



PROGRAMMA SEMINARIO 2016

COSA PUÒ ACCADERE DURANTE UNA VISITA DI CONTROLLO?

La relazione medico-paziente può □
essere uno strumento di educazione per
affrontare il riconoscimento della
comorbosità □ ?



Giovanni Guaraldi
Università di Modena



UNIVERSITÀ DEGLI STUDI
DI MODENA E REGGIO EMILIA

The healthcare professional (HCP)–patient relationship in the HIV setting

The healthcare professional (HCP)–patient relationship in the HIV setting

Unique

- Chronic disease with a unique story

Strong investment from HIV community

- Numerous HIV associations and meetings
- There is a strong view that healthcare professionals (HCPs) working with people living with HIV (PLWHIV) are more focussed on their patients than their 'medical world'

Close HCP teams but casual relationships within them

- "When HIV broke out, physicians, like nurses, had very little means to combat it. Holding the patients hands and listening to their fear of death was often all they could do."
- As a result teams are close, with a more casual nature to their working relationships, which reflects on HCP-patient relationships

Relational pathology

- Psychiatrist Dr Linard's theory

Secrecy about the condition

- HCPs are often the only people who know a patient's HIV status, families are rarely involved
- The hospital/clinic may be the only place where patients discuss their condition

Existing resources

Community organisations	<ul style="list-style-type: none">• Meetings• Magazines• Websites
Websites from institutions & companies	<ul style="list-style-type: none">• www.treat-hiv.com
Apps	<ul style="list-style-type: none">• www.patientsknowbest.com/
Tools to help prepare for meeting HCPs	<ul style="list-style-type: none">• Patient-reported outcome measures (PROMs)• Tools from Gilead



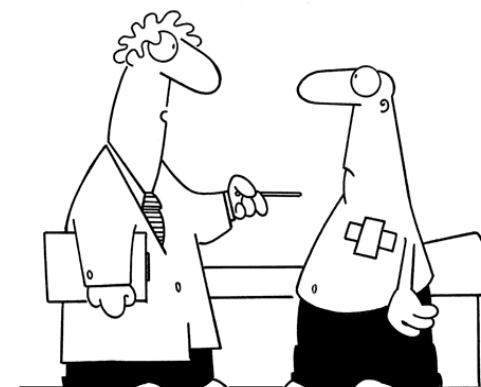
treat.info

vih.org



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"It's a pacemaker for your heart,
plus you can download apps for your
liver, kidneys, lungs, and pancreas!"

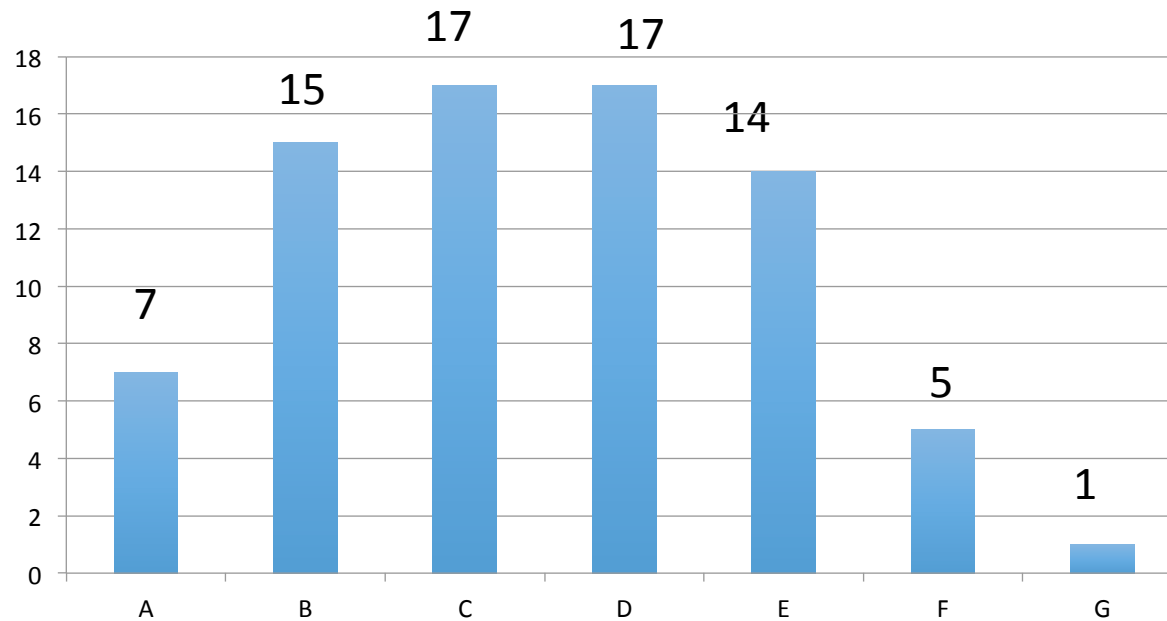
Note: Confidentiality is extremely important

The importance of a strong HCP-patient relationship

- A strong HCP-patient relationship can:
 - Support adherence
 - Enhance self-efficacy and self-esteem
 - Improve quality of life
 -

Relazione con il medico

COME GIUDICHI LA RELAZIONE CON IL TUO MEDICO INFETTIVOLOGO?



N = 76

- A. Pienamente soddisfacente perché ascoltarlo è sempre interessante.: 9%
- B. Pienamente soddisfacente perché parlo di tutto e quindi lo sento “amico/a”.: 20%
- C. Pienamente soddisfacente perché, tramite le nostre conversazioni, agisco conseguentemente per gestire al meglio il mio stato di salute modificando anche il mio stile di vita, se necessario.: 22%
- D. Abbastanza soddisfacente. Non ho particolari questioni da segnalare.: 22%
- E. Abbastanza soddisfacente, anche se vorrei parlare di più con lui/lei, perché penso di avere bisogno di alcuni consigli sul mio stato di salute che per varie ragioni non riesco a ottenere.: 19%
- F. Non soddisfacente perché parliamo poco e c'è sempre poco tempo.: 7%
- G. Non soddisfacente.: 1%

Improving the relationship

Time

“Developing trusting relationships – through respect and partnership–was something that both patients and providers saw as occurring over time”

Respect

“Respect may be particularly important for patients who have been marginalized or stigmatized because of their HIV status or for other reasons”

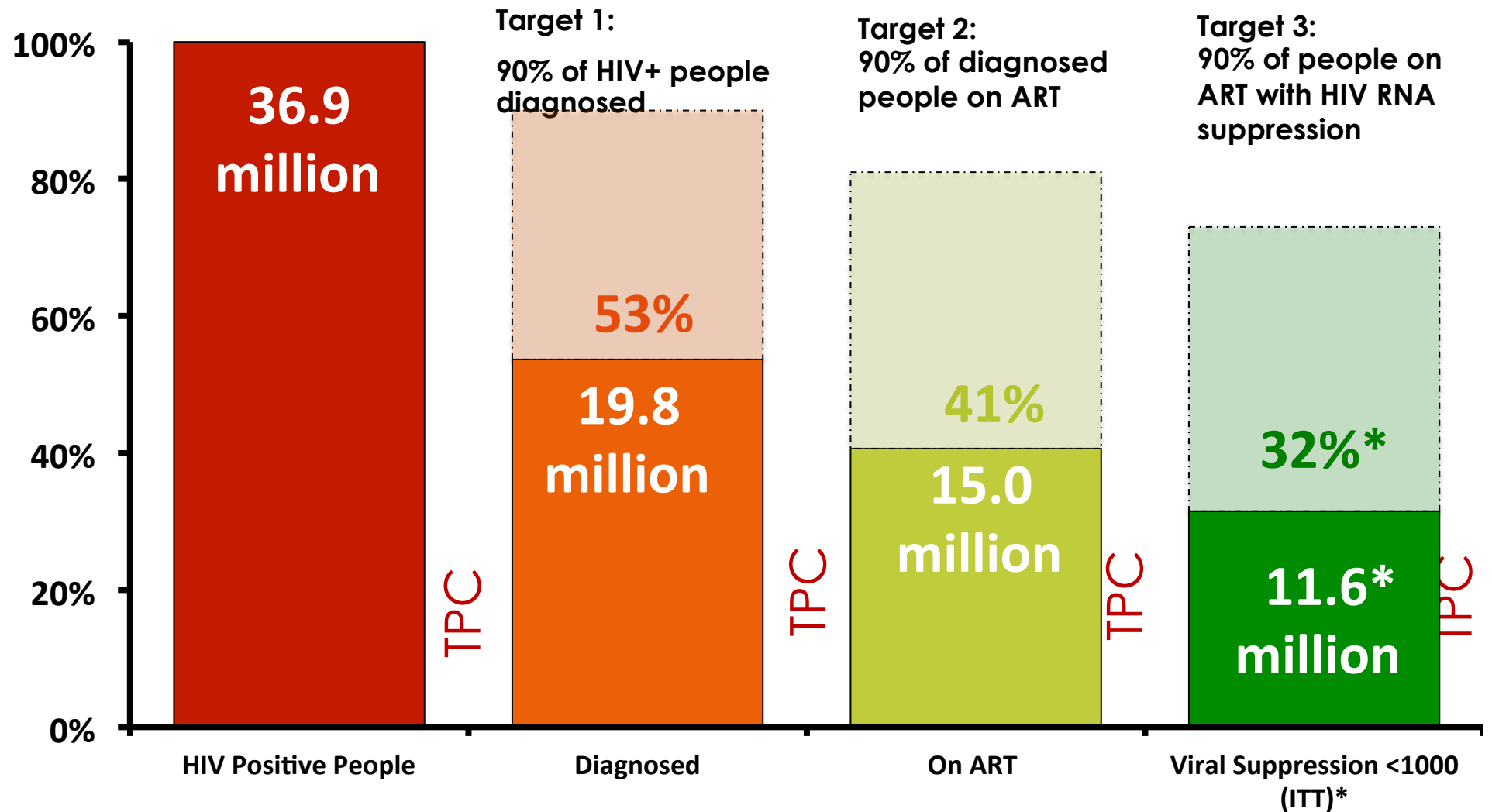
Partnership

“The relationship between patient and provider must be a partnership, in which both sides share their knowledge and understanding of HIV”

Trust

“Not only did patients need to trust providers, but providers also needed to trust their patients”

TOTAL PATIENT CARE VS BEYOND UNDETECTABILITY

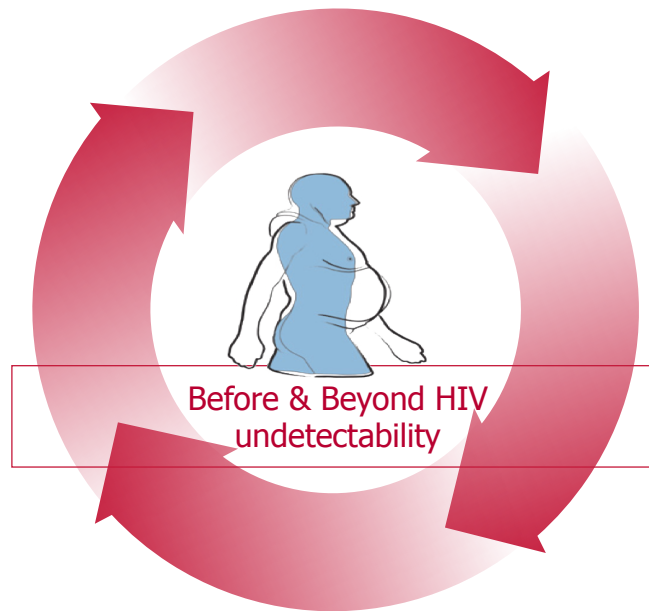


Ref: The Joint United Nations Programme on HIV/AIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. 2014; JC2684 (Numbers as of March 2015) How Aids Changed Everything. Fact Sheet. UNAIDS 2015. MDG 6: 15 YEARS, 15 LESSONS OF HOPE FROM THE AIDS RESPONSE July 2015.

TOTAL PATIENT CARE: a patient centered multidimensional assessment of HEALTH

How to **screen** for comorbidities:

1. Collect Modifiable and not modifiable risk factors
2. Estimate risk probability with algorithms
3. Evaluate patient unitability with markers of subclinical disease



How to **treat** comorbidities:

1. Get HIV undetectability
2. Reactive or pre-emptive ARV switch
3. Treat risk factors or existing comorbidities
4. Empower the patients for life style changes

Case 1

ModenaB “Gennaro”

The skeleton

What is it?

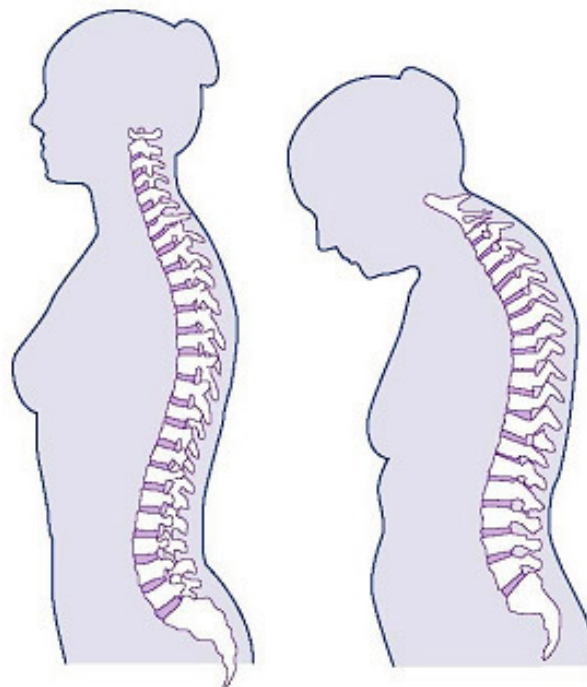
- Framework that supports your body, protects your organs
- Adult skeleton has 206 bones
- Entire skeleton is 'remodeled' every ten years

What is it made of?

- A collagen matrix, mineral crystals and living bone cells (osteocytes, osteoblasts and osteoclasts)
- Bones have a cavity containing bone marrow. Red bone marrow produces blood cells
- Bone is either spongy or compact-compact bone is hard and provides an outer protective shell

What is osteoporosis?

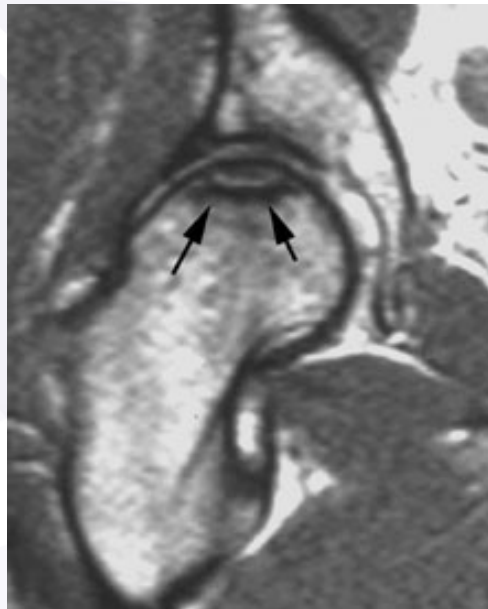
- Osteoporosis is a condition where the bones lose mass and structure, leading to weakness and increased risk of fracture. Fractures are the important and only clinical consequence of osteoporosis.



What is osteonecrosis?

Osteonecrosis = bone death due to poor blood supply, can lead to joint replacement, often very painful.

This is a rare condition.



What is Vitamin D?

- Adequate vitamin D is essential for bone health
- Low Vitamin D levels are very common
- Main source of Vitamin D is sunlight
- Blood tests can check for Vitamin D levels
- Vitamin D deficiency can be corrected by exposure to sunlight and/or Vitamin D supplements

What is osteomalacia?

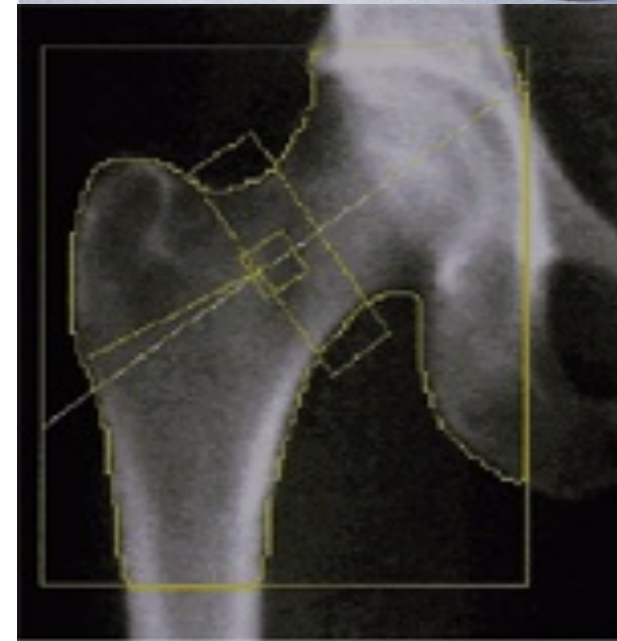
- Often caused by Vitamin D deficiency
- In children it is known as rickets
- Osteomalacia may cause bone pain and may be associated with fractures
- Has been linked to kidney abnormalities such as Fanconi syndrome, though would likely take years to develop
- Very rare

Does my gender affect my risk of fracture?

- Over the age of 50...
 - 1 in 2 women will have an osteoporotic fracture during their remaining lifetime
 - 1 in 5 men will have an osteoporotic fracture during their remaining lifetime

What is a bone scan?

- DXA stands for Dual X-ray absorptiometry
 - DXA measures X-ray absorption by bones and gives a value for bone mineral density (BMD)
- Measurements are usually made in the spine and the hip
- Bone Mineral Density is used to predict fracture risk
- Non-invasive
 - Takes 20 minutes
 - No needles
 - No tunnels
 - Low radiation (less than being outside for a day)



Calculating your fracture risk

- Your doctor can help you do this using www.shef.ac.uk/FRAX

The screenshot shows the FRAX WHO Fracture Risk Assessment Tool interface. The header includes the FRAX logo and navigation links: HOME, CALCULATION TOOL, PAPER CHARTS, FAQ, and REFERENCES. A language selection dropdown is visible. The main heading is 'Calculation Tool'. Below this, a message asks the user to answer questions to calculate the ten-year probability of fracture with BMD. The form includes a country selection (UK), a name/ID field, and a questionnaire with 12 items. Items 1-4 are demographic: 1. Age (between 40-90 years) or Date of birth (with separate fields for Y, M, D); 2. Sex (Male/Female); 3. Weight (kg); 4. Height (cm). Items 5-12 are clinical: 5. Previous fracture; 6. Parent fractured hip; 7. Current smoking; 8. Glucocorticoids; 9. (unlabeled, likely falls); 10. Secondary osteoporosis; 11. Alcohol 3 or more units per day; 12. Femoral neck BMD (g/cm²) with a 'Select DXA' dropdown. 'Clear' and 'Calculate' buttons are at the bottom right. On the left, there are weight and height conversion tools with 'convert' buttons.

- If your fracture risk is high, your doctor may recommend treatment
- (Frax is only validated for post menopausal women and men aged 50 or above)

Age and fracture risk

- As you get older, your risk of fracture is higher for any given BMD
 - People fall over more when they get older
 - There may also be changes in composition of your bone as you get older
- For a BMD at the threshold of osteoporosis the likelihood of fracture in the next ten years is approximately 5% for a 50 year old woman and over 30% for an 80 year old woman

Age and fracture risk

Modifiable

- Low body mass index
- Use of oral glucocorticoids (steroids)
- Secondary causes of osteoporosis
- Current tobacco smoking
- Daily intake of alcohol >3 units
- Bone mineral density (measured by DXA)

Non-modifiable

- Age
- Gender
- Prior low trauma fracture
- Parental history of hip fracture

Risk factors used in the calculation of 10-year risk of fracture

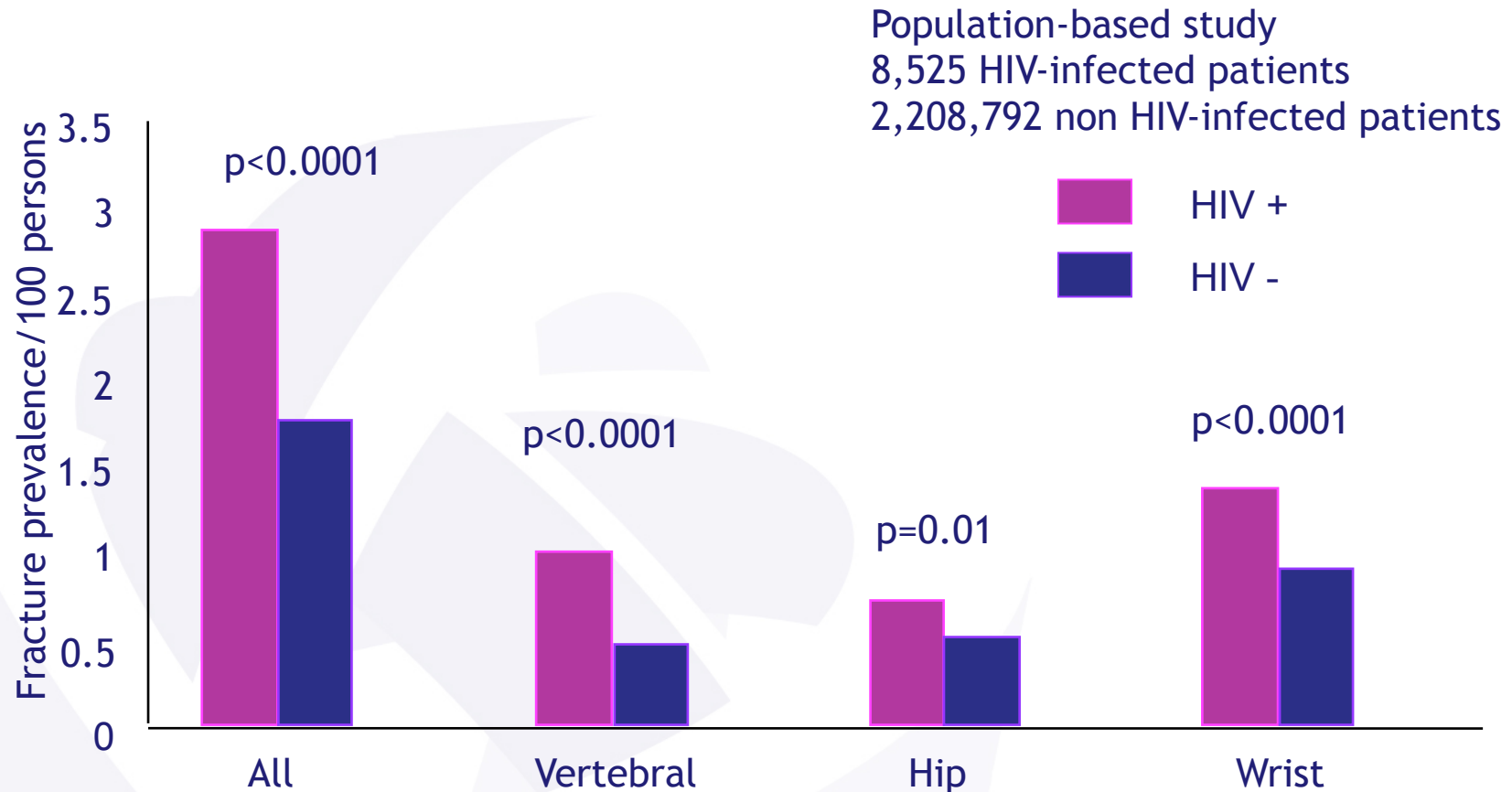
- Age (increasing)
- Gender (female > male)
- Low body mass index
- Prior low trauma fracture
- Parental history of hip fracture
- Use of oral glucocorticoids (steroids)
- Secondary causes of osteoporosis
- Current tobacco smoking
- Daily alcohol intake of > 3 units
- Bone mineral density (measured by DXA)

HIV and Bone Disease

HIV and bone disease

- How common is it?
- How does it develop?
- How is it assessed and diagnosed?
- How can it be managed?

People with HIV are at greater risk of fractures



Anti-retroviral therapy and bone loss

- Data are conflicting with bone loss, stable bone mass and increased bone mass all reported in treated patients
- Many studies have been small
- Some studies indicate higher prevalence of bone loss in people treated with protease inhibitors than other classes
- Specific association between NRTIs, especially NtNRTI, and Fanconi syndrome

What are the possible risk factors for osteoporosis in HIV +ve people?

Modifiable

- Low body mass index
- Hypogonadism (sex hormone deficiency)
- Infection/inflammation
- Low Vitamin D levels
- Smoking
- Heavy alcohol use

Potentially modifiable

- Anti-retroviral therapy

HIV and bone: what tests can be done?

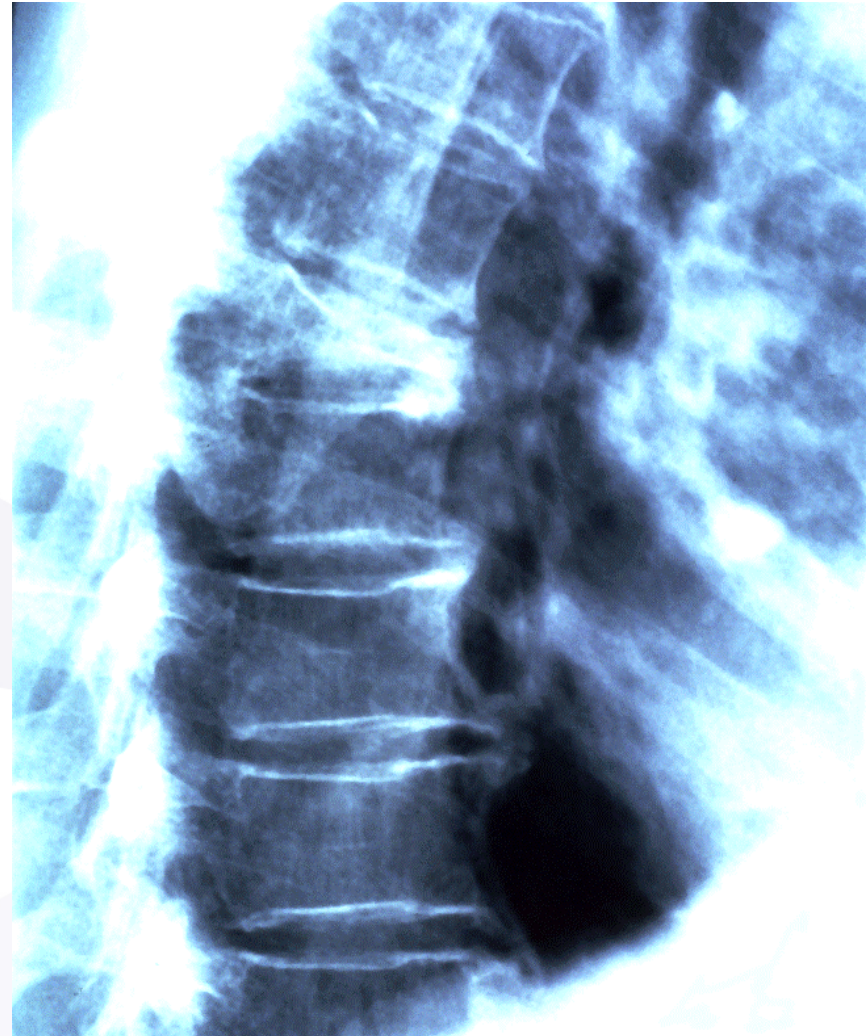
- Bone function tests (serum calcium, phosphate and alkaline phosphatase)
- Serum vitamin D and parathyroid hormone
- Serum testosterone (men)
- Bone scan (DXA)
- X-ray of the spine
- Tests to exclude other causes of osteoporosis

Management of osteoporosis: general measures

- Good diet with maintenance of normal body weight
- Adequate calcium intake (around 1g/day), dietary or as supplement
- Vitamin D supplementation if required (1,000 to 2,000 IU/day)
- Stop smoking and avoid excessive alcohol use
- Encourage physical activity
- Avoid falls

Treatments for osteoporosis

- Bisphosphonate drugs
- Hormone Replacement Therapy
- Calcium and vitamin D

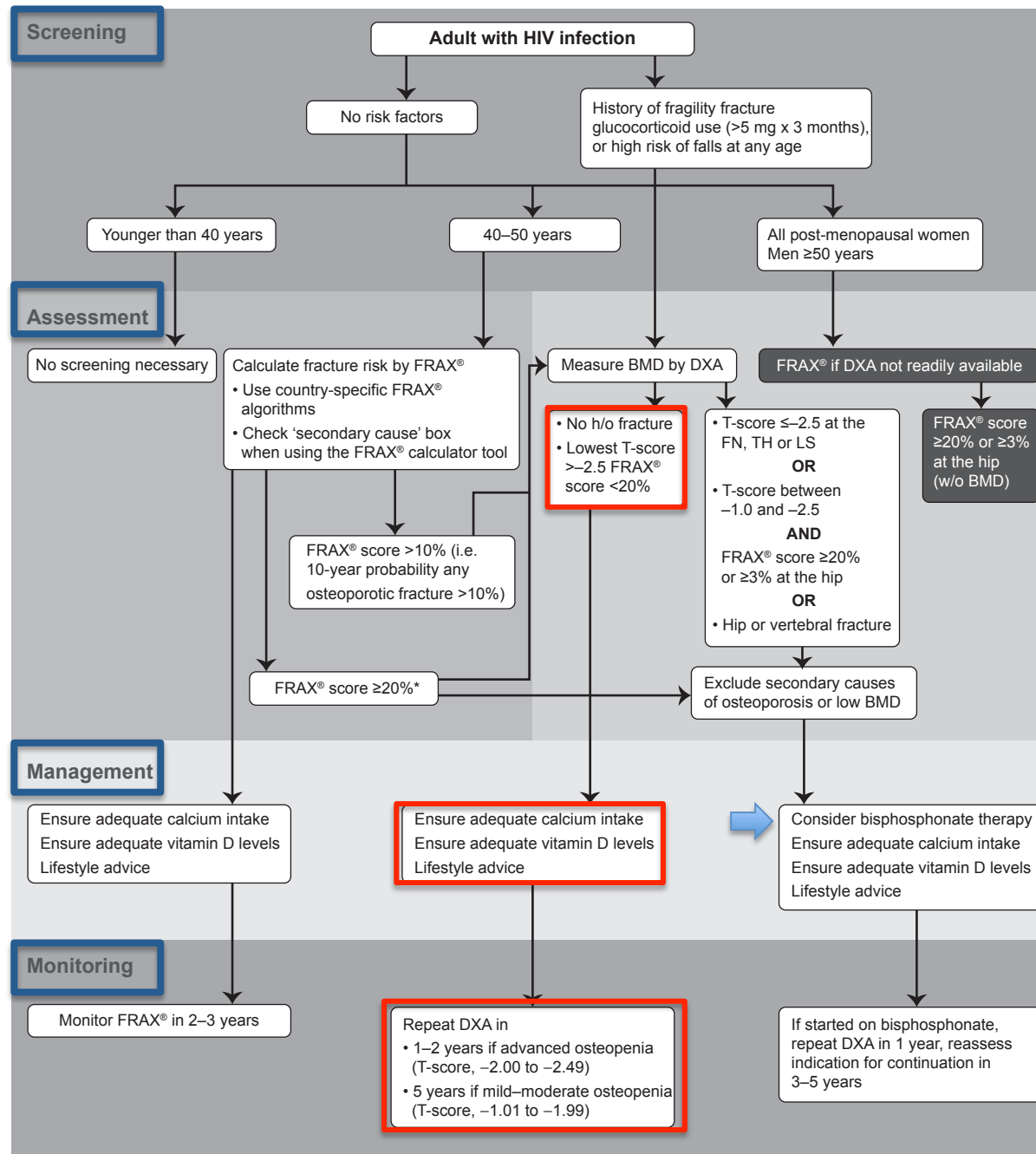


Recommendations for Evaluation and Management of Bone Disease in HIV

Todd T. Brown,¹ Jennifer Hoy,² Marco Borderi,³ Giovanni Guaraldi,⁴ Boris Renjifo,⁵ Fabio Vescini,⁶ Michael T. Yin,⁷ and William G. Powderly⁸

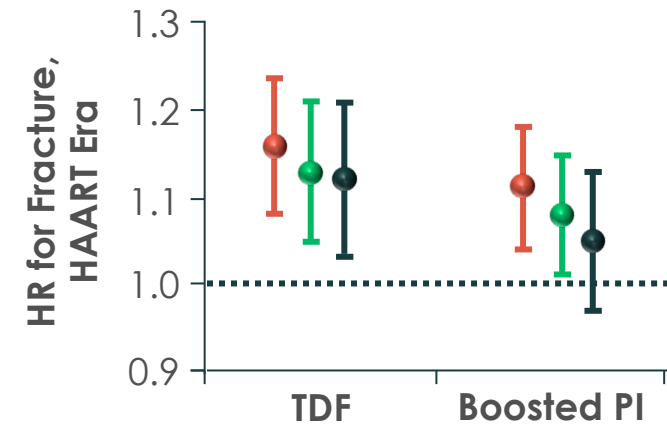
¹Division of Endocrinology, Diabetes and Metabolism, Johns Hopkins University School of Medicine, Baltimore, Maryland; ²Department of Infectious Diseases, Alfred Hospital and Monash University, Melbourne, Australia; ³Infectious Diseases Unit, Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, and ⁴Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena, Italy; ⁵Global Medical Affairs Virology, Global Pharmaceutical Research and Development, AbbVie, North Chicago, Illinois; ⁶Endocrinology and Metabolism Unit, University Hospital "Santa Maria della Misericordia," Udine, Italy; ⁷Department of Medicine, Columbia University Medical Center, New York, New York; and ⁸Division of Infectious Diseases, Washington University School of Medicine, St Louis, Missouri

Thirty-four human immunodeficiency virus (HIV) specialists from 16 countries contributed to this project, whose primary aim was to provide guidance on the screening, diagnosis, and monitoring of bone disease in HIV-infected patients. Four clinically important questions in bone disease management were identified, and recommendations, based on literature review and expert opinion, were agreed upon. Risk of fragility fracture should be assessed primarily using the Fracture Risk Assessment Tool (FRAX), without dual-energy X-ray absorptiometry (DXA), in all HIV-infected men aged 40–49 years and HIV-infected premenopausal women aged ≥ 40 years. DXA should be performed in men aged ≥ 50 years, postmenopausal women, patients with a history of fragility fracture, patients receiving chronic glucocorticoid treatment, and patients at high risk of falls. In resource-limited settings, FRAX without bone mineral density can be substituted for DXA. Guidelines for antiretroviral therapy should be followed; adjustment should avoid tenofovir disoproxil fumarate or boosted protease inhibitors in at-risk patients. Dietary and lifestyle management strategies for high-risk patients should be employed and antiosteoporosis treatment initiated.



Cumulative use of TDF and/or boosted PIs and risk of osteoporotic fractures

- Retrospective analysis of 56,660 HIV-positive male veterans enrolled from 1988–2009
 - Osteoporotic fractures assessed from ICD-9 codes
- Cumulative use of TDF and/or boosted PI associated with higher risk in ART era, after controlling for risk factors
 - Highest risk with concomitant use
- Cumulative use of LPV/r also associated with higher fracture risk
 - PI association limited to LPV/RTV
- Cumulative use of ABC, thymidine analogues, NNRTIs not associated with higher risk
- Limitations
 - Retrospective cohort study
 - BMD data not available
 - Fractures not verified to be osteoporotic



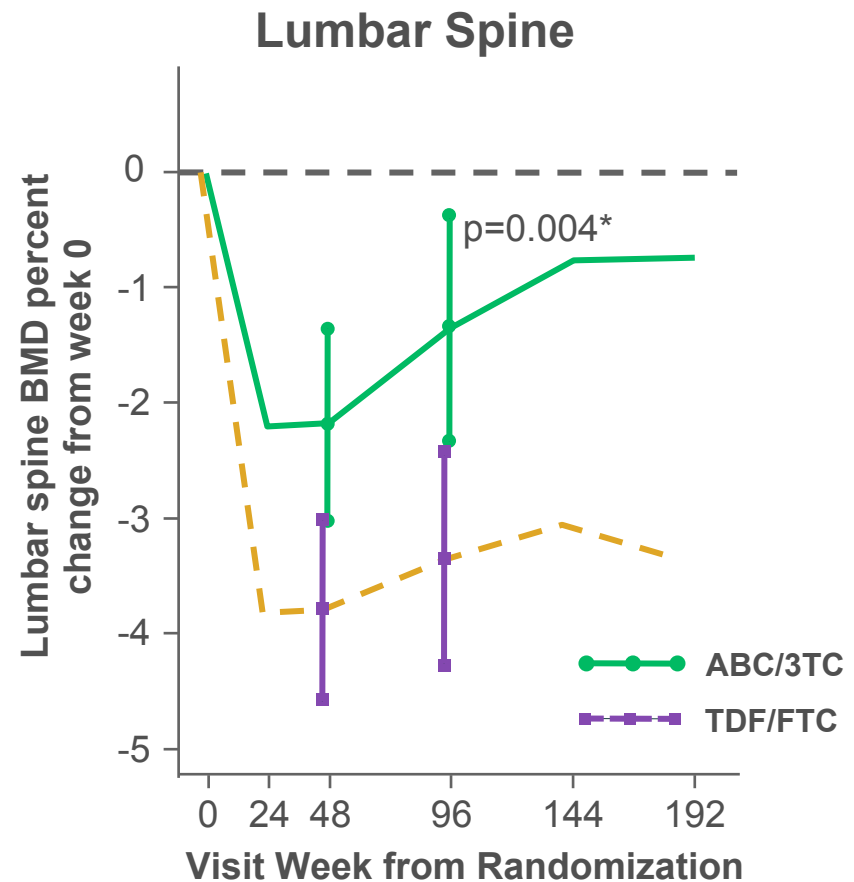
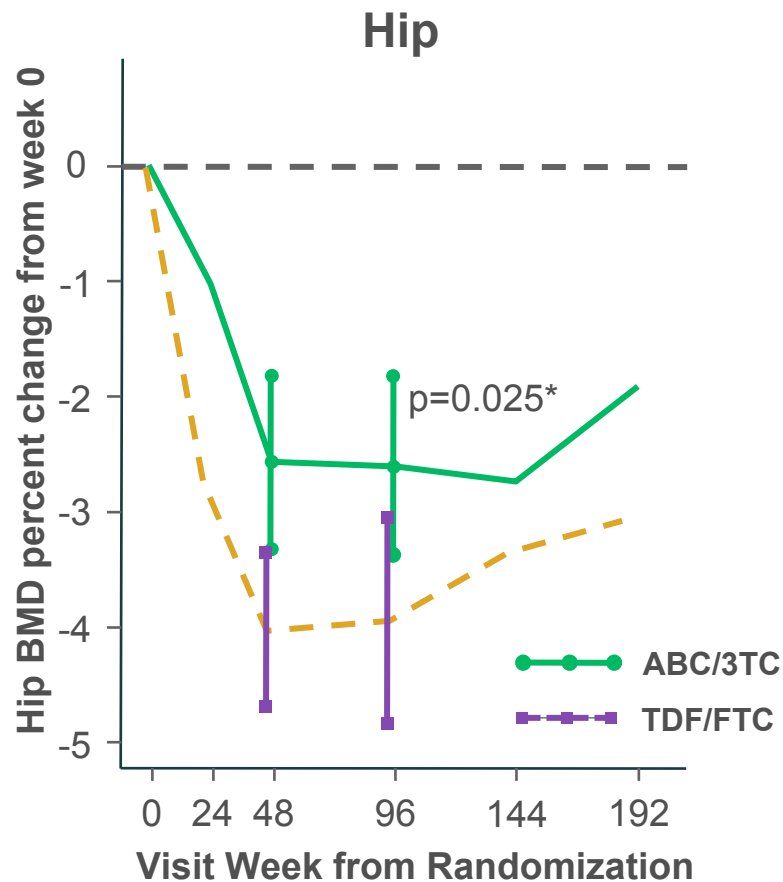
● Univariate analysis

● Model 1: Controlled for effects of CKD, age, race, smoking, DM, BMI, and HCV

● Model 2: Controlled for covariates in Model 1 plus concomitant exposure to ARVs



ACTG 5224s: Mean (95% CI) percent change in lumbar spine BMD and hip BMD (ITT) - ABC/3TC vs TDF/FTC



No. of subjects

TDF/FTC	126	109	105	96	85	53
ABC/3TC	128	119	104	99	79	54

*linear regression

McComsey GA, et al. J Infect Dis. 2011;203:1791–801.

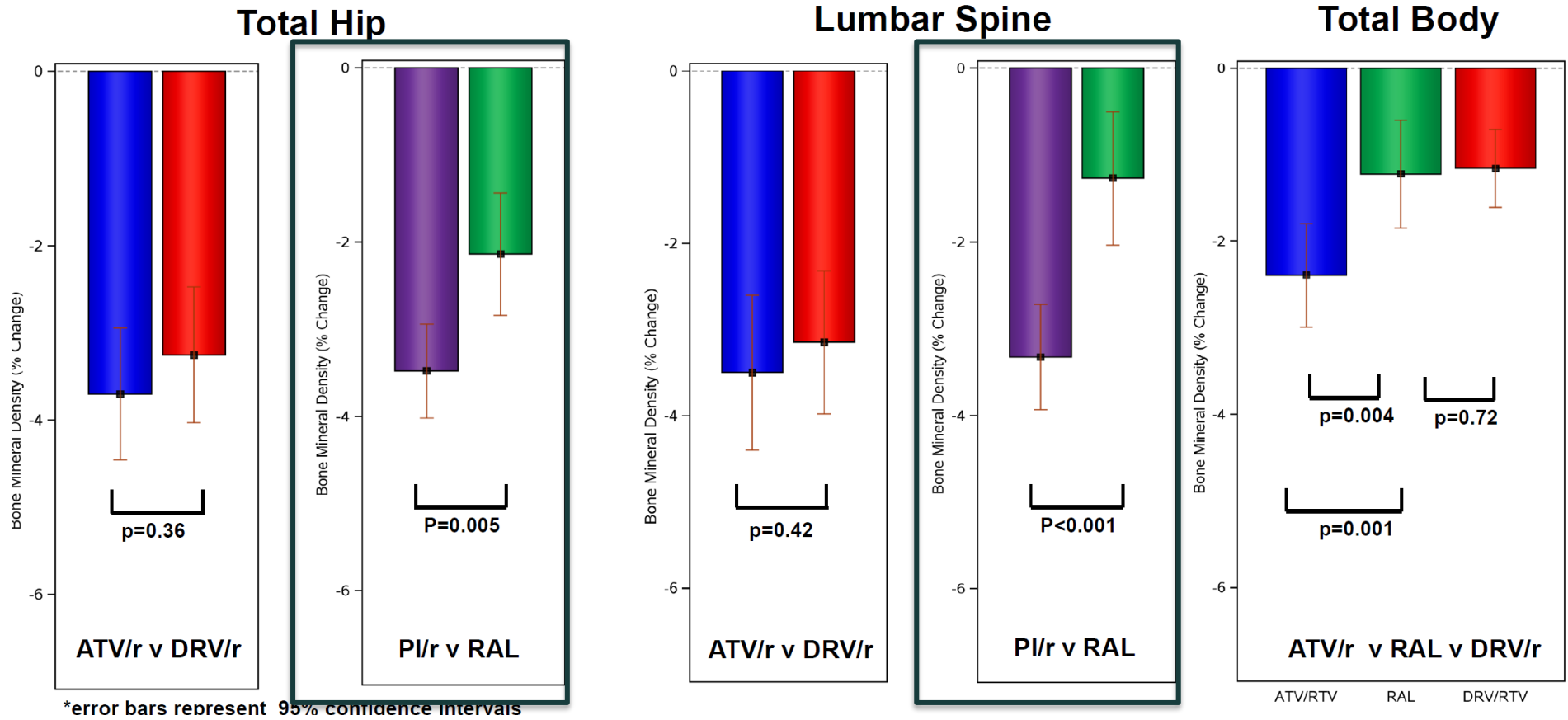
No. of subjects

TDF/FTC	128	111	106	97	87	53
ABC/3TC	130	122	106	101	80	53

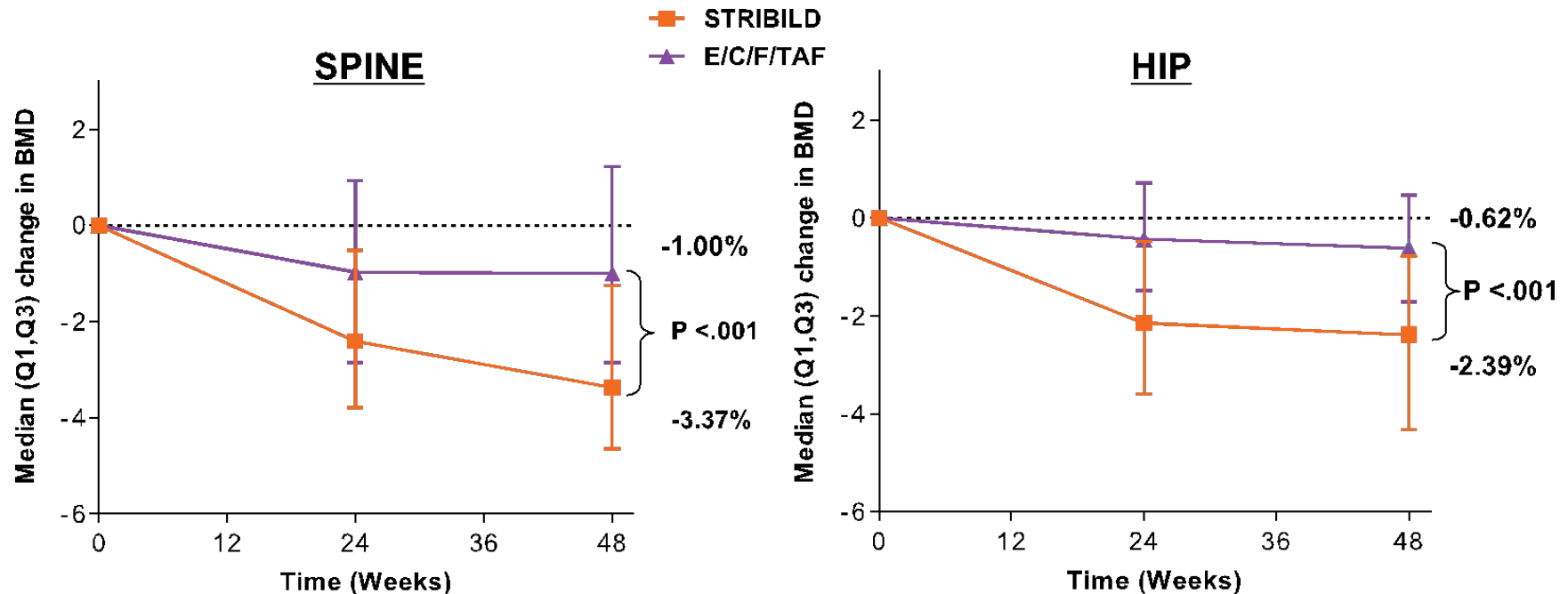


Bone Mineral Density at 96w. Substantial less impact of RAL on BMD

Mean Percentage Change in BMD over 96 Weeks by Treatment Regimen*



Changes in Spine and Hip BMD at Week 48



Significantly less spine and hip BMD loss with E/C/F/TAF vs Stribild

Percentages of subjects with no change in BMD at week 48

Spine BMD: 37% E/C/F/TAF vs 11% Stribild (p <0.001)

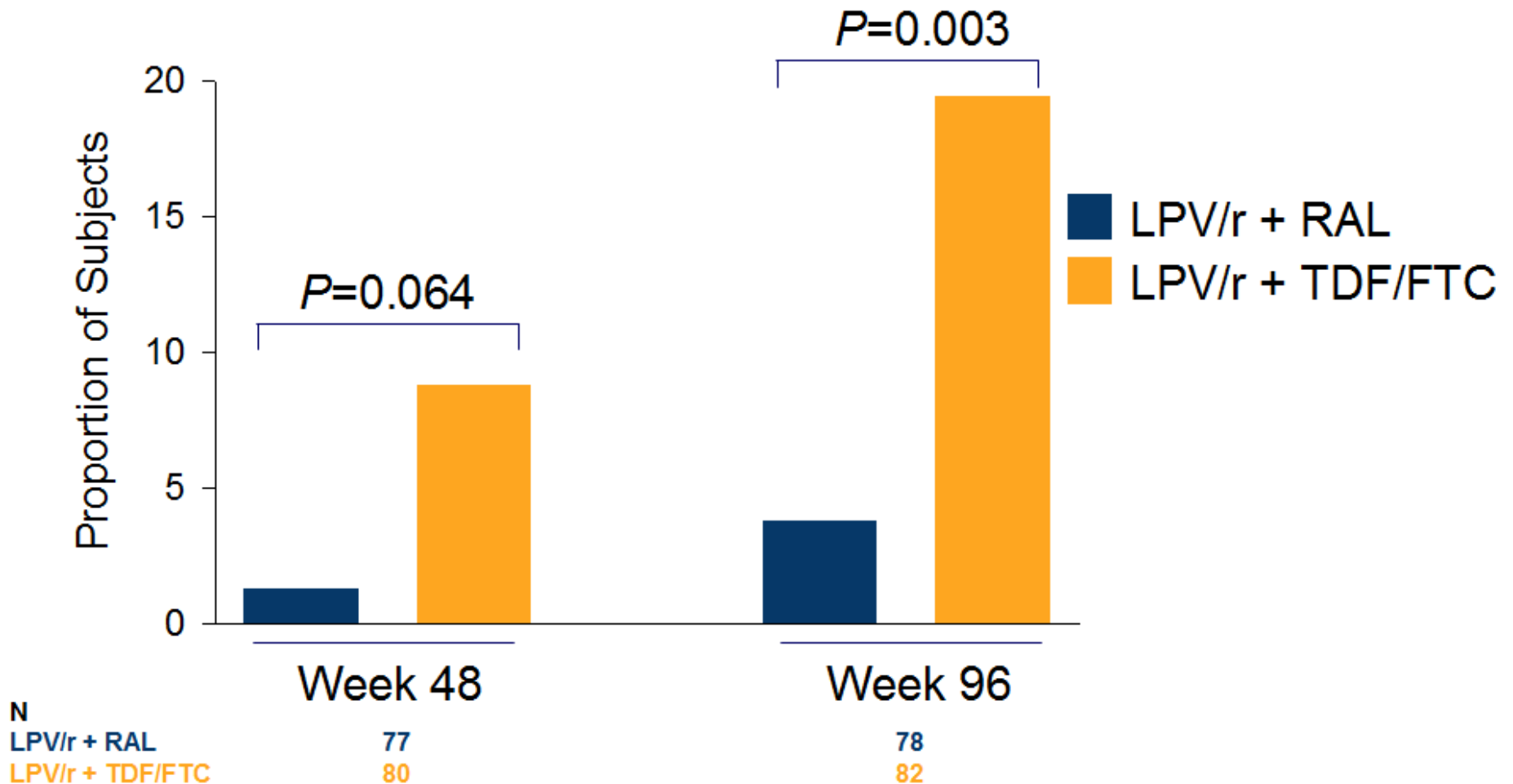
Hip BMD: 32% E/C/F/TAF vs 7% Stribild (p <0.001)

There were no fragility fractures in either group

PROGRESS:



Proportion of Subjects with $\geq 5\%$ Decrease from Baseline in Total Bone Mineral Density



P-values calculated using Fisher's exact test

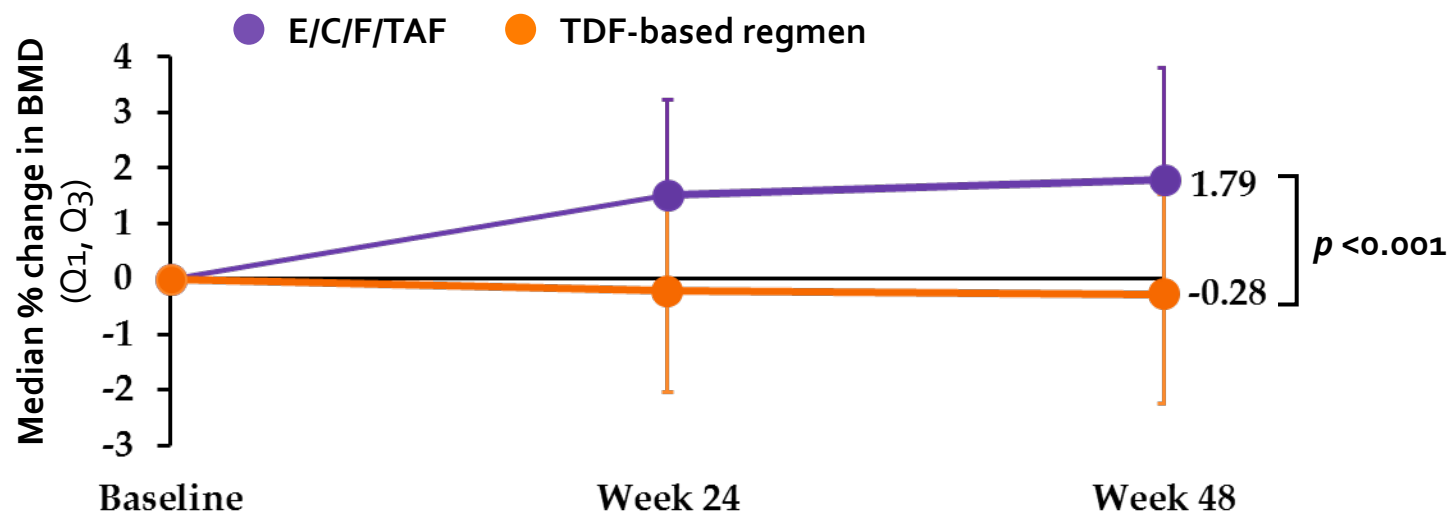
July 14, 2011

Switching TDF to TAF

DXA scan results: Spine BMD



Change from baseline to week 48
All participants (N=1,369)



- Regardless of prior treatment regimen, differences between arms were statistically significant
- More than 2% difference between the arms at Week 48

Conclusions

- HIV infection is associated with an increased risk of osteoporosis and fracture
- There are many reasons why osteoporosis develops in people with HIV and a number of risk factors are modifiable. The contribution of ARVs is still under debate
- Bone health should be assessed in all HIV positive people
- Treatment with bone protective therapy should be considered in patients with fracture, after exclusion of osteomalacia, and in those with a high risk of fracture



PROGRAMMA SEMINARIO 2016

COSA PUÒ ACCADERE DURANTE UNA VISITA DI CONTROLLO?

La consapevolezza del rischio e la buona gestione della comorbidità possono condurre a un miglioramento della qualità della vita intervenendo sugli stili di vita?



Giovanni Guaraldi
Università di Modena



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Case 2

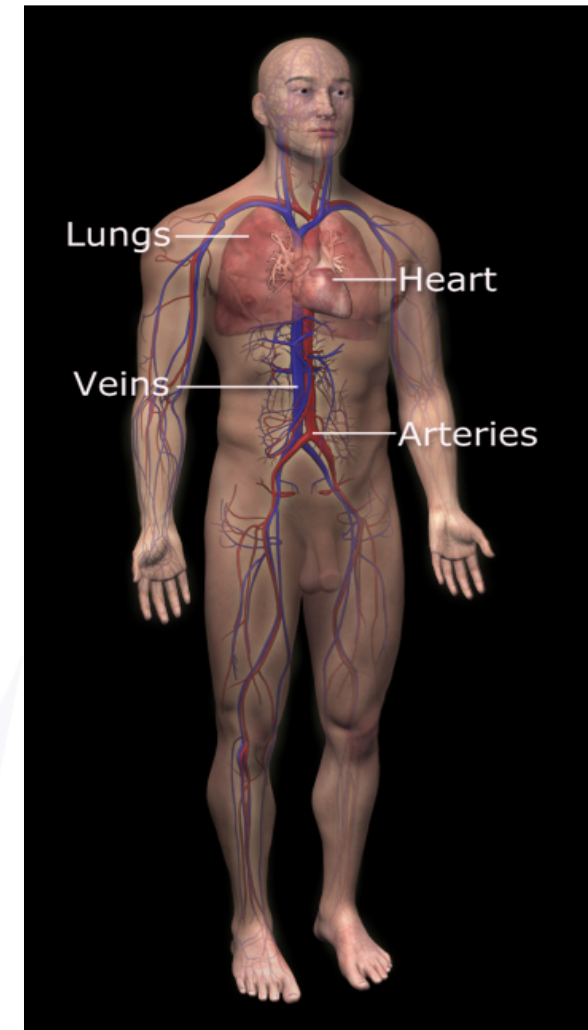
ModenaH “PIETRO”

In this presentation

- What is the cardiovascular system (CVS)?
- What is heart disease (HD)?
- Who is affected by HD?
- Why is it important to know about it?
- What are the causes?
- What tests can be done to check your heart?
- What can you do to keep your heart healthy?

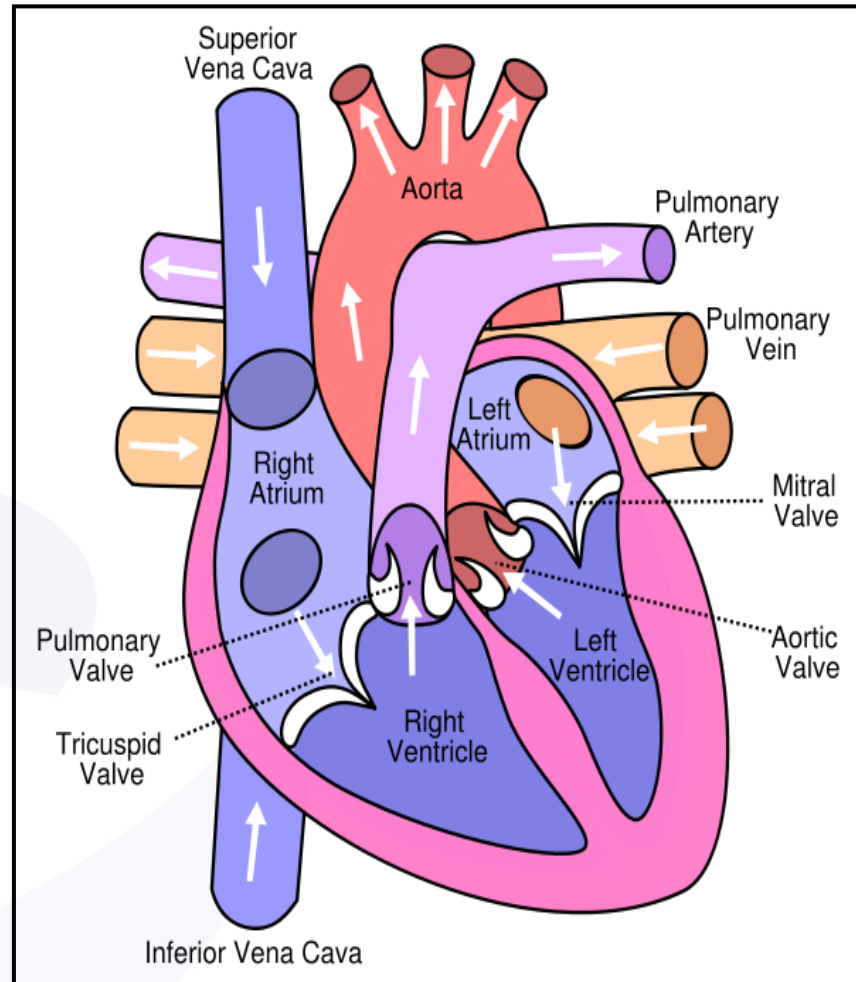
What is the cardiovascular system (CVS)?

- Function: it maintains the circulation of blood to all parts of our body to deliver nutrients, remove waste and exchange oxygen and carbon dioxide
- Main organs: heart, blood vessels (arteries and veins)



The Heart

- A muscle, located in the chest between the two lungs, slightly to the left and protected by the rib cage
- It pumps blood to the various parts of our body by repeated rhythmic contractions
- A normal heart beat is 60-80 beats per minute



What is heart disease (HD)?

Heart disease is also known as:

- Coronary heart disease (CHD)
- Cardiovascular disease (CVD)
- It covers all diseases that affect the heart and circulatory system including:
 - Heart attack, also known as myocardial infarction (MI)
 - Angina
 - Stroke
- HD is the most common cause of death in the developed world

Who is affected by heart disease?

- As we get older the heart muscle begins to lose its function
- Factors which affect the likelihood of developing heart disease (known as risk factors) are:
 - Family history of early heart disease
 - Pre-existing heart disease
 - Sex
 - Smoking
 - Unhealthy diet
 - Lack of exercise
 - Being overweight
 - High blood pressure

Why is it important to know about heart disease?

- Heart disease is a dangerous, and potentially lethal condition
- The HIV infected population in the developed world is aging and therefore at increased risk of CHD
- HIV infection increases the risk of heart attack
- Some ARVs have been shown in studies to increase the risk of MI
- Some life-style habits, more common to people with HIV, increase the risk of heart disease
- Interventions and life-style changes can reduce the risk of heart disease

What are the causes of heart disease?

Modifiable

- Smoking
- High cholesterol
- High triglycerides
- High blood pressure, especially systolic
- High levels of sugar in blood
- Diabetes and insulin resistance
- Diet and exercise
- Weight
 - e.g. a BMI > 30 kg/m²

Non-modifiable

- Older age
- Sex
- Family history
- Previous CHD
- HIV

Potentially modifiable

- Lipodystrophy (dyslipidaemia and body shape changes)

What tests do the doctors use to check for HD?

- Physical assessment

- Smoking
- Blood pressure
- Weight, height and waist to hip ratio
- Blood tests
 - Cholesterol
 - Total
 - Differential
 - Triglycerides
 - Glucose

- Medical history

- Previous MI or CHD
- Family history
- Level of fitness-physical activity

- Other types of test, examinations

- Chest x-ray
- ECG
- Angiogram
- MRI scan

How often will these tests be done?

- **At each clinic visit**

- Weight
- Blood pressure
- A urine test (dip stick) for glucose

- **Just before, one month after starting/changing treatment or 6-monthly to yearly (if stable)**

- Total cholesterol, HDL, LDL and triglycerides

- **Before starting or changing therapy then yearly**

- A cardiovascular risk assessment
 - Modified Framingham score - this calculation gives you an estimated risk of you developing CVD over the next 10 years

What do my results mean?

- Blood pressure
 - There is an upper reading (systolic) and a lower reading (diastolic)
 - Normal result is 120/80
 - Increases slightly with age
- Blood
 - Cholesterol
 - Triglycerides



What do my results mean? (i)

- Fasted triglycerides:
 - Normal <2.2 mmol/l
 - Borderline 2.2-4.4 mmol/l
- Cholesterol:
 - A total cholesterol level is usually measured
 - <4 mmol/l is usually considered as good
 - >5mmol then a further test will indicate the levels of the 'good' cholesterol known as high density lipoprotein (HDL) and 'bad' cholesterol known as low density lipoprotein (LDL) cholesterol



Target levels keep changing

What do my results mean? (ii)

- **LDL cholesterol**
 - Target level: < 2 mmol/l
 - Increased risk of CVD > 3 mmol/l
- **HDL cholesterol**
 - Target level: over 0.9 mmol/l

What do my results mean? (iii)

- Models available to calculate risk of developing HD
 - These can be found on the internet
 - Blood pressure
 - Smoking /non smoking
 - Cholesterol (TC:HDL)
 - Age
- Framingham score
 - A calculation of your 10 year risk of myocardial infarction and coronary death
 - Risk results come as:
 - Low, average, high or
 - % risk of developing over next 10 years
- Limitations
 - Does not take in to account HIV status
 - Not applicable to all races and socio-economic status and younger age

Blood pressure (mmHg)					
Other risk factors, OD or disease	Normal SBP 120-129 or DBP 80-84	High normal SBP 130-139 or DBP 85-89	Grade 1 HT SBP 140-159 or DBP 90-99	Grade 2 HT SBP 160-179 or DBP 100-109	Grade 3 HT SBP \geq 180 or DBP \geq 110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1-2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors, MS, OD or diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Established CV or renal disease	Very high added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

Stratification of CD Risk in four categories

Do antiretrovirals affect my heart?

- The SMART study showed that being on ARV therapy and having an undetectable viral load (VL) is protective for heart disease, compared to not being on ARVs and having a detectable VL
- Benefits of ARVs far outweigh the possible risks
- Some ARVs affect the blood lipids (increases)
 - These include some of the protease inhibitors
- A large study of cohort of patients known as the D:A:D study reported an increase of risk of cardiac events such as heart attack (myocardial infarction or MI) with certain drugs
 - These drugs will still be used, but with caution and careful monitoring

What will my doctor do if I have HD or I am at a high risk?



- Your doctor will advise you to change your lifestyle to:
 - Give up smoking
 - Reduce your fat intake from your food, alcohol intake, and salt
 - Increase your intake of fruit and vegetables and oily fish
 - Increase your level of exercise and fitness
 - Reduce your stress levels
- You may be prescribed medicines to:
 - Decrease your blood pressure (antihypertensives)
 - Decrease your lipids (cholesterol and triglycerides reducing agents such as statins, fibrates, omega-3 fish oil, niacin)
 - Control your blood sugar
- You may be started on an ART, associated with a lower risk
- One or more medicines in your cART may be changed

Are there any interactions between my ARVs, CVD drugs and supplements / herbs that I take?

- Before you start any new medicine check with your doctor or pharmacist or treatment counsellor that it is safe to do so
 - This should include also a discussion about any:
 - non-prescription medicines
 - Supplements
 - herbs and herbal preparations
 - recreational drugs
- Some drugs must not be used together and some require a dose modification

What things should I tell my doctor?

- If you had heart disease in the past
- If a blood relative of yours had heart disease
- Whether you have any liver disease, kidney disease, diabetes, blood clotting problems or other medical conditions
- All prescription, non-prescription, recreational drugs, as well as herbs, supplements, potassium and potassium containing salt substitutes that you are taking at the moment
- How much alcohol you drink - per day / per week
- If you smoke or have ever smoked
 - the number of cigarettes per day

What can I do to improve my heart health and avoid CVD?

- **The important things to do are:**

- Find out what your estimated CV risk is
- Review your lifestyle and risks and make changes



- **If you smoke**

- To stop smoking is the number one thing that you can do to reduce your risk
- It is thought that the dangerous effects of smoking on your heart are reversible
- Ask your doctor, nurse or pharmacist or peer counsellor about programmes or means available to help you stop smoking
 - This includes agents such as nicotine patches, lozenges and medicines to stop you craving for nicotine

Summary

- The incidence of HD in PLWHs is increasing
- The risk factors for developing HD are known
- Make sure you know what your risk is
- You can make changes to your lifestyle to reduce your risk
- Your doctor will check your blood to monitor the lipids, and sugar in your blood as well as your blood pressure
- Treatment with medicines can be used to control blood sugar levels, lipids and your blood clotting