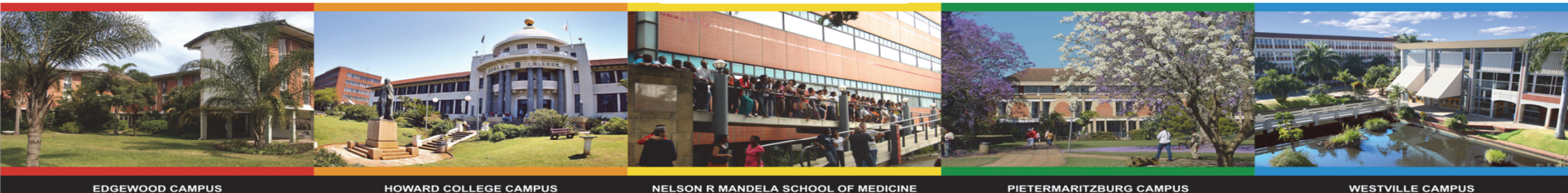




TB and HIV co-infection including IRIS

Richard Lessells

SAHCS Conference 2018



EDGEWOOD CAMPUS

HOWARD COLLEGE CAMPUS

NELSON R MANDELA SCHOOL OF MEDICINE

PIETERMARITZBURG CAMPUS

WESTVILLE CAMPUS

UKZN INSPIRING GREATNESS

Clinical scenario 1



36-year-old male

Presents with cough, fever & weight loss

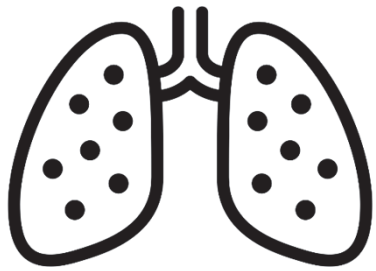
HIV test positive (new diagnosis)

Sputum Xpert Ultra - MTB detected, rifampicin resistance not detected

Commenced on TB treatment (HRZE)

When will you initiate ART?

Timing of ART initiation in adults with TB



Person with pulmonary TB



CD4+ ≤ 50



Start ART within 2 weeks



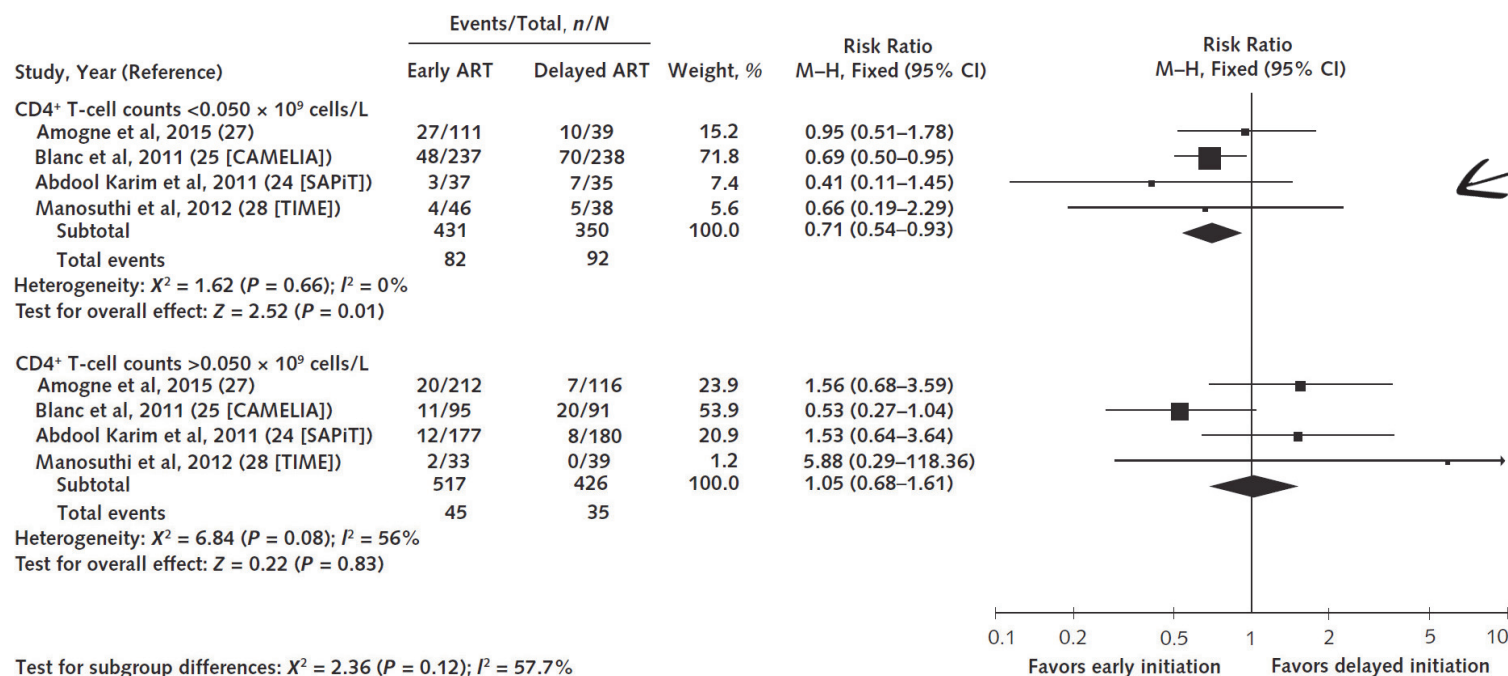
CD4+ > 50



Start ART within 2-8 weeks

Timing of ART initiation in adults with TB

Meta-analysis of RCTs comparing early ART (1-4 weeks after TB treatment) and delayed ART (8-12 weeks after TB treatment)



Reduction in mortality with early ART if CD4⁺ ≤50 cells/μL

No difference in mortality if CD4⁺ >50 cells/μL

Uthman Ann Intern Med 2015

Clinical scenario 2



36-year-old male

Hospitalised with headache & fever

HIV test positive (new diagnosis)

CSF Xpert Ultra - MTB detected, rifampicin resistance not detected

Commenced on TB treatment (HRZE) & prednisone

When will you initiate ART?

Timing of ART initiation in adults with TB



Person with TB meningitis



Irrespective
of CD4+
count



Start ART after 8 weeks

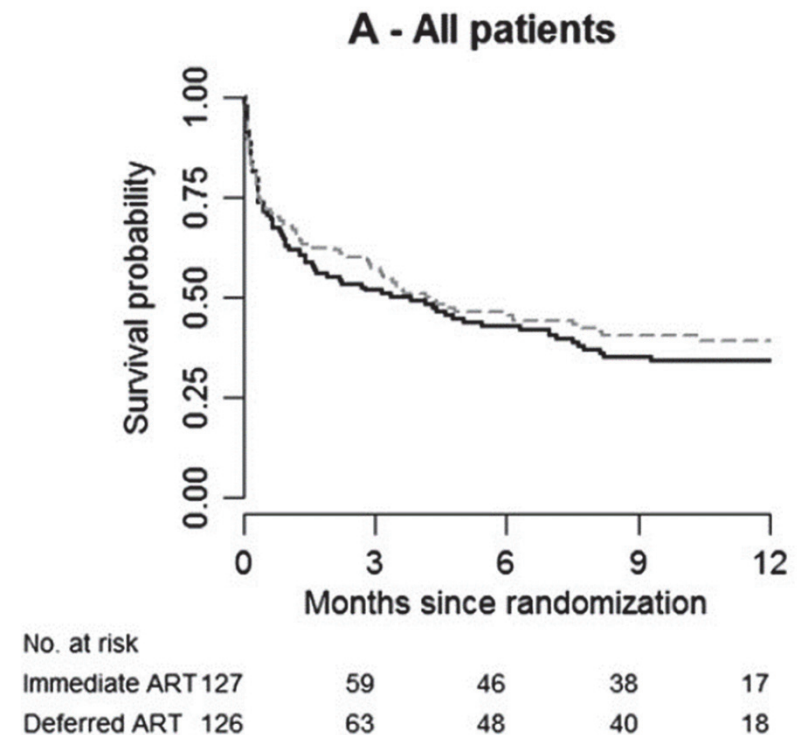
Timing of ART initiation in adults with TB meningitis

RCT HIV-positive adults with TBM, Vietnam

Immediate ART (within 7d) vs. deferred ART (after 2 months)

Immediate ART was not associated with improved survival at 9 months

Some evidence that immediate ART was associated with increased risk of grade 4 adverse events



Torok CID 2011

Clinical scenario 3



36-year-old male

HIV test positive (new diagnosis)

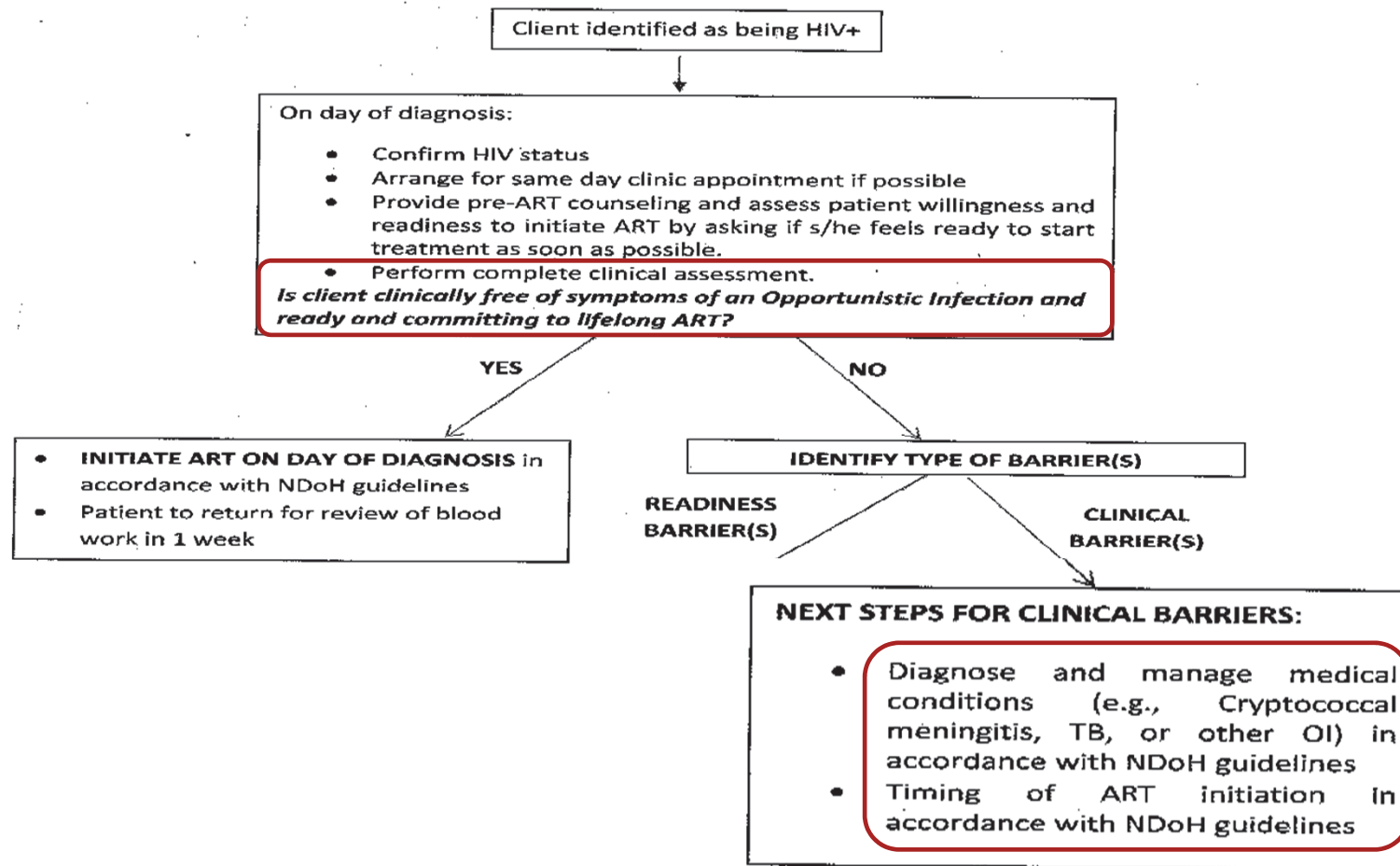
Reports cough, fever & weight loss

Sputum sent for Xpert Ultra

Commenced on FDC (same-day initiation)

Was this the correct management?

Same-day ART initiation



NDoH Memo Sep 2017

Clinical scenario 4



36-year-old male

HIV positive, on TDF/FTC/EFV (FDC)

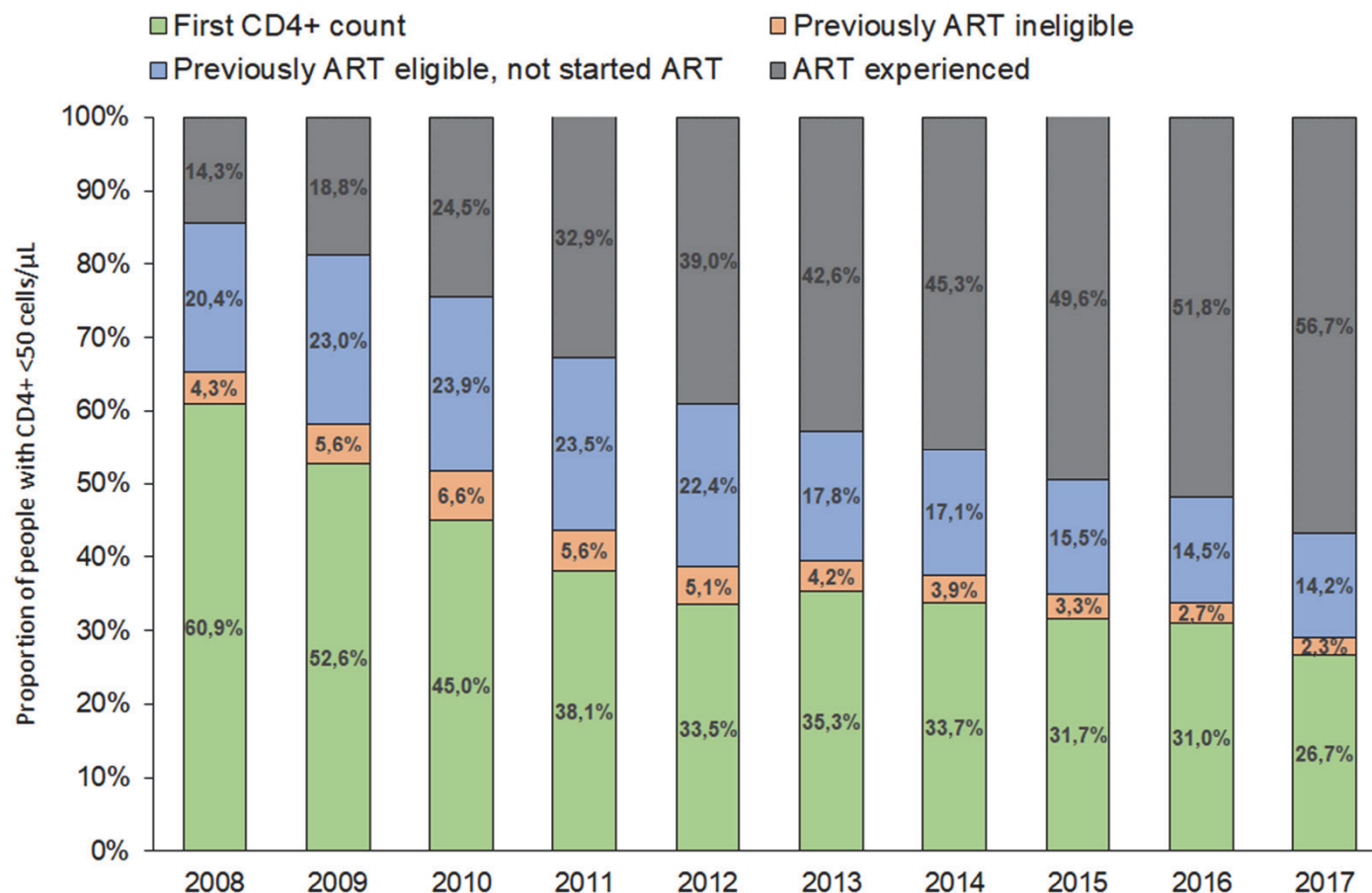
Presents with cough, fever & weight loss

Sputum Xpert Ultra – MTB detected, rifampicin resistance not detected

How will you assess this patient and manage their antiretroviral therapy?

Changing profile of people with very advanced HIV disease

Western Cape public sector cohort



Most people with CD4+ <50 cells/μL are now ART experienced

Osler CID 2018

Changing profile of people with possible TB



Rapid urine-based screening for tuberculosis in HIV-positive patients admitted to hospital in Africa (STAMP): a pragmatic, multicentre, parallel-group, double-blind, randomised controlled trial



Ankur Gupta-Wright, Elizabeth L Corbett, Joep J van Oosterhout, Douglas Wilson, Daniel Grint, Melanie Alufandika-Moyo, Jurgens A Peters, Lingstone Chiume, Clare Flach, Stephen D Lawn*, Katherine Fielding

HIV-positive medical admissions, Edendale Hospital, KZN, Oct 2015 – Sep 2017

90% had one or more TB symptom (cough, fever, night sweats, or weight loss)

Median CD4+ count 236 cells/ μ L (30% <100 cells/ μ L)

Overall, 72% were ART experienced (most were currently on ART)

Gupta-Wright Lancet 2018

Clinical scenario 4



36-year-old male

HIV positive, on TDF/FTC/EFV (FDC)

Presents with cough, fever & weight loss

Sputum Xpert Ultra – MTB detected, rifampicin resistance not detected

Important to evaluate for virological failure - check VL results (current & historical)

Timing of ART switch in adults with TB and virological failure

- No specific evidence to guide timing of ART switch in context of TB and virological failure
- Same principles apply as with initiating ART in naïve patients – treating TB is the first priority, ensure tolerating TB treatment, reduce risk of shared toxicities, reduce risk of paradoxical IRIS
- Aim to switch ART regimen within 2-8 weeks depending on clinical condition and CD4+ count

Clinical scenario 5



36-year-old HIV-positive male

On TB treatment 8 weeks (diagnosed by CXR, Xpert negative)

On TDF/FTC/EFV 6 weeks

Pre-treatment CD4+ count 40 cells/ μ L

Presents with worsening cough & dyspnoea

Is this IRIS?

TB-IRIS

- TB-IRIS remains a clinical diagnosis
- Important to revisit original TB diagnosis, e.g. check for sputum culture result, review CXR
- Important to consider alternative diagnoses/problems
 - Poor adherence
 - TB drug resistance
 - Other opportunistic infection (e.g. PCP, bacterial pneumonia)

Will IRIS be more common with dolutegravir?

- Some evidence from European cohort studies that IRIS (especially TB-IRIS) more common with INSTIs than NNRTIs or PIs
- This observation not supported by evidence from RCTs of DTG, but small number of events overall and most trials excluded people with more advanced disease
- No specific concerns reported from national roll-out programmes of DTG (Botswana, Brazil)

Treatment of TB-IRIS

- No indication to stop ART with paradoxical TB-IRIS
- Prednisone use is supported by RCT data and can be used in treatment of paradoxical TB-IRIS
- Key point is not to rush to diagnosis and treatment without thorough clinical assessment

Prevention of TB-IRIS



- RCT of 4-week course of prednisone vs placebo in ART-naïve adults at high risk of TB-IRIS (CD4+ count <100 cells/ μ L, within 30 days of starting TB treatment)
- Prednisone reduced incidence of paradoxical TB-IRIS - 32.5% vs. 46.7%, relative risk 0.70 (95%CI 0.51-0.96)
- Prednisone reduced need for corticosteroids as treatment – 13.3% vs. 28.3%, relative risk 0.47 (95%CI 0.27-0.83)
- No evidence of harms associated with prednisone use

Meintjes CROI 2018

Summary

- Good quality evidence to guide timing of ART initiation in ART-naïve adults
- Many HIV-positive adults with TB are now ART experienced - either returning to care or viraemic on ART. Thorough assessment and careful management required to achieve good outcomes
- Promising results around use of prednisone to prevent TB-IRIS, but precise role uncertain