APPROACH TO PRIMARY CARE FOR PEOPLE LIVING WITH HIV

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Louis Stokes Cleveland VA Medical Center
Case Western Reserve University School of Medicine
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 PMH includes HTN, diabetes and CKD. He reports smoking since the age of 15. In addition, he reports heavy alcohol use. He reports history of injection opioid use but has been in remission for several years. He reports frequent condomless sex with multiple casual female partners.

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)

Review approaches to comorbid disease prevention in HIV

Review screening and immunization guidelines for PLWH
Making the Case for an Integrated Care Model

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

Joel E. Gallant, Adaora A. Adimora, J. Kevin Carmichael, Michael Horberg, Mari Kitahata, E. Byrd Quinlivan, James L. Raper, Peter Selvin, and Steven Bruce Williams

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

A. Ben Appenheimer, Barbara Bokhour, D. Keith McInnes, Kelly K. Richardson, Andrew L. Thurman, Brice E. Beck, Mary Vaughan-Sarrazin, Steven M. Asch, Amanda M. Midboe, Thom Taylor, Kelly Dverin, Allen L. Gifford, and Michael E. Obi

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

Gemmae M. Fix, PhD, Steven M. Asch, MD, MPH, Hemen N. Saifu, MPH, Michael D. Fletcher, MHP, BA, Allen L. Gifford, MD, and Barbara G. Bokhour, PhD

Open Forum Infect Dis. 2017 Feb 3;4(1):ofx005.
• Management of HIV
• Prevention of Co-conditions
• Social Determinants
• Management of Comorbidities
• Behavioral Factors
Elements of a Primary Care Visit

• ART history
• Risk factors for HIV
• SH including social support/coping, sexual history
• PMH including OI hx, mental health and substance use
• Other medications
• Comprehensive PE
• Follow-up visits:
  • Adherence to ART
  • Sexual history
  • Tobacco and other substance use

LABORATORY

• 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 Promotion

- Screening
  - Age appropriate cancer screening

- Metabolic conditions

- Co-infections

- Prevention
  - Immunizations

- Sexual/mental health

- Lifestyle modification

- Substances
  - Tobacco

- Alcohol

- Drugs
Screening
Cancer

Normal → Hyperplasia → Dysplasia → Cancer
Cancer in PLWH

- Increased Risk
- Average Risk
- Lower Risk
- Modifying Risk Factors

Cancer in PLWH

- 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

Increased Risk
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
Cancer Screening

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Specific to HIV infection

* 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
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**

*AIDS 2018, Vol 32 No 10; CROI 2019, Abstract # 15*
What is the optimal screening criteria?

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<td>15</td>
<td>82%</td>
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CROI 2019, Abstract # 15
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)


![Graph showing cardiovascular event rates in PLWH and uninfected individuals.](image-url)
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 ≥ 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

BP thresholds and recommendations for treatment and follow-up

- Normal BP (BP <120/80 mm Hg)
  - Promote optimal lifestyle habits
    - Reassess in 1 y (Class Ila)

- Elevated BP (BP 120–129/<80 mm Hg)
  - Nonpharmacological therapy (Class I)
    - Reassess in 3–6 mo (Class I)

- Stage 1 hypertension (BP 130–139/80–89 mm Hg)
  - Nonpharmacological therapy (Class I)
    - Reassess in 3–6 mo (Class I)

- Stage 2 hypertension (BP ≥140/90 mm Hg)
  - Nonpharmacological therapy and BP-lowering medication (Class I)
    - Reassess in 1 mo (Class I)
    - BP goal met
      - Yes: Nonpharmacological therapy and BP-lowering medication (Class I)
        - Reassess in 3–6 mo (Class I)
      - No: Assess and optimize adherence to therapy
        - Consider intensification of therapy

Clinical ASCVD or estimated 10-y CVD risk ≥10%*

*2017 ACC/AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults
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.

*Clin Infect Dis. 2015 Feb 1;60(3):453-62.*
### HgA1c goals

<table>
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<tr>
<th>Major Comorbidities or Physiologic age</th>
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<td>Absent &gt;10-15 years life expectancy</td>
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<tr>
<td>Present 5-10 years like expectancy</td>
<td>7.0-8.0%</td>
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<tr>
<td>Marked &lt;5 years life expectancy</td>
<td>8.0-9.0%</td>
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</table>
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.

Curr Opin HIV AIDS. 2016 May;11(3):277-84.
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 ≥ 20% major osteoporotic AND/OR ≥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
- Penumococcal: 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.

Clin Infec Dis 2018;67:1339-1346
What about vaccinating after age 26?

2 studies have evaluated efficacy in older PLWH.

A Canadian study enrolled a cohort of 432 HIV+ girls & women aged 9–65yrs (median age 39yrs, IQR 34–45yrs, median CD4 500, 69% HIV VL < 50) to receive 3 doses of G4 vaccine.

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+ women aged 24–45yrs showed: vaccinated women without HIV - 0.1/100py; vaccinated women with HIV – 1.2/100py; unvaccinated women with HIV – 1.5/100py.

Clin Infec Dis 2019;68:788-794
# Vaccinations for Travellers with HIV

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<td>Typhoid, Ty21a</td>
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<tr>
<td>Varicella</td>
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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

Clinical Infectious Diseases 2013;56(5):727–34
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

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<td>Varenicline 2 mg/day</td>
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<td>Bupropion SR</td>
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<tr>
<td>Nicotine spray</td>
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<tr>
<td>Patch + bupropion SR</td>
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*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