

17<sup>TH</sup> ANNUAL CONFERENCE OF THE  
BRITISH HIV ASSOCIATION (BHIVA)

British HIV Association  


# Dr Patrick Mallon

University College Dublin, Ireland

6-8 April 2011, Bournemouth International Centre

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Dr Patrick Mallon:	Dr Mallon has acted in a consultancy capacity, or as a speaker or received research funding from Gilead Sciences, GlaxoSmithKline, ViiV Healthcare, Abbott, MSD and Janssen.
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# Broken bones: is it worth the worry?

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Scoil an Leighis agus  
Eolaíocht An Leighis UCD



# Broken bones: is it worth the worry?

10 slides in favour

10 slides against



## Broken bones: is it worth the worry?



**Well of course it is!**

## Prevalence of low BMD is alarmingly high!

Publication	Number of patients		% ↓ BMD	
	HIV+	HIV–	HIV+	HIV–
Amiel <i>et al</i> 2004	148	81	<b>82.5</b>	35.8
Brown <i>et al</i> 2004	51	22	<b>63</b>	32
Bruera <i>et al</i> 2003	111	31	<b>64.8</b>	13
Dolan <i>et al</i> 2004	84	63	<b>63</b>	35
Huang <i>et al</i> 2002	15	9	<b>66.6</b>	11
Knobel <i>et al</i> 2001	80	100	<b>87.5</b>	30
Loiseau-Peres <i>et al</i> 2002	47	47	<b>68</b>	34
Madeddu <i>et al</i> 2004	172	64	<b>59.3</b>	7.8
Tebas <i>et al</i> 2000	95	17	<b>40</b>	29
Teichman <i>et al</i> 2003	50	50	<b>76</b>	4
Yin <i>et al</i> 2005	31	186	<b>77.4</b>	56

Adapted from Brown TT & Qaqish RB. *AIDS* 2006; **20**:2165-2174

## Significant declines in BMD are common.

*Spain.* N=391.

49% osteopenic, 22% osteoporosis.

Progression after 2.5 years:

- 12.5% to osteopenia
- 15.6% to osteoporosis

*Aquitaine cohort.* N=255. 68% men. Age 44 yrs. All on ART.

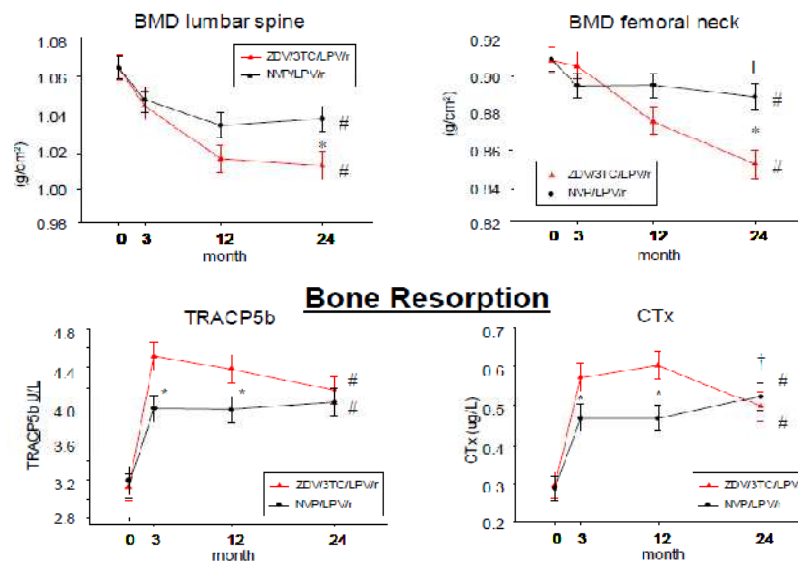
72% osteopenic (osteoporosis excluded)

Progression after 2.3 years:

- 7.8% to osteopenia
- 11.4% to osteoporosis

Cazanave C et al. 17<sup>th</sup> CROI 2010. Abstract 747. Bonjoch A et al. 18<sup>th</sup> IAC 2010. Abstract THPDB104.

## Antiretroviral therapy makes BMD worse!



Van Vonderen et al. CROI 2011. abstract 833

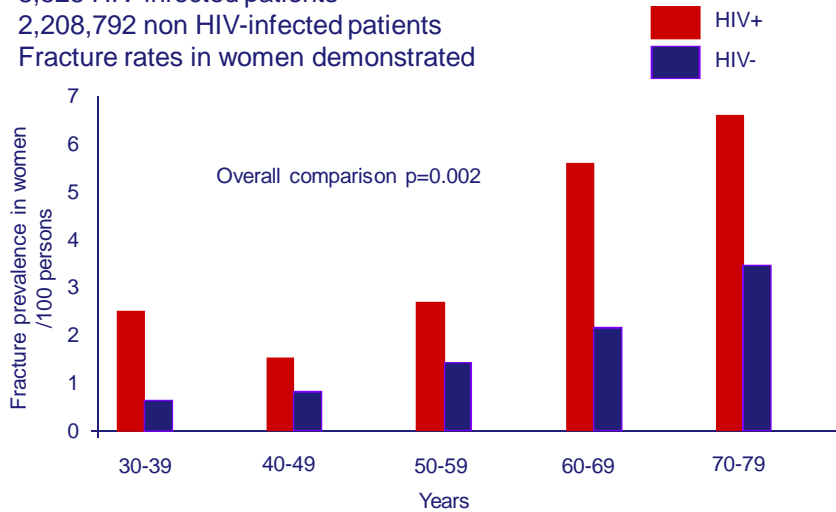
## Fractures are much more prevalent

Healthcare Registry study

8,525 HIV-infected patients

2,208,792 non HIV-infected patients

Fracture rates in women demonstrated

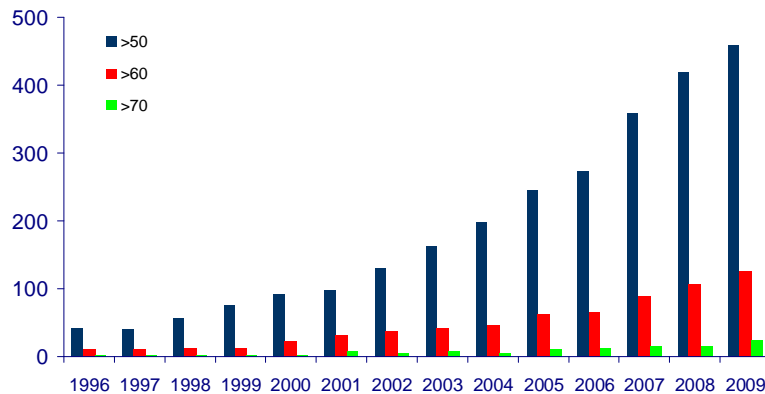


Triant VA et al, JCEM 2008;93:3499-3504

## HIV+ patients are getting much older!

Patient age in Brighton cohort: 1996-2009

Most of the age increase is in the 50-60 age group



The increase in the over 50s is greater than the overall cohort

Personal communication, M. Fisher

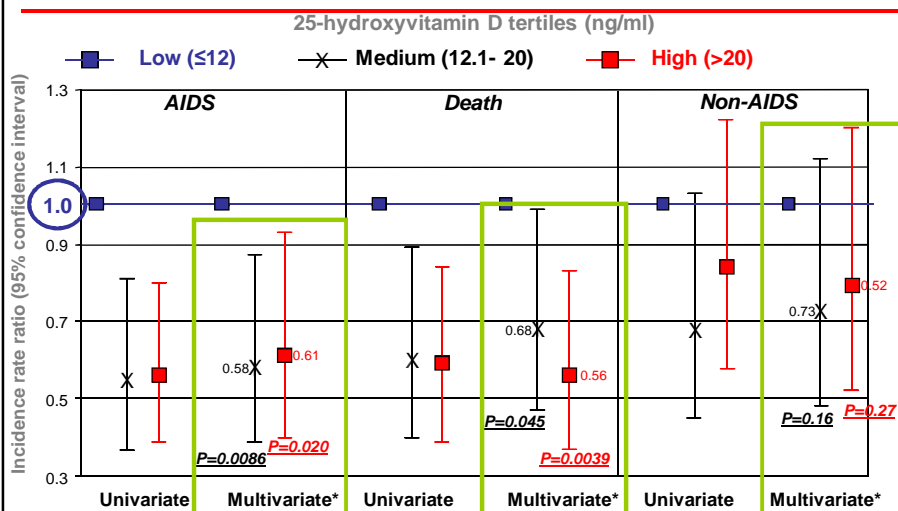
## Everyone has low vitamin D!

*almost*

	N	% caucasian	Insufficient (<75nmol/L)	Deficient (<30nmol/L)
SUN study	672	58%	72%	-
Swiss HIV Cohort	215	80%	-	41%
ICONA	852	-	54%	7%
C&W cohort	312	-	35% (<70nmol/L)	21% (<40nmol/L)
Crutchley (USA)	200	40%	64% (<50nmol/L)	20% (<27.5nmol/L)
NYC (St Luke's)	342	-	85%	-

1. Dao, CN et al, CROI 2010 #750, 2. Fux et al. CROI 2010t #749 3. Muller N. et al. CROI 2010 #752 4. Borderi M et al CROI 2010 #751, Rashid T et al. AIDS 2010 Vienna. Crutchley et al. AIDS 2010, Vienna. Gandhi et al. AIDS 2010, Vienna.

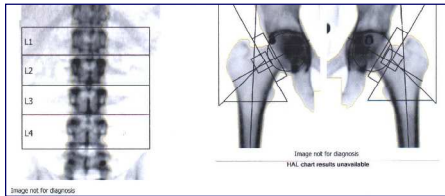
## Lower vitamin D = worse outcomes!



\*Adjusted for baseline values of gender, ethnic origin, HIV risk group, region of Europe, HBsAg and HCV antibody status, prior AIDS, exposure to antiretrovirals, age, CD4 count, Nadir CD4, HIV-RNA viral load, date of baseline sample date, season of sample and date of recruitment to EuroSIDA

Viard JP et al. IWADR, 2010

## Low BMD is easy and cheap to diagnose!



- Low cost
- Low radiation exposure
- Standardised interpretation

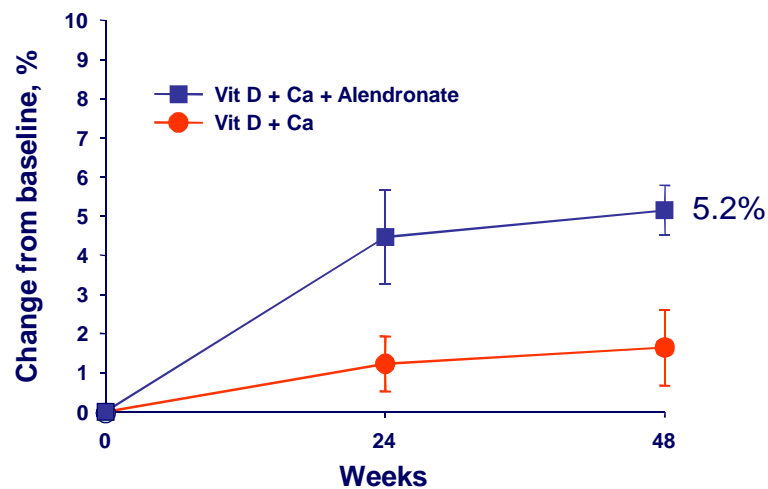
Disorder	T score
Normal	> -1.0
Osteopenia	-2.5 to -1.0
Osteoporosis	< -2.5
Disorder	Z score
Osteoporosis	< -2.0



NIH consensus development panel on osteoporosis prevention, diagnosis and therapy. *JAMA* 2001; **285**:785–795 2.

## Treatment of low BMD in HIV is effective

Change in lumbar BMD with alendronate (70mg weekly)  
 $n=31$ .  $t$ -score <1.



Mondy K, et al. *J Acquir Immune Defic Syndr* 2005; **38**:426–431

**What is the consequence of inaction?**

**Do we really want to watch our patients experiencing debilitating fractures knowing that we had the know-how to identify those most at risk and were able to intervene with effective medications?**



## Broken bones: is it worth the worry?



**Of course not! Don't be silly!  
There are much more important things to  
worry about!**

**guardian.co.uk**

### Budget 2011: coalition criticised as NHS spending power cut by £1bn

New inflation forecasts show the NHS in England will suffer a cut  
of almost £1bn in its spending power by 2015

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Denis Campbell, health correspondent  
guardian.co.uk, Thursday 24 March 2011 21.12 GMT

- Steadily increasing numbers of patients
- Arguably more patients on ART
- Little scope for budget increases
- Potentially tighter controls on how you treat
- Unclear who is responsible.....

## Should we really be screening for low BMD?

1. The condition should be an important health problem.
2. There should be a treatment for the condition.
3. Facilities for diagnosis and treatment should be available.
4. There should be a latent stage of the disease.
5. There should be a test or examination for the condition.
6. The test should be acceptable to the population.
7. The natural history of the disease should be adequately understood.
8. There should be an agreed policy on whom to treat.
9. The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole.
10. Case-finding should be a continuous process, not just a "once and for all" project.

Wilson JMG et al. WHO 1968;22(11):473

## Who should we be treating for low BMD?



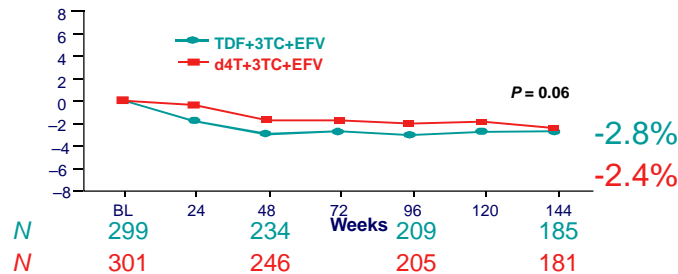
***National Institute for  
Health and Clinical Excellence***

**Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women (amended)**

- No guidance for HIV-infected patients
- Little guidance for primary prevention in men
- Lack of consensus regarding current guidance
- Uptake of guidance in the general population poor

## After 1 year on ART does BMD change?

- Little to suggest further declines in BMD after 48 weeks<sup>1</sup>

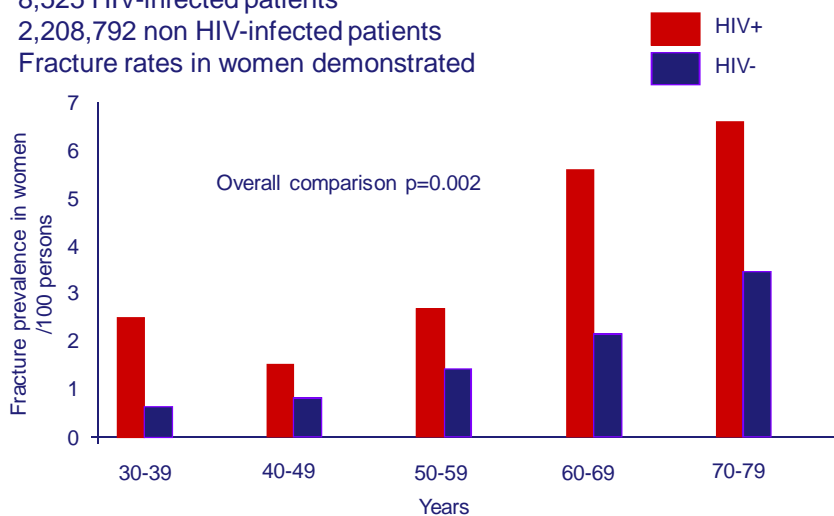


- HIV+ men on ART have stable or increasing BMD<sup>2</sup>
- Rates of change in BMD similar between HIV+ and HIV- women<sup>3</sup> and men<sup>4</sup>
- Rates of loss per year <0.5% - within the normal range<sup>5</sup>

1. Gallant JE, et al. *JAMA* 2004; 292:191-201. 2. Nolan D et al. *AIDS* 2001;15:1275-80. 3. Dolan SE et al. *JCEM* 2006;91:2938-45. 4. Bolland MJ et al. 2007. 5. Rozenberg S et al. *IWADR*, 2010

## Will treatment of low BMD lower fractures?

Healthcare Registry study  
 8,525 HIV-infected patients  
 2,208,792 non HIV-infected patients  
 Fracture rates in women demonstrated



Triant VA et al, *JCEM* 2008;93:3499-3504

## IF YOU DON'T FALL YOU WON'T FRACTURE!

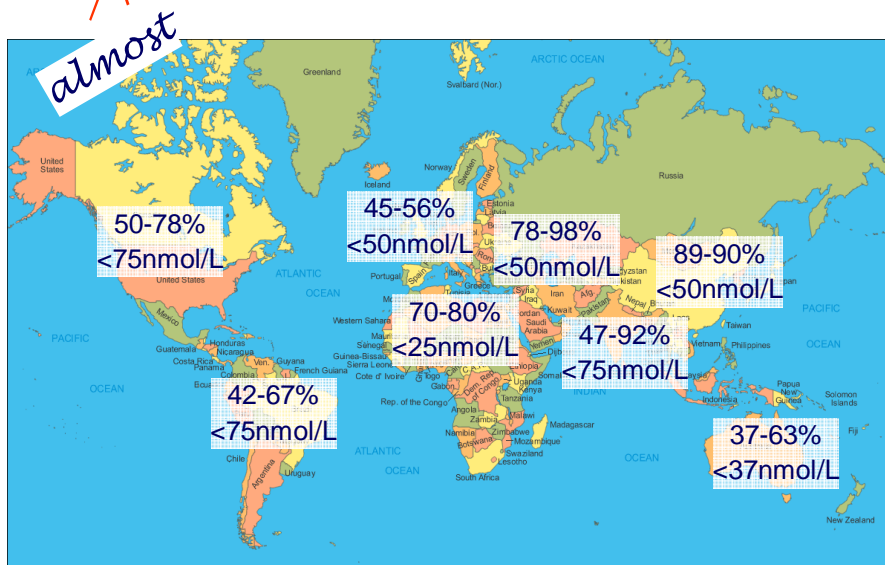
- 'Fragility' poorly defined – young populations  
ASSERT – 37yrs
- Cause of fragility may not be directly HIV related  
- IVDU / Alcohol
- Is increasing BMD the best intervention?
- Is it right to target interventions in one particular group?

## Vitamin D.....what's the '*panic*'?

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- Vitamin D associated with a low bone turnover state
- Bone loss in HIV associated with a high bone turnover state
- Rates of symptomatic clinical osteomalacia very low
- Is vitamin D lower in HIV+ versus HIV-?
- *What difference does it make?* – the benefits of vitamin D replacement on clinical outcomes have not been demonstrated
- It may be better to measure PTH than vitamin D (in those with low BMD)

## Everyone has low vitamin D!



Mithal A et al. Osteoporosis int 2009;20:1807-1820

## Everyone has low vitamin D!

**Women's Interagency HIV Study (WIHS).** N=1650 (71% HIV+)

23% Vit D insufficient (20-30ng/mL), 63% deficient (<20ng/mL)

**Vit D levels HIV+ 16 [10-25] versus HIV- 14 [9-20] ng/ml**

**REACH cohort (US).** 87% low Vit D (<37.5nmol/L)

- Latitude, vitamin D intake and ETOH 3 strongest predictors of vitamin D concentrations

	HIV+	HIV-
Vit D (nmol/L)	20.3 [1.1]	19.3 [1.7]

Adeyemi OM et al. AIDS 2010, Vienna. WEPDB101. Stephensen CB, et al. Am J Clin Nutr 2006; 83:1135-41

## Who is right?

### No need to 'ask' – there are guidelines....

	EACS 2009 <sup>1</sup>	CID 2010 <sup>2</sup>
HIV as 2 <sup>o</sup> cause OP*	Consider	Yes
Post-menopausal women	Yes	Yes
Men > 50 yrs	Yes	Yes
Repeat risk assessment	2 years	2-5 years
Steroid exposure	Yes	Screen
Hypogonadism	Yes	Screen
FRAX	All >40 yrs	T>-2.5 and ≤-1
Fragility fracture	Yes	Yes

\* OP = osteoporosis

1. EACS Prevention and Management of Non-Infectious Co-Morbidities in HIV 2009.

2. McComsey GA et al. CID 2010;51:937-46

## Who to consider for therapy\*:

	EACS 2009 <sup>1</sup>	CID 2010 <sup>2</sup>
Post-menopausal women and men >50 yrs with T<-2.5	Yes	Yes
History of fragility fracture and T<-2.5**	Yes	Yes
Follow-up DXA	2 years	1-2 years

\*Bisphosphonate therapy standard first-line

\*\*Regardless of age, gender or menopausal status

1. EACS Prevention and Management of Non-Infectious Co-Morbidities in HIV 2009.

2. McComsey GA et al. CID 2010;51:937-46

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Ireland

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