HIV Comorbidities: Treat, Switch ART, or Both?

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Comorbidities: change ART or treat?
Background

- ~25,000 existing HIV+ pts, with 90%+ on ART
- ~ 1,000 new HIV infections annually – number will fall
- So issue of what to start will recede, and issue of what should patients continue will grow
- Comorbidities more common in HIV+ than age-matched controls
- Comorbidities cause more deaths than AIDS in adults on ART in resource-rich countries

Schouten et al, Clin Infect Dis 2014; DAD study group, AIDS 2010

Comorbidities: change ART or treat?
Outline

- Conditions
  - CVD / dyslipidaemia / diabetes
  - HAND
  - chronic kidney disease
  - low bone mineral density / fracture
- Change ART, treat, or both?
  - Can I switch / treat?
  - Should I switch / treat?
  - Should I do anything else?
  - 2-drug ART?

Comorbidities: change ART or treat?
Outline

- **Conditions**
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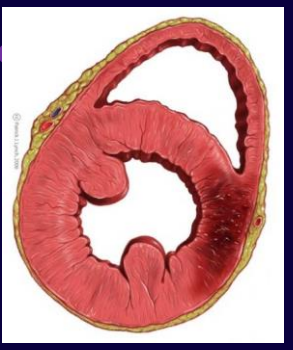
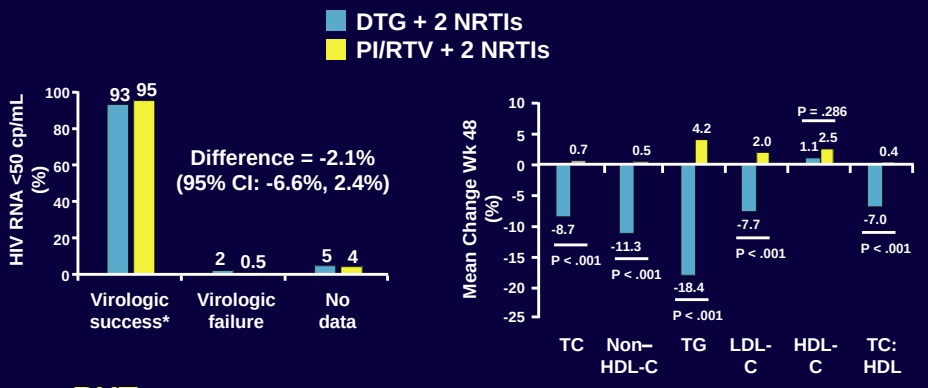


Comorbidities: change ART or treat?
CVD: PIr switching



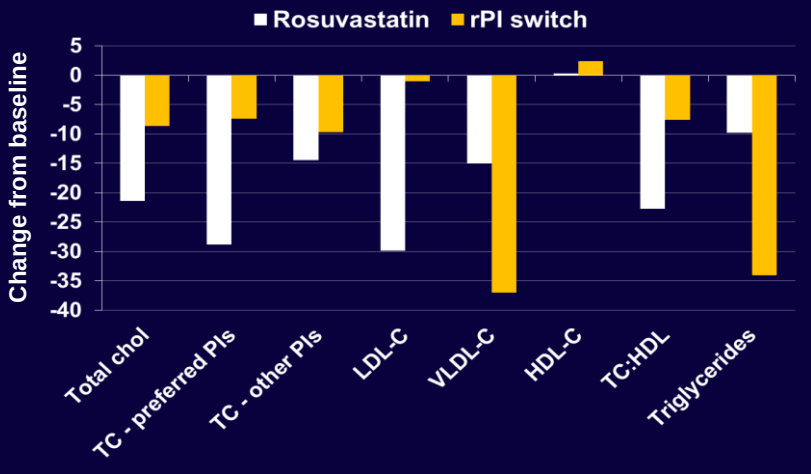
- **BUT**
  - no fewer gd 3/4 AEs, SAEs, AE-related discontinuations
  - no less atheroma / CV function

Gatell JM, et al. IAS 2017. Abstract TUAB0102

Comorbidities: change ART or treat?

CVD: PI switch vs. treat

Adults with Framingham score >8% on a boosted PI



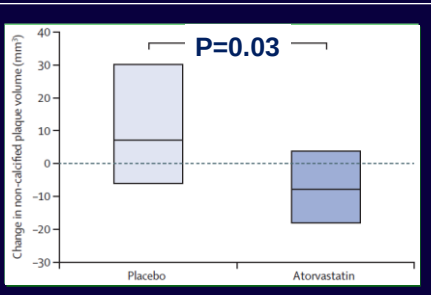
Lee et al, HIV Med 2016

Comorbidities: change ART or treat?

CVD: statins and carotid plaque

Change at 12 months	Placebo	Atorvastatin 20 mg daily	Diff.	P
Total chol	0.12	-1.23	1.35	<0.0001
LDL-Chol	0.30	-1.00	1.30	<0.0001

Carotid plaque volume



Lo et al, CROI 2015, Abstract 136; Lo et al, Lancet HIV 2015

Comorbidities: change ART or treat?

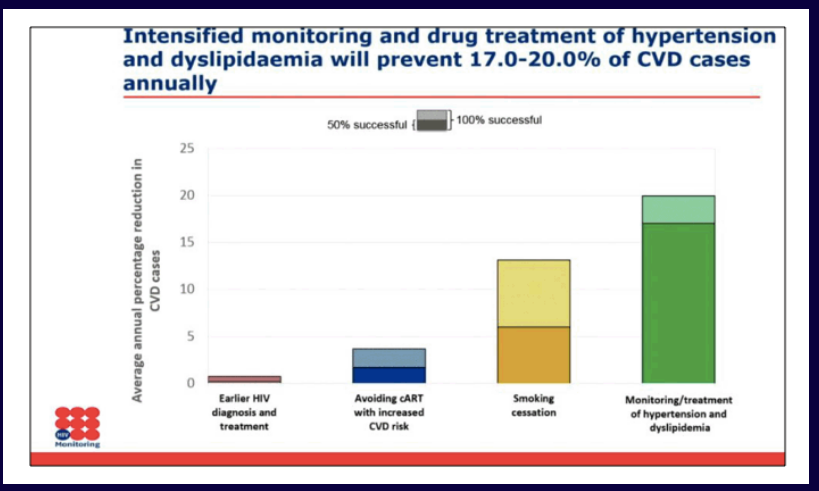
CVD: risk assessment

Framingham n=5573	DAD model n=22625	HR for MI	% n=5719
Age	Age (per 5 year increment)	1.93	
Sex	Male sex	1.34	
Current smoking	Current smoking	4.02	48%
..	Ex-smoking	2.01	
..	Diabetes	2.28	
Total cholesterol	Total chol (per 1 mmol/l higher)	1.28	47%
HDL cholesterol	HDL chol (per 1 mmol/l higher)	0.66	
Systolic BP	Systolic BP (per 1 mmHg higher)	1.04	31%
..	Indinavir (per year exposure)	1.07	
..	Lopinavir/r (per year exposure)	1.12	
..	Abacavir (current exposure)	2.04	

Friis-Møller et al, Eur J Cardiovasc Prev Rehab 2010; Shahmanesh et al, ADR workshop 2013

Comorbidities: change ART or treat?

CVD: traditional risk factors vs. ART choice



van Zoest et al, CROI 2017, Abstract 129

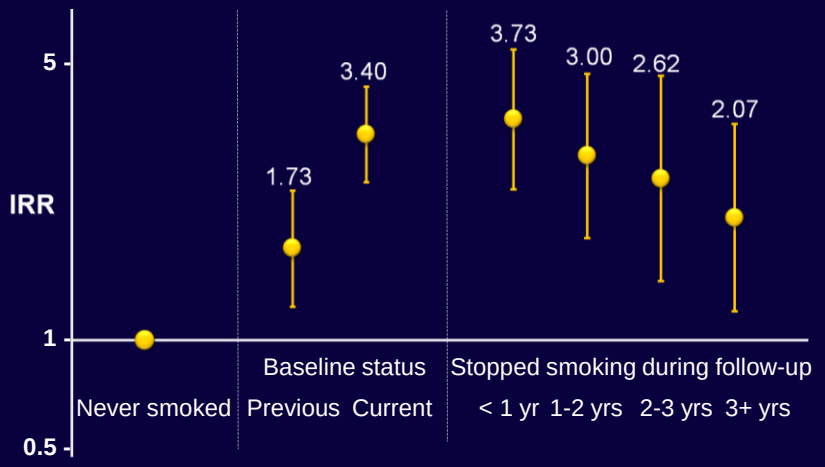
Comorbidities: change ART or treat?

CVD: traditional risk factors

- Similar approach as in general population
  - Smoking
    - counselling
    - nicotine replacement
    - varenicline (CNS side effects similar to EFV)
  - Hypertension
    - weight and salt reduction
    - A = ACE inhibitor / ARB
    - C = Calcium blocker
    - D = diuretic
  - Diabetes
    - weight reduction
    - metformin

Comorbidities: change ART or treat?

CVD: smoking cessation



Adjusted for: age, sex, cohort, calendar year, antiretroviral treatment, family history of CVD, diabetes, and time-updated lipids and blood pressure assessments

Petoumenos et al, AIDS 2012

Comorbidities: change ART or treat?
Outline

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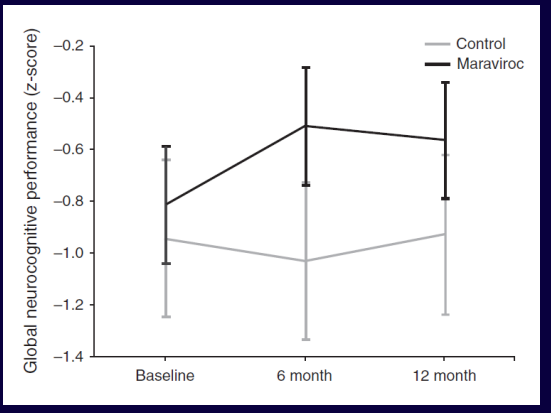
Comorbidities: change ART or treat?
HAND: ART intensification



- **No RCT data showing improvement with ART switching or traditional interventions**

Gates et al, AIDS 2016

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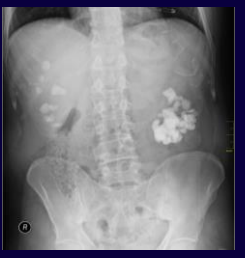
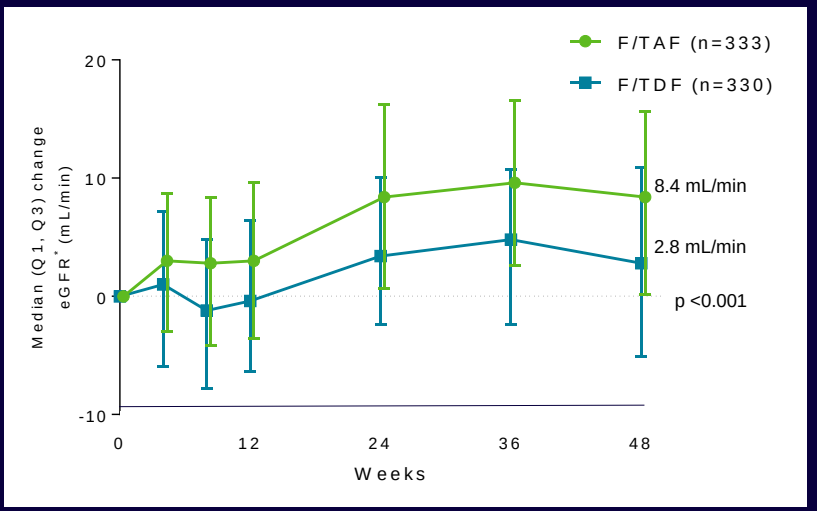


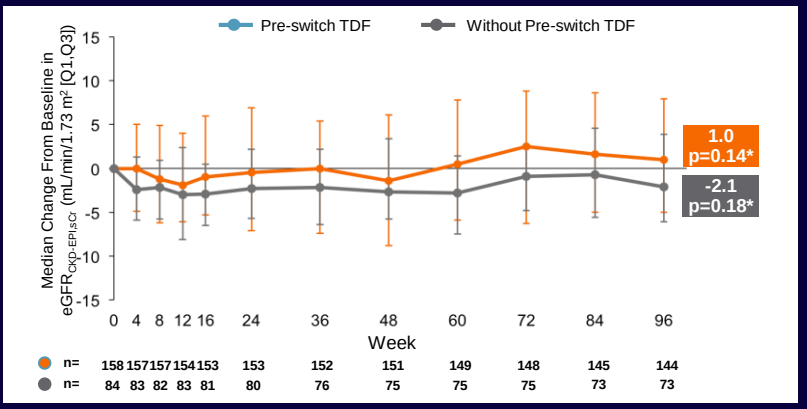
Comorbidities: change ART or treat?
Chronic kidney disease: switch TDF to TAF



Gallant et al, Lancet HIV 2016

Comorbidities: change ART or treat?

Chronic kidney disease: switch TDF to TAF



- No data on conventional CKD treatments (e.g. hypertension, diabetes)

Pozniak et al, JAIDS 2016

Comorbidities: change ART or treat?

Chronic kidney disease: treatment

- When measuring eGFR, ensure patient is
  - well hydrated and
  - not taking creatine supplements
- Avoid nephrotoxic drugs e.g. NSAIDs
- Assess and treat other risk factors including diabetes, blood pressure, HCV, HBV as in HIV-neg adults
- Switch? - declining eGFR more likely to be TDF if
  - glycosuria +
  - urinary phosphate +
  - blood pressure normal
  - no diabetes, active HCV or active HBV

Comorbidities: change ART or treat?
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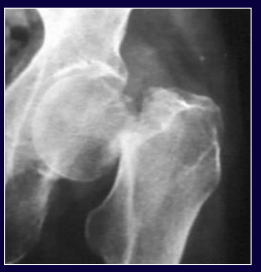
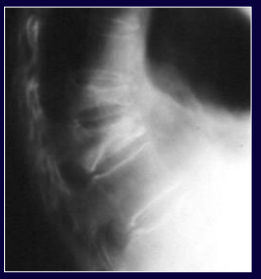
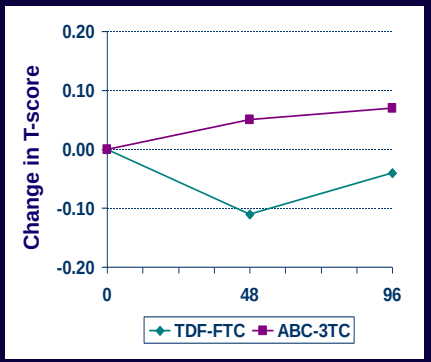
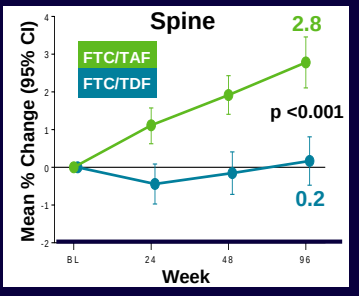
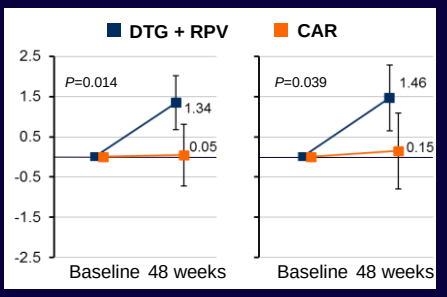




Comorbidities: change ART or treat?
Low BMD: switch TDF to ABC, TAF or no NRTI



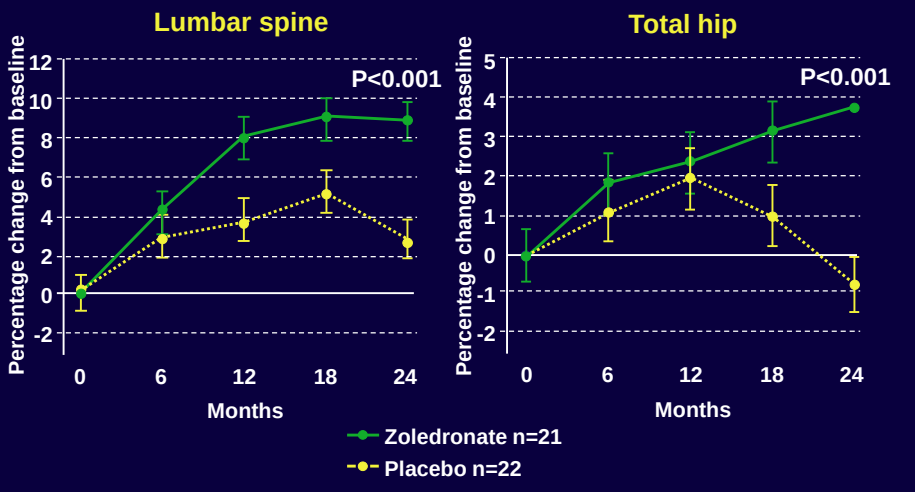




Martin et al, Clin Infect Dis 2009;
Yazdanpanah Y, et al. IAS 2017 #MOPEB0292; McComsey et al. IAS 2017, #TUPDB0205LB

Comorbidities: change ART or treat?

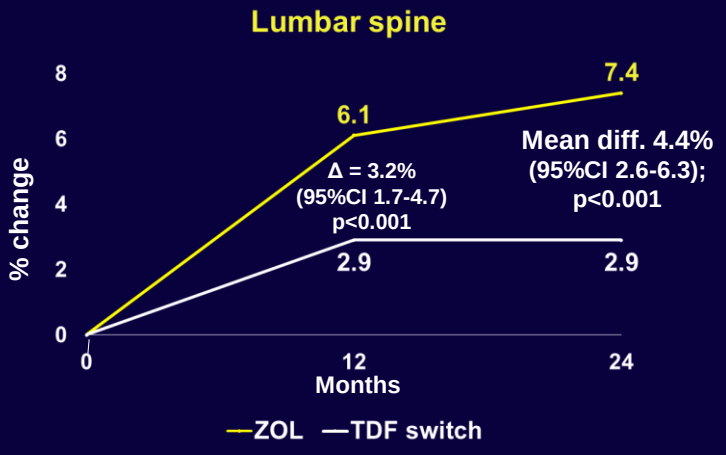
Low BMD: zoledronic acid



Bolland et al, J Clin Endocrinol Metab 2007

Comorbidities: change ART or treat?

Low BMD / fractures

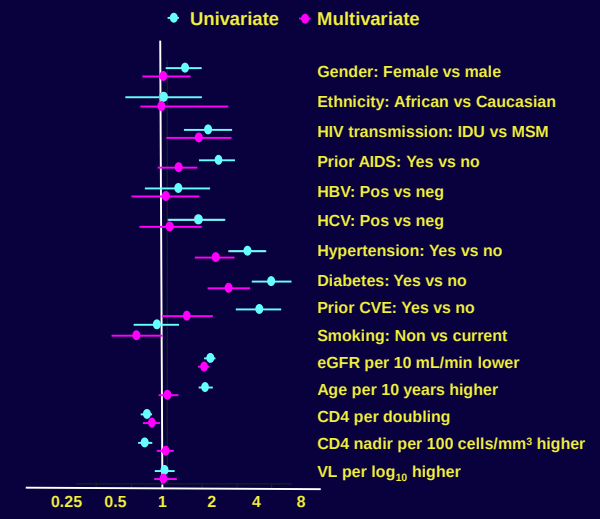


- Fractures: ZOL, n = 1; TDF switch = 7

Hoy et al. IAS 2017

Comorbidities: change ART or treat?

Low BMD / fractures: traditional risk factors

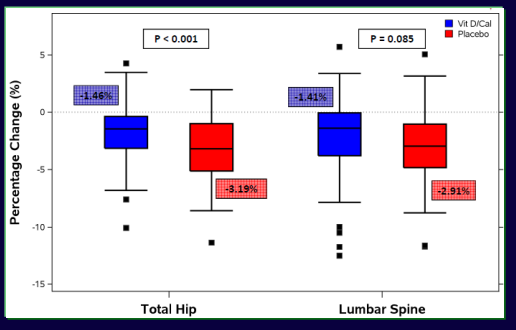


Ryom L, et al. AIDS 2014

Comorbidities: change ART or treat?

Low BMD: general measures

- Reduce risk of falls
- Exercise
  - weight-bearing
  - muscle strength
  - balance training
- Calcium and vitamin D



http://www.nof.org/files/nof/public/content/resource/913/files/580.pdf; Overton et al, CROI 2014

Comorbidities: change ART or treat?
Summary

Comorbidity	Switch ART	Treat	Comment
CVD	PIr (except AZV) to anything	Potent statin, aspirin, etc	Conventional risk factors #1
Cholesterol	PIr (except AZV) to anything	Potent statin	
Diabetes	No data	As in HIV-neg	
HAND	Add maraviroc?	No data	Intervene early?
CKD	Switch or omit TDF	No data	TDF largely irreversible
Low BMD / fractures	Switch or omit TDF	Bisphosphonate +/- 2° causes	

Comorbidities: change ART or treat?
Summary / homilies

- If it ain't broke, don't fix it
  If it's about to break → switch +/- treat
  If it's broken → treat and (probably) switch
- Just because you can switch, does not mean you should
- If you do switch, new ART should
  - be just as effective
  - yield a clinical advantage (don't just treat numbers)
  - not introduce new toxicity / interaction