PRIMARY CARE FOR PATIENTS WITH HIV INFECTION

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LEARNING OBJECTIVES

- Discuss reduction of cardiovascular risk in patients with HIV, including management of hypertension, hyperlipidemia and diabetes in these patients
- Discuss causes of renal disease and management in patients with HIV
- Describe screening indications and management of osteoporosis in patients with HIV
- Review options for tobacco cessation and discuss the relationship between obstructive lung disorders and HIV
- Summarize cancer screening recommendations for patients with HIV

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TOPIC OVERVIEW

- With long-term anti-retroviral therapy (ART), the life expectancy of people with HIV infection has increased dramatically
- HIV clinical care is therefore transitioning to a chronic disease model
- Since ART is preventing progression of HIV, most deaths among patients who are receiving effective ART are now related to conditions other than AIDS
- Clinicians providing primary care to people with HIV infection must be able to recognize and manage common primary care conditions and deliver evidence-based prevention measures

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CARDIOVASCULAR RISK

- Patients with HIV have a 1.5- to 2-fold greater risk of cardiovascular disease than those without HIV
- Kaiser Observational Study: Over 4,000 patients studied, showing patients with HIV had higher rates of both MI and hospitalization for CAD compared to patients without HIV
- Veterans Aging Cohort Study: Analyzed data from nearly 90,000 veterans and showed an increased risk of MI among veterans with HIV across all age groups. Also found that low CD4 cell counts and high RNA levels increase the risk of myocardial infarction.

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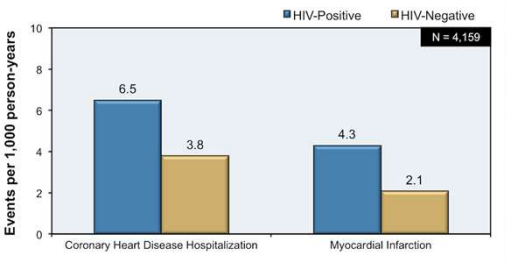
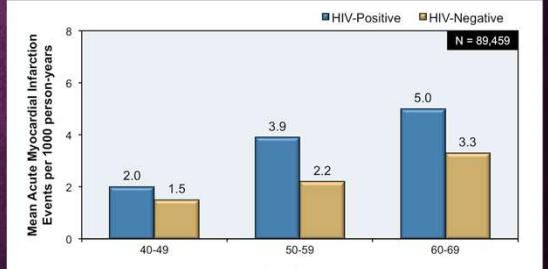
CARDIOVASCULAR RISK

Kaiser Observational Study (1996-2001)



Veterans Aging Cohort Study, 2003-2009



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CARDIOVASCULAR RISK

Multiple factors contribute to increased risk of atherosclerotic disease in patients with HIV:

- Traditional risk factors such as dyslipidemia, obesity and cigarette smoking
- Metabolic alterations related to ART such as insulin resistance and dyslipidemia
- Factors linked to HIV itself including immune activation and inflammation

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CARDIOVASCULAR RISK

- Disproportionately increased risk among Hispanics and blacks with HIV
- Studies using carotid ultrasound, CT and PET scans show increased prevalence of atypical, non-calcified, vulnerable coronary plaques as well as increased arterial inflammation
- Rate of heart failure, stroke, pulmonary hypertension and sudden cardiac death are higher for people with HIV, even those taking ART with a suppressed viral load
- Many experts now consider HIV as an independent risk factor for cardiovascular disease particularly with more advanced immunosuppression

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CARDIOVASCULAR RISK

- The optimal approach to cardiovascular risk reduction in patients with HIV infection has not been precisely defined but it is widely accepted that the same risk reduction strategies that are used in uninfected individuals should apply
- These strategies include aspirin use, statin therapy, blood pressure control and management of diabetes as indicated
- Additionally, counseling about lifestyle interventions should address potentially modifiable risk factors, such as smoking, obesity, excessive alcohol use, diet, and lack of physical activity

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CARDIOVASCULAR RISK AND ART

- The relationship between ART and cardiovascular risk remains controversial
- Studies examining individual drug and class effects have raised concerns regarding the contribution of protease inhibitors and abacavir to cardiovascular risk
- The Data Collection on Adverse Events of Anti-HIV Drugs (D;A;D) study found that recent abacavir use conferred the highest relative rate of MI (relative rate of 1.89, even after controlling for traditional cardiovascular risk factors)
- Most experts would avoid abacavir in patients with cardiovascular disease and many would avoid abacavir based on significant cardiovascular risk factors alone

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2017 HYPERTENSION GUIDELINES

2017 American College of Cardiology/American Heart Association Clinical Practice Guidelines
Categories of Blood Pressure for Adults*

Blood Pressure Category	Systolic BP		Diastolic BP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120 – 129 mm Hg	and	<80 mm Hg
Hypertension: Stage 1	130 – 139 mm Hg	or	80 – 89 mm Hg
Hypertension: Stage 2	≥140 mm Hg	or	≥90 mm Hg

*Individuals with SBP and DBP in 2 categories should be designated to the higher BP category.

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HYPERTENSION AND HIV

- Hypertension increases the risk of acute MI independent of, and in addition to, that contributed by HIV
- In patients with HIV, hypertension is associated with traditional risk factors such as increasing age, obesity, African American race, diabetes or hyperlipidemia
- In a cross-sectional study at two Navy medical centers, hypertension was most strongly associated with age over 40 years and duration of HIV infection of greater than 10 year
- Diabetes, African American race, and elevated BMI also contributed to increased odds of developing hypertension according to this study

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HYPERTENSION AND ART

- Data are conflicting regarding the association of HIV, ART and hypertension
- Some early studies linked hypertension to ART, in particular protease inhibitors, but this has not been supported in more recent investigations
- In both the Navy study and the Women's Interagency Study, there was no association between hypertension and ART
- In the D:A:D study, neither the type of ART at baseline nor the cumulative exposure to protease inhibitors or nucleoside reverse transcriptase inhibitors (NRTIs) predicted hypertension but exposure to non-nucleoside reverse transcriptase inhibitors (NNRTIs) was associated with decreased risk of hypertension

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MANAGEMENT OF HYPERTENSION IN PATIENTS WITH HIV

- Not specifically addressed by the 2017 Hypertension Guidelines or by the HIVMA Primary Care Guidelines
- Given that both hypertension and HIV are cardiovascular risk factors, both should be managed aggressively
- Clinicians must consider the risk of drug interactions when adding any anti-hypertensive medication to a medication regimen that includes ART
- Caution should be used when administering calcium channel blockers in patients taking protease inhibitors or cobicistat, since these medications can raise levels of calcium channel blocker drugs
- EKG monitoring is recommend if a calcium channel blocker is used with either atazanavir or saquinavir

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HIV AND HYPERLIPIDEMIA

- Dyslipidemia has been associated with traditional risk factors as well as with HIV itself and ART
- Chronic HIV infection causes a rise in triglyceride levels and a decrease in total cholesterol, HDL, and LDL that is consistent with a chronic inflammatory state
- The mechanisms for these latter changes are likely multifactorial, due to a combination of genetic factors, patient lifestyle, increased triglycerides, insulin resistance, increased activity of various hepatic enzymes, and abnormal HDL metabolism
- Compared to individuals without HIV infection, those with HIV infection have also been shown to have a higher prevalence of atypical, high-risk coronary plaques

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LIPID CHANGES AFTER INITIATION OF ART

- After starting ART, a patient's lipid levels typically return to baseline and then rise above pre-treatment levels, except for HDL, which remains persistently low
- The magnitude of lipid changes following the introduction of ART depends on many factors:
  - Gender
  - Race/ethnicity
  - Underlying genetic polymorphisms
  - The lipid profile of the specific antiretroviral regimen

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EFFECT OF ART ON LIPIDS

- Each class of ART has a distinct effect on baseline lipid levels
- Protease inhibitors generally cause the greatest increases in lipid levels, especially LDL and triglycerides
- Integrase inhibitors exert the least effect on lipid levels
- Within classes, certain agents are recognized to cause more adverse lipid effects than others

Impact of Antiretroviral Medication on Lipids

Class	Impact on Lipids
NRTIs	• Stavudine > Zidovudine > Abacavir: ⇧TG and ⇧LDL • Tenofovir alafenamide > Tenfovir DF: ⇧TG, ⇧LDL, ⇧HDL (no change in TC:HDL ratio)
NNRTIs	• Efavirenz: ⇧TG, ⇧LDL, ⇧HDL
PIs	• All ritonavir- or cobicistat-boosted PIs: ⇧TG, ⇧LDL, ⇧HDL • Lopinavir-ritonavir = Fosamprenavir + Ritonavir: ⇧TG • Lopinavir-ritonavir > Darunavir + Ritonavir: ⇧TG • Atazanavir + Ritonavir: ⇧TG
ISTIs	• Elvitegravir-Cobicistat: ⇧TG, ⇧LDL, ⇧HDL
EIs	• NA

Abbreviations: NRTIs = nucleoside reverse transcriptase inhibitors; NNRTIs = nonnucleoside reverse transcriptase inhibitors; PIs = protease inhibitors; ISTIs = integrase strand transfer inhibitors; EIs = entry inhibitors

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TREATMENT OF DYSLIPIDEMIA IN PATIENTS WITH HIV

- The 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults comments that individuals with HIV infection have an increased risk of developing ASCVD, but does not make any specific treatment recommendations for this population
- The prevalence of dyslipidemia among patients with HIV is as high as 80%, yet as few as 5% of persons with HIV infection who are on antiretroviral therapy are also taking a statin
- Studies have shown that the 2013 ACC/AHA Guideline and the adjunctive 10-year ASCVD risk calculator likely underestimate cardiovascular risk in patients with HIV even as they expand the overall statin-eligible population
- Many experts encourage more aggressive management of dyslipidemia and other cardiac risk factors (obesity, smoking, hypertension, diabetes mellitus, etc) in patients with HIV

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HIV-SPECIFIC LIPID MANAGEMENT

The 2013 Primary Care Guidelines for the Management of Persons Infected with HIV issued the following recommendations:

- All patients with HIV should have fasting lipid screening at entry into care, prior to and within 1 to 3 months of initiating ART, then every 6 to 12 months while on ART
- Individuals who are not on ART should have annual fasting lipid measurements
- Manage according to the 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk
- If indicated, use the lowest possible dose of a statin titrated to tolerability and response

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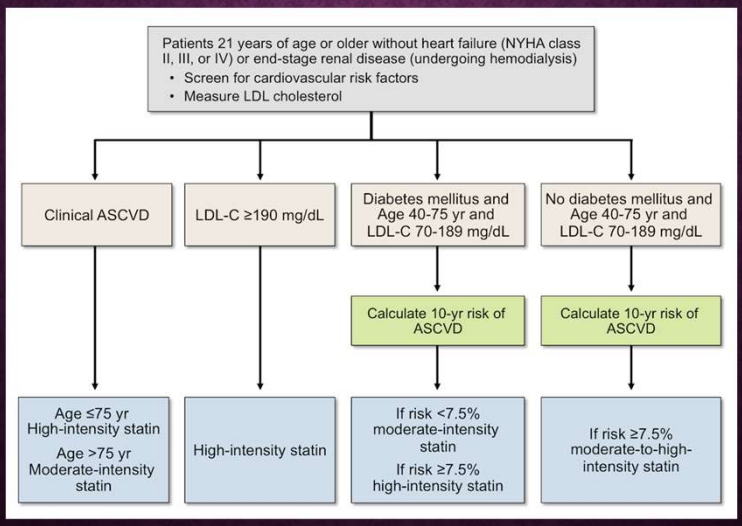
ACC-AHA CHOLESTEROL GUIDELINES FOR USE OF STATIN THERAPY



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STATINS AND ART

- Statin should be selected based on careful review of the patient's ART for possible drug interactions, which differs from the 2013 ACC/AHA recommendation
- Potentially dangerous drug interactions can occur between statin therapy and ART, particularly with PIs, NNRTIs and pharmacologic boosters ritonavir and cobicistat
- Ritonavir and cobicistat can dramatically increase serum levels of simvastatin and lovastatin, increasing the risk of statin-related hepatotoxicity, myopathy, and rhabdomyolysis
- Simvastatin and lovastatin are therefore contraindicated in combination with ritonavir- or cobicistat-containing regimens
- The NNRTI efavirenz induces statin metabolism so may decrease efficacy of some statins
- In general, pravastatin, low-dose atorvastatin, pitavastatin, and rosuvastatin are less likely to cause drug interactions with ART and are therefore the preferred agents for patients on ART, particularly regimens containing a PI or NNRTI

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HYPERTRIGLYCERIDEMIA AND HIV

- Elevated triglyceride levels are common among patients with HIV
- Management of hypertriglyceridemia in patients with HIV is the same as it is for the general population except that the triglyceride target is < 200 mg/dL (as opposed to < 150mg/dL in the general population)
- Dietary modification is considered first-line therapy
- Exercise, smoking cessation, and aggressive control of hyperglycemia for diabetic patients are all additional lifestyle factors that help reduce triglyceride levels
- When dietary modification is insufficient, fibrates are considered first-line pharmacologic therapy with fenofibrate preferred over gemfibrozil due to fewer drug interactions
- Second line therapies include fish oil and niacin

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HYPERTRIGLYCERIDEMIA AND HIV

According to the 2003 IDSA Guideline for the Management of Dyslipidemia in HIV-infected Adults Receiving Antiretroviral Therapy, initial approach to elevated triglycerides is as follows:

- TGs 200 to 500 mg/dL and elevated LDL: Initiate therapy with statin alone
- TGs > 500 mg/dL: Initiate therapy with fibrates or, alternatively, with fish oil or niacin
- Options for hypertriglyceridemia refractory to fibrate therapy:
  - Consider adding fish oil or niacin to fibrate therapy
  - Assess whether ART is contributing to refractory hypertriglyceridemia and weigh risk versus benefits of changing ART if this appears to be the case
  - Adding a statin is unlikely to have significant additional clinical benefit and increases the risk of myopathy

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DIABETES AND HIV

- Patients with HIV have an increased risk of diabetes, further heightened by ART
- The Multicenter Cohort Study demonstrated diabetes had a prevalence of 5% among men with HIV, 7% among men with HIV infection not taking ART, and 14% among men with HIV taking ART
- After adjustment for BMI and age, this represents a 4-fold increase in the incidence of diabetes in men with HIV taking ART compared to men without HIV
- Certain factors may make diabetes management in patients with HIV more challenging
  - Patients with HIV have higher rates of anemia, which can falsely lower HgbA1c levels due to decreased red blood cell survival
  - Patients with HIV have higher rates of abnormal renal function and lactic acidosis can increase the risk of metformin toxicity

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DIABETES AND HIV

The Primary Care Guidelines for the Management of Persons Infected with HIV make the following recommendations related to diabetes for persons with HIV:

- Fasting glucose or HbA1c should be measured at entry into care, prior to starting medications, and repeated within 1 to 3 months after starting ART
- For persons with HIV on ART, using a lower HbA1c cutoff to diagnose diabetes mellitus (5.8% or greater) increases the sensitivity of the screening test but the 6.5% cutoff is still considered the standard for diagnosis
- Individuals with prediabetes should be managed aggressively with lifestyle modifications per ADA guidelines to prevent progression to frank diabetes
- In most cases, persons with HIV and mild blood glucose abnormalities can be effectively managed with lifestyle changes
- Manage according the ADA guidelines once therapeutic intervention is warranted

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DIABETES AND HIV

- Patients with HIV and diabetes should undergo HbA1c level monitoring every 6 months, with a goal of less than 7% in accordance with the ADA guidelines
- In addition to routine monitoring of kidney function, patients with HIV should have annual monitoring of urine albuminuria in accordance with the ADA guidelines
- No evidence that switching ART is beneficial for impaired glucose tolerance but a careful evaluation for drug interactions should be conducted in these patients
- For example, protease inhibitors and cobicistat can increase drug levels of quetiapine or certain corticosteroids (inhaled or oral) and thus cause hyperglycemia

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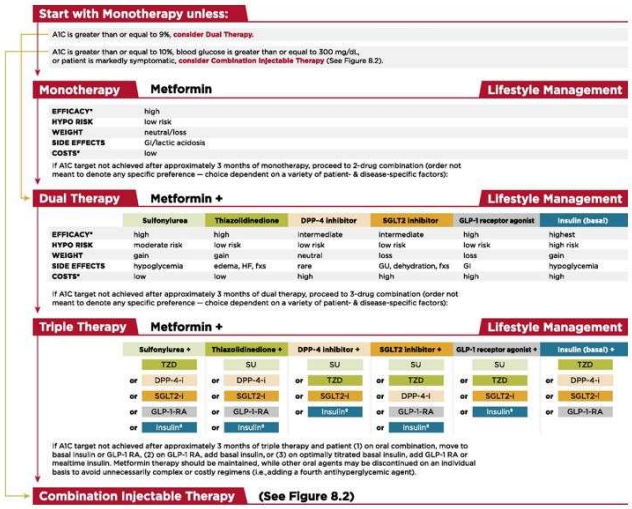
Antihyperglycemic therapy in type 2 diabetes: general recommendations.



American Diabetes Association Dia Care 2017;40:S64-S74

American Diabetes Association.

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CHRONIC KIDNEY DISEASE AND HIV

- Patients with HIV should have routine laboratory monitoring of renal function at the time of diagnosis, when ART is initiated or changed and at least twice annually in stable patients
- The risk of developing renal disease is higher in those patients with CD4 less than 200 cells/mm^3, elevated HIV RNA levels, black race, female sex, older age, or comorbidities such as diabetes, hypertension, and hepatitis C
- Tenofovir DF carries a risk of nephrotoxicity that is increased in patients taking lopinavir/ritonavir and in patients with lower body weight and lower creatinine clearance at tenofovir DF initiation
- Other predictors of tenofovir DF-related renal toxicity are still being studied

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OSTEOPOROSIS AND HIV

- Lower bone density is more prevalent among patients with HIV, largely explained by lower body weight and increased smoking rates but also by HIV-related factors
- Specific osteoporosis risk factors that are unique to persons with HIV infection include increased inflammation, altered bone metabolism, and antiretroviral-related toxicities
- Initiation of ART is associated with a 2 - 6% decrease in bone mineral density during the first 2 years of therapy, which varies with the specific ART regimen used
- Tenofovir DF and boosted protease inhibitors, in particular, have been linked to greater loss of bone density compared with other ART agents
- In contrast, tenofovir alafenamide does not cause significant loss of bone mineral density

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OSTEOPOROSIS SCREENING AND HIV

- Screen all postmenopausal women with HIV and men age 50 years and older with HIV with a DXA scan. Also use DXA scan in all adults with HIV who have a major risk factor for fragility fracture (personal history, chronic glucocorticoid treatment and/or high risk of falls)
- Assessment of morning testosterone levels is recommended in adult men with HIV who present with decreased bone mass, a low trauma fracture, decreased libido, erectile dysfunction, hot flashes, or sweats, and should be considered for nonspecific symptoms such as depression and fatigue.
- In men 40-49 with HIV and premenopausal women with HIV 40 and older without a major risk factor for osteoporotic fracture, assess fracture risk using the Fracture Risk Assessment Tool (FRAX tool)
  - Risk assess every 2-3 years or when a new clinical risk factor develops
  - When using the FRAX tool, some experts recommend checking the "secondary osteoporosis" box to better estimate the increased risk of osteoporosis conferred by HIV
  - If the FRAX tool determines the 10-year risk of major osteoporotic fracture is greater than 10%, perform a DXA scan

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OSTEOPOROSIS SCREENING AND HIV

- For DXA results, use T-scores for patients 50 years and older and Z-scores for patients under 50 years
- Optimal screening intervals (for DXA or FRAX assessment) are not clear for persons with HIV
  - Consider repeat DXA scanning after 1 - 2 years for patients with advanced osteopenia (T-score -2.0 to -2.49) and after 5 years in those with mild-to-moderate osteopenia (T-score of -1.01 to -1.99)
  - Some experts suggest rescreening persons with an initial normal DXA after 15 years based on data in the general population
  - Consider repeating DXA scan sooner in persons with a new fragility fracture or new risk factors for osteoporosis

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MANAGEMENT RECOMMENDATIONS

- Avoid tenofovir DF or boosted protease inhibitors in patients with osteoporosis
- Address possible treatable secondary causes for decreased bone mineral density including smoking, alcohol use, sedentary lifestyle, low BMI, exposure to medications associated with bone loss (glucocorticoids, phenytoin, PPIs, thiazolidinediones), vitamin D deficiency, renal disease, hyperparathyroidism, thyroid disease, and hypogonadism
- Supplement calcium and vitamin D for high-risk patients
- Lifestyle modifications for persons with osteopenia or osteoporosis include regular weight-bearing and muscle strengthening exercise, avoidance of falls, smoking cessation, and reduction in alcohol consumption
- Rule out osteomalacia (can be caused by tenofovir DF-induced renal phosphate wasting and/or vitamin D deficiency) before treating with bisphosphonates

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PHARMACOTHERAPY RECOMMENDATIONS

- In general, the management of osteopenia or osteoporosis in persons with HIV should follow established guidelines for the general population without HIV, but there are exceptions
- The National Osteoporosis Foundation recommends initiating treatment in women and men with osteopenia 50 and older with an estimated 10-year hip fracture risk of 3% or greater or a 10-year major osteoporosis-related fracture risk 20% or greater (based on FRAX calculator)
- When therapy is indicated for patients with HIV at risk for osteoporotic fractures, use alendronate or zoledronic acid, since other therapies not adequately studied in patients with HIV
- Treatment duration should be individualized, though the 2017 ACP guideline recommends discontinuing treatment after 5 years in the general population
- Some experts repeat DXA scan after 3 - 5 years of pharmacotherapy and switch to alternate treatment such as zoledronic acid or teriparatide for patients with worsening BMD, a new fracture, poor adherence with bisphosphonate therapy or greater than 1 cm height loss
- Data are limited with teriparatide and other osteoporosis pharmacotherapies in patients with HIV

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SMOKING AND HIV

- Individuals with HIV smoke at approximately twice the rate of those without HIV
- The excess mortality of smokers is tripled and the population-attributable risk of death associated with smoking is doubled among patients with HIV compared with those without HIV
- Smoking is linked to multiple medical problems among patients with HIV, including major cardiovascular disease, non-AIDS-defining cancers, and bacterial pneumonia
- A study of women with HIV starting ART found that smokers had poorer virologic and immunologic responses to ART, higher risk of death, and higher rates of progression to AIDS
- In the HIV Outpatient Study, a prospective observational cohort study of patients with HIV receiving care since 1993, the attributable risk of incident cardiovascular disease events for tobacco smoking was 26.7%, which was similar to the attributable risk associated with baseline CD4 count less than 500 cells/mm^3 and greater than the attributable risks associated with male sex or diabetes
- There are no significant drug interactions between varenicline and antiretroviral therapy, though interactions can occur between bupropion and antiretrovirals that may result in lower bupropion levels

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OBSTRUCTIVE LUNG DISEASE AND HIV

- Evidence suggests possible association between HIV and obstructive lung disease, independent of smoking
- Poor HIV control (higher viral load) and advanced immunosuppression (lower CD4) may contribute to increased risk
- Compared with the prevalence of obstructive lung disease of 6.8% in the general adult population, studies have shown a prevalence of over 16% among individuals with HIV
- Investigators have proposed a mechanism whereby HIV enhances the risk of developing obstructive lung disease, but has not been fully elucidated
- Besides higher smoking rates among those with HIV, other factors that may predispose to lung disease include increased CD8 T-cell activation, increased levels of inflammatory cytokines, decreased antioxidant defenses, and more frequent episodes of pneumonia
- Currently, no HIV-specific guidelines exist for the management of obstructive lung disease in this population so it is reasonable to follow existing asthma and COPD guidelines that pertain to the general population
- Smoking cessation should be strongly encouraged in smokers with HIV

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COMPLICATIONS WITH INHALED CORTICOSTEROIDS

- Respiratory medications commonly recommended for COPD, particularly inhaled corticosteroids, may pose increased risk of complications in persons with HIV
- Associated with oral candidiasis, bacterial pneumonia, and tuberculosis among individuals without HIV, and this risk could be augmented by HIV
- In addition, the metabolism of corticosteroids, especially fluticasone and budesonide, is inhibited by PIs and potentially by cobicistat-containing antiretroviral regimens
- This can cause dangerous systemic levels of corticosteroids and induce serious side effects (Cushing's syndrome and osteoporosis)
- Salmeterol levels may also increase significantly when used concomitantly with PIs (particularly ritonavir) or cobicistat
- Use caution when considering this long-acting β-agonist due to concerns about increased risk of salmeterol-associated cardiovascular events

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CANCER AND HIV

- Data from the ongoing HIV/AIDS Cancer Match Study and the CDC showed a sharp increase in non-AIDS-defining cancers among persons with HIV during the 15-year period from 1991 and 2005
- Kaposi sarcoma and non-Hodgkin's lymphoma (both AIDS-defining malignancies) along with lung cancer are currently the most common cancers in persons with HIV
- In a recent study examining excess cancers among patients with HIV in the US, half of all excess deaths were due to AIDS-defining cancers (Kaposi's sarcoma, non-Hodgkin lymphoma, cervical cancer) and half were due to non-AIDS-defining cancers (lung, anal, liver, oral/pharyngeal cancers)
- Most of these cancers are mediated by viral coinfections
- In this same study, there was no excess of colon, breast or prostate cancer among persons with HIV compared with the general population
- Other studies have shown rates of prostate and colorectal cancer are similar to, or slightly lower, than that those in the general population
- There is no data to suggest that ART medications are associated with an increased rate of malignancy
- Indeed, intermittent ART (compared with continuous therapy) is associated with an increase in the rate of non-AIDS-defining cancers

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Cancers in people living with HIV

Risk factors

Immune Dysregulation
Low CD4 T-cell count
Chronic immune activation
T-cell exhaustion

Oncogenic viruses
EBV, KSHV, HPV, HBV, HCV

Smoking
Inflammation

Aging
Immune senescence

Outcome disparities

Cancer-specific factors
Advanced stage at presentation
Delayed diagnosis
Other medical co-morbidities

Treatment related factors
Inadequate HIV treatment
Inadequate supportive care
Lack of access to clinical trials
Less aggressive or no cancer treatment

Health system factors
Co-ordination of HIV and cancer care
Lack of multidisciplinary support
Stigma

The Changing Face of HIV-Associated Malignancies: Advances, Opportunities, and Future Directions

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CANCER SCREENING AND HIV

- The shifting spectrum of cancer in persons with HIV underscores the importance of incorporating standardized cancer surveillance practices in the care of the persons with HIV, including those with relatively preserved immune function
- Rates of colon cancer, prostate cancer and breast cancer are similar among persons with HIV to those without HIV so the screening recommendations for these types of cancer are the same as for the general population
- Due to disproportionate risks of developing cervical and anal cancer among individuals with HIV infection, these cancers warrant different screening protocols

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CERVICAL CANCER SCREENING AND HIV

- Abnormal cervical cytology is nearly 11 times more common among women with HIV compared with the general female population and is associated with HPV infection and immune dysfunction.
- Sexually active women with HIV should undergo cervical cancer screening at initial entry to HIV care and again and again 6-12 months later
- Although initiation of cervical cancer screening is recommended at age 21 years in the general population, young women with HIV should be screened for cervical cancer within 1 year of onset of sexual activity, and by age 21 at the latest, due to concerns about more rapid progression of cervical abnormalities in women with HIV
- Cervical cancer screening should continue throughout the life of a woman with HIV, as opposed to the recommendation to stop after age 65 in the general population
- Cervical cancer screening recommendations for women with HIV are not altered if they have received prior HPV vaccine

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ANAL CANCER SCREENING AND HIV

- Relative incidence of anal cancer is increased in those with HIV compared to the general population
- Risk is particularly high among men who have sex with men (MSM), with one study estimating 83% excess cases of anal cancer in this group
- HPV has been implicated in the pathogenesis of most anal malignancies
- The Primary Care Guidelines for the Management of Persons Infected with HIV recommend:
  - Anal Pap smears should be performed in MSM, women with a history of receptive anal intercourse OR abnormal cervical Pap test results, AND all patients with HIV who have genital warts
  - HPV testing is not recommended as part of screening at this time, although an annual digital rectal examination may detect masses and should be considered as part of anal health screening
  - Abnormal anal Pap testing (ASC-US or worse) requires follow-up with high-resolution anoscopy and possible biopsy and treatment
  - When implementing anal Pap testing in clinical settings, it is critical to establish a follow-up plan and ensure access to providers who can deliver these services

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SUMMARY POINTS

- Cardiovascular diseases are an area of special concern to patients with HIV and risk reduction should be prioritized
- Calcium channel blockers should be avoided in patients taking PIs or cobicistat due to risk of drug interactions
- There is limited trial data to inform clinical decision-making regarding lipid management in persons with HIV infection and this has likely led to undertreatment of lipid disorders in this population
- For patients with HIV infection on ART who would benefit from statin therapy, rosuvastatin offers the best combination of safety and efficacy but low-dose atorvastatin, pitavastatin, and pravastatin are other alternatives
- Simvastatin and lovastatin should be avoided due to drug interactions with certain ART medications
- Patients with HIV should be screened regularly for the development of diabetes mellitus but there is no role for switching ART regimens in patients with impaired glucose tolerance
- Patients with HIV should have routine laboratory monitoring of renal function
- The risk of developing renal disease is higher in patients with CD4 less than 200 cells/mm^3, elevated viral load, black race, female sex, older age, or comorbidities such as diabetes, hypertension, and hepatitis C

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SUMMARY POINTS

- Tenofovir DF carries a risk of nephrotoxicity that is higher in patients taking lopinavir/ritonavir and in patients with lower body weight and lower creatinine clearance at tenofovir DF initiation
- All postmenopausal women and all men 50 years of age and older should receive DXA scans
- Assessment of morning testosterone levels is recommended in adult men with HIV who present with decreased bone mass, a low trauma fracture, decreased libido, erectile dysfunction, hot flashes, or sweats, and should be considered for nonspecific symptoms such as depression and fatigue.
- Persons with HIV smoke at twice the rate of those without HIV
- Kaposi's sarcoma, non-Hodgkin lymphoma, and lung cancer are the most common cancers among patients with HIV
- Colon cancer, breast cancer, and prostate cancer screening recommendations are the same for persons with HIV infection as for the general population
- Due to disproportionate risks of developing cervical and anal cancer among patients with HIV infection, these cancers warrant different screening protocols

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REFERENCES

- National HIV Curriculum
- Palella FJ Jr, Baker RK, Moorman AC, et al. Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. J Acquir Immune Defic Syndr. 2006;43:27-34.
- Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. JAMA Intern Med. 2013;173:614-22.
- Shah ASV, Stelzle D, Lee KK, et al. Global Burden of Atherosclerotic Cardiovascular Disease in People Living With HIV. Circulation. 2018;138:1100-12.
- Feinstein MJ, Hsue PY, Benjamin LA, et al. Characteristics, Prevention, and Management of Cardiovascular Disease in People Living With HIV: A Scientific Statement From the American Heart Association. Circulation. 2019;140:e98-e124.
- Aberg JA, Gallant JE, Ghanem KG, et al. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV medicine association of the Infectious Diseases Society of America. Clin Infect Dis. 2013;58:e1-34.
- Malvestutto CD, Aberg JA. Management of dyslipidemia in HIV-infected patients. Clin Lipidol. 2011;6:447-462.
- Brown TT, Cole SR, Li X, et al. Antiretroviral therapy and the prevalence and incidence of diabetes mellitus in the multicenter AIDS cohort study. Arch Intern Med. 2005;165:1179-84.
- Lucas GM, Ross MJ, Stock PG, et al. Clinical Practice Guideline for the Management of Chronic Kidney Disease in Patients Infected With HIV: 2014 Update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis. 2014;59:e96-e138.
- Brown TT, Hoy J, Borderi M, et al. Recommendations for Evaluation and Management of Bone Disease in HIV. Clin Infect Dis. 2015;60:1242-51.
- Mdodo R, Frazier EL, Dube SR, et al. Cigarette smoking prevalence among adults with HIV compared with the general adult population in the United States: cross-sectional surveys. Ann Intern Med. 2015;162:335-44.
- Gingo MR, Morris A, Crothers K. Human immunodeficiency virus-associated obstructive lung diseases. Clin Chest Med. 2013;34:273-82.
- Patel P, Hanson DL, Sullivan PS, et al. Incidence of types of cancer among HIV-infected persons compared with the general population in the United States, 1992-2003. Ann Intern Med. 2008;148:728-36.
- Robbins HA, Pfeiffer RM, Shiels MS, Li J, Hall HI, Engels EA. Excess cancers among HIV-infected people in the United States. J Natl Cancer Inst. 2015;107:

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