Primary Care for People Living with HIV

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Disclosures

- The speaker does not have any financial relationships with commercial entities to disclose.
- The speaker will not discuss any off-label use or investigational product during the program.

This slide set has been peer-reviewed to ensure that there are no conflicts of interest represented in the presentation.

What does high quality primary care look like to you?

Learning Objectives

- Appreciate the key to great primary CARE!
- Compare and contrast different models for providing primary care to people living with HIV
- List important drug-drug interactions and complications seen with antiretroviral therapy (ART)
- Describe how HIV and ART impact screening, monitoring and management of chronic medical conditions
- Describe how HIV changes preventive care: cancer screening, immunizations

Background

- Antiretroviral therapy (ART) has dramatically altered the natural history of HIV
- Near normal life expectancy
  - Greater than 50 percent of deaths in individuals infected with HIV receiving ART are now related to conditions other than AIDS
- **Primary Care Providers and Professionals needed!**

1. PLoS One. 2013;8(12):e81355. Epub 2013 Dec 18.
2. AIDS. 2002;16(12):1663

How and where?

Models of Care

- Fenway Community Health
  - Managed by generalists trained in HIV care
- UF Health
  - Co managed primary care and ID
- Others
  - ID only, managing HIV and all other issues
  - Telehealth
  - Traveling Infectious Diseases physician

Physician Specialization and the Quality of Care for Human Immunodeficiency Virus Infection

MAJOR ARTICLE

Differences between Infectious Diseases–Certified Physicians and General Medicine–Certified Physicians in the Level of Comfort with Providing Primary Care to Patients

Arch Intern Med. 2005;165:1133-1139
Clinical Infectious Diseases 2005; 41:738–43

The Key to Great Primary Care

"The treatment of a disease may be entirely impersonal; ***the care of a patient must be completely personal***. The significance of the intimate personal relationship between physician and patient cannot be too strongly emphasized, for in an extraordinarily large number of cases both diagnosis and treatment are directly dependent on it, and the failure of the young physician to establish this relationship accounts for much of their ineffectiveness in the care of patients."

- Francis Peabody MD, *The Care of the Patient* (JAMA, 1927)

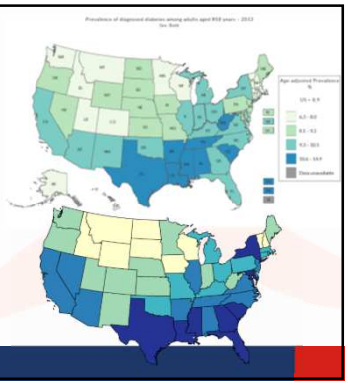
Behavior Change

- Behavior change is **personal**
- The primary care provider is optimally positioned to provide the collaborative, supportive, nurturing environment to promote behavior change

Breakout Session Case Review

Chronic Disease

- Cardiovascular Disease
- Dyslipidemia
- Diabetes mellitus
- Osteoporosis
- Mental Health
- Substance Abuse



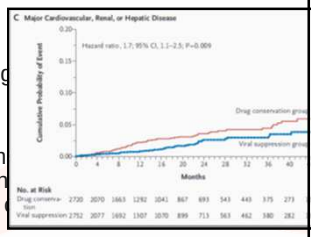
Question?

- HIV increases your risk of coronary artery disease and diabetes?
  - True
  - False
  - Not Sure

Cardiovascular Disease

Table 4. Time-Updated Analyses Assessing the Association of HIV-1 RNA and CD4 Cell Count Values and the Risk of AMI in Separate Models[a]

Category	HR (95% CI)	*P* Value[b]
HIV-1 RNA		
Uninfected	1 [Reference]	.05
≥500	1.75 (1.40-2.18)	
<500	1.39 (1.17-1.66)	
CD4 cell count		
Uninfected	1 [Reference]	.04
<200	1.88 (1.46-2.40)	
≥200	1.43 (1.21-169)	

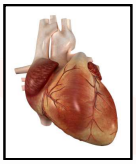


- Discontinuation of ART associated with higher risk

JAMA Intern Med. 2013;173(8): 614-622
N Engl J Med 2006; 355: 2283-96

Abacavir and CVD Risk

- Possible association between abacavir and increased risk of cardiovascular disease
- Increases with cumulative abacavir exposure



J Acquir Immune Defic Syndr 2015;69:413–421

Hypertension

- ART/HIV NOT felt to increase risk of hypertension
- Treat aggressively given increased risk of CVD risk
- Beware: Drug-Drug interaction
  - Dihydropyridine calcium channel blockers and Pis/Cobicistat
    - Example: Amlodipine or Nifedipine

Dyslipidemia

- Lower HDL and LDL levels, and greater triglyceride levels, independent of any exposure to ART
- **ART Impact:**
  - PI Raise LDL, TG
  - Ritonavir boosted PI regimens (eg atazanavir/darunavir) tend to have less unfavorable effects
  - Efavirenz associated with increases in the HDL, LDL, TG
  - NRTI limited impact on lipids
  - Integrase inhibitors are also associated with favorable lipid profiles

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Diabetes

- Glucose intolerance/diabetes are an important toxicity associated with PI/NRTI
- Unclear association with newer agents

Table 3. Incidence of Diabetes Mellitus Among 680 Men Between April 1999 and March 2003

Patient Group (n = 680)	No. of End Points	Person-years	Rate Per 100 Person-Years (95% CI)	Crude Rate Ratio* (95% CI)	Adjusted Rate Ratio* (95% CI)
Overall	38	1451.4	2.6 (1.9-3.6)	NA	NA
HIV seronegative	10	709.3	1.4 (0.8-2.6)	1	1
HIV infected not using HAART	4	236.3	1.7 (0.6-4.5)	NA	NA
HIV infected using HAART	24	505.8	4.7 (3.2-7.1)	3.32 (1.58-6.94)	4.11 (1.85-9.16)

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Arch Intern Med. 2005;165:1179-1184

What to do

ASSESS

- Fasting lipid levels: prior to ART, 6 and 12 months after initiation, annually if nl
- HgbA1c/fasting blood sugar: prior to ART and every 3 -6 months after initiation, annual if nl
- Measure blood pressure, waist circumference, body mass index
- Know your patient! smoking habits, diet, level of exercise activity
- Family history

Calculate

- American Heart Association CV Risk Calculator

Prevent and/or Treat

- Lifestyle modification
- Smoking cessation
- Aspirin
- Statin, Change ART Regimen
- Control blood pressure and blood sugar

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aidsinfo.nih.gov

Osteoporosis

- Higher rates of bone loss in patients with HIV
- Studies have shown possible link with ART (PIs, tenofovir)

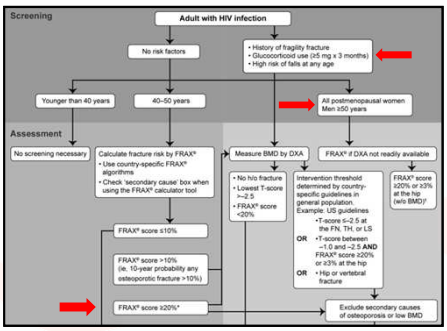
What to do

- screen postmenopausal women and men aged 50 years of age or older
- rule out secondary causes (ie. hypogonadism, vitamin D deficiency, hyperparathyroidism, and thyroid disease)
- **Treat:** calcium, vitamin D, weight bearing exercise, bisphosphonate therapy

AETC Southeast

Slide 19

ZM32 able to get a clearer shot of this table? A little blurry
Zoe Muller, 5/4/2017



Clinical Infectious Diseases 2015;60(8):1242–51

Mental Health and Substance Abuse

- A disproportionate number of people with HIV have substance abuse and/or psychiatric disorders
- Leads to disease progression secondary to poor adherence as well as increased risk of HIV/STI transmission

Mental Health and Substance Abuse

What to do

- Screen and aggressively treat psychiatric and substance use disorders
- **Depression** "PHQ 2"
  - Over the past two weeks have you been bothered by any of the following problems?
    - Little interest or pleasure in doing things
    - Feeling down or hopeless
- **Substance Abuse**
  - How many times in the past year have you had five (four for women) or more drinks in a day?
  - How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons?
- **Neurocognitive conditions**
  - Do you experience frequent memory loss (eg, do you forget the occurrence of special events, even the more recent ones, appointments, etc.)?
  - Do you feel that you are slower when reasoning, planning activities, or solving problems?
  - Do you have difficulties paying attention (eg, to a conversation, a book, or a movie)?

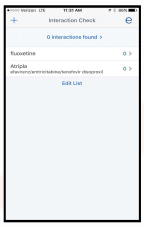
Breakout Session Case Review

Anti-Retroviral Therapy

- Even if not prescribing, the generalist should understand drug-drug interactions, complications and assess/counsel regarding ART adherence

Drug-Drug Interactions

- **Lists**
- **Interaction checker**
- **Ask an expert**

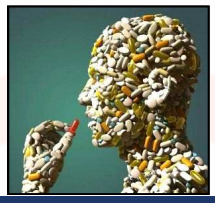


Question?

- Simvastatin can cause a dangerous interaction with which class of antiretrovirals?
  - Protease inhibitors
  - Nucleoside reverse transcriptase inhibitors
  - Non-nucleoside reverse transcriptase inhibitors
  - Integrase inhibitors
  - All of the above

Drug-Drug Interactions

- Statins
- Steroids
- Metformin
- Acid-Reducing Agents
- Herbs



Statins

- Lovastatin/Simvastatin **Contraindicated** with PIs and cobicistat; increases statin levels
- fluvastatin, pitavastatin, pravastatin least interaction
- atorvastatin, rosuvastatin use with caution with PIs and cobicistat

Start low and go slow!

Steroids

- Inhaled/Intranasal budesonide, fluticasone, mometasone do not coadminister with ***ritonavir and/or cobicistat.*** ***Beclomethasone is an alternative***
- Methylprednisolone, prednisolone, triamcinolone injections do not coadminister with ***cobicistat and/or ritonavir***
- Prednisone, dexamethasone use with caution with cobicistat and/or ritonavir

★ **Increased steroid levels = adrenal insufficiency and Cushing's syndrome**

Metformin

- Caution is advised when administering **dolutegravir** with metformin, as coadministration may increase exposure to metformin
- If these drugs are used in combination, the total daily dose of metformin must not exceed 1000 mg when starting, and close monitoring of blood glucose is recommended. Can increase dose if hyperglycemic
- When stopping dolutegravir, the metformin dose may need to be increased

Start low and go slow!

Acid-Reducing Agents

Rilpivirine with Acid-Reducing Agents	
Antacids	Avoid 2 hours after and 4 hour before
H2 receptor Antagonists	Give 12 hours before or 4 hours after
Proton Pump Inhibitors	Contraindicated

Adapted from DHHS Guidelines Available at www.aidsinfo.nih.gov. Accessed 4/25/16.

Atazanavir Dosing with Acid-reducing Agents

Acid-reducing Agents	ARV-naive	ARV-exp
Antacids or buffered medications	• ATV, ATV/c, ATV/r: Give **≥ 2 hours before or 1 to 2 hours after** antacid or buffered medication	
H2 Receptor Antagonists (H2RAs)	**ARV-naive with or without TDF** • ATV: Give **≥ 2 hours before or 10 hours after** H2RA. Max dose of famotidine 20 mg bid (not to exceed 20 mg in single dose) [or equivalent]. • ATV/r or ATV/c: Give simultaneously **with or ≥ 10 hours after** H2RA. Max dose of famotidine 40 mg bid [or equivalent].	**ARV-exp without TDF** • ATV/r or ATV/c: Give simultaneously **with or ≥ 10 hours after** H2RA. Max dose of famotidine 20 mg bid [or equivalent]. **Treatment-exp with TDF** • ATV/r (400/100 mg) or ATV/c (400/150 mg): Give simultaneously **with or ≥ 10 hours after** H2RA. Max dose of famotidine 20 mg bid [or equivalent].
Proton Pump Inhibitors (PPIs)	• ATV: **not recommended** • ATV/r or ATV/c: Max dose of omeprazole 20 mg once daily [or equivalent] **taken ≥ 12 hours prior to** ATV/r	• ATV/r or ATV/c: **not recommended**

Adapted from DHHS Guidelines Available at www.aidsinfo.nih.gov. Accessed 4/25/16.

Herbs

- St Johns Wart: **Contraindicated**, decreases antiretroviral levels

Others

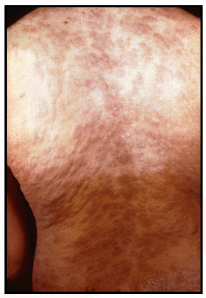
- Clopidogrel **contraindicated** with etravirine, prevents activation of clopidogrel
- Apixaban/Rivaroxaban **avoid use** with ritonavir and/or cobicistat, increases anticoagulant level

ART Complications - Monitoring

- Variety of bone marrow, kidney, and liver abnormalities
  - **CBC** with differential every 3-6 months
  - **Basic chemistry**, including BUN and creatinine, 2-8 weeks following ART initiation and every 3-6 months thereafter
  - **Urinalysis** following ART initiation or change and every 12 months thereafter (or every 6 months while on tenofovir-containing regimens)
  - **ALT/AST/Total Bilirubin** 2-8 weeks following ART initiation and every 3-6 months thereafter

http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf

Breakout Session Case Review



http://www.cdc.gov/std/syphilis/images/rash-gbr.htm, accessed 4/26/16

Cancer Screening/Prevention

- With ART the incidence of AIDS-defining malignancy has decreased but ***non-AIDS-defining cancers are on the rise***
- No current changes to standard guidelines except related to ***HPV associated neoplasia***
- ***Vaccinate: HPV and Hepatitis B***
- ***Smoking Cessation***
- ***Treat Hepatitis C***

Clinical Infectious Diseases 2012;55(9):1228–35

Table 1. Standard Incidence Ratios of Selected Non–AIDS-Defining Cancers [2, 5–8]

Non–AIDS-Defining Cancer	Cancer Risk (Standardized Incidence Ratio)
Anal	33.4–42.9
Hodgkin's Lymphoma	14.7–31.7
Liver	7.0–7.7
Skin	
Squamous cell carcinoma/Basal cell	3.2
Melanoma	1.1–2.6
Head and Neck	1.0–4.1
Lung	2.2–6.6
Leukemia	2.2–2.5
Renal	1.8–2.2

HPV associated neoplasia

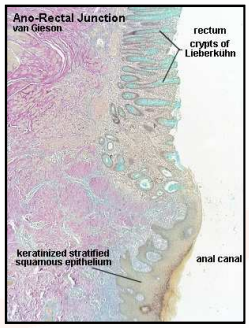
Cervix

- <30 years old
  - Start within first year of sexual activity and no later than age 21
  - If normal repeat 12 months (some argue for 6 months if newly diagnosed)
  - After 3 negative, screen 3 year interval
- ≥30 years old
  - At diagnosis if normal repeat 12 months, after 3 negative, screen 3 year interval
  - ***HPV cotesting,*** if negative, screen 3 year interval
  - Continue lifelong

Anal Cancer Screening

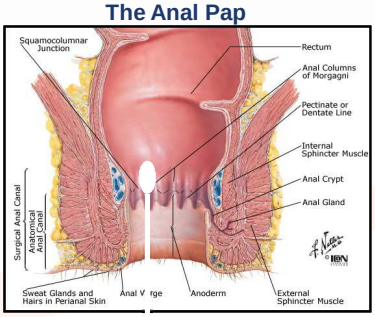
- **Consider if access to high resolution anoscopy and biopsy**
  - MSM HIV + incidence 42 to 137 per 100,000 person years
  - Others: HIV + women engaging in receptive anal intercourse or abnormal pap smears, or HIV+ with Anal/Genital warts
- Two cost-effectiveness studies have shown anal pap for MSM to be comparable with other accepted preventive measures in clinical medicine
  - HIV+: 1-2 years
  - HIV-: 2-3 years

Curr Infect Dis Rep (2010) 12:126–133
JAMA. 1999;281:1822-1829
AmJ Med. 2000;108:634–641
Clin Infect Dis. 2014 Jan;58(1):1-10.



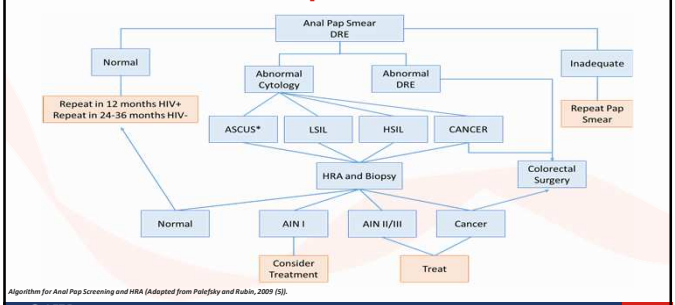
https://embryology.med.unsw.edu.au/embryology/index.php/Gastrointestinal_Tract_-_Colon_Histology

The Anal Pap



https://www.netterimages.com/rectum-and-anal-canal-labeled-multiple-publications-gastroenterology-frank-h-netter-4491.html

Anal Pap Follow UP



Algorithm for Anal Pap Screening and HRA (Adapted from Palefsky and Rubin, 2009 (5)).

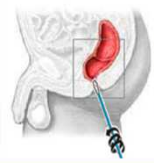
Curr Infect Dis Rep (2010) 12:126–133

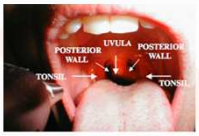
Question?

- A 50 yo male presents for routine follow up. He reports being sexually active exclusively with men and engages in oral and receptive anal sex. He is asymptomatic. What screening for sexually transmitted infection would you recommend?

Screening for Infection

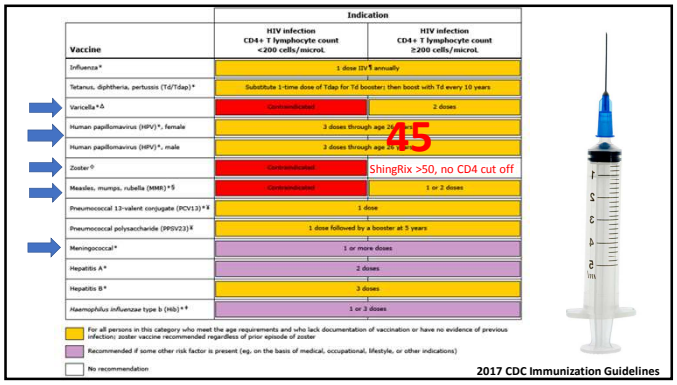
- STIs, Hepatitis (A,B,C),TB screening at initial evaluation
- Further testing based on risk
- Test at site of exposure





Question?

- What vaccinations are recommended routinely for people with HIV?
  - Pneumococcal Vaccinations (prevnar and penumovax)
  - Annual Influenza
  - Meningococcal
  - Herpes Zoster (ShingRix) vaccine if >50 years of age
  - HPV vaccine
  - All of the above



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Remember!

- ***"One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in <u>caring</u> for the patient."***

  – Francis W. Peabody, MD

- Behavior change relies on a collaborative, supportive, nurturing environment
- As individuals living with HIV live longer the role of a generalist is key in the comanagement/management of chronic disease

Slide 51

ZM30 could inclide a reference slide at the end or a 'questions?' slide to end

Zoe Muller, 5/4/2017

Questions?

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