

APPROACH TO PRIMARY CARE FOR PEOPLE LIVING WITH HIV

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Usual clinic day....

WC is a newly diagnosed 56-year-old man who presents to establish care in HIV clinic. He was told he has HIV when he recently went to donate blood. He was diagnosed with Hep C at the same time.

His DMH includes



Objective findings are relevant for a BP of 168/96, FBG of 158, Creatinine of 1.5.

Objectives

Outline the components of the initial and follow-up primary care visits for People Living With HIV (PLWH) approaches to comorbid disease prevention in HIV

Review screening and immunization guidelines for PLWH

Making the Case for an Integrated Care Model

IDSA PUBLIC POLICY

Essential Components of Effective HIV Care:
A Policy Paper of the HIV Medicine Association
of the Infectious Diseases Society of America and
the Ryan White Medical Providers Coalition

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James L. Raper,⁶ Peter Selwyn,⁷ and Steven Bruce Williams⁸

Open Forum Infectious Diseases

MAJOR ARTICLE



Should Human Immunodeficiency Virus Specialty Clinics
Treat Patients With Hypertension or Refer to Primary
Care? An Analysis of Treatment Outcomes

A. Ben Appenheimer,^{1,2} Barbara Bokhour,^{3,4} D. Keith McInnes,^{3,4} Kelly K. Richardson,¹ Andrew L. Thurman,¹ Brice F. Beck,¹ Mary Vaughan-Sarrazin,^{1,2}
Steven M. Asch,^{5,6} Amanda M. Midboe,⁶ Thom Taylor,⁶ Kelly Dvorin,⁴ Allen L. Gifford,^{3,4} and Michael E. Ohl^{1,2}

**Delivering PACT-Principled Care: Are Specialty Care Patients
Being Left Behind?**

Gemmae M. Fix, PhD^{1,2,3}, Steven M. Asch, MD, MPH^{3,4,6}, Hemen N. Saifu, MPH^{3,5},
Michael D. Fletcher, MHP, BA^{3,5}, Allen L. Gifford, MD^{1,2,3}, and Barbara G. Bokhour, PhD^{1,2,3}

Clin Infect Dis. 2011 Dec;53(11):1043-50.

Open Forum Infect Dis. 2017 Feb 3;4(1):ofx005.

J Gen Intern Med. 2014 Jul;29 Suppl 2:S695-702.

- **Management of HIV**
 - **Prevention of Co-conditions**
 - **Social Determinants**
 - **Management of Comorbidities**
 - **Behavioral Factors**

- ART history
- Risk factors for HIV
- SH including social support/coping, sexual history
- PMH including OI hx, mental health and substance use
- Other medical issues

Elements of a Primary Care Visit

- Comprehensive PE
- **Follow-up visits:**
- Adherence to ART
- Sexual history
- Tobacco and other substance use

• LABORTORY

- **Initial visit:**
- CD4, HIV VL, Genotype (new diagnosis or VF)
- HLA-B*5701, G6PD
- Pregnancy test*
- CBC, CMP, Lipid Panel, fasting glucose, Hgb A1c, UA, Serum testosterone*
- Coinfection screening^{see next}
- STI screening^{see next}
- **Follow-up visit:**
- HIV VL – q3-6 mo. OR 2-8 weeks after ART start or change
- CD4 – q3-6 mo. (first 2 yrs.) q12 mo. – optional (based on CD4 count)
- CBC, CMP – q3-6mo.
- Hgb A1c, lipids – q12mo.
- UA/urine microalbumin* – q12mo

* if indicated

• COUNSELLING

- **All visits:**

Disease Prevention & Health

• Screening **Promotion**

- Age appropriate cancer screening

- Metabolic conditions

- Co-infections

• Prevention

- Immunizations

- Sexual/mental health

- Lifestyle modification

• Substances

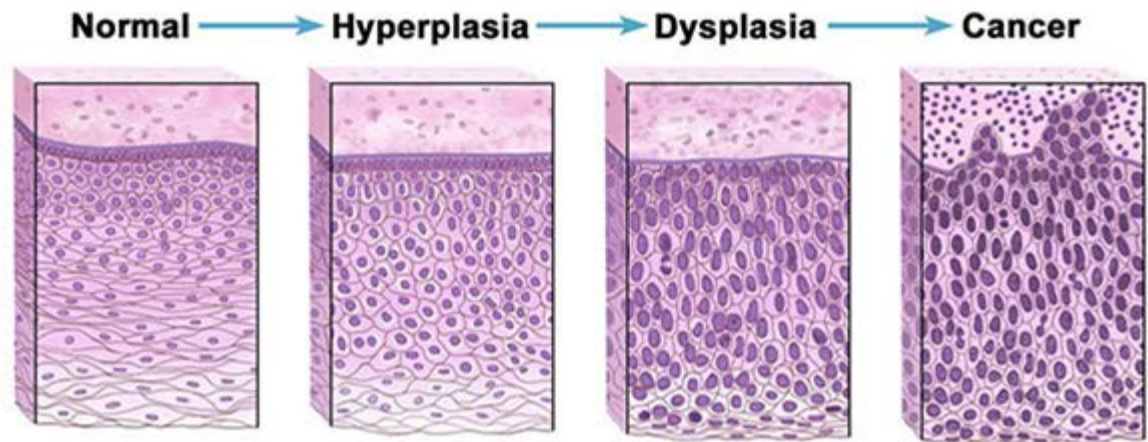
- Tobacco

- Alcohol

- Drugs

Screening

Cancer



Cancer in PLWH



Increased Risk

Average Risk

Lower Risk

Modifying Risk Factors

Cancer in PLWH

Increased Risk

- Infection-related cancers that are both AIDS defining (ADC), including Kaposi sarcoma, cervical cancer and non-Hodgkin lymphoma, and non-AIDS-defining cancers (NADC), including anal squamous cell cancer and liver cancers
- Infection unrelated cancers are also increased in ART-treated individuals, including Hodgkin disease, melanoma, and lung cancer
- Lung cancer is the most common NADC

Cancer in PLWH

Average or lower risk

- By contrast, the risk of prostate and breast cancer, two of the most prevalent age-associated malignancies in the general population, are not increased and may be lower in PLWH
- Colon cancer average risk

Cancer in PLWH

Risk Factors

- Higher prevalence of carcinogenic exposure, including smoking and possibly alcohol use
- Immunosuppression and chronic inflammation
- ART mitigates the risk of ADC: immediate initial ART in persons with CD4 cell counts of greater than 500 cells/mL was associated with reduced incidences of infection-related cancers (HR, 0.26) and with nonsignificant decreases in non-infectious cancers (HR, 0.49) in the Strategic Timing of Antiretroviral Treatment trial

Cancer Screening

- Not impacted by HIV infection
 - **Colon cancer***: fecal occult blood testing, sigmoidoscopy or colonoscopy beginning age 50 until age 75
 - Age 76-85 – no routine screening
 - Age 85 or older – recommend against screening
 - **Breast cancer***: biennial screening mammography for women age 50-74
 - Before 50 – individual discussion
 - Age 75 or older – not enough evidence for or against
 - USPSTF recommends AGAINST self breast exams
 - **Prostate cancer***: Age 55-69 based on shared decision making
 - Age 70 or older: do not screen
 - Risk factors: older age, AA, family history
 - **Lung cancer***: Low dose CT annually
 - age 55-77, 30 pack-years of smoking, current or quit within 15 years
- Specific to HIV infection
 - **Cervical cancer**#: sexually active women with HIV undergo cervical PAP at entry into care, q12 mo. thereafter; within one year of sexual activity, age 21 at the latest Screening should continue throughout life (as opposed to 65 in general population) Younger than age
 - 30- annual PAP testing, if 3 consecutive tests are negative - q3yrs Age 30 or
 - older- co-testing with PAP and HPV, if negative then q3yrs.
 - **Anal cancer**@: Anal pap at baseline and annually in MSM, women who report anal receptive intercourse OR abnormal cervical PAP OR anyone with genital warts. ASCUS or worse requires high-resolution anoscopy and/or exam

* U.S. Preventive Services Task Force (USPSTF) guidelines

US Department of Health and Human Services HIV Guidelines @ NY State Health Dept. of Health AIDS Institute Guidelines

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Specific to HIV infection

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How does the USPSTF criteria for lung cancer screening perform in PLWH?

USPSTF lung cancer screening criteria was validated using cases of lung cancer and matched controls from the MACS and WIHS cohorts

Women's Interagency HIV Study (WIHS): 4982 participants, 3677 with HIV

Sensitivity: 16%

Specificity: 93%

Multicenter AIDS Cohort Study (MACS): 7357 participants, 3914 with HIV

Sensitivity: 24%

Specificity: 94%

USPSTF Criteria has low sensitivity in PLWH

What is the optimal screening criteria?

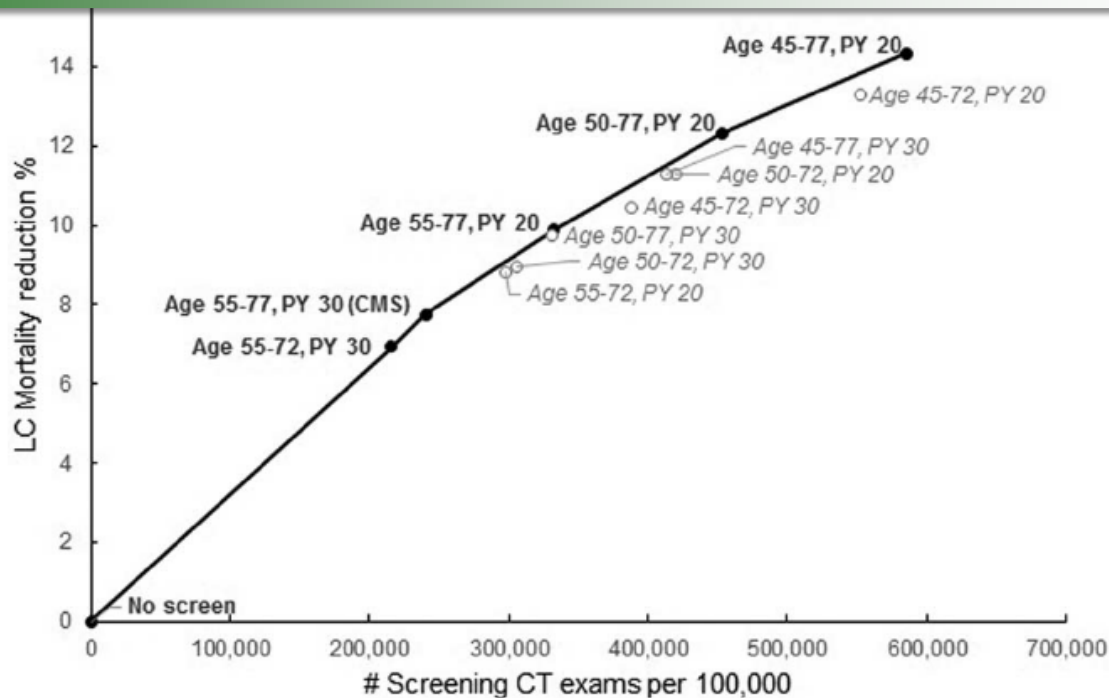
WIHS					
	AGE	Pack-years	Quit time	Sensitivity	Specificity
USPSTF	55	30	15	16%	93%
Optimal	49	16	15	52%	75%

MACS					
	AGE	Pack-years	Quit time	Sensitivity	Specificity
USPSTF	55	30	15	24%	94%
Optimal	43	19	15	82%	76%

Utility of LDCT Screening in PLWH

In PLWH (virally suppressed and CD4 cell count at least 500 cells/ml) screening using the Centers for Medicare & Medicaid Services criteria would reduce lung cancer mortality by **18.9%**

Alternative screening strategies increase mortality reduction, but require more LDCT examinations



Impact of Anal Cancer Screening

- ❑ Swiss HIV Cohort Study
Yearly screening of HIV-positive MSM may reduce anal cancer incidence substantially
- ❑ The numbers needed to screen over 15 years to prevent one anal cancer case were:

384 for yearly cytology

313 for yearly anoscopy

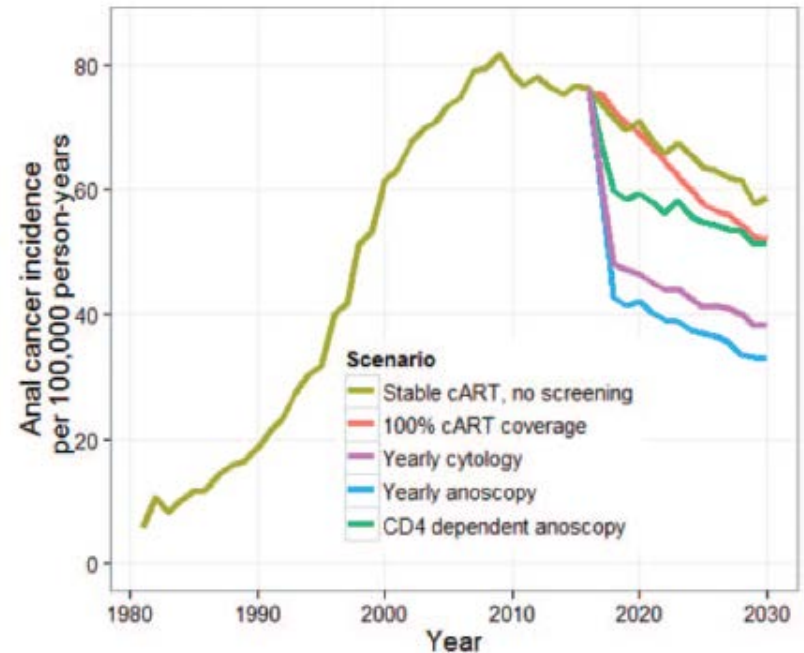


Fig. 2. Simulated anal cancer incidence assuming different intervention scenarios.

Coinfections



Screening for Sexually Transmitted Illnesses



• Women

- ***Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis*** at entry into care
- Repeat testing periodically, depending on risk and the prevalence of STIs in the community
- Retest in 3 months if positive
- Nucleic acid amplification testing (NAAT) or PCR of urine is the preferred method of screening, but for clinics that do not have urine PCR testing for trichomoniasis, screening should utilize a wet mount or culture for *T. vaginalis*
- **Syphilis:** at entry into care with a treponemal or non-treponemal test and periodically if ongoing risk factors exist

Screening for Sexually Transmitted Illnesses



• Men

- ***Neisseria gonorrhoeae* & *Chlamydia trachomatis*** at entry into care and at least annually thereafter, depending on risk and the prevalence of STIs in the community.
- Retest in 3 months if positive
- All **MSM** should have testing for urethral and rectal gonorrhea and chlamydia, as well as testing for oral gonorrhea—if they report receptive sex at these sites
- When testing for urethral infection, testing of a urine sample (not a urethral swab) with a NAAT is the preferred approach
- There are no guidelines for screening men for ***T. vaginalis***
- **Syphilis:** at entry into care with a treponemal or non-treponemal test and periodically if ongoing risk factors exist (q6-12 mo.)

Screening for Coinfections

- Hepatitis

- **Screen for evidence of prior infection or immunity**

- **Hepatitis A:** HAV ab at entry into care

- **Hepatitis B:** HBsAg, anti-HBs, and anti-HBc at entry into care; anti-HBs for immunity

- **Hepatitis C:** HCV ab at entry into care then annual testing for high risk (IDU, MSM with condom less sex, incarceration)

- Mycobacterium

- **Screen for latent or active disease**

- ***Mycobacterium tuberculosis*:** TST or IGRA: entry into care; repeat if negative and CD4 increases >200 after ART; only need to repeat annually in those with risk of exposure or known exposure – HCW, homelessness, incarceration, household contact

- ***Mycobacterium avium*:** prior to initiating prophylaxis consider screening for MAC infection with AFB blood cultures in CD4 <50

- Miscellaneous

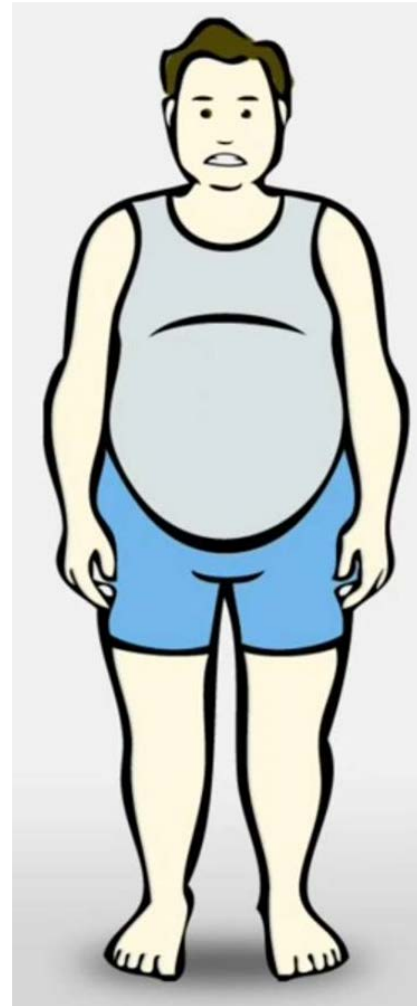
- **Screen for exposure**

- ***Toxoplasma gondii*:** Toxo IgG at entry into care, if negative counsel on ways to avoid exposure; if CD4 drops <100 and negative at baseline, recheck

- **CMV:** routine screening not recommended for MSM, PWID (presumed positive); CD4<50 should receive education on sx. of CMV retinitis and routine eye exams

- **Cryptococcal disease:** some experts recommend checking cryptococcal antigen in newly diagnosed with CD4<100

Comorbidities

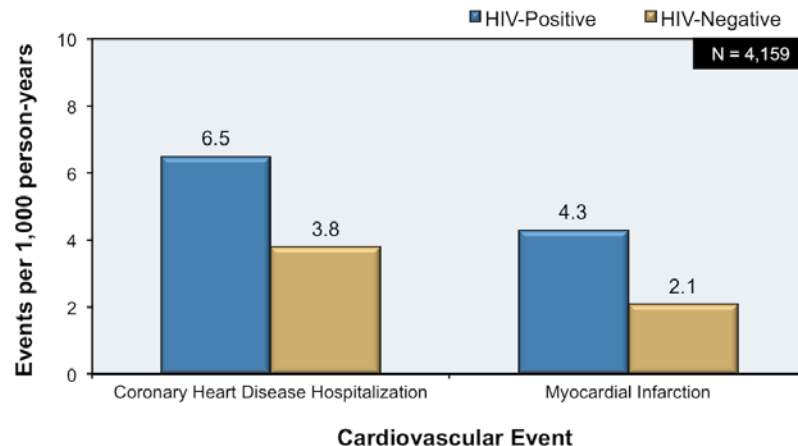


Cardiovascular Risk

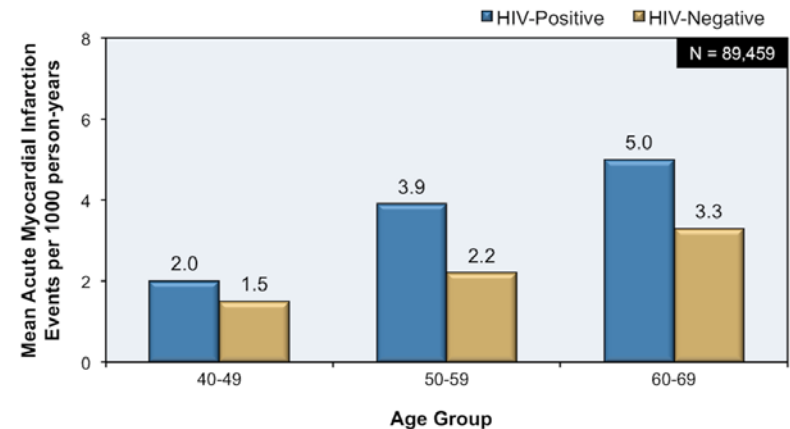
1.5- to 2-fold greater risk of cardiovascular disease in PLWH

- ❑ Traditional risk factors such as dyslipidemia, obesity, and smoking
- ❑ Metabolic alterations related to antiretroviral therapy (ectopic fat, insulin resistance, and dyslipidemia)
- ❑ HIV (immune activation and inflammation)

Kaiser Observational Study (1996-2001)



Veterans Aging Cohort Study, 2003-2009



J Acquir Immune Defic Syndr. 2002 Aug 15;30(5):471-7

JAMA Intern Med. 2013 Apr 22;173(8):614-22.

Assessing CV Risk in PLWH

Several controversies exist: differing guidelines (American College of Cardiology/American Heart Association (ACC/AHA vs. European guidelines)

Risk scores differ in their prediction ability (FHS-CVD and FHS-CHD, a higher overall CVD risk was attributed to PLWH than when using the D:A:D, ASCVD and SCORE-NL models)

ACC/AHA identifies four statin benefit groups in which the potential for an ASCVD risk reduction benefit clearly exceeds the potential for adverse effects

- Clinical ASCVD
- Primary elevations of LDL-C \geq 190 mg/dL
- Age 40 and 75 years with diabetes and LDL-C 70–189 mg/dL
- No clinical ASCVD or diabetes who are 40 to 75 years of age with LDL-C 70–189 mg/dL and an estimated 10-year ASCVD risk of 7.5% or higher)

Common Clinical Questions

- What is the best risk prediction tool to use?
- When to start a statin?
- Which statin to use?
- Should we use statin in subclinical atherosclerosis?
- Should we use LDL targets in PLWH?
- Aspirin for primary prevention?

Some Practical Advice

STATIN

- ACC/AHA guidelines are simple to use, well validated and take into account non-fatal events

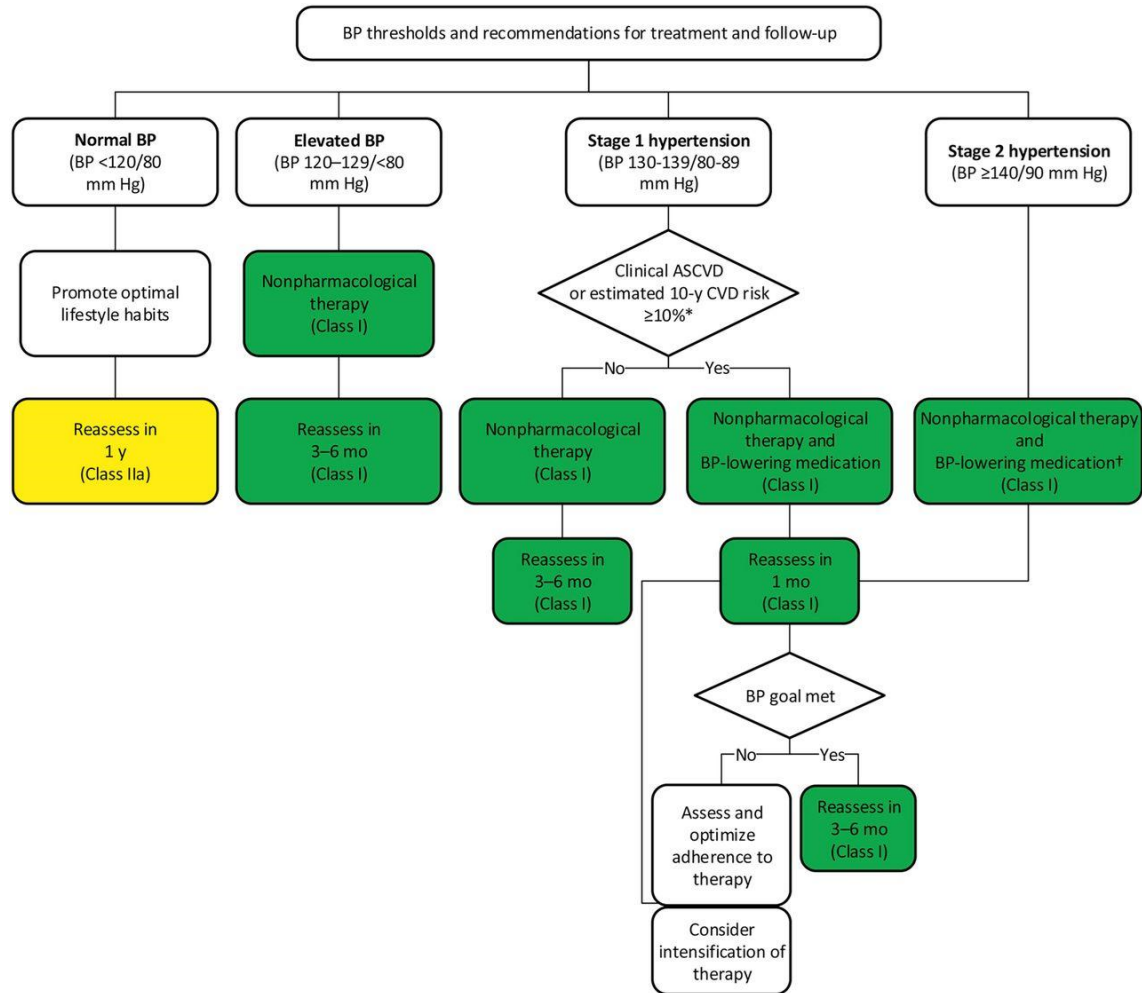
STATIN

- Start statin therapy at 10-year risk of 10% or more.
- Weigh risk vs. benefits in 7.5-10%
- Consider D-D-I and statin intensity when choosing statin

Aspirin

- Weigh risk of bleeding and pill burden against the benefit
- Use in patients with ASCVD risk of 20% or more who are adherent and have low risk of bleeding

Hypertension



Diabetes Mellitus – Key Points

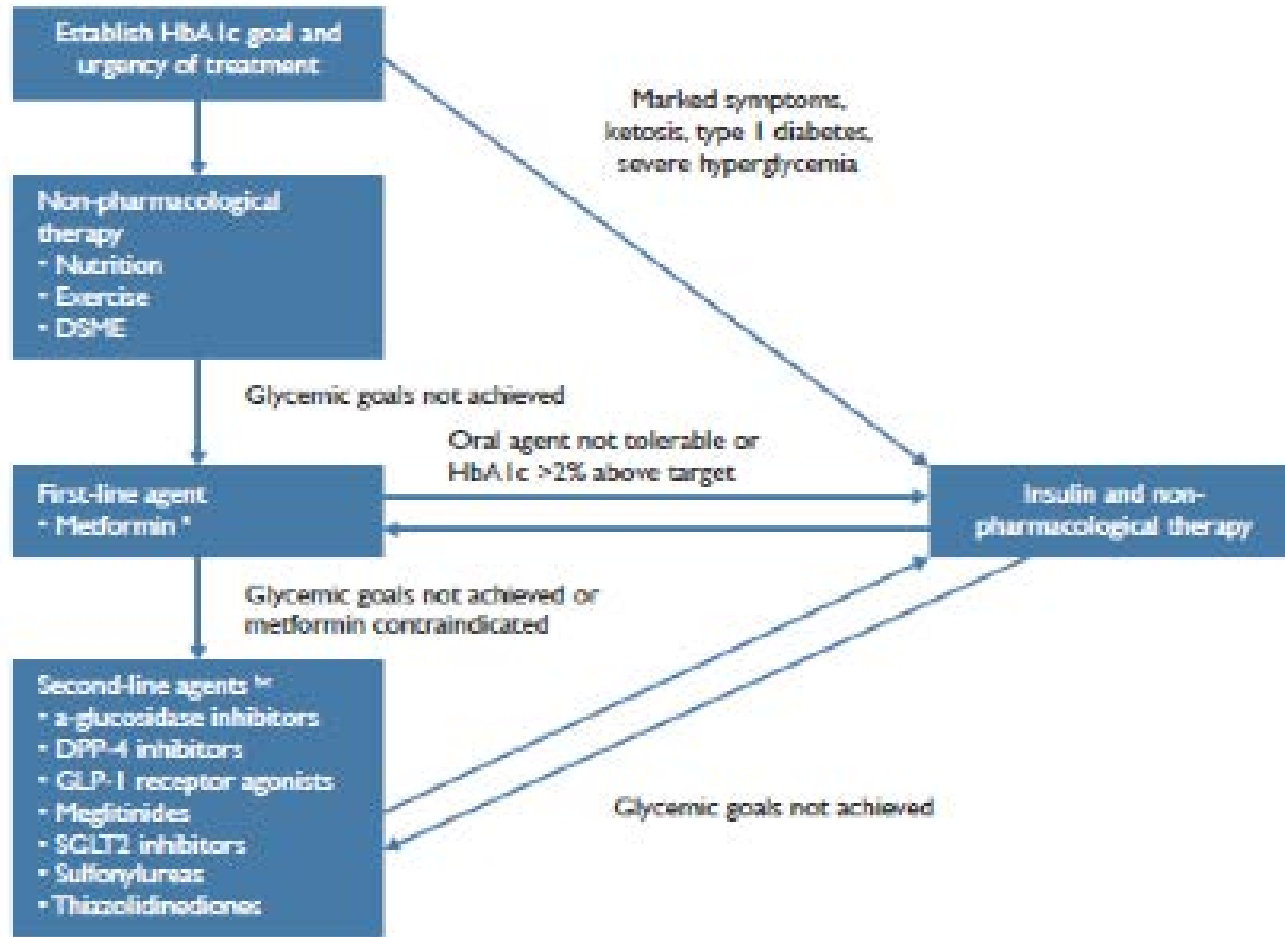
The prevalence of DM in PLWH has been reported to range from 2% to 14%

There is conflicting evidence on whether HIV infection is an independent risk factor for DM, with some studies showing increased risk and others showing no independent effect of HIV on DM or showing an inverse effect

HbA1c may underestimate glycemia in PLWH (higher mean corpuscular volume, nucleoside reverse transcriptase inhibitor use, specifically abacavir, and lower CD4 count)

Fasting blood glucose testing should be performed every 6–12 months in all PLWH

Diabetes Mellitus – Key Points



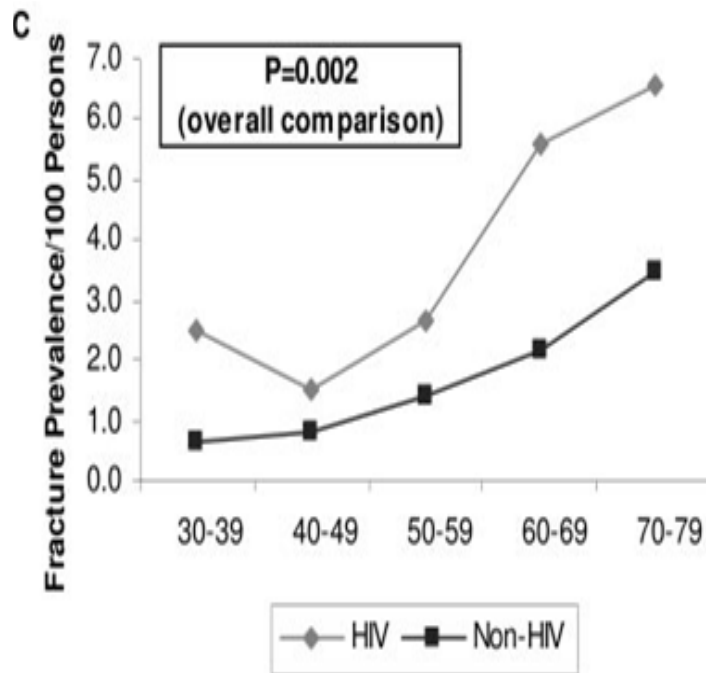
HgA1c goals

Major Comorbidities or Physiologic age	Microvascular Complications		
	Absent or mild	Moderate	Advanced
Absent >10-15 years life expectancy	6.0-7.0%	7.0-8.0%	7.5-8.5%
Present 5-10 years like expectancy	7.0-8.0%	7.5-8.5%	7.5-8.5%
Marked <5 years life expectancy	8.0-9.0%	8.0-9.0%	8.0-9.0%

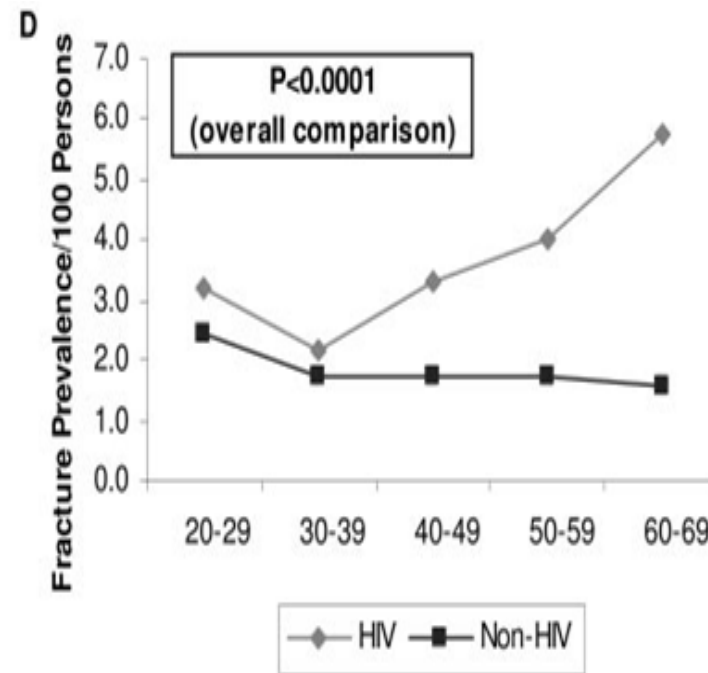
Bone Health

HIV infection is related to premature bone loss

Women



Men



Role for Vitamin D in PLWH

Vitamin D deficiency is common in PLWH

Traditional risk factors, specific antiretroviral agents and chronic HIV-associated immune activation all contribute to low vitamin D

There is an association between low vitamin D and low BMD in HIV-infected individuals

While the data are limited, vitamin D supplementation appears to be safe and beneficial especially for the prevention of bone loss with ART initiation and in conjunction with bisphosphonate therapy for treatment of low BMD.

Because of the high prevalence of osteopenia and osteoporosis in the aging HIV population, screening for vitamin D deficiency with serum 25(OH)D levels and strong consideration for vitamin D supplementation should be made for both the treatment and prevention of bone disease in HIV-infected patients.

Approach to Bone Health in PLWH


- Assess risk factors:
 - Age, sex, hx of fractures, secondary causes
- Lifestyle advice:
 - Smoking cessation, vit. D, calcium intake, weight bearing exercise
- When to consider DEXA
 - <50 years (men), premenopausal women, AND no hx of fracture
 - Wait
 - 50 or older (men), postmenopausal women AND/OR hx. of fracture
 - Measure BMD by DEXA


Approach to Bone Health in PLWH

- T-score ≤ -2.5 OR fragility fx.
 - Evaluate potential secondary causes
 - Secondary cause
 - Treat secondary cause

- T-score > -2.5 and ≤ -1 , NO fragility fx.
 - Calculate FRAX score
 - 10 year fx. risk $\geq 20\%$ major osteoporotic AND/OR $\geq 3\%$ hip
 - Consider bisphosphonates or other treatment
 - Monitor DEXA in 1-2 years

YES NO YES NO



- T-Score > -1 , NO fragility fx.
 - Lifestyle advice, continue ART
 - Monitor DEXA in 2-5 years

Screening and Management of Chronic Kidney Disease

Appropriate treatment selection and/or dose reduction is warranted for ART agents or other medications that are primarily eliminated by the kidneys

Check basic chemistry every 3-6 months, UA (+/-microalbumin/Cr) if on TDF, every 12 months otherwise

Referral to a nephrologist for GFR<60 or proteinuria

ACEi for microalbuminuria

Prevention

Prevention with Positives



- Empowering PLWH with information about ways they can protect their own health
- Developing strategies to improve adherence to treatment
- Counseling, behavioral interventions such as promoting condom use in PLWH to prevent transmission of HIV and reduce risk of STIs
- Discussing strategies for disclosing HIV status to sexual partners
- Counseling on risk of alcohol and drugs in context of sexual health
- Providing all HIV-positive women and with support to prevent mother-to-child transmission

Immunization Summary

ALL

Influenza: Annually

Tdap: Once followed by Td booster every 10 years

Pneumococcal: PCV13 (once) ->
PPSV23 (every 5 years (twice) ->
PPSV23 after 65

Hepatitis B: 3 dose series (consider double dose for non-responders)

Conjugate Meningococcal ACWY: 2 dose series, booster every 5 years

Some

HPV: 3 dose series (upto 26 yrs)
(consider up to 45)

Hep A: 2 dose series (MSM, liver dz, travel, HCW, IDU)

MMR and Varicella: lack immunity (CD4 > 200)

Recombinant Zoster Vaccine: 2 dose series (>50yrs)

Contraindicated

All PLWH: MMRV, LIAV, Oral Typhoid

CD4 < 200: Varicella, ZVL, Yellow Fever, MMR

Non-specific

HiB, Conjugate Meningococcal B

HPV



What about vaccinating after age 26?

2 studies have evaluated efficacy in older PLWH

The 1* endpoint was vaccine efficacy (VE) against new persistent HPV 6,11,16,18 (qHPV) anal infection, ± single final visit detection.

VE against new persistent anal qHPV was 22% (95% CI -31%–53%) which was not significantly different than placebo.

High baseline HPV seropositivity was noted, which suggests that VE may have been compromised by prevalent sub-clinical/latent infections not detected at study entry.

HPV



What about vaccinating after age 26?

A Canadian study enrolled a cohort of 452 HIV + ve girls & women aged 9–26 yrs (mean age = 17.7 yrs) with a mean CD4 count of 500 (99% HIV VL < 20) to receive 3 doses of G4 vaccine.

2 studies have evaluated efficacy in older PLWH

Comparison of rates of a combined endpoint of qHPV related infection and disease/100py with non-contemporary groups of qHPV vaccinated women and unvaccinated HIV + ve women aged 24–45yrs showed: vaccinated women without HIV - 0.1/100py; vaccinated women with HIV - 1.2/100py; unvaccinated women with HIV - 1.3/100py.

Vaccinations for Travellers with HIV

	CD4>200	CD4<200
<u>Live Vaccines</u>		
LAIV	X	X
MMR	✓	X
Typhoid, Ty21a	X	X
Varicella	✓	X
Yellow Fever	Precaution	X
<u>Inactivated Vaccines</u>		
Hep A	✓	✓
Hep B	✓	✓
Influenza	✓	✓
Japanese encephalitis	✓	✓
Meningococcal conjugate	✓	✓
PCV13 ->PPSV23	✓	✓
Rabies	✓	✓
Td/TdaP	✓	✓
Typhoid, Vi	✓	✓

Substance Use

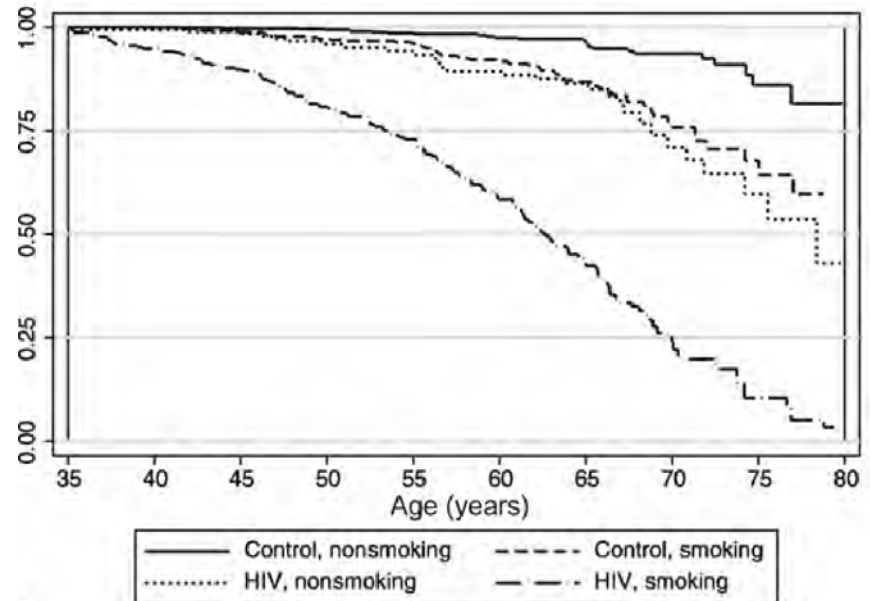
Tobacco Cessation

✓ PLWH are **TWICE** as likely to use tobacco

✓ PLWH lose more life-years to **SMOKING** than to HIV

✓ The excess mortality of smokers is **TRIPLED**

✓ The population-attributable risk of death associated with smoking is **DOUBLED** among HIV patients compared to the background population



Tobacco Cessation

WHAT WORKS

ASK

about tobacco use at every visit

ADVISE

all tobacco users to quit

ASSESS

willingness to quit (in the next 30 days)

ASSIST

the patient in quitting (medications, counseling)

ARRANGE

referral and follow-up contact

Effectiveness and abstinence rates at 6-months post-quit

Medication	Estimated Abstinence Rate* (95% CI)
Placebo	13.8
Monotherapy	
Varenicline 2 mg/day	33.2
Bupropion SR	24.2
Nicotine spray	26.7
Nicotine gum (> 14 weeks)	26.1
Nicotine inhaler	25.4
Nicotine patch (> 14 weeks)	23.7
Combination Therapy	
Patch + nicotine gum or spray	36.5
Patch + bupropion SR	28.9
*Abstinence rate 6-months post quit	

Mental health and Substance abuse

- ✓ More than 25% of PLWH in the United States meet criteria for one or more substance use disorders
- ✓ Substance use disorders are linked to decreased adherence to antiretroviral medications, risk-taking behaviors, and HIV disease progression (independent of non-adherence behaviors)
- ✓ The prevalence of depression, anxiety, and posttraumatic stress disorder is also significantly higher among PLWH
- ✓ Screening for mental health conditions, including HIV-associated neurocognitive disorders, among PLWH require interdisciplinary approach, working closely with HIV mental health specialists

To Summarize....

- Providing good primary care to PLWH requires an interdisciplinary, multifaceted approach.
- Special attention needs to be given to primary disease prevention, screening for co-morbid conditions and health promotion.
- When possible, interventions such as smoking cessation and statin therapy can have a high impact.
- Addressing social and behavioral determinants of health are a critical part of primary care delivery for PLWH

