currently recommended
Promising findings **ACTG 5279 (BRIEF TB)** study 1/12 rifapentine and isoniazid non inferior to 9/12 INH

TB treatment



Treatment of active drug-sensitive TB

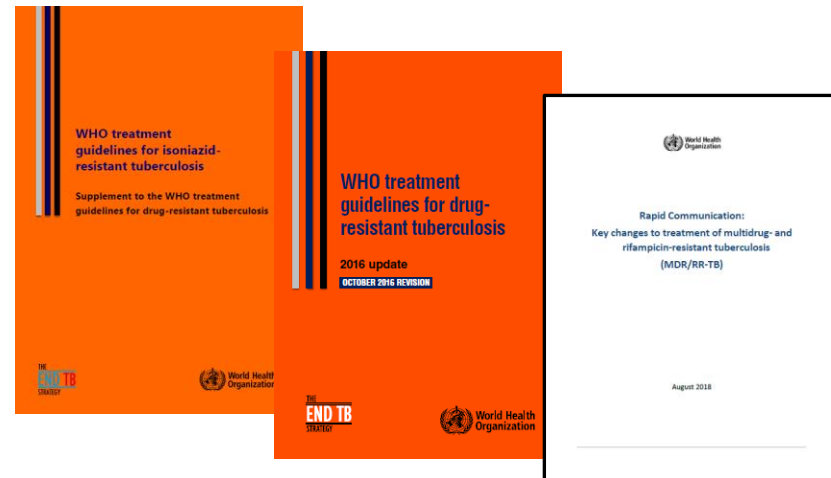
- We recommend **DAILY** administration of standard TB therapy in patients with drug-sensitive TB (GRADE 1A)*
- **2RHZE/4RH**
- **CNS TB: 2RHZE(+steroids)/7-10RH**
- Fixed-dose combination tablets



*Vernon et al, Lancet 1999; Burman et al, J Respir Crit Care Med 2006; Narendran et al, CID 2014; Gopalan et al, JAMA Intern Med 2018;

Management of drug-resistant TB

Isoniazid mono-resistance (~6%):
rifampicin, ethambutol, **levofloxacin** and
pyrazinamide
daily for 6 months (GRADE 1C)



All individuals with rifamycin-resistant (including MDR*) TB should be managed in conjunction with **expert centre** in the management of drug-resistant TB

*MDR/TB definition**: resistance to at least isoniazid and rifampicin

When to start antiretroviral therapy (in the ART-naïve)

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ESTABLISHED IN 1812

OCTOBER 20, 2011

VOL. 365 NO. 16

Earlier versus Later Start of Antiretroviral Therapy in HIV-Infected Adults with Tuberculosis

François-Xavier Blanc, M.D., Ph.D., Thim Sok, M.D., Didier Laureillard, M.D., Laurence Borand, Pharm.D., Claire Rekeciewicz, M.D., Eric Nerrienet, Ph.D., Yoann Madec, Ph.D., Olivier Marcy, M.D., Sarin Chan, M.D., Narom Prak, M.D., Chindamony Kim, M.D., Khemarin Kim Lak, M.D., Chanroenrui Hak, M.D., Bunnet Dim, M.D., Chhun Im Sin, M.D., Sath Sun, M.D., Bertrand Guillard, M.D., Borann Sar, M.D., Ph.D., Sirenda Vong, M.D., Marcelo Fernandez, M.D., Lawrence Fox, M.D., Ph.D., Jean-François Delfraisse, M.D., Ph.D., and Anne E. Goldfeld, M.D., for the CAMELIA (ANRS 1295-

The NEW ENGLAND JOURNAL

ORIGINAL ARTICLE

Timing of Antiretroviral Therapy for HIV-1 Infection and

Diane V. Havlir, M.D., Michelle A. Kendall, M.S., Prudence Ive, M.D., Johnstone Kumwenda, M.B., B.S., Susan Swindells, M.B., B.S., Sarojini S. Qasba, M.D., Anne F. Luetkemeyer, M.D., Evelyn Hogg, B.A., James F. Rooney, M.D., Xingye Wu, M.S., Mina C. Hosseini, M.D., Umesh Laloo, M.B., Ch.B., Valdilea G. Veloso, M.D., Fatuma F. Some, M.B., Ch.B., N. Kumarasamy, M.D., Nesri Padayatchi, M.D., Breno R. Santos, M.D., Stewart Reid, M.D., James Hakim, M.B., Ch.B., Lerato Mohapi, M.D., Peter Mugenyi, M.D., Jorge Sanchez, M.D., Javier R. Lama, M.D., Jean W. Pape, M.D., Alejandro Sanchez, M.D., Aida Asmelash, M.D., Evans Moko, M.B., Ch.B., Fred Save, M.B., Ch.B., Janet Andersen, Sc.D., and Ian Sanne, M.D., for the AIDS Clinical Trials Group Study A5221*

Time to Initiate Antiretroviral Therapy Between 4 Weeks and 12 Weeks of Tuberculosis Treatment in HIV-Infected Patients: Results From the TIME Study

Weerawat Manosuthi, MD,* Wiroj Mankatitham, MD,* Aroon Lueangniyomkul, MD,* Supeda Thongyen, MPH,* Sirirat Likanonsakul, MSc,* Pawita Suwanvattana, MSc,* Unchana Thawornwan, MSc,* Busakorn Suntisuklappon, BSc,* Samruay Nilkamhang, BC,* and Somnuek Sungkanuparph, MD,† for the TIME Study Team

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Integration of Antiretroviral Therapy with Tuberculosis Treatment

Salim S. Abdool Karim, M.B., Ch.B., Ph.D., Kogieleum Naidoo, M.B., Ch.B., Anneke Grobler, M.Sc., Nesri Padayatchi, M.B., Ch.B., Cheryl Baxter, M.Sc., Andrew L. Gray, M.Sc.(Pharm.), Tanuja Gengiah, M.Clin.Pharm., M.S.(Epi.), Akshmi Gengiah, M.A.(Res.Psych.), Med.Sci.(Pharm.), Niraksha Jithoo, M.B., Ch.B., M.P.H., Wafaa M. El-Sadr, M.D., M.P.H., M.D., and Ouarraisha Abdool Karim, Ph.D.

Initiation of highly active antiretroviral therapy in HIV-infected adults with newly diagnosed

pulmonary tuberculosis (TB-HAART): a prospective, international, randomised, placebo-controlled trial

Sayoki G Mfinanga*, Bruce J Kirenga*, Duncan M Chanda*, Beatrice Mutayoba, Thuli Mthiyane, Getnet Yimer, Oliver Ezechi, Cathy Connolly, Vincent Kapotwe, Catherine Muwonge, Julius Massaga, Edford Sinkala, Wanze Kohi, Lucinda Lyantumba, Grace Nyakoojo, Henry Luwaga, Basra Doulla, Judith Mzyezye, Nathan Kapota, Mahnaz Vahedi*, Peter Mwaba*, Saidi Egwaga*, Francis Adatu*, Alex Pym*, Moses Jobaba, Roxana Rustumjee, Alimuddin Zumla*, Philip Onyiah*

CAMELIA 2011, SaPiT 2010, STRIDE 2011, TB-HAART 2014, TIME 2012

STRIDE results

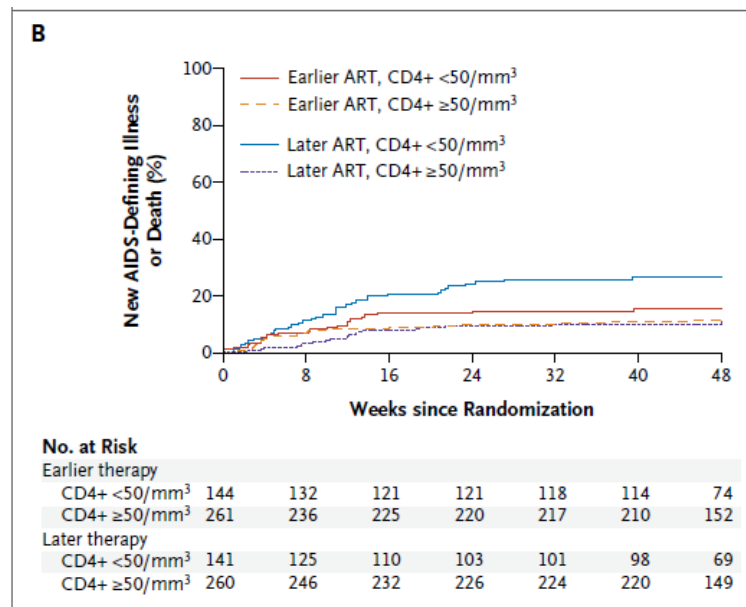
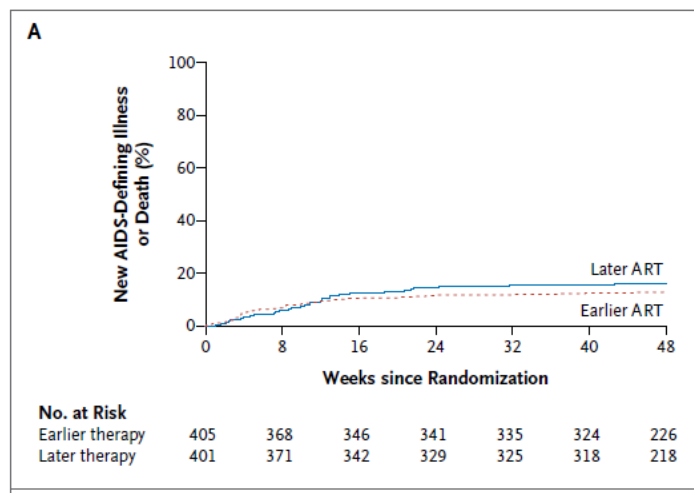


Figure 2. Time to New AIDS-Defining Illness or Death.

Shown are the times to the end point of a new AIDS-defining illness or death for the entire study population (Panel A) and for the study population according to CD4+ T-cell count (Panel B).

Early = within 2 weeks of TB Rx

Later = 8 – 12 weeks

Update to 2011 guidance – was low grade, with CD4 cut off = 100 cells/ μ L

When to start antiretroviral therapy (in the ART-naïve)

No early initiation of ART in individuals with TB meningitis
(GRADE 1A)

Published in final edited form as:

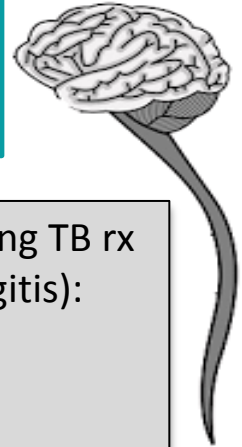
Clin Infect Dis. 2011 June ; 52(11): 1374–1383. doi:10.1093/cid/cir230.

Timing of Initiation of Antiretroviral Therapy in Human Immunodeficiency Virus (HIV)–Associated Tuberculous Meningitis

M. Estee Török^{1,2}, Nguyen Thi Bich Yen³, Tran Thi Hong Chau⁴, Nguyen Thi Hoang Mai⁴, Nguyen Hoan Phu⁴, Pham Phuong Mai⁴, Nguyen Thi Dung⁴, Nguyen Van Vinh Chau⁴, Nguyen Duc Bang³, Nguyen Anh Tien³, N. H. Minh³, Nguyen Quang Hien³, Phan Vu Khac Thai³, Doan The Dong³, Do Thi Tuong Anh³, Nguyen Thi Cam Thoa³, Nguyen Hai³, Nguyen Ngoc Lan³, Nguyen Thi Ngoc Lan³, Hoang Thi Quy³, Nguyen Huy Dung Tran Tinh Hien⁴, Nguyen Tran Chinh⁴, Cameron Paul Simmons^{2,5}, Menno de Jong^{2,6}, Marcel Wolbers^{2,5}, and Jeremy James Farrar^{2,5}

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CORTICOSTEROIDS
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PHASE



ART immediately vs 2 months after starting TB rx
(253 patients with HIV-related TB meningitis):

No survival benefit

More frequent severe adverse events

Which ART to start (in the ART-naïve)

- **Efavirenz**¹ (standard dose) (GRADE 1B)
- **Raltegravir**² 400 mg bd/800 mg bd or
- **Dolutegravir**³ (DTG) 50 mg bd (GRADE 2C)
- If need for a **ritonavir-boosted PI**: use **rifabutin** (GRADE 1C)

Do not use:

nevirapine or cobicistat

TAF or bictegravir - until clinical outcome data available



Evidence for integrase inhibitors with rifampicin

Raltegravir: Reflate study

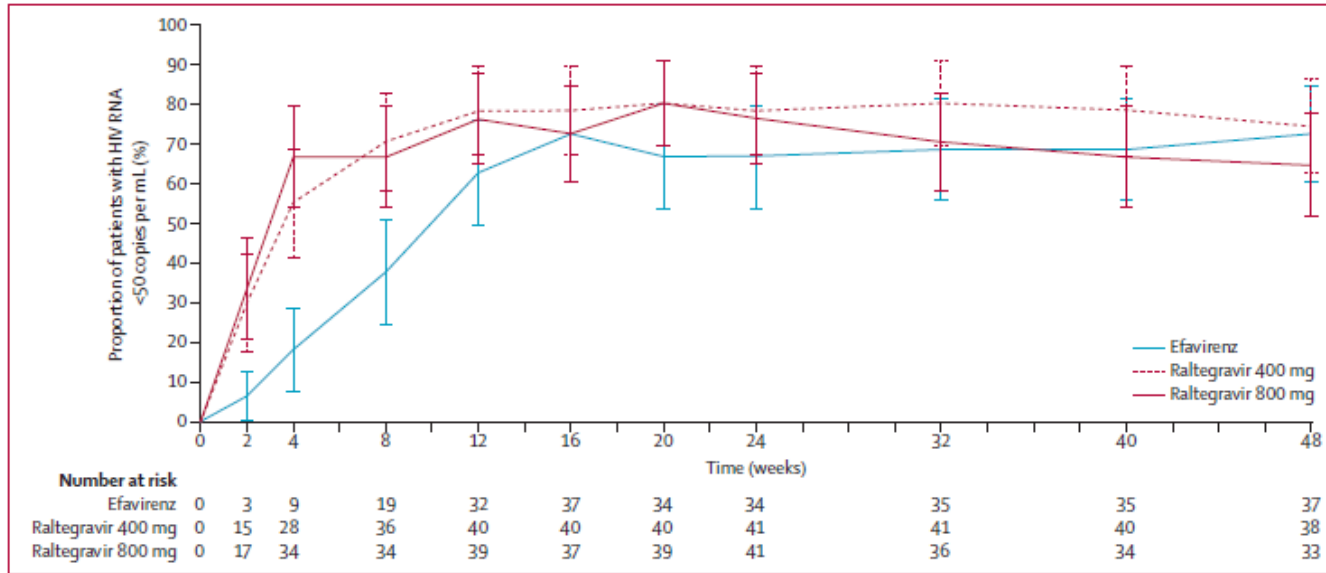
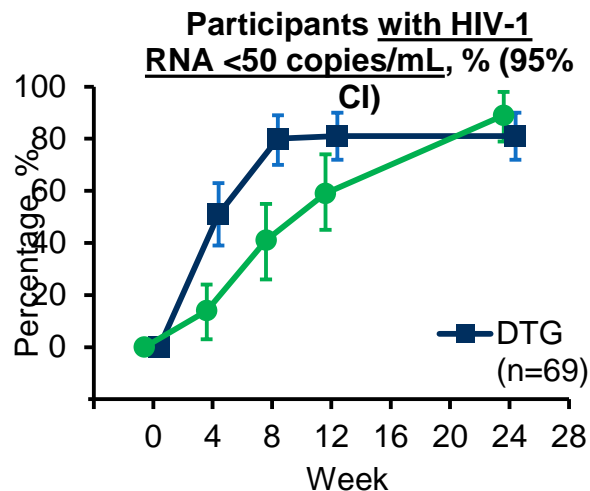


Figure 2: Virological response

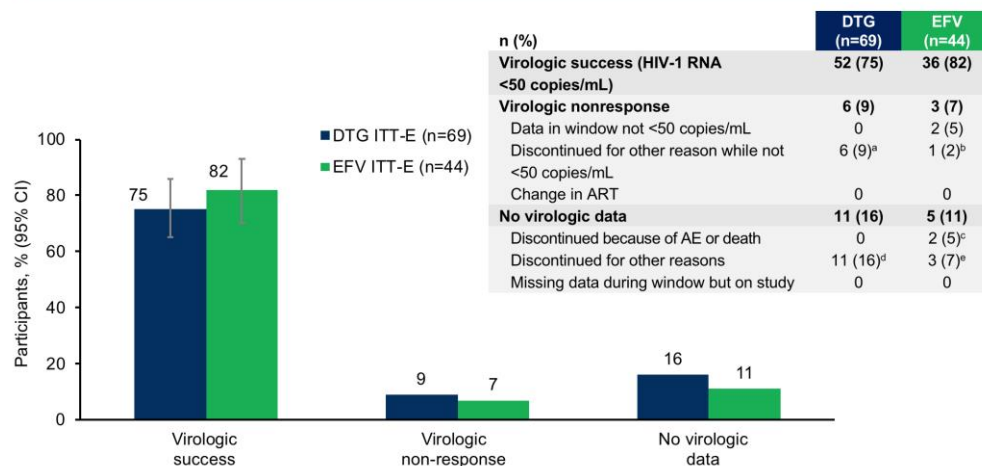
Error bars are 95% CIs.

Evidence for integrase inhibitors with rifampicin

Dolutegravir: INSPIRING study



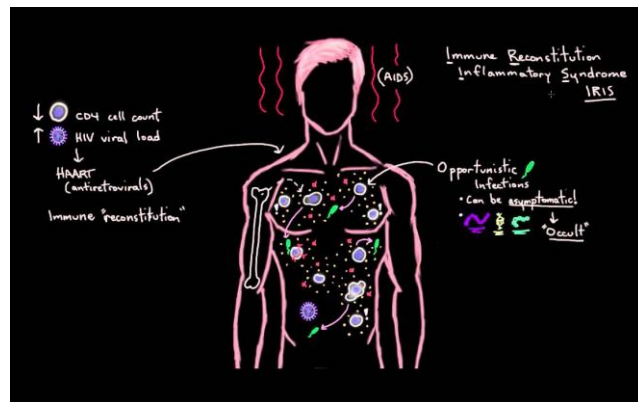
Modified FDA Snapshot Outcomes at Week 48



IRIS (immune reconstitution inflammatory syndrome)

'Paradoxical' & 'Unmasking'

Paradoxical IRIS: *worsening or appearance of new signs, symptoms or radiographic abnormalities, occurring after the initiation of ART*



Criteria*:

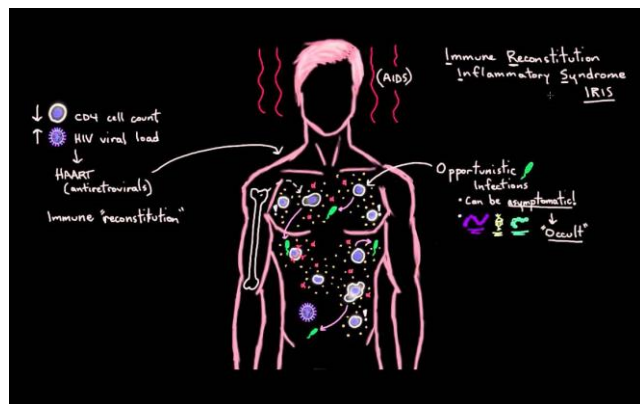
- temporal association with initiation of ART
- demonstration of response to ART (VL ↓, CD4+↑)
- clinical deterioration with an inflammatory process
- exclusion of other causes that could explain deterioration

* Meintjes et al, Lancet 2008; khanacademy <https://www.youtube.com/watch?v=NGJY4yvgqv8>

IRIS (immune reconstitution inflammatory syndrome)

Risk factors

- ✓ low baseline CD4+ & rapid recovery of CD4+;
- ✓ rapid decline in HIV viral load;
- ✓ dissemination of TB outside the lung;
- ✓ Short time between anti-TB Rx and ART;



If clinically significant IRIS: use corticosteroids, tapered over 4–6 weeks (GRADE 1C)
[Prednisone or methylprednisolone at a dose of 1–1.5 mg/kg]

Recurrent IRIS and complex cases can be difficult to manage: seek advice from centre of expertise in managing TB

Control of transmission and contact tracing

All hospitals and HIV units should have a TB infection control plan

Notification/tracing of contacts

Do not delay contact tracing until notification

Screen close contacts of any person with pulmonary or laryngeal TB

New: enhanced contact tracing for PLWH, including contacts of people with EPTB should be implemented where feasible

NICE

National Institute for
Health and Care Excellence



Summary

- Evidence still lacking in some areas
- some movement on treatment for DRTB
- some new evidence on newer antiretroviral agents, with clinical outcomes
- testing for latent TB in HIV-positive individuals at risk is part of routine HIV care
- need more push for more contact tracing if we are to reduce TB incidence

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**HIV-associated tuberculosis: new
guidelines for the UK**

Questions?

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BHIVA TB/HIV Guidelines Writing Group

NW TB conference, 2018