



TB/HIV Integration

TB Infection control training



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Objectives for this session

- Describe how TB and HIV influence each other
- Describe the link between TB and HIV activities
- Describe the impact of HIV on the diagnosis of TB
- Describe the importance of TB screening in HIV patients
- Describe the management of TB/HIV co-infection



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Paradigm Shift in TB/HIV Advocacy



" We can't fight AIDS unless we do much more to fight TB as well "

Nelson Mandela, Bangkok, July 2004



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TB and HIV co-infection

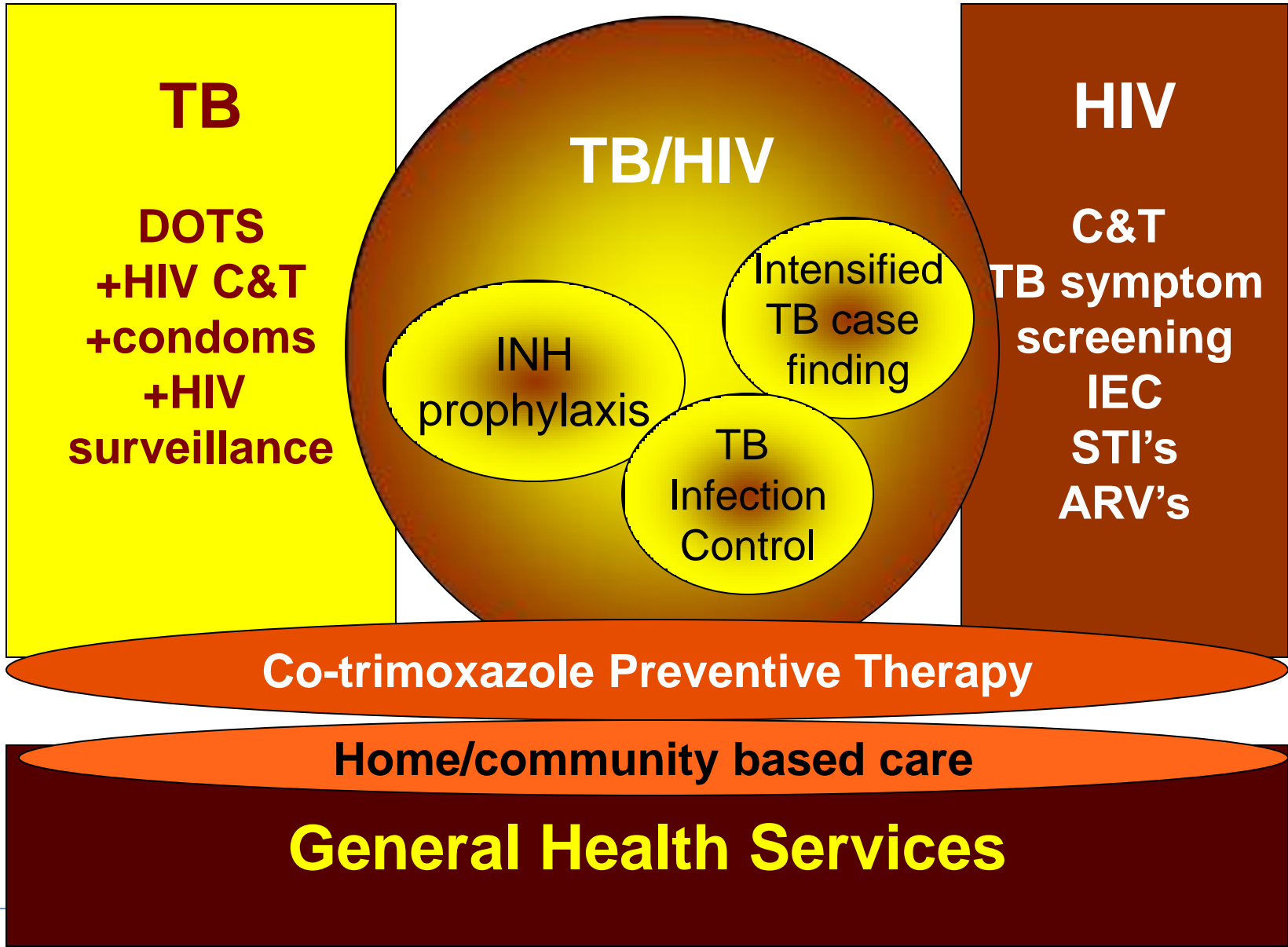
- Without HIV, about 10% of people infected with TB will develop TB disease
- In people co-infected with HIV and TB, about 50% may develop TB disease
- TB accelerates HIV disease progression
- TB is the leading cause of death in people living with HIV & AIDS
- TB can usually be cured whether a patient is co-infected with HIV or not, with the same treatment regimen



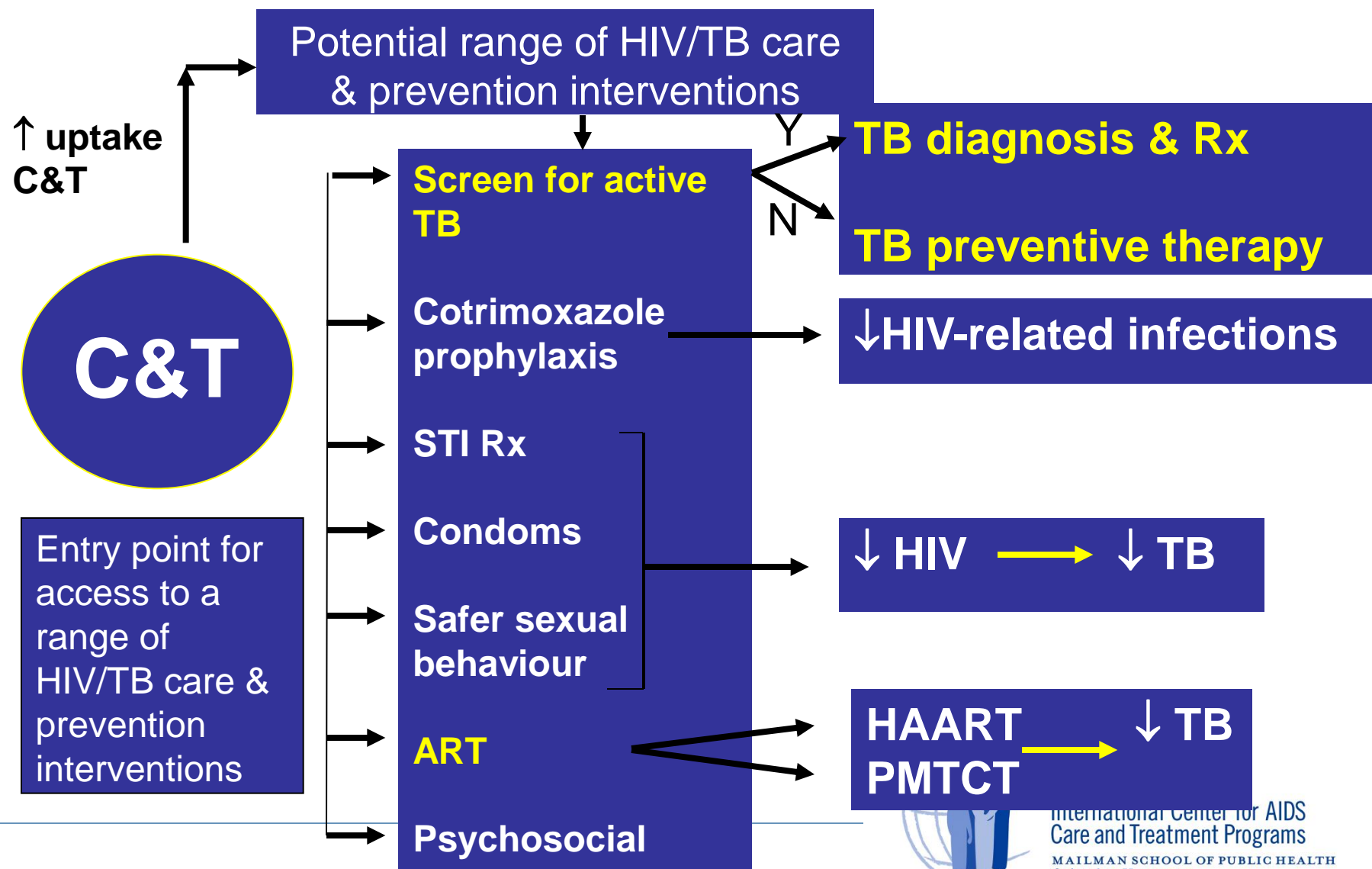
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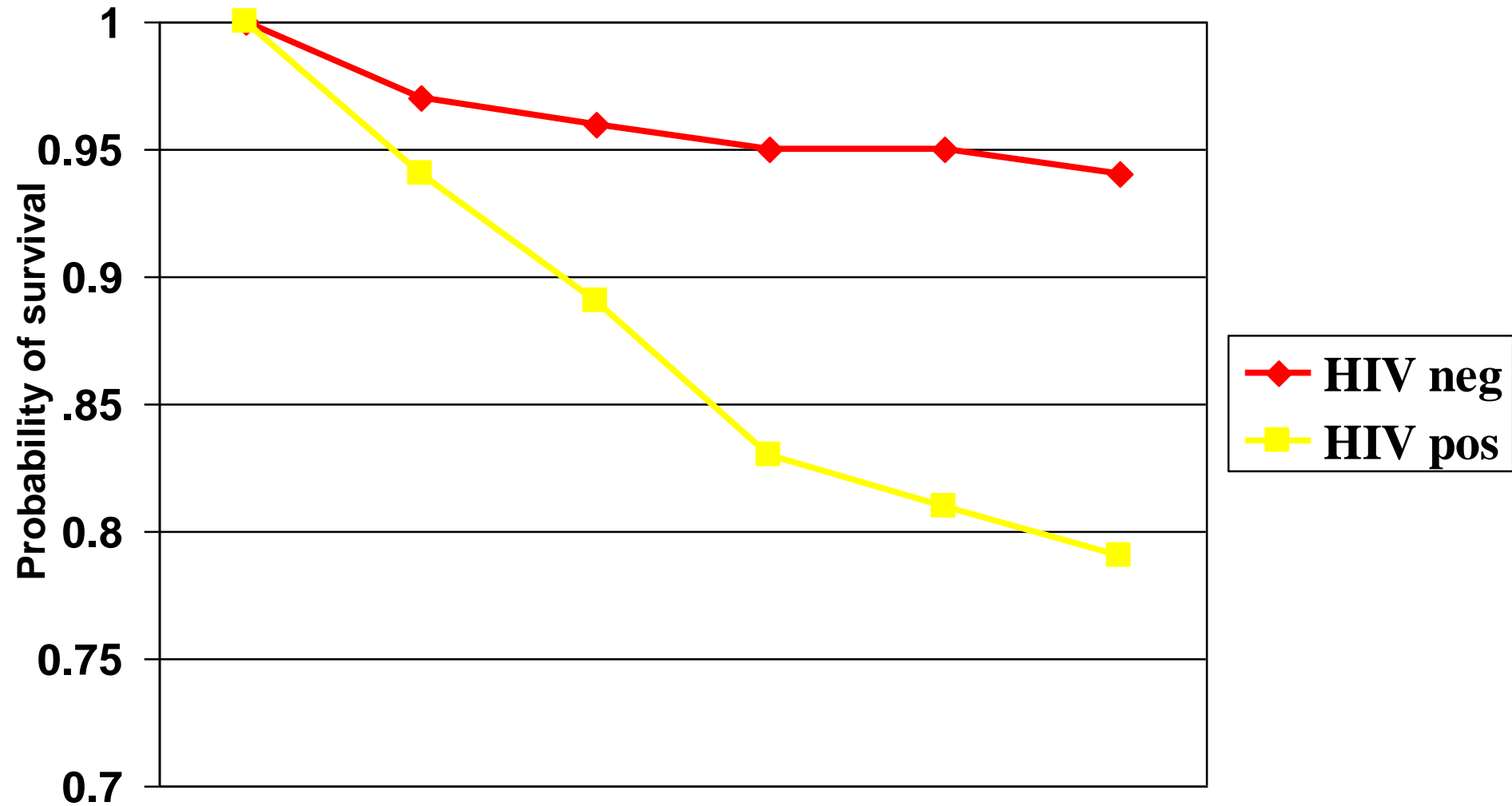
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The link between TB & HIV activities



Probability of survival during TB Rx



Nunn P et al
Am Rev Respir Dis 1992;146:849-54

Problems with TB in HIV+ patients

- ✓ Over-diagnosis of sputum smear-negative PTB
- ✓ Under-diagnosis of sputum smear-positive PTB
- ✓ Missed diagnosis of extra-pulmonary TB
- ✓ Low cure rates
- ✓ High mortality rates during treatment
- ✓ High rates of TB recurrence



Why are sputum smears more commonly negative in HIV+ patients?

- Bacillary load in lung tissue is actually higher
- Immunocompromised status results in poor granuloma formation
- Less caseous necrosis, cavity formation
- Bacilli are not expectorated
 - Sputum negative (but often culture positive) PTB



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Alternative diagnostic methods useful in HIV+ pts

- Induced sputum (also when suspecting EPTB)
- Lymph node needle biopsy (67-90% AFB +)
- Lymph node excisional biopsy
- Aspirate of effusion: ADA, leukocyte counts
- TB blood culture (26-42% pos)
- Urine for TB culture (40% pos)
- Ultrasound abdomen / CT chest
- Bronchoscopy (30-73% AFB+ or granulomas)
- Bone marrow biopsy (40% pos)

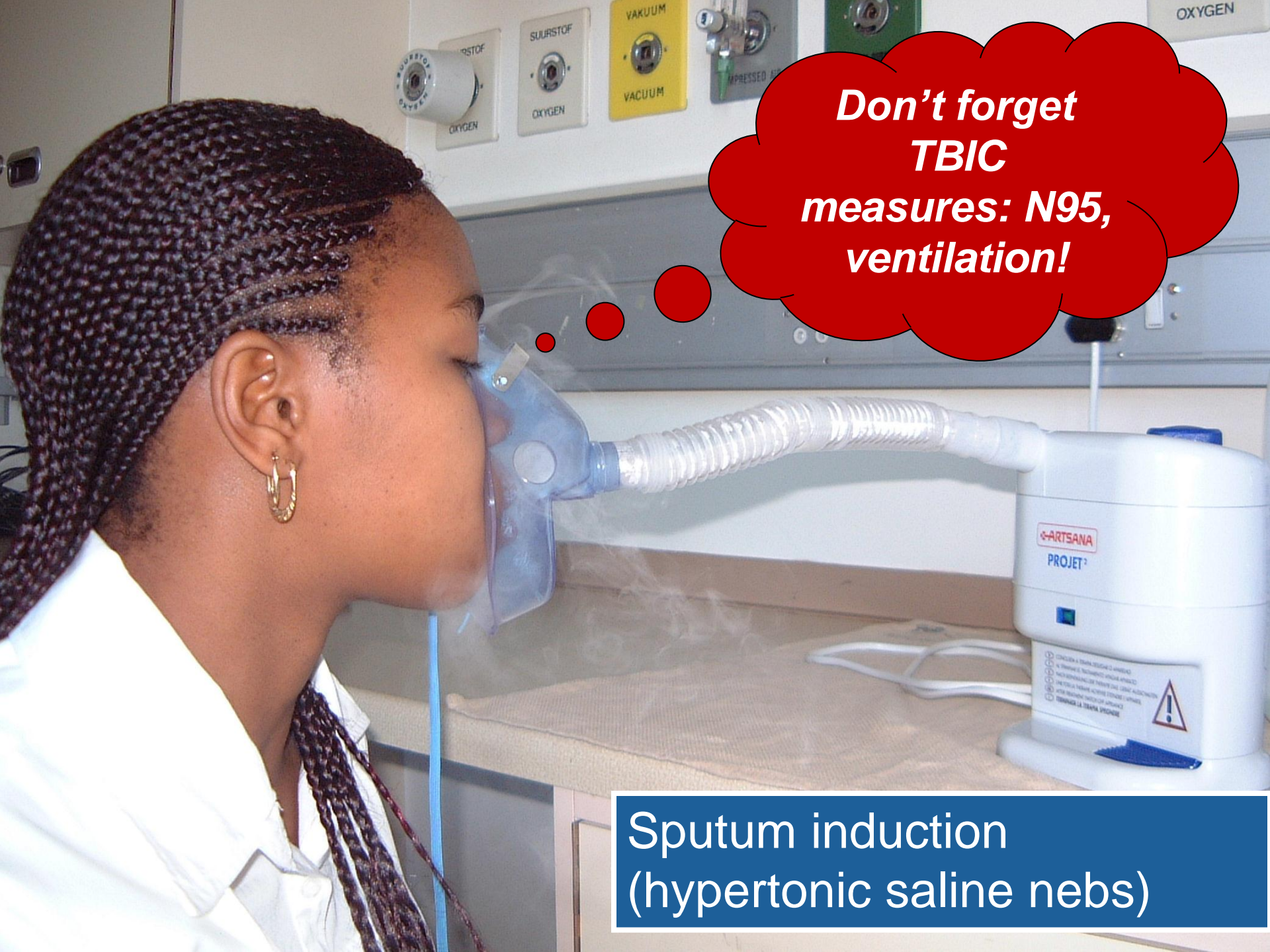




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**Don't forget
TBIC
measures: N95,
ventilation!**

**Sputum induction
(hypertonic saline nebs)**

The effect of HIV infection on symptoms and signs of TB

Symptom/sign	HIV+ (%)	HIV- (%)
Dyspnea	97	81
Fever	79	62
Sweats	83	64
Weight loss	89	83
Diarrhoea	23	4
Hepatomegaly	41	21
Splenomegaly	40	15
Lymphadenopathy	35	13

Chest 1994;106:1471-6



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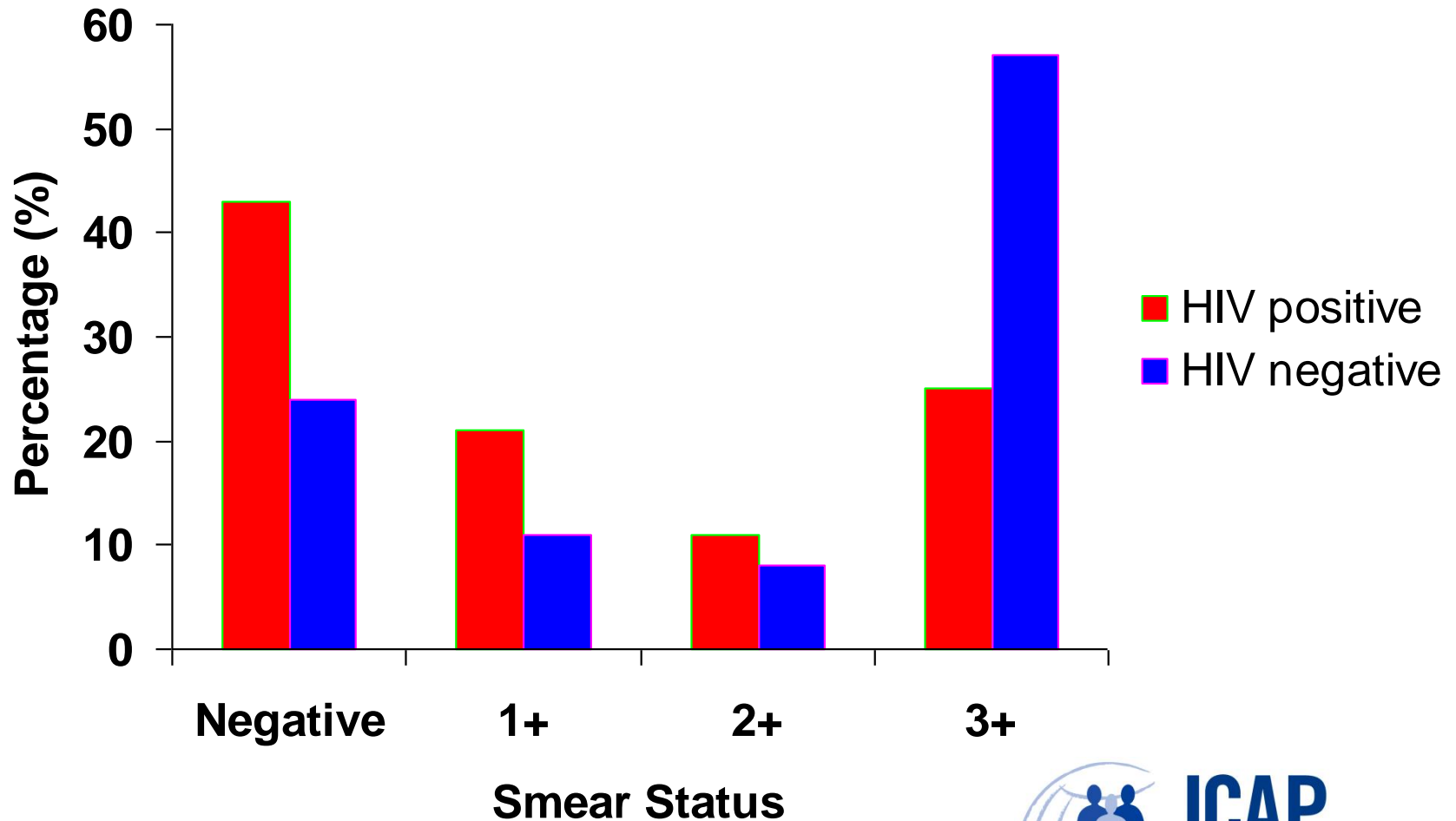
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Presentations and HIV Status

Site	HIV Positive (%)	HIV Negative (%)
Pulmonary	40 %	72 %
Extra-pulmonary	34 %	16 %
Both	26 %	12 %
Pleural	31 %	19 %
Pericardial	15 %	3 %
Lymph node	19 %	3 %



Diagnosis: Sputum Smear Result and HIV Status



TB Presentations in HIV (1)

With *mild immunosuppression*:

- ✓ Clinical picture often resembles post-primary pulmonary TB (PTB)
- ✓ Sputum smear is usually positive
- ✓ “Typical” chest x-ray (CXR) findings include:
 - upper lobe and or bilateral infiltrates
 - cavitation
 - pulmonary fibrosis
 - shrinkage



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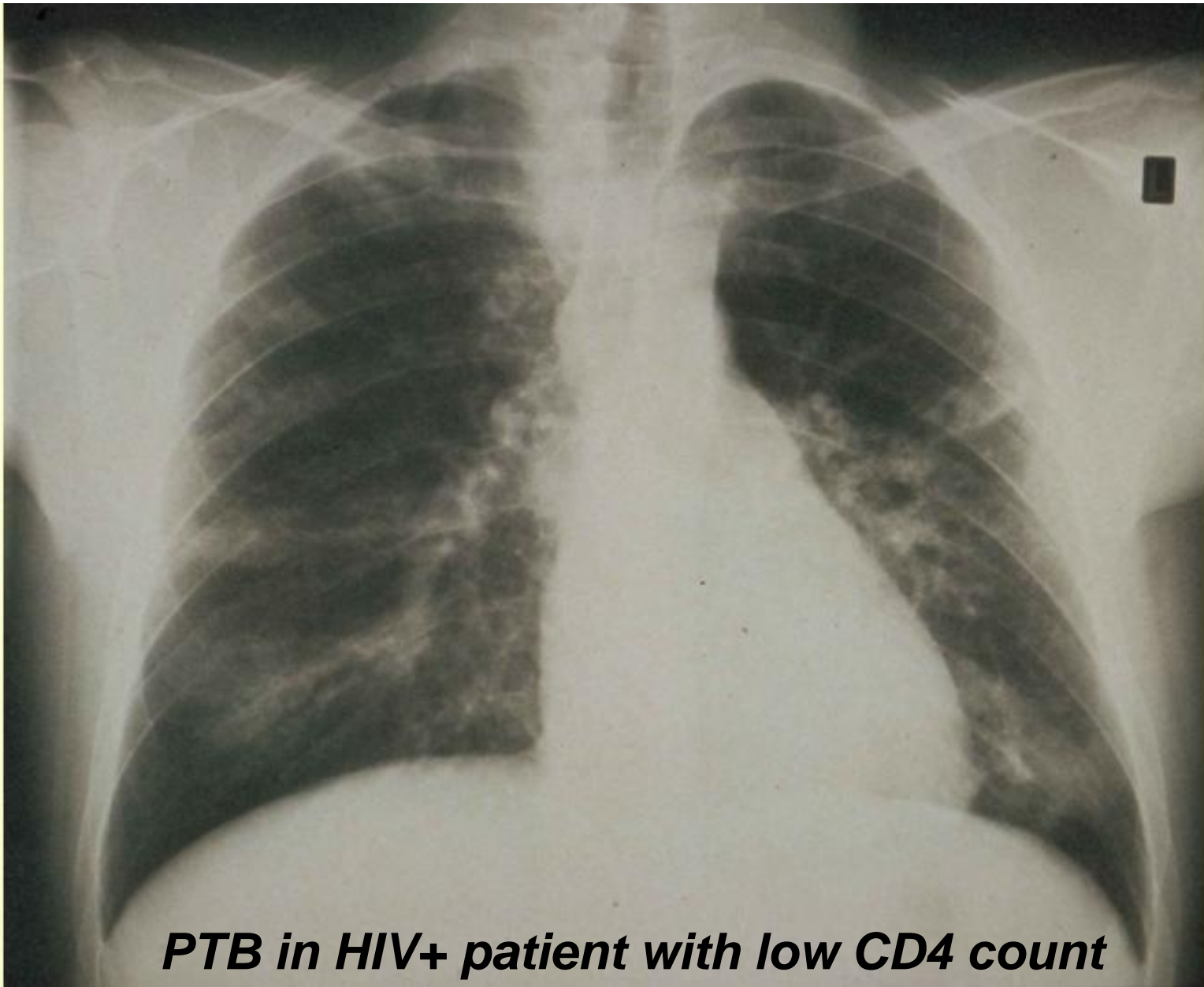
TB Presentations in HIV (2)

With severe immunosuppression:

- ✓ Atypical features, resembling that of primary PTB:
 - Sputum smear often negative
 - CXR: interstitial infiltrates especially in lower zones; no features of cavitation and fibrosis
 - CXR may look exactly like bacterial pneumonia
 - Higher number of extra-pulmonary manifestations:
 - Immune system is less able to prevent growth and local spread of *M. tuberculosis*

In the setting of an HIV epidemic, it is **not possible** to look at a CXR and say that it is or is not TB



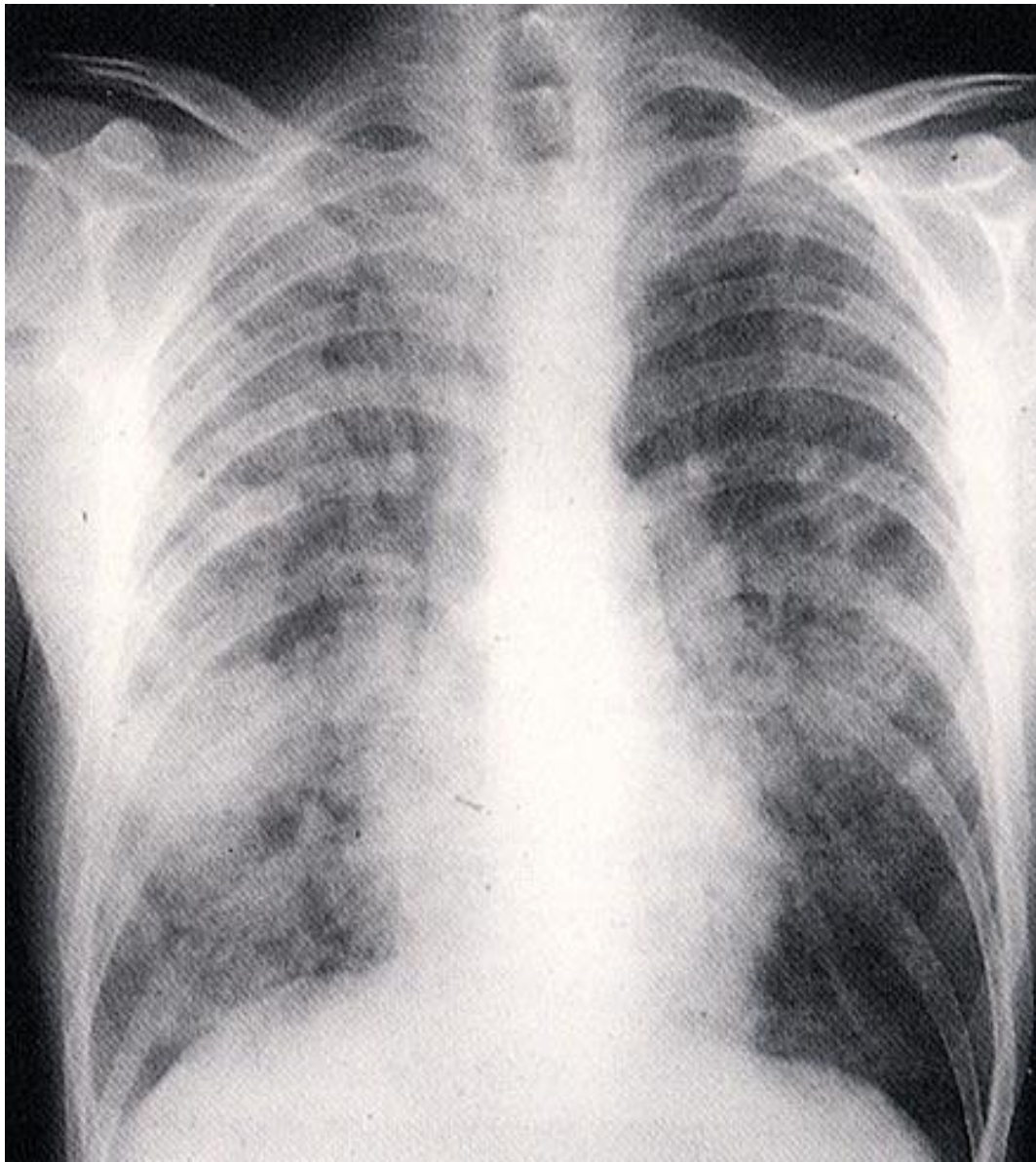


PTB in HIV+ patient with low CD4 count



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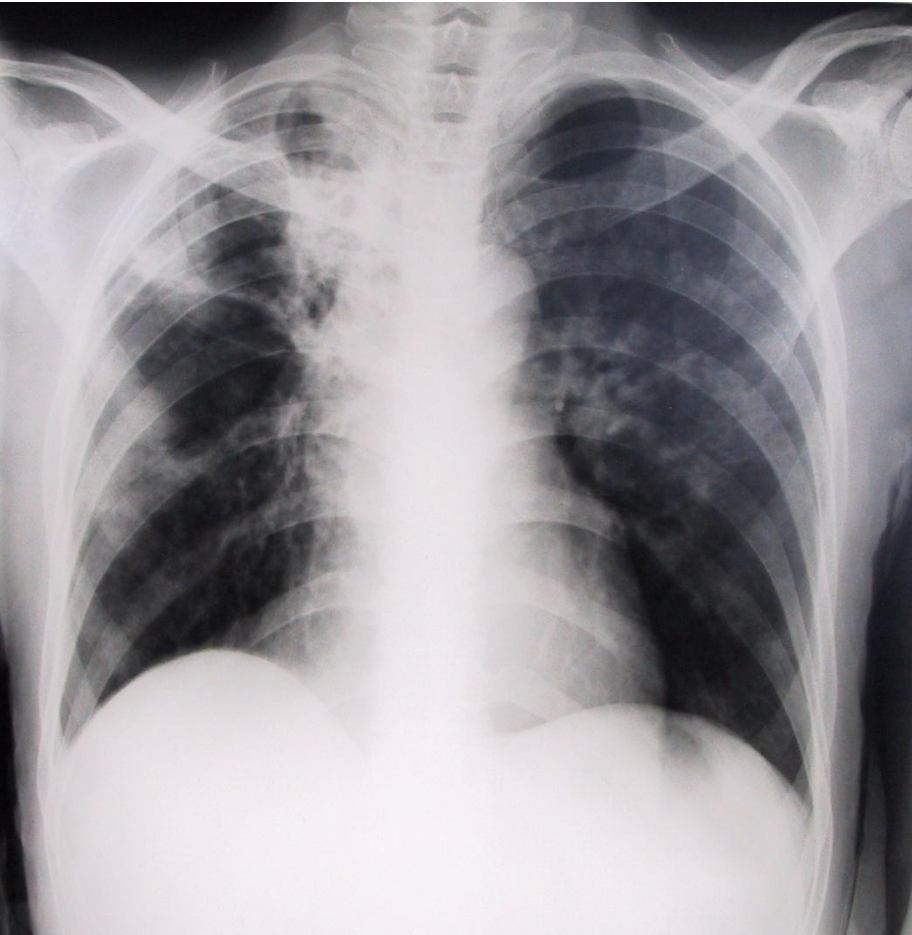
***X-ray in a TB patient may look like this one
(patient with confirmed PCP)***

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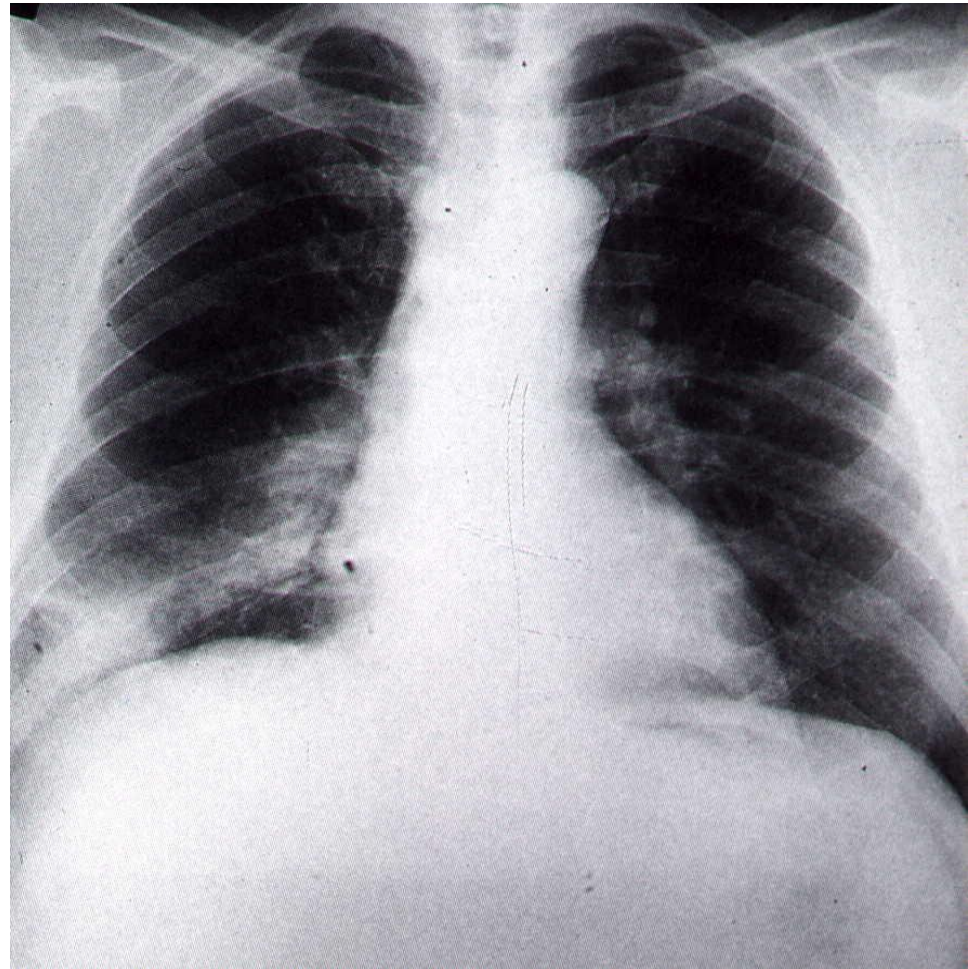
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Pulmonary Tuberculosis

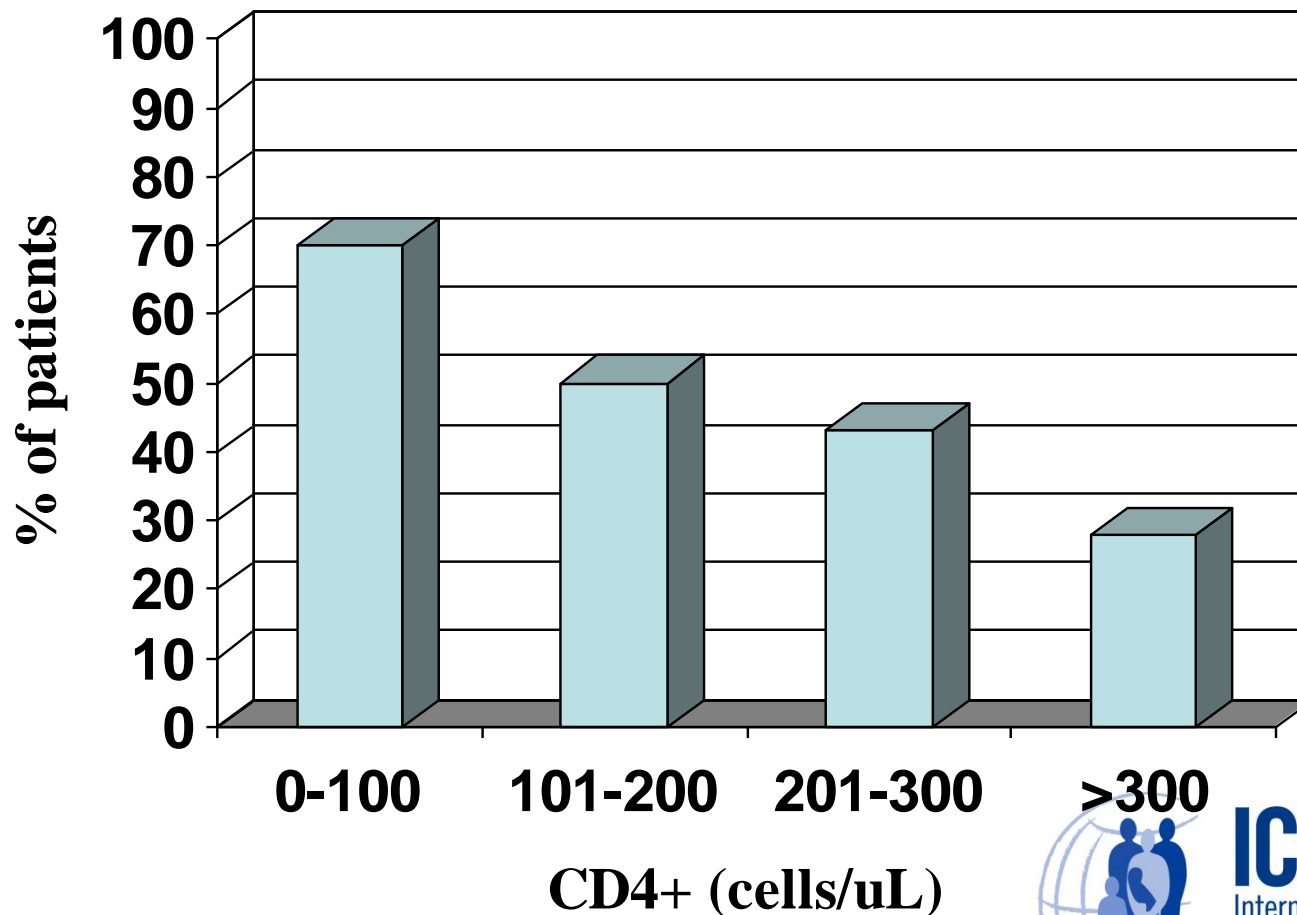


CD4 > 200



CD4 < 200

Frequency of Extra-pulmonary TB according to CD4 count



**Prompt and accurate diagnosis of
pulmonary tuberculosis (PTB)
is fundamental
to effective control of the disease.**

under diagnosis:

**is bad for patients and the control of
transmission.**

over diagnosis:

**is bad for patients and leads to misuse of
scarce resources (drug budgets and staff)**



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TB screening in HIV patients

- What is TB screening?
 - Method to intensify TB case finding among HIV+ patients
 - Part of WHO 3 I's strategy (Intensified Case Finding, IPT, Infection Control) to reduce burden of TB among HIV+ people
 - Asking questions about TB symptoms to find out if the patient may have active TB
 - Not just taking sputum for AFB's!!!



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TB symptom questionnaire

TB should be suspected if any one of the following symptoms is present:

1. Weight loss (more than 1.5kg in 4 weeks)
2. Cough for more than 2 weeks (with or without haemoptysis)
3. Night sweats (drenching) for more than 2 weeks
4. Fever for more than 2 weeks
5. Swollen lymph-nodes (need to examine to confirm)
6. Chest-pains or other respiratory symptoms

TB Rx		TB SCREEN (tick if present)*						
On TB treatment (if initial phase tick)	On TB treatment (if continuation phase tick)	Weight loss	Cough > 2 weeks	Night sweats > 2 weeks	Fever > 2 weeks	Swollen lymph nodes	Respiratory symptoms / chest pain	NO TB SYMPTOMS

TB Treatment columns

TB Screening questions: patients with symptoms will get a tick in any of these columns

Patients without TB symptoms will get a tick here

* If any of these TB symptoms present, do sputum x3 (2xAFB + TB culture) and/or other investigations to rule out active (P)TB



The patient has symptoms

– now what?

- If the patient has any one of these TB symptoms, he is a TB suspect and needs to be investigated:
 - Do sputum AFB x2 and TB culture
 - Hypertonic saline nebulizations improve sputum quality
 - Refer for further assessment if sputa come back negative and still symptomatic, and not responding to a 7 day course of antibiotics
 - Refer for CXR if pleural effusion or miliary TB is suspected
 - Refer for Fine Needle Aspirate Biopsy (FNAB) if suspicious lymphadenopathy detected
 - Refer for other investigations if other types of extra-pulmonary TB suspected



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TB screening

- Focus is on detecting smear or culture positive PTB patients
 - These are infectious and transmit TB
 - Consequences for infection control
- At the same time:
 - We should not forget patients with smear negative PTB and/or EPTB
 - These need to start treatment before starting HAART
 - Consequences for individual patient management (IRIS)

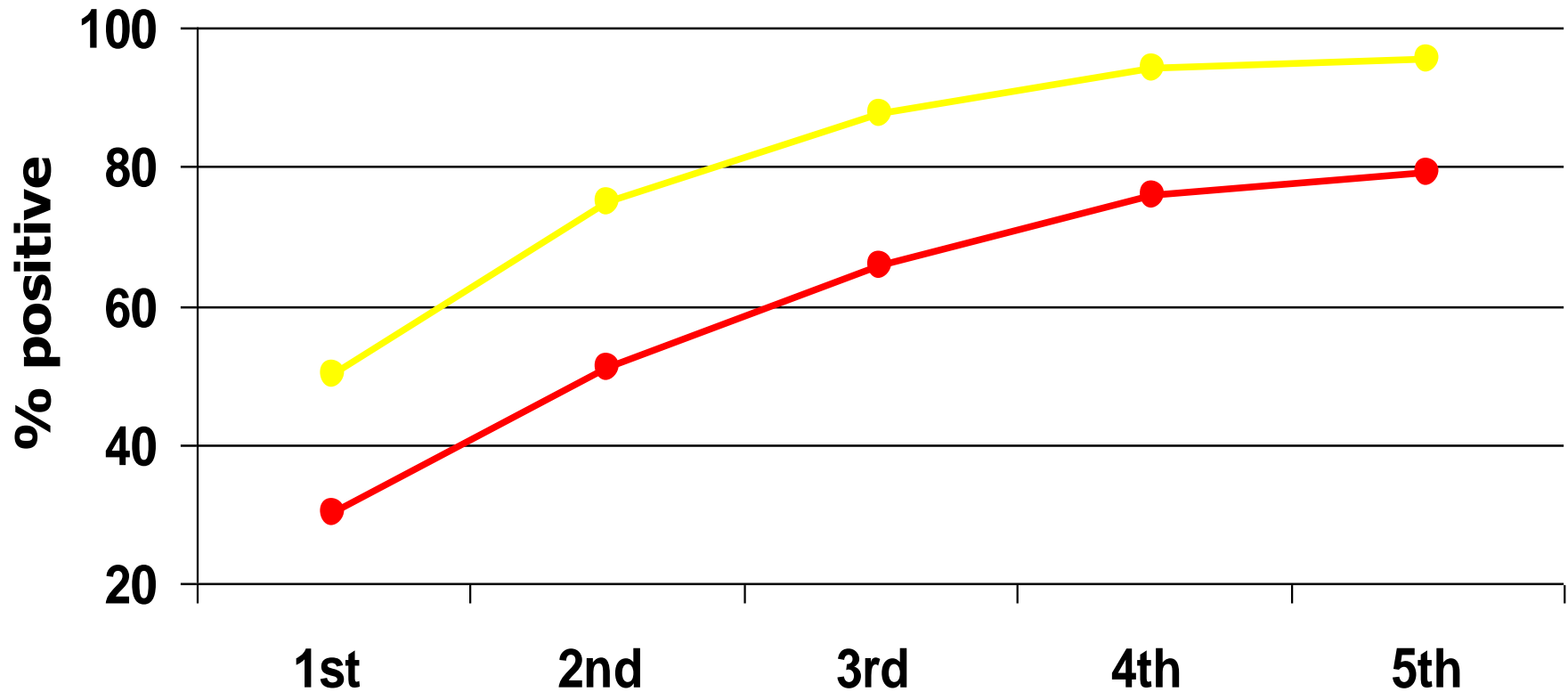


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Multiple sputum stains



Sputum stains

—●— HIV neg —●— HIV pos

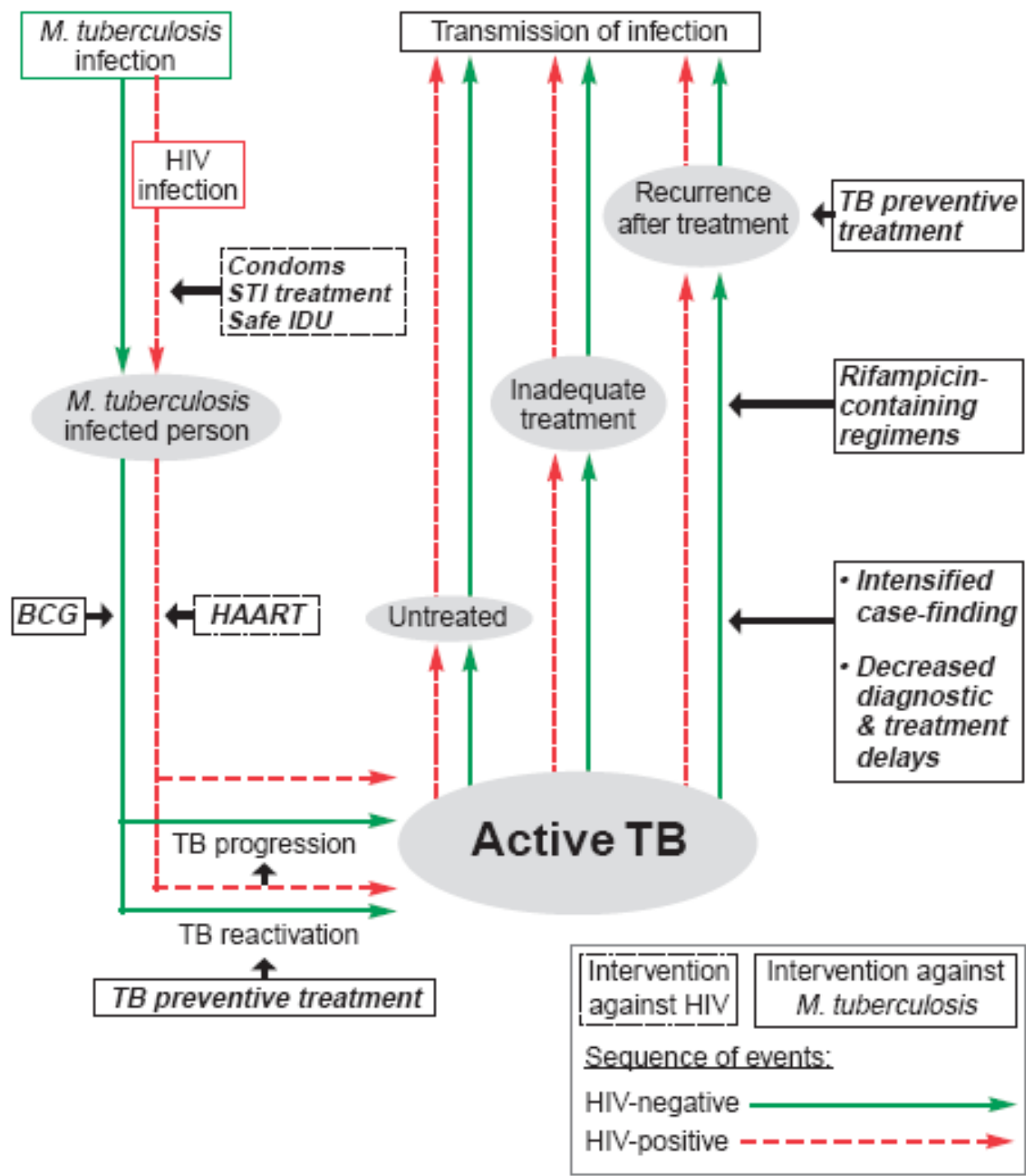


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Interventions to interrupt the sequence of events by which HIV fuels the TB epidemic



STRATEGIC FRAMEWORK TO DECREASE THE BURDEN OF TB/HIV

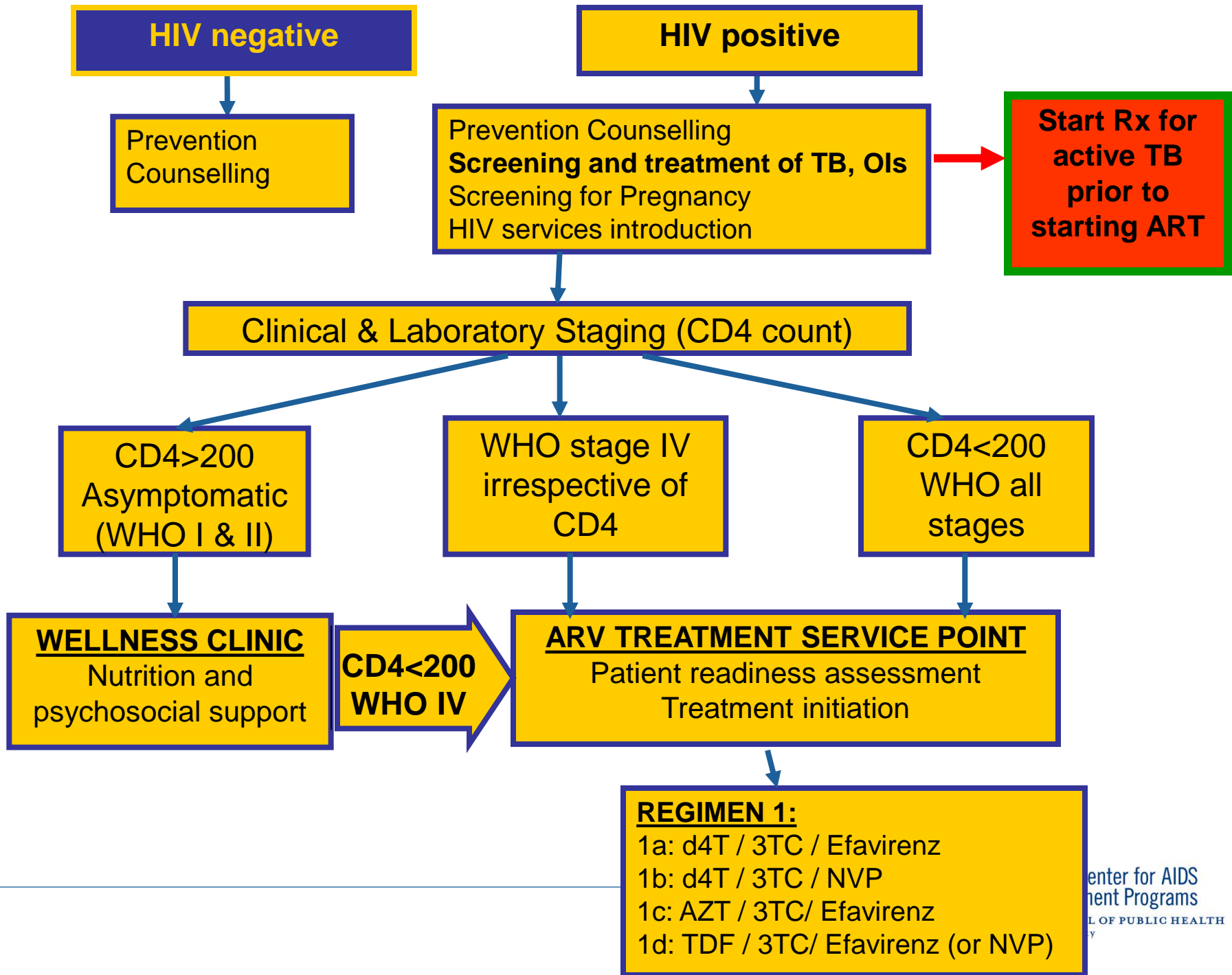
Management of TB/HIV co-infection



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HIV negative

Prevention
Counselling

HIV positive

Prevention Counselling
Screening and treatment of TB, OIs
Screening for Pregnancy
HIV services introduction

**Start Rx for
active TB
prior to
starting ART**

Clinical & Laboratory Staging (CD4 count)

CD4 > 200
Asymptomatic
(WHO I & II)

WHO stage IV
irrespective of
CD4

CD4 < 200
WHO all
stages

WELLNESS CLINIC
Nutrition and
psychosocial support

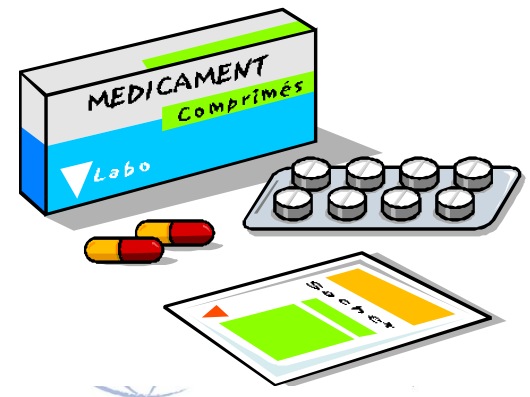
**CD4 < 200
WHO IV**

ARV TREATMENT SERVICE POINT
Patient readiness assessment
Treatment initiation

REGIMEN 1:
1a: d4T / 3TC / Efavirenz
1b: d4T / 3TC / NVP
1c: AZT / 3TC / Efavirenz
1d: TDF / 3TC / Efavirenz (or NVP)

Principles of TB treatment

- Use multiple drugs in combination tablets
- Directly Observed Treatment (DOT)
- Standardised treatment regimens
- Cure patients the first time round
- Give the correct drugs for the correct period of time
- Standard TB regimens applicable to HIV patients
- ***No trials of therapy!***



Influence of HIV on TB Treatment

- More adverse effects of TB treatment
 - Cutaneous hypersensitivity
 - Non-cutaneous adverse effects
 - Hepatotoxicity, gastro-intestinal, thrombopenia
- Reduced treatment efficacy
 - Less drug absorption due to enteropathy
 - Not a major issue for most patients
 - Currently not enough evidence to prolong treatment for HIV+ patients



Challenges related to adherence when starting multiple medications

Would you like start all of the following
medications on the same day?

Isoniazid, Rifampin, Ethambutol, Pyrazinamide

AND

Stavudine (d4T), Lamivudine (3TC), Efavirenz

AND possibly

Cotrimoxazole, Fluconazole ?



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Patient develops TB while on ART

ART should be continued throughout TB treatment **with changes to schedules and monitoring as follows:**

- **Regimen 1 (a/b):**

- A change to **Efavirenz** is recommended for patients on Nevirapine wherever possible
- If still on **NVP**: more frequent monitoring of liver function

- **Regimen 2:**

- Lopinavir/ritonavir (Lop/r: Kaletra):
 - increase the dosage of **Ritonavir** to **400 mg** every 12 hours (3 extra caps of Ritonavir)
- OR: increase Lop/r dose to 6 caps bd (800/200mg bd)
 - Continue until 2 weeks after completion of TB Rx



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Patient presents with TB before commencing ART

- **No history of WHO Stage 4 illness and CD4 > 200 cells/mm³: antiretroviral therapy is not yet needed**
The need for ARVs should be reassessed on completion of TB treatment.
- **History of WHO Stage 4 illness and/or a CD4 between 50 and 200 cells/mm³: complete 2 months of TB therapy before commencing ARVs**
- **CD4 count <50 cells/mm³ or current Stage 4 illness: complete at least 2 weeks of TB treatment and make sure patient is tolerating before initiating ARVs**

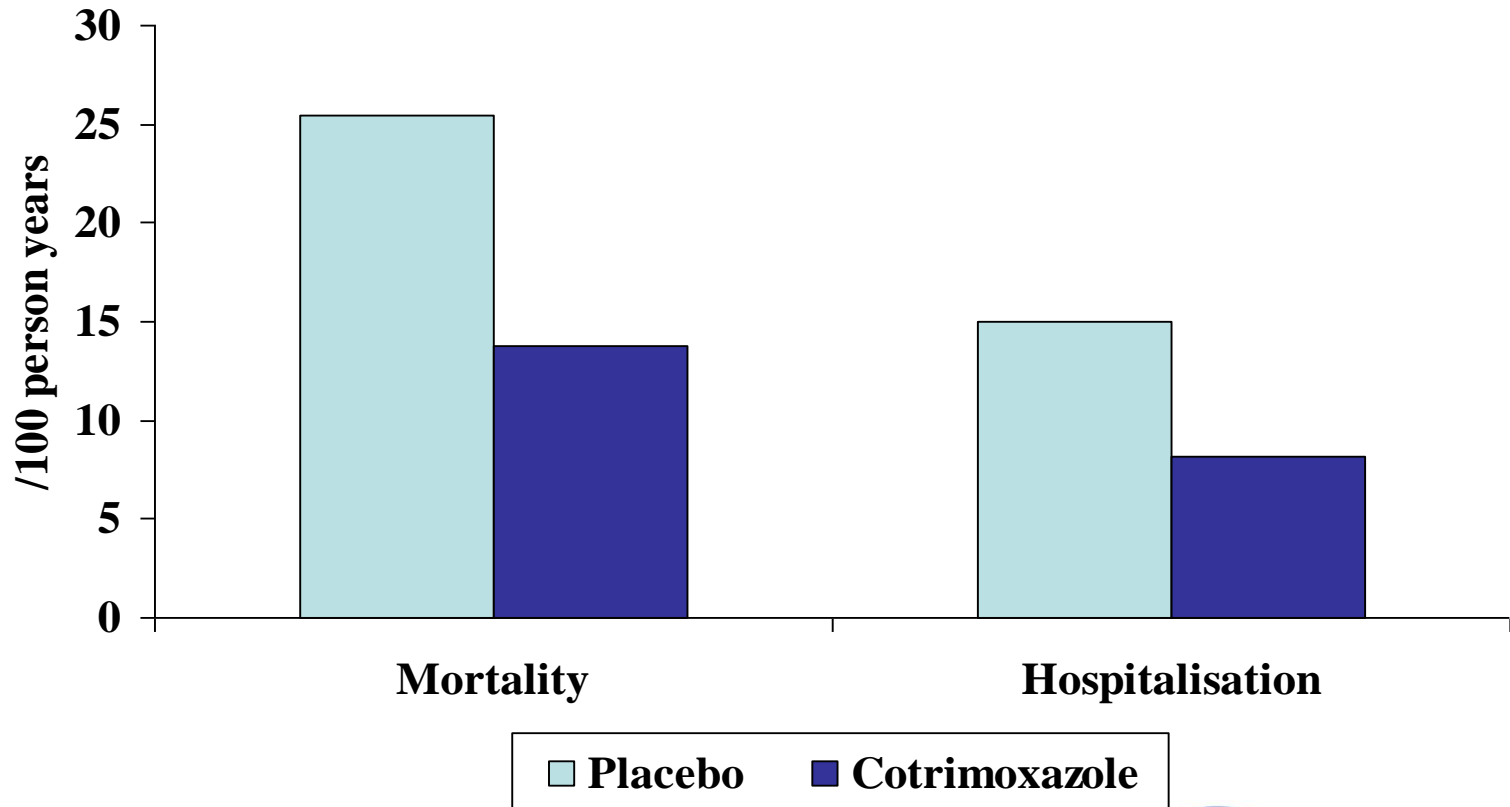


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Co-trimoxazole preventive therapy (CPT) in TB/HIV



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Co-trimoxazole prophylaxis (CPT)

- All symptomatic HIV-infected patients
 - WHO stage 2, 3 and 4
- Patients on HAART:
 - Discontinue if 2 consecutive CD4+ counts >200
- Dosage: 960mg daily (2 single strength tabs)

All HIV+ patients with PTB (stage 3) or EPTB (stage 4) qualify for CPT!



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Drug-Drug Interactions

- Effects of Rifamycins on **levels of ART drugs**
 - **Decreased** levels of EFV, NVP, PIs via induction of Cytochrome P450 system
- Effects of ART on **levels of Rifamycins**
 - **Increased** levels of Rifamycins, especially Rifabutin
 - Especially with Ritonavir
 - Via inhibition of cytochrome P450
- Effects of Rifamycins on **other drugs**
 - **Decreased** levels of oral contraceptives, ketoconazole, warfarin
 - Decreased efficacy **requires higher dosage**



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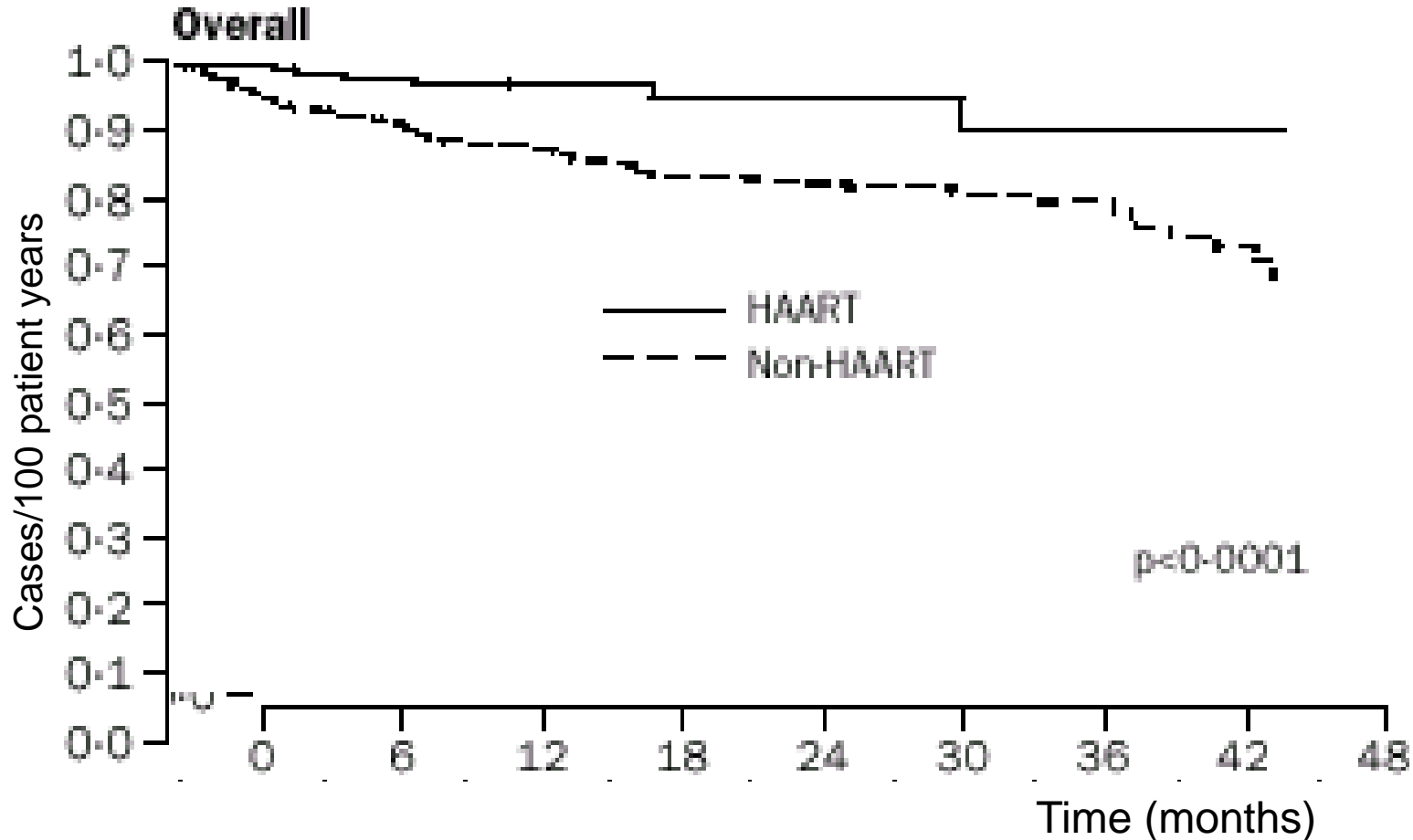
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Overlapping side effects: TB Rx – ARVs

	<i>Possible causes</i>	
	Anti-TB drugs	ARVs
Skin rash	PZA RIF INH EMB	NVP EFV
Nausea, vomiting	PZA RIF INH RBT	AZT ddi RTV IDV
Peripheral neuropathy	INH	ddi d4T
Hepatitis	PZA RIF INH RBT	NVP EFV PIs IRIS
Leukopenia, anemia	RIF RBT	AZT



HAART and TB prevention



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Definition: IPT

Preventive therapy against TB:
the use of
one or more anti-tuberculosis drugs
given to individuals with **latent** infection
with ***M. tuberculosis***
in order to prevent the **progression**
to active disease

HIV is the strongest risk factor for the
progression of latent infection into active TB



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Who is eligible for IPT?

All HIV positive people with no signs and symptoms of TB are eligible for TB preventive therapy

- Particular attention to: miners, prisoners, TB contacts, HCW's
- Pregnant mothers without symptoms of TB
- IPT and ART:
 - Patients who receive IPT and need ART can complete IPT even if ART is started
 - Patients on ART for more than 6 months without active TB can benefit from IPT



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Who is NOT eligible for IPT?

- Patients with active liver disease or active alcohol abuse should not be offered TB preventive therapy
 - Potential hepatotoxicity of the drug used for preventive therapy
- HIV negative patients



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Regimen

The standard regimen for TB preventive therapy is:

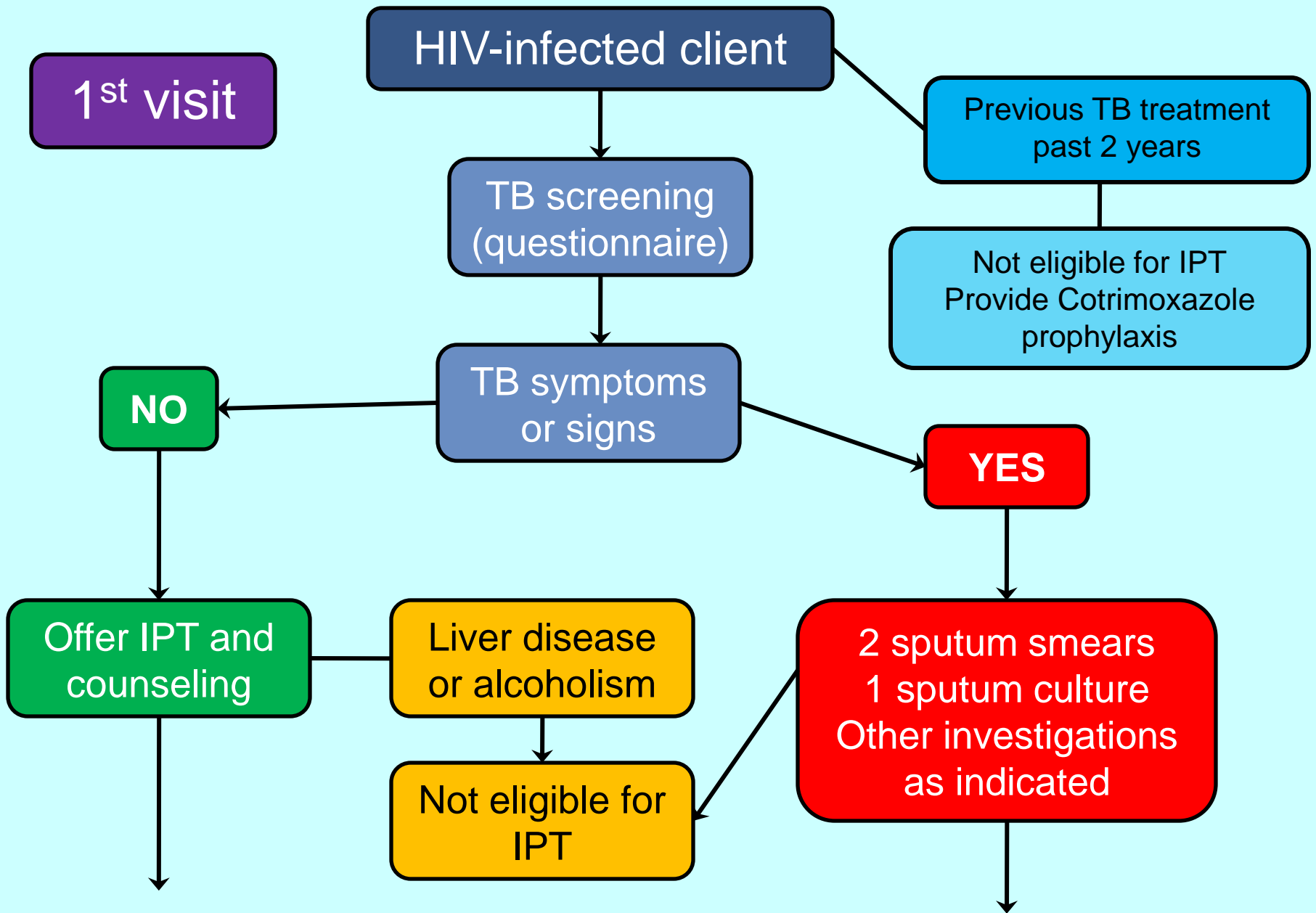
Isoniazid (INH) daily

The dose (for adults) is: **5 mg/kg/day** (maximum **300 mg per day**)

The recommended duration is: **6 months**

Provide Pyridoxine 50mg daily to prevent peripheral neuropathy as well.





2nd visit

Asymptomatic patient

Review patient, offer IPT and counseling

Start IPT

Patient refuses IPT

Symptomatic patient
Smear/culture

Smear/culture
negative

Smear/culture
positive

Antibiotics

Poor response to antibiotics

Good response to antibiotics

TB treatment
Co-trimoxazole
Prophylaxis

Refer for further investigations for PTB/ EPTB/other

Reassess and reconsider IPT after 3 months

Not eligible for IPT, provide CPT

