

# Primary Care Guidance for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America

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Advances in antiretroviral therapy (ART) have made it possible for persons with human immunodeficiency virus (HIV) to live a near expected life span, without progressing to AIDS or transmitting HIV to sexual partners or infants. There is, therefore, increasing emphasis on maintaining health throughout the life span. To receive optimal medical care and achieve desired outcomes, persons with HIV must be consistently engaged in care and able to access uninterrupted treatment, including ART. Comprehensive evidence-based HIV primary care guidance is, therefore, more important than ever. Creating a patient-centered, stigma-free care environment is essential for care engagement. Barriers to care must be decreased at the societal, health system, clinic, and individual levels. As the population ages and noncommunicable diseases arise, providing comprehensive healthcare for persons with HIV becomes increasingly complex, including management of multiple comorbidities and the associated challenges of polypharmacy, while not neglecting HIV-related health concerns. Clinicians must address issues specific to persons of childbearing potential, including care during preconception and pregnancy, and to children, adolescents, and transgender and gender-diverse individuals. This guidance from an expert panel of the HIV Medicine Association of the Infectious Diseases Society of America updates previous 2013 primary care guidelines.

**Keywords.** HIV primary care; HIV care engagement; HIV monitoring; HIV comorbidities; sexually transmitted infections.

Although substantial inequities exist by region and population, with continuous engagement in high-quality human immunodeficiency virus (HIV) care and uninterrupted access to antiretroviral therapy (ART), people with HIV now have the possibility of an expected life span that approaches that of persons not living with HIV, free of opportunistic diseases and without horizontal transmission to partners or vertical transmission to infants [1–4]. Ending the HIV epidemic, however, has proven challenging in the United States, with only 59.8% of those aware of their HIV diagnosis achieving viral suppression, and even lower rates among African-Americans, Hispanic/Latinos, transgender women, persons aged 13–24 years, persons who inject drugs (PWID), and those who live in the South [5]. Identifying and overcoming barriers to care engagement and continuous ART, therefore,

must be an overarching priority of HIV primary care. Ensuring stigma-free, culturally appropriate, and patient-centered care experiences is essential to maximize care engagement, treatment adherence, and viral suppression. While ART has become more potent, less toxic, and simpler, other aspects of HIV care have become increasingly complex as people with HIV live longer and experience increased comorbidities across the life span, requiring additional attention to issues associated with aging with HIV [6–10]. Recommendations that are affected by age are noted throughout this guidance. Noncommunicable diseases, including metabolic complications, require guidance for prevention and management, particularly as the population ages. Persons of childbearing potential, children, adolescents, and transgender and gender-diverse individuals experience unique clinical challenges. As ever-increasing numbers of people are living with HIV and require both HIV-specific and primary medical care, the need for updated recommendations necessitated this update to the 2013 HIV Primary Care Guidelines from the HIV Medicine Association (HIVMA) of the Infectious Diseases Society of America (IDSA) [11]. “People First” language that places the person before the disease is used in this document to acknowledge the dignity of people with HIV, and gender-neutral language is used, where appropriate [12].

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## METHODS

### Panel Composition

Participants on the panel are HIVMA members who are experts in the care of persons with HIV and who volunteered to participate. Two co-chairs (M. A. T. and M. A. H.) with experience in developing guidelines and guidance led the expert panel.

### Literature Review, Analysis, and Consensus Development of Evidence-based Recommendations

The expert panel conducted a literature review to identify new contributions to the field from the date of the last guideline publication in 2013 to December 2019, with the exception of Centers for Disease Control and Prevention (CDC)/Advisory Committee on Immunization Practices (ACI) guidelines released in January 2020 and coronavirus 2019 COVID-19 comments, including peer-reviewed presentations at recent scientific conferences. Panel members responsible for each section evaluated the evidence and developed recommendations accordingly. The entire panel reviewed all recommendations, and decisions on final recommendations were made by consensus, based on the evidence. The full panel participated in reviewing and editing the final document. A medical writer contributed to copy editing and formatting prior to submission.

### Conflicts of Interest

All members of the panel complied with the IDSA policy on conflicts of interest, which requires disclosure of any financial or other interest that might be construed as constituting an actual, potential, or apparent conflict. Members of the panel were provided with the IDSA's conflict of interest disclosure statement and asked to identify ties to companies that develop products that might be affected by promulgation of the guidance. Information for panel members and spouses was requested regarding employment, consultancies, stock ownership, honoraria, research funding, expert testimony, and membership on company advisory committees. The panel made decisions on a case-by-case basis as to whether an individual's role should be limited as a result of a conflict or potential conflict. No limiting conflicts were identified.

## RECOMMENDATIONS FOR THE PRIMARY CARE OF PERSONS WITH HIV

While these recommendations seek to provide optimal medical care for persons with HIV, establishing a relationship of trust should guide the structure of the medical visit, the order of ascertainment of medical information, and the delivery of care and treatment. For persons who experience stigma and discrimination, optimal care outcomes are dependent on a stigma-free and welcoming care environment. Attention to other barriers that impact care engagement and continuous ART access is essential for successful outcomes.

Many recommendations throughout this document refer to other guidelines, with the recognition that these sources evolve over time and that no single primary care guidance publication can fully anticipate these changes. In general, recommendations from the most current versions of guidelines should be followed.

## I. OPTIMIZING CARE ENGAGEMENT, MEDICATION ADHERENCE, AND VIRAL SUPPRESSION

### Recommendations

1. All persons with HIV should be provided timely access to routine and urgent primary medical care, including approaches to expand access such as extended/weekend hours or telehealth.
2. HIV care sites should make every effort to provide care in a way that is linguistically and culturally appropriate.
3. HIV care sites should implement programs that incorporate evidence-based and evidence-informed interventions shown to improve HIV care engagement and viral suppression.
4. HIV care sites should use a multidisciplinary model but identify a primary clinician for each patient and support the development of trusting long-term, patient-clinician relationships.

### Evidence Summary

The long-term effectiveness of ART is dependent on durable suppression of viral replication. Clinicians should emphasize that adherence to antiretrovirals not only improves the patient's health but prevents HIV transmission to others [12–16]. Undetectable = Untransmittable messaging is welcomed and encouraged by communities with HIV and should be part of routine messaging in the clinic as a means to mitigate stigma. The primary reason for treatment failure, particularly among patients who take initial regimens, is suboptimal adherence to care or treatment regimens [17, 18]. Adherence to care not only means medication adherence but also medical visit attendance and continual engagement in care [19, 20]. Low adherence to visits and poor engagement in care have been found to predict approximately 50% higher mortality among persons with HIV [21]. Thus, it is critically important that HIV care providers and clinics have evidence-based and evidence-informed strategies to effectively engage and assist patients in staying in care [22]. Drivers of poor treatment adherence are many and include inconsistent access to medications (eg, inability to afford medications, limited pharmacy hours, requirements to pick up prescription refills monthly), structural societal barriers (eg, inadequate transportation; health system barriers to engagement; food or housing insecurity; stigma and discrimination based on HIV status, race, and ethnicity; gender identity; sexual orientation; disability; immigration status), clinic level barriers (eg, stigmatizing or discriminatory language or practice

by office staff or clinicians, restrictive hours, inaccessible location, lack of an effective patient–clinician relationship), and patient-level barriers (eg, mental health and substance use issues, pill fear, pill fatigue, stigma) [23–28]. Additionally, the postpartum period is a time when a high proportion of women are lost to follow-up, and these populations warrant dedicated programs to assist with care engagement [29]. All of these factors must be considered when designing systems to improve care engagement.

A national expert panel in which HIVMA and IDSA participate has developed HIV quality-of-care performance metrics [30]. These metrics are endorsed by the National Quality Forum and the Center for Medicare & Medicaid Services and have been adopted by many care organizations. Importantly, mortality decreases when performance measures are met [31].

With few exceptions (such as in cases of cryptococcal meningitis or tuberculosis), there is no reason to delay initiation of ART among newly diagnosed or ART-naïve populations who desire therapy. Ideally, patients should be initiated on ART on the day of diagnosis or as soon thereafter as feasible [32]. It is clear that eliminating barriers to care engagement leads to shorter times to viral suppression, and there is increasing evidence that patients engaged through rapid entry programs have excellent retention and viral suppression upon longer-term follow-up [33–38]. Rapid ART initiation approaches are endorsed by the Department of Health and Human Services (DHHS) Adult and Adolescent Antiretroviral Guidelines Panel, International Antiviral Society–USA Antiretroviral Panel, and New York Department of Health AIDS Institute [39, 40]. Long waiting time for an initial appointment for HIV care has been shown to be one predictor of failure to engage in care [40–42].

The quality of the patient–provider relationship is often cited as one of the most important factors in care engagement. Having a provider with whom the patient feels comfortable and can communicate effectively and honestly is key to developing this type of relationship [26, 43–45]. The multidisciplinary care model for care coordination often helps patients remain in care, identifies unmet care needs, and improves adherence to medications [46–49]. Having an HIV team that includes a case manager, social worker, or staff with similar responsibilities and skills has been shown to enhance adherence to care and engagement [50]. Other team members may include physicians, HIV clinical pharmacists, nurses, nurse practitioners, physician assistants, mental health professionals, social workers, health educators, patient navigators, and nutritionists. Culturally and linguistically competent care is critical to successfully engage and retain patients in care. A broad range of components, from having staff of the same race, culture, or lifestyle to having art and reading material in the clinic that reflects the culture of the local community, may be useful in facilitating this goal [51, 52]. Dedicated attention to tailored programs that facilitate care engagement is an essential component of effectively caring for

persons with HIV. Ensuring the meaningful involvement of people with HIV in program design and implementation is critical to shaping clinical programs that prioritize access and care engagement.

Components that could provide a foundation for individual care engagement programs include social engagement programs, reminders around the clinic about the importance of retention, patient navigation (eg, enhanced personal contacts), financial incentives, nutrition assistance, coordination with public health surveillance data, and mobile health (mHealth) platforms that leverage mobile devices to better engage patients [53–58]. Intake assessments and ongoing assessments of barriers to care should include social and economic factors such as stigma, violence, social support, food insecurity, unstable housing, and transportation challenges. Lack of adequate food or safe housing can impact the ability to remain adherent to a treatment regimen and even increase risk of death [59]. Early assessment by a qualified social worker or case manager is essential, and ongoing access to effective case management teams is necessary [60–62].

## II. INITIAL EVALUATION AND IMMEDIATE FOLLOW-UP FOR PERSONS WITH HIV

### Recommendation

5. A comprehensive present and past medical history that includes HIV-related information, medication/social/family history (Tables 1 and 2), review of systems, and physical examination (Table 3) should be obtained for all patients upon initiation of care, ideally at the first visit or, if not feasible, as soon as possible thereafter. In particular, in settings of rapid ART initiation, clinicians may initially truncate parts of the comprehensive history and physical and provide a more targeted exam but with close follow-up to complete the essential and more comprehensive assessment. As many patients will not be able to recall details of prior treatments and laboratory results, medical records should be requested and reviewed, and the current medical record updated accordingly. Baseline laboratory assessments should be obtained at the initial visit (Table 4).

### Family Medical History

A family medical history has become more important now that persons with HIV are living longer and are at increased risk for age- and sex-specific conditions in addition to HIV- and treatment-related complications. Clinicians should ask about family history of conditions that might predispose them to malignancies, neurologic diseases, osteoporosis, and atherosclerotic disease and whether there is a family history of early coronary heart disease.

### Social History

Clinicians should ask how the patient is coping with the diagnosis of HIV, whom they have informed of their HIV status,

**Table 1. Initial Assessment: History of the Present Illness and Human Immunodeficiency Virus–specific History**

History of the present illness
<ul style="list-style-type: none"> <li>Initial questions should focus on establishing rapport, putting the patient at ease, and ascertaining the patient's primary reason for the visit, if not simply to establish the patient in HIV care</li> <li>Assess the patient's level of knowledge about HIV treatment and prevention, evaluate educational needs, and determine what ancillary and social support might be necessary (ideally, in collaboration with effective case management)</li> <li>If not previously treated with ART, assess the patient's readiness to begin ART immediately, including on the day of the first visit if feasible</li> <li>If previously but not currently on ART, assess the patient's readiness to reinstate ART immediately, including on the day of the first visit if feasible and if adequate information is available to choose an appropriate regimen</li> <li>Assess the need for assistance with social services, such as housing, transportation, and food access, and involve support staff early if appropriate</li> </ul>
HIV-specific history
<ul style="list-style-type: none"> <li>Approximate date of HIV diagnosis</li> <li>Approximate date of HIV acquisition, which can sometimes be determined on the basis of prior negative test results, occurrence of symptoms suggestive of acute retroviral infection, or timing of activities that may have resulted in exposure</li> <li>Prior HIV care</li> <li>Nadir CD4 cell count and highest viral load</li> <li>Current and past exposure to antiretroviral drugs <ul style="list-style-type: none"> <li>Use of pre- or postexposure prophylaxis (including medications and date of last use)</li> <li>ART for prevention of perinatal transmission</li> <li>Prior antiretroviral treatment <ul style="list-style-type: none"> <li>Drug regimens taken and HIV RNA level while on those regimens</li> <li>Duration of therapy</li> <li>Reasons for changing regimens (eg, virologic failure, tolerability, simplification) and adherence challenges</li> </ul> </li> <li>Past medical record review (request records if not available)</li> <li>Results of all prior resistance testing</li> </ul> </li> <li>Prior HIV-associated conditions <ul style="list-style-type: none"> <li>Opportunistic infections and/or malignancies according to Centers for Disease Control and Prevention stage 3 definition [247]</li> <li>Other HIV-related conditions (eg, thrush)</li> </ul> </li> </ul>
People who currently inject drugs
<ul style="list-style-type: none"> <li>Current drug-use practices</li> <li>Source of needles and needle-sharing practices</li> </ul>

Abbreviations: ART, antiretroviral therapy; HIV, human immunodeficiency virus.

and what support they have been receiving from family and friends. If needed, patients should be offered assistance with the disclosure process. Work and educational histories should be discussed, including whether these have been affected by the diagnosis of HIV. Other pertinent information includes insurance issues, financial status, marital and family status, and plans for having children.

It is critical to obtain a sexual history in an open, nonjudgmental manner, asking about past and current practices [69]. Counseling and education should focus on attaining viral suppression for optimal personal health and elimination of HIV transmission to sexual partners (including education that Undetectable = Untransmittable), and risk reduction for other sexually transmitted pathogens. Clinicians should ask about partners, sexual practices (including all exposure sites, condom and contraceptive use), past sexually transmitted infections (STIs), HIV status of partner(s), and whether the patient has informed their partner(s) of their HIV status. Laws vary from state to state regarding the obligation of healthcare providers to notify sex partners, and clinicians should be aware of laws in their own jurisdiction. All clinicians should familiarize themselves with basic discussions about gender identity, including

communication about appropriate pronouns, and fundamentals of care for transgender and gender-diverse individuals [70]. Please see Section VIII for further discussion of transgender and gender-diverse health.

#### **Allergies and Medications**

A discussion of allergies and intolerances should include questions about hypersensitivity reactions to antibiotics and ART. Clinicians should ask about all current medications, including dietary or herbal supplements, some of which have been shown to interact with ART. All prior ART regimens, including years of use, prior side effects, and reasons for switching, should be recorded. It is also important to assess prior adherence to medications and document viral loads while on each regimen.

#### **Review of Systems**

The review of systems should be comprehensive and include questioning about common HIV-related symptoms (see Table 3). Patients should be questioned about how their current weight compares with their baseline, along with a dietary assessment. Depression is common among people with HIV, especially women, and the review of systems should include questions that focus on changes in mood,

**Table 2. Other Medical and Surgical History**

Comorbidities: current or past chronic medical conditions that might affect the choice of therapy or response to therapy
<ul style="list-style-type: none"> <li>• Prior and present gastrointestinal disease</li> <li>• Liver disease, including viral hepatitis</li> <li>• Cardiovascular disease and risk factors, including hyperlipidemia, hypertension, diabetes mellitus, smoking</li> <li>• Osteopenia or osteoporosis</li> <li>• Kidney disease</li> <li>• History of receipt of blood products, organ transplant, or tattoos</li> </ul>
Other past medical conditions that may have implications for persons with HIV
<ul style="list-style-type: none"> <li>• History of chicken pox or shingles, measles</li> <li>• <i>Mycobacterium tuberculosis</i> illness, exposure, treatment; prior testing or treatment for latent tuberculosis</li> <li>• STIs, including syphilis, chlamydia, gonorrhea, herpes simplex, trichomoniasis, chancroid, HPV</li> <li>• Abnormal anal cytology; past anorectal disease including warts, fissures</li> </ul>
Gynecologic and obstetric history
<ul style="list-style-type: none"> <li>• Past pregnancies and plans for future pregnancy; history of artificial insemination by an unidentified donor</li> <li>• Birth control practices</li> <li>• Last cervical Pap test, abnormal Pap test ever, colposcopy, loop electrosurgical excision procedure, biopsy (cone/knife)</li> <li>• Menstrual history</li> <li>• Other gynecologic conditions including pelvic inflammatory disease</li> </ul>
Mental health history, current and past
<ul style="list-style-type: none"> <li>• Previous or current psychotherapy and medication treatment</li> <li>• Anxiety disorders, bipolar disorder, depression, violent behavior</li> <li>• Suicidal, homicidal ideation; history of hospitalization due to mental health issues</li> <li>• History of trauma, including sexual and physical abuse, intimate partner and other violence; post-traumatic stress disorder (with appreciation for the sensitive nature of these inquiries and the emotional responses they may elicit)</li> </ul>
Current or past use of psychoactive substances
<ul style="list-style-type: none"> <li>• Tobacco including e-cigarettes; years of use and estimate of cumulative exposure</li> <li>• Cannabis and cannabinoids (including vaping)</li> <li>• Vaping (regardless of substance)</li> <li>• Alcohol use: quantify weekly/monthly use</li> <li>• Stimulants, including methamphetamine, cocaine, crack cocaine</li> <li>• Opioids</li> <li>• Other nonprescription drugs</li> <li>• Misuse or overuse of prescription drugs</li> <li>• Other substances primarily used with sex (amyl nitrate [poppers], erectile dysfunction drugs)</li> <li>• Past injection drug use (regardless of substance used); history of needle sharing; hospitalizations related to injection drug use</li> </ul>
Past hospitalizations, surgical procedures, transfusions or blood product receipt, especially during 1975–1985 or outside United States/Canada
Immunization status (obtain from past medical records if possible)
<ul style="list-style-type: none"> <li>• Childhood vaccination including for measles, mumps, rubella</li> <li>• Hepatitis A and B</li> <li>• HPV</li> <li>• Influenza</li> <li>• Meningococcus</li> <li>• Pneumococcus—13 valent and 23 valent</li> <li>• Varicella zoster</li> <li>• Tetanus/diphtheria or tetanus/diphtheria/pertussis</li> <li>• Travel vaccinations</li> </ul>
Travel and residential history pertinent to endemic infectious diseases that may be reactivated (eg, histoplasmosis [Ohio and Mississippi River valleys] or coccidioidomycosis [southwestern deserts])
Pediatric
<ul style="list-style-type: none"> <li>• Maternal obstetric and birth history</li> <li>• Exposure to perinatal antiretrovirals</li> <li>• Exposure to infectious diseases</li> <li>• Growth and development</li> </ul>
Family medical history
<ul style="list-style-type: none"> <li>• Diabetes</li> <li>• Early heart disease: myocardial infarction in a first-degree relative before the age of 55 years in male relatives and before the age of 65 years in female relatives</li> <li>• Hypertension</li> <li>• Hyperlipidemia</li> <li>• Cancer</li> </ul>

**Table 2. Continued**

Social history
• Race and ethnicity
• Gender identity and sexual orientation; pronouns
• Patient birthplace, residence, and travel history
• Employment history
• Incarceration history
• Education history
• Financial support
• Children: ages, plans for having children in the future; HIV status of children
• Pets
• Diet and exercise
• Sexual history: types of activity including partners and practices; sexual exposure sites; STI prevention including condom use; past STIs; prior preexposure prophylaxis use
• Marital/relationship status
◦ Partner(s) health and HIV status
◦ Partner(s) access to healthcare, including HIV testing (if appropriate)
◦ Disclosure of HIV status to partner(s)
• Social support and participation in support groups
• Disclosure history: friends, family, work colleagues
• Access to stable housing, food, transportation
• For minors, review legal guardianship and consent/assent
Medications
• Current medications, including over-the-counter medications, supplements
• Use of complementary or alternative therapy or treatment
Allergies and intolerance: dates and types of reactions, including hypersensitivity reactions to antiretroviral therapy
Healthcare maintenance and preventative health screenings (as appropriate)
Dates of last
• Mammogram
• Bone density
• Colonoscopy
• Abnormal aortic aneurysm screening
• Dental visit
• Dilated eye exam

Abbreviations: HIV, human immunodeficiency virus; HPV, human papillomavirus; STI, sexually transmitted infection.

libido, sleeping patterns, appetite, concentration, and memory. As part of the initial evaluation and at periodic intervals thereafter, providers should assess the presence of depression, post-traumatic stress disorder, and sexual or physical abuse, including domestic violence, by means of direct questions or validated screening tools (Patient Health Questionnaire-9 [PHQ-9] and Generalized Anxiety Disorder 2-item [GAD-2]) [71, 72]. Persons with HIV have high rates of adult sexual and physical abuse and of childhood sexual abuse.

#### **Physical Examination**

A complete physical examination should be performed at the initial encounter or as soon afterward as possible. In addition to recording all vital signs (including height and weight), head circumference should be measured in children aged <3 years and plotted against standard growth curves. Furthermore, developmental assessment is important in infants and children. Older persons should be assessed for frailty. For all patients, the overall body habitus should be assessed, looking for evidence of wasting, obesity, or, particularly in patients who have received older ART regimens, evidence of drug-related

lipohypertrophy (eg, dorsocervical fat pad, gynecomastia, or visceral abdominal fat accumulation) and/or lipoatrophy (eg, loss of subcutaneous fat in the face, extremities, or buttocks). All adult patients with advanced HIV disease (CD4 cell count <50 cells/ $\mu$ L) as well as infants and young children with profound immunodeficiency should be referred to an ophthalmologist for a dilated fundoscopic examination. Though persistent generalized lymphadenopathy is common among untreated persons with HIV, it does not correlate with prognosis or disease progression. However, focal or rapidly progressive lymphadenopathy may require further evaluation, including biopsy. Additionally, if lymphadenopathy does not quickly resolve with initiation of ART, diagnostic studies should be pursued. Neurology and/or neuropsychology referral for assessment of neurocognitive disorders, dementia, and focal neuropathies may be indicated [73, 74]. Cervical motion and uterine or adnexal tenderness on bimanual pelvic examination suggest pelvic inflammatory disease and should prompt STI testing. An anorectal examination is important to evaluate for anal warts, other STIs, and anal cancer, with

**Table 3. Initial Assessment—Review of Systems and Physical Examination**

Review of Systems	Physical Examination
A complete review of systems with special attention to the areas listed below:	A complete physical examination should be performed, with special attention to the following areas:
<ul style="list-style-type: none"> <li>• General: unexplained weight loss or gain, night sweats, fever, changes in body habitus</li> <li>• Skin: discoloration, rash, ulcers, or lesions</li> <li>• Lymph nodes: localized or generalized enlargement of lymph nodes</li> </ul>	<ul style="list-style-type: none"> <li>• Vital signs: including height and weight</li> <li>• General: including body habitus, evidence of obesity, wasting, lipodystrophy, assessment of frailty, and ambulatory ability</li> <li>• Skin: seborrheic dermatitis, ecchymoses, purpura, petechiae, Kaposi sarcoma, herpes simplex or zoster, psoriasis, molluscum contagiosum, onychomycosis, folliculitis, condylomata, cutaneous fungal infections, acanthosis</li> </ul>
<ul style="list-style-type: none"> <li>• Eyes: vision change or loss</li> <li>• Mouth: gum disease, ulcers, oral lesions, or pain</li> <li>• Cardiopulmonary: chest pain, palpitations, wheezing, dyspnea, orthopnea</li> </ul>	<ul style="list-style-type: none"> <li>• Lymph nodes: generalized or localized lymphadenopathy</li> <li>• Eyes: retinal exudates or cotton wool spots, hemorrhages, pallor, icterus</li> <li>• Cardiovascular: heart exam, peripheral pulses, presence/absence of edema or bruits</li> </ul>
<ul style="list-style-type: none"> <li>• Gastrointestinal: odynophagia, dysphagia, diarrhea, nausea, pain</li> <li>• Endocrinology: symptoms of hyperglycemia, thyroid disease, hypogonadism</li> </ul>	<ul style="list-style-type: none"> <li>• Chest: lung examination</li> <li>• Breast: nodules, nipple discharge</li> </ul>
<ul style="list-style-type: none"> <li>• Neurologic and psychiatric: persistent and severe headaches, memory loss, loss of concentration, depression, apathy, anxiety, mania, mood swings, lower extremity paresthesias, pain, or numbness, paralysis or weakness, cognitive difficulties, dizziness, seizures, sleep disorders</li> <li>• Genitourinary: dysuria, urethral or vaginal discharge or lesions, hematuria</li> </ul>	<ul style="list-style-type: none"> <li>• Abdomen: hepatomegaly, splenomegaly, masses, tenderness</li> <li>• Genitourinary: ulcers, warts, chancres, rashes; gynecologic exam including bimanual exam, discharge; if born male: testicular exam; evaluation for hernia</li> </ul>
<ul style="list-style-type: none"> <li>• Orthopedic: hip pain, joint pain, fractures, diagnosis of or risk factors for osteopenia/osteoporosis</li> <li>• Anorectal: anal discharge, rectal bleeding, rectal itching, pain or fullness in anal area</li> </ul>	<ul style="list-style-type: none"> <li>• Anorectal: ulcers, warts, fissures, internal or external hemorrhoids, masses, Kaposi sarcoma; prostate exam when appropriate</li> <li>• Neuropsychiatric: depression, mania, anxiety, signs of personality disorder, difficulties in concentration, attention, memory, signs of dementia, speech problems, gait abnormalities, focal deficits (motor or sensory), lower extremity vibratory sensation, deep tendon reflexes</li> </ul>
<ul style="list-style-type: none"> <li>• Developmental milestones: for infants and young children assess for motor or speech delays</li> </ul>	

screening for prostate abnormalities if born male (as age appropriate).

#### Baseline Laboratory Evaluation

A number of initial laboratory studies are indicated upon presentation with a new HIV diagnosis or for persons who reengage in care (see Table 4). Other tests may be indicated depending on the age and sex of the patient and/or symptoms. In settings where rapid initiation of ART is possible, it is important to obtain baseline laboratory tests. However, ART initiation need not be delayed until results are received, including for HIV RNA, CD4 cell count, resistance testing, and safety assessments. The absence of results for human leukocyte antigen subtype B\*5701 (HLA B\*5701), genotype, and hepatitis B surface antigen will influence the choice of antiretrovirals for rapid initiation. HIV diagnosis should be ascertained, preferably using rapid testing with a fourth-generation antigen/antibody test if results of HIV screening are not available for review.

#### HIV-Specific Tests for All Persons With HIV and HIV Screening Recommendation

6. Patients who have no documentation of their HIV status or who were tested anonymously should have an HIV antigen/antibody screening test performed upon initiation of care.

#### Evidence Summary

Clinicians should be familiar with the current CDC HIV testing algorithms and interpretation of results based on algorithm and assays used [75, 76]. Confirming an HIV diagnosis is especially important in patients who are asymptomatic and have a normal CD4 cell count and an undetectable or very low viral load. In addition, patients may present to care with misinformation regarding previous test results.

#### CD4 Cell Counts and Percentages Recommendations

7. A CD4 cell count with percentage should be obtained upon initiation of care.
8. Measurement of the CD8 cell count and the ratio of CD4 cells to CD8 cells are unnecessary, as the results are not used in clinical decision-making.

#### Evidence Summary

The initial CD4 cell count is used to stage HIV infection, to help establish the risk of specific HIV-associated complications, and to determine the need for prophylaxis against opportunistic infections. It is important that the clinician and patient be aware of the substantial variation in CD4 cell counts, especially during acute illness. CD4 cell counts

**Table 4. Recommended Initial Laboratory Screening and Other Studies in Persons With Human Immunodeficiency Virus**

Test	Comment(s)
HIV-specific tests for all persons with HIV	
HIV antigen/antibody testing	If written evidence of diagnosis not available or if viral load low or undetectable
CD4 cell count and percentage	Assess need for OI prophylaxis
Plasma HIV RNA polymerase chain reaction (HIV viral load)	Establish baseline and monitor viral suppression
HIV resistance testing	Baseline genotype for protease inhibitor, nonnucleoside reverse transcriptase inhibitor, nucleoside/nucleotide reverse transcriptase inhibitor mutations for persons who have never initiated therapy or who are reengaging in care and not on therapy or with inconsistent access to therapy. INSTI genotype is recommended only if suspicion for INSTI mutation transmission.
HIV-related tests in select patients	
Coreceptor tropism assay	If use of C-C motif chemokine receptor 5 antagonist is being considered
Human leukocyte antigen subtype B*5701	If use of abacavir is being considered
Other laboratory tests	
Complete blood cell count with differential	Assess for anemia, neutropenia, thrombocytopenia
Alanine aminotransferase, aspartate aminotransferase, total bilirubin, alkaline phosphatase	Assess for evidence of liver damage, hepatitis, or systemic infection (eg, elevated alkaline phosphatase with some OIs)
Total protein and albumin	High total protein common with untreated HIV infection due to increased immunoglobulin fraction secondary to B-cell hyperplasia. Low albumin may indicate nutritional deficiency or nephrotic syndrome.
Electrolytes, blood urea nitrogen, creatinine	Assess kidney function. Use creatinine to calculate estimated glomerular filtration rate.
Lipid profile and blood glucose; hemoglobin A1c	Fasting not needed for initial lipid and glucose assessment; if abnormal, repeat fasting. Hemoglobin A1c should be measured prior to ART initiation but is not used for diagnosis of diabetes in those on ART [63–65].
Urinalysis	Assess for evidence of proteinuria, hematuria
Screening for coinfections	
Gonorrhea, chlamydia	Nucleic acid amplification testing with sites based on exposure history (eg, urine, vaginal, rectal, oropharyngeal; 3 site testing preferred for all patients)
Trichomoniasis	In all persons who have vaginal sex
Syphilis	Using local protocol (either rapid plasma regain or treponemal-specific antibody tests)
Latent <i>Mycobacterium tuberculosis</i>	Tuberculin skin test or IGRA; IGRA preferred if history of BCG vaccination
Varicella virus	Anti-varicella IgG if no known history of chicken pox or shingles
Viral hepatitis A, B, and C	HBsAg, HBsAb, HBeAb, HCV antibody; HAV total or IgG antibody. If HBsAg+, or HBeAb+, order HBV DNA level; if HCVAb+, order HCV RNA level and HCV genotype. Screen for hepatocellular carcinoma for all adult patients with cirrhosis and noncirrhotic patients with chronic HBV for an extended period [66, 67].
Measles titer	Adequate evidence of immunity includes being born in the United States before 1957, written documentation of adequate vaccination, or serologic evidence of immunity [68]. Persons born in the 1960s may have been vaccinated with a vaccine other than MMR and may have waning immunity. Patients may opt to receive a booster MMR vaccine rather than check serology.
Tests that may be performed under certain circumstances	
Chest radiography	For patients with evidence of latent <i>Mycobacterium tuberculosis</i> infection. Consider in patients with underlying lung disease for use as comparison in evaluation of future respiratory illness.
Cytology: cervical and/or anal Pap test	Cervical; anal if indicated. Abnormal results require follow-up with colposcopy or high-resolution anoscopy.
Glucose-6-phosphate dehydrogenase	Screen for deficiency in appropriate racial or ethnic groups to avoid use of oxidant drugs including dapsone, primaquine, sulfonamides
Pregnancy test in persons of childbearing potential	Pregnancy status is required to inform choice of ART and discussions about conception in persons of childbearing potential
Serum testosterone level	In cisgender males with fatigue, weight loss, loss of libido, erectile dysfunction, or depression or who have evidence of reduced bone mineral density. Morning free testosterone preferred. See Section IV for management of hypogonadism.
Tests that are not recommended for general screening purposes	
HSV IgG, CMV IgG, toxoplasma IgG, biomarkers of inflammation	In asymptomatic persons, routine testing for all persons is not recommended for HSV, CMV, and toxoplasma. Biomarkers of inflammation are not recommended. Toxoplasma IgG and cryptococcal antigen should be obtained in the context of suspicion for clinical disease. Toxoplasma IgG may be obtained in patients for whom prophylaxis is indicated. CMV IgG may be considered if blood transfusion is contemplated in a person at low risk for CMV exposure. A negative CMV IgG may support use of CMV-free blood products.
Serum cryptococcal antigen in persons with CD4 cell count $\geq 100/\text{mm}^3$	Serum cryptococcal antigen may be considered for persons with CD4 cell count $< 100/\text{mm}^3$

Abbreviations: ART, antiretroviral therapy; BCG, Bacillus Calmette–Guérin; CMV, cytomegalovirus; HAV, hepatitis A virus; HBcAb, HBsAb, Hepatitis B core antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HCVAb, Hepatitis C antibody, HIV, human immunodeficiency virus; HSV, herpes simplex virus; IgG, immunoglobulin G; IGRA, interferon- $\gamma$  release assay; INSTI, integrase strand transfer inhibitor; MMR, measles mumps rubella; OI, opportunistic infection.



may be affected by a variety of medications and intercurrent illnesses, so caution should be applied when interpreting CD4 cell counts during these situations. Although the absolute CD4 cell count is the number most often used in clinical practice, the CD4 cell percentage can also be used to assess immune function and is somewhat less variable than the absolute count. Total CD4 cell counts of 200 and 500 cells/ $\mu$ L generally correspond to CD4 cell percentages of 14% and 29%, respectively. In children aged <5 years, there is more variability in the absolute CD4 cell count; therefore, CD4 percentage is generally preferred for monitoring immune status.

#### **Plasma HIV RNA Levels**

##### **Recommendation**

9. A quantitative HIV RNA (viral load) level should be obtained upon initiation of care.

##### **Evidence Summary**

The initial HIV RNA level defines the patient's baseline so that response to therapy can be measured. The US Food and Drug Administration (FDA) has approved several viral load assays for clinical use. Clinicians should be aware of changes in the type of assay used, the associated variability, and differences in interpretation of results between assays. Thresholds for lower limits of detection for the most commonly used assays range from 20–50 copies/mL. Viral load should be measured during the initial evaluation of the untreated patient upon establishing care or when a patient reengages in care. Viral suppression is defined as a viral load persistently below the level of quantification of the assay; however, the threshold for prevention of HIV sexual transmission is considered to be <200 copies/mL [77].

#### **HIV Resistance Testing**

##### **Recommendations**

10. Patients should be assessed for transmitted drug resistance with a genotype assay for protease inhibitor (PI), nonnucleoside reverse transcriptase inhibitor (NNRTI), and nucleoside reverse transcriptase inhibitor (NRTI) mutations upon initiation of care.
11. Resistance testing should be obtained for patients who reengage in care and who are currently not on ART or who have not had consistent ART access, recognizing that the absence of resistance mutations does not guarantee the absence of resistance when no selective pressure is present.
12. Resistance testing, including for integrase strand transfer inhibitor (INSTIs), if appropriate, is indicated for patients who are experiencing virologic failure to guide modification of ART and should be performed while the patient is on the failing ART regimen or within 4 weeks of discontinuing the ART regimen.
13. If transmitted INSTI resistance is suspected, genotypic testing for INSTI resistance should be obtained.

##### **Evidence Summary**

Drug-resistant HIV can be transmitted from one person to another; however, this is currently less common with INSTIs [78]. The purpose of baseline genotypic resistance testing is to assess for transmitted resistance that would compromise the initial ART regimen. Currently, DHHS ART guidelines recommend baseline genotypic resistance testing for PI, NRTI, and NNRTI mutations for all persons beginning treatment [32]. A modeling study has suggested that, for patients starting bicitgravir or dolutegravir-based triple-drug regimens, baseline genotype testing offers minimal clinical benefit in persons newly diagnosed with HIV [79]. Lack of genotypic testing, however, limits the regimens that may be prescribed, including 2-drug regimens such as dolutegravir/lamivudine fixed-dose combination, or other combinations in which resistance to one drug would result in functional monotherapy. In persons who reengage in care and who have been off therapy for 4 or more weeks, resistance mutations may be absent due to lack of selective pressure rather than absence of resistance, and results should be interpreted with this in mind [32].

Patients who take a failing antiretroviral regimen (HIV RNA >200 copies/mL) should undergo resistance testing to guide interventions in order to improve viral control. In addition, those with prior ART history, quantifiable viral load >200 copies/mL, and no prior documentation of resistance results should undergo resistance testing.

Routine baseline testing for resistance to integrase inhibitors is not currently recommended because of the low frequency of transmitted resistance. However, that may change with the increasing use of integrase inhibitors in clinical practice. Baseline integrase genotypes should be considered in patients who have evidence of transmitted reverse transcriptase or protease mutations or in patients who may have acquired HIV infection from an individual known to have been taking an integrase inhibitor-based regimen [79, 80].

#### **HIV-related Tests in Select Patients and Coreceptor Tropism Assay**

##### **Recommendation**

14. Tropism testing should be performed if the use of a C-C motif chemokine receptor 5 (CCR5) antagonist is being considered.

##### **Evidence Summary**

Coreceptor tropism testing is needed to determine which patients are appropriate candidates for therapy with a CCR5 antagonist [32]. CCR5 antagonists should not be used in patients with X4- or dual/mixed-tropic (D/M) virus. The use of a CCR5 inhibitor in this population could increase the risk of virologic failure and resistance to the other drugs in the regimen. Tropism screening may fail to detect X4 or D/M virus present at very low levels, and patients may experience treatment failure with

CCR5 antagonists because of the presence of preexisting X4 or D/M virus not detected by the tropism assay. Routine tropism testing is not recommended prior to initiation of other regimens because of cost and lack of demonstrated benefit. Patients who exhibit virologic failure while taking a CCR5 antagonist may also be considered for tropism testing.

#### **HLA B\*5701**

##### **Recommendations**

15. HLA B\*5701 testing should be performed before initiation of abacavir therapy.
16. Patients who are positive for the HLA B\*5701 haplotype are at high risk for abacavir hypersensitivity reaction and should never be treated with abacavir (this should be noted appropriately in the medical record).

##### **Evidence Summary**

Screening for the HLA B\*5701 haplotype is recommended in patients being considered for abacavir therapy in order to identify those who are at high risk for the abacavir hypersensitivity reaction [32]. A negative test result does not rule out the possibility of a hypersensitivity reaction but makes it extremely unlikely. Patients who have negative test results should still be counseled about a hypersensitivity reaction before being treated with abacavir. If HLA B\*5701 screening is not available or the patient declines testing, it is reasonable to initiate abacavir with appropriate counseling and monitoring for symptoms or signs of a hypersensitivity reaction [32].

#### **Laboratory Tests to Assess Safety and General Health**

##### **Recommendations**

17. A complete blood count with differential white blood cell count, chemistry panel with calculated creatinine clearance (or estimated glomerular filtration rate [eGFR]) and glucose level, and urinalysis should be obtained upon initiation of care.
18. Because many antiretroviral drugs, HIV infection itself, and host factors are associated with increased cholesterol and triglyceride levels, a lipid profile should be obtained upon initiation of care and repeated fasting, if appropriate.

##### **Evidence Summary**

Anemia, leukopenia, and thrombocytopenia are common among persons with untreated HIV. The complete blood count also is used to calculate the absolute CD4 cell count. A chemistry panel (including electrolytes, glucose, creatinine, blood urea nitrogen, total protein, albumin, total bilirubin, aspartate transaminase, and alanine transaminase) is an important tool to assess renal and hepatic function and to look for evidence of preexisting liver injury or hepatitis.

Kidney function is abnormal in up to 30% of persons with untreated HIV, and HIV-associated nephropathy is a relatively common cause of end-stage renal disease, especially in black persons with HIV, although both rates and mortality have

declined with more effective ART [81, 82]. A calculated creatinine clearance or eGFR should be obtained to further assess baseline renal function. The eGFR assists in prescribing antiretroviral agents and other commonly used medications that require renal dosing. Clinicians should be aware that some medications such as cobicistat, dolutegravir, and trimethoprim may affect creatinine secretion and elevate serum creatinine without affecting renal function [83]. A screening urinalysis for proteinuria should be considered at initiation of care and annually thereafter, especially in patients who are at increased risk for developing kidney disease (eg, black patients; those with CD4 cell counts <200 cells/ $\mu$ L or viral loads >4000 copies/mL; and those with diabetes mellitus, hypertension, or hepatitis C virus [HCV] coinfection) [32]. Patients with proteinuria of grade  $\geq 1$  by dipstick analysis or reduced kidney function should be referred to a nephrologist for consultation and should undergo additional studies, including quantification of proteinuria, renal ultrasound, and possible renal biopsy. Screening for glucose intolerance and diabetes mellitus is recommended because of the increased prevalence in this population [84]. In young children, fasting blood studies are more problematic because of feeding schedules, and clinicians may obtain fasting levels when nonfasting levels are abnormal [77] (see Section V). The lipid profile is important because of high rates of cardiovascular disease in this population and the importance of managing risk factors. Additionally, several antiretrovirals affect lipid levels (see Section IV).

#### **Screening for Coinfections and Screening for STIs**

Rates of STIs have increased substantially in the United States since 2014, and screening rates have been found to be suboptimal in clinical care settings [80, 85]. All clinicians who care for persons with HIV should implement CDC STI screening and treatment guidelines as appropriate for their populations [86]. CDC also provides detailed recommendations for quality STI clinical services in primary care and STI specialty settings [87]. Persons diagnosed with an STI should be encouraged to inform partners in order to decrease further transmission. Expedited partner therapy (EPT), that is, the delivery of STI treatment directly to sexual partners by the person diagnosed with an STI, should be considered.

#### **Chlamydia, gonorrhea, trichomoniasis**

##### **Recommendations**

19. Persons with HIV should be screened for gonorrhea and chlamydia infection at initial presentation. Screening should include all sites of contact (oral, anal, urethral [urine], and vaginal). Those found to have gonorrhea or chlamydia on initial screening should be treated and rescreened in 3 months because of high reinfection rates.
20. All persons who have receptive vaginal sex should be screened for trichomoniasis at entry into care. Those found to have trichomoniasis on initial screening should be

treated and rescreened in 3 months because of high reinfection rates.

### Evidence Summary

Screening and treatment for chlamydia, gonorrhea, and trichomonas should follow CDC STI guidelines [86]. Many STIs (often known to patients as sexually transmitted diseases [STDs]) are asymptomatic. Screening for gonorrhea and chlamydia at all sites of sexual contact (oral, anal, genital [urine]) is recommended for all persons with HIV upon presentation to care, regardless of sex. Nucleic acid amplification tests (NAATs) have the highest sensitivity for detecting gonorrhea, chlamydia, and trichomoniasis and are preferred at all sites of contact, but conditional on the clinical laboratory being Clinical Laboratory Improvement Amendments–certified for the assay at each site of testing. Vaginal swabs in women and urine in men are the preferred specimens for genital testing with NAATs. Other specimens (eg, urethral swabs, endocervical swabs) are also appropriate. Whenever a person has received a diagnosis of a specific STI for which there is curative treatment, immediate therapy should be given according to CDC guidelines. Sexual contacts should be evaluated and presumptively treated, including use of EPT if allowed. All patients treated for gonorrhea and chlamydia or trichomoniasis should be retested 3 months later because short-term reinfection rates are high.

### Syphilis

#### Recommendations

21. All patients should be screened for syphilis upon initiation of care.
22. A lumbar puncture should always be performed for patients with a reactive syphilis serology who have neurologic or ocular symptoms or signs, irrespective of past syphilis treatment history.
23. A lumbar puncture should be performed in patients who experience serologic treatment failure (ie, whose nontreponemal titers fail to decline 4-fold after stage-appropriate therapy or whose titers increase 4-fold if reinfection is ruled out).

#### Evidence Summary

Serologic testing for syphilis should be performed at baseline. Between 2013 and 2017, the annual rate of reported primary and secondary syphilis increased 72.7%. Although the highest rates are in men who have sex with men and transgender women, there was a 155.6% increase among women. Among women and heterosexual men with primary or secondary syphilis, methamphetamine, injection drug, and heroin use doubled during 2013–2017 [88]. Syphilis testing can be done by traditional algorithm or reverse-sequence algorithm. Both treponemal and nontreponemal tests should be followed by a

confirmatory test [89]. Biologic false-positive rapid plasma regain and Venereal Disease Research Laboratory test results are generally of low titer (ie, <1:8). Expert opinion varies on the need for lumbar puncture in neurologically asymptomatic persons with HIV and syphilis. There is a higher incidence of cerebrospinal fluid abnormalities when the nontreponemal test result is positive at a high titer (ie,  $\geq 1:32$ ) or when the CD4 cell count is  $\leq 350$  cells/ $\mu\text{L}$ , regardless of syphilis stage. Persons with syphilis should be treated according to CDC guidelines [86, 90].

### Latent Tuberculosis

#### Recommendations

24. Upon initiation of care, persons living with HIV without a history of tuberculosis or a prior positive tuberculosis screening test should be screened for *Mycobacterium tuberculosis* infection using either a PWID, people who inject drugs; tuberculin skin test (TST) or an interferon- $\gamma$  release assay (IGRA). Those with positive test results should be treated for latent *M. tuberculosis* infection after active tuberculosis has been excluded.
25. Persons with HIV who are close contacts of persons with infectious tuberculosis should be treated for latent *M. tuberculosis* infection regardless of their TST or IGRA results, age, or prior courses of tuberculosis treatment; active tuberculosis should be excluded first.

#### Evidence Summary

All persons with HIV should be tested for *M. tuberculosis* infection using TST or IGRA upon initiation of care [32, 85, 91]. A TST or IGRA should be performed any time there is concern of a recent exposure. For those with CD4 cell count  $\leq 200/\mu\text{L}$ , testing should be repeated after the CD4 cell count increases to  $>200$  cells/ $\mu\text{L}$  following initiation of ART. For a person with HIV, induration of  $>5$  mm by TST is considered a positive result and should prompt chest radiography and other evaluation, as warranted, to rule out active tuberculosis [92]. Annual testing should be considered for those who have negative results by TST or IGRA but are at ongoing risk for exposure [85, 93]. Routine cutaneous anergy testing is not recommended because of lack of standardization of reagents and poor predictive value and because prophylaxis provided to anergic persons has been shown to prevent few cases of tuberculosis [94]. The QuantiFERON-TB Gold test, the QuantiFERON-TB Gold In-tube test (Cellestis Limited), and the T-SPOT TB test (Oxford Immunotech) are approved by the FDA as aids for detecting latent *M. tuberculosis* infection. A large meta-analysis suggests that IGRAs perform similarly to TST when identifying persons with HIV with latent tuberculosis infection [95]. However, prior vaccination with BCG vaccine may result in a positive TST result; whereas there is less cross-reactivity with IGRA. IGRAs that are reported as

weakly positive should be repeated, as follow-up testing may be negative. The CDC states that use of an IGRA is preferred over TST in patients with a history of BCG vaccination and in patients with a low likelihood of returning to have their skin test read. Advanced immunosuppression may be associated with false-negative results in all types of immunologically based tests used for detection of *M. tuberculosis* infection. The routine use of IGRA in children, especially those aged <5 years, is currently not recommended due to limited data and some evidence of lower sensitivity.

### **Hepatitis A, B, and C Recommendations**

26. Persons with HIV should be screened for evidence of hepatitis B virus (HBV) infection upon initiation of care by detection of hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), and antibody to hepatitis B total core antigen (anti-HBc or HBcAb). If HBsAg is positive, HBV viral load should be ordered.
27. Persons with HIV should be screened for evidence of immunity to hepatitis A virus (HAV) with HAV immunoglobulin G (IgG).
28. Persons with HIV should be screened for HCV antibody upon initiation of care. If positive, HCV RNA should be ordered to assess for active HCV infection. Curative therapy should be offered to all who are diagnosed with HCV.
29. Infants born to persons with HBV and/or HCV should be tested for HBV and HCV transmission.
30. Persons who are not immune to HAV and HBV should be immunized according to Advisory Committee on Immunization Practices (ACIP) guidelines. Please see Section III for further discussion.

### **Evidence Summary**

Screening and prevention of HBV and HAV are critical in the management of HIV [96]. Persons with HIV who have HBV and/or HCV coinfection should be managed according to published guidelines [85, 97, 98]. Hepatitis A vaccination is especially important in persons with unstable housing, for PWID, for men who have sex with men, for those with current or prior incarceration, and for those with chronic liver disease due to recent outbreaks in certain communities [99]. Prevacination screening for HAV infection is cost-effective when there is a seroprevalence of >30% in the patient population [66]. Because of worse outcomes for persons with HIV and HBV coinfection, persons with HIV who also have HBV should be adequately treated for HBV [32]. Because many persons with HIV may be treated with tenofovir-based ART that also suppresses HBV, stopping ART may result in a flare of HBV. Persons with HBV are at higher risk for hepatocellular carcinoma (HCC) even in the absence of cirrhosis. Screening for HCC in persons with HBV should be conducted according to the American Association

for the Study of Liver Diseases guidelines [97]. Persons not immune to HAV and HBV should be immunized according to ACIP guidelines (see Section III).

HCV RNA should also be measured in persons who are HCV-seronegative with a history of injection drug use or with unexplained increased serum transaminases because approximately 3%–6% of persons with HIV/HCV coinfection do not develop HCV antibodies [67]. The rate of mother-to-infant HCV transmission is up to 3-fold higher among women with HIV, according to multiple studies [100]. Infants can be tested for HCV RNA after age 2 months or for HCV antibody after age 18 months [101]. All persons diagnosed with HCV should be offered curative treatment. Eradication of HCV reduces but does not eliminate the risk of HCC in persons with cirrhosis; therefore, ongoing HCC screening in this group is warranted. Screening for HCC is recommended in all patients with cirrhosis due to hepatitis B or C or other nonviral etiologies (ie, alcohol use, fatty liver disease) [102].

### **Measles, Mumps, and Rubella Recommendations**

31. All persons with HIV born in 1957 or after should be tested for immunity to measles, mumps, and rubella (MMR) by measuring antibodies.
32. MMR vaccine should be given to protect against measles, mumps, and rubella if persons were born in 1957 or after and have not received this vaccine or do not have immunity to these infections.

### **Evidence Summary**

In 2019, 1282 individual cases of measles were confirmed in 31 states, the largest number of cases reported in the United States since 1992 [103]. The majority were among people not vaccinated against measles. Acceptable evidence of immunity against measles includes at least 1 of the following: written documentation of adequate vaccination, laboratory evidence of immunity, laboratory confirmation of measles, or birth in the United States before 1957 [104, 105].

### **Varicella Zoster Virus Recommendation**

33. Serologic screening for varicella zoster virus (VZV) may be considered for persons who have not had chicken pox or shingles and who have not been previously vaccinated (see Section III).

### **Evidence Summary**

It is advisable to determine anti-varicella IgG levels for patients who are unable to give a history of chicken pox or shingles [106, 107].

### **Tests That May Be Performed Under Certain Circumstances: Chest Radiography Recommendation**

34. A baseline chest radiograph should be obtained in all persons with HIV who have a positive tuberculosis screening

test result in order to rule out active tuberculosis. It may also be useful in other patients who are likely to have preexisting lung abnormalities.

#### **Evidence Summary**

Persons with HIV are susceptible to a variety of pulmonary complications. PWID are especially likely to have radiographic abnormalities that may be mistaken for infiltrates. A radiograph obtained at baseline in persons with a history of pulmonary disease may be useful for comparison in the evaluation of future respiratory complaints [68,108–110].

#### **Cervical Cancer Screening Recommendations**

35. Persons with a uterus and who are aged <30 years should have a cervical Pap test performed within 1 year of the onset of sexual activity but not later than age 21 years. Persons with HIV aged between 21 and 29 years and who have a uterus should have a cervical Pap test at diagnosis, if not performed within the last year. Routine human papillomavirus (HPV) testing is not recommended for women with HIV aged < 30 years, unless the Pap test is abnormal.
36. Persons with a uterus and who are aged >30 years should have a cervical Pap test performed at diagnosis. A Pap test alone or in combination with HPV testing can be performed.
37. Persons with atypical squamous cells of unknown significance on cytology or negative cytology with positive high-risk HPV (HRHPV) may have the Pap smear repeated in 1 year or should undergo colposcopy. If the Pap test shows negative cytology but HRHPV 16 or 18, atypical squamous cells and cannot rule out high-grade squamous intraepithelial lesion (ASC-H), atypical glandular cells, low-grade or high-grade squamous intraepithelial lesion, or squamous carcinoma noted by Pap testing, the patient should undergo colposcopy and directed biopsy, with further treatment as indicated by results of evaluation.
38. Following hysterectomy for benign disease, routine screening for vaginal cancer is not recommended for persons with HIV. Those with a history of high-grade Cervical intraepithelial neoplasia (CIN) adenocarcinoma in situ or invasive cervical cancer should be followed with annual vaginal cuff Pap tests.

#### **Evidence Summary**

Cervical cancer screening is an essential component of care for all persons with HIV who have a uterus. Patients with HIV are at a greater risk for cervical cancer than the general population, especially those with low CD4 cell counts. However, despite this association, the impact of ART on cervical dysplasia and cervical cancer remains uncertain [111, 112]. HPV

infection remains a major risk factor for the development of cervical dysplasia and invasive cervical cancer. HPV acquisition occurs through sexual transmission. The majority of infections are transient and resolve without intervention or treatment. HPV, specifically oncogenic strains (16,18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59), may persist, a necessary but not sufficient step in the development of cervical dysplasia and ultimately cervical cancer.

The Pap and HPV tests are the principal components of screening. The Pap test should be performed with liquid-based cervical cytology to improve reliability and should be reported according to the Bethesda system [113]. Cervical cancer screening can be performed by cytology alone or, for those aged >30 years, cytology may be combined with HPV testing. HPV testing can detect oncogenic HPV types in clinical specimens. Some commercially available tests specify HPV subtype including HPV 16 and/or 18. The Pap results should include a statement on specimen adequacy and a general categorization (negative for intraepithelial lesion or malignancy, epithelial cell abnormality, or other), and those reported as unsatisfactory for evaluation should be obtained again.

#### **Anal Cancer Screening Recommendation**

39. Persons with a history of receptive anal intercourse or abnormal cervical Pap test results and all persons with genital warts should have an anal Pap test if access to appropriate referral for follow-up, including high-resolution anoscopy, is available.

#### **Evidence Summary**

Persons with HPV are at increased risk for anal dysplasia and cancer. Currently, there are no national screening guidelines for the use of anal Pap tests. HPV-related anal dysplasia is seen at a lower frequency among heterosexual men. If anal cytologic screening using an anal Pap test is performed and indicates atypical or abnormal cells, then high-resolution anoscopy should be performed with biopsy of abnormal areas and appropriate therapy based on biopsy results [85, 114]. Access to appropriate referral and follow-up is necessary if anal Pap screening is performed. See Section III for discussion of HPV immunization.

#### **Glucose-6-Phosphate Dehydrogenase Recommendation**

40. Screening for glucose-6-phosphate dehydrogenase (G6PD) deficiency is recommended before starting therapy with oxidant drugs such as dapsone, primaquine, or sulfonamides in patients with a predisposing racial or ethnic background.

#### **Evidence Summary**

G6PD deficiency is a genetic condition that may result in hemolysis after exposure to oxidant drugs. Black individuals and

men from the Mediterranean, India, and Southeast Asia have higher risk for these genetic variants. Dapsone, primaquine, and sulfonamides are often used to treat persons with HIV and can lead to hemolysis in the presence of G6PD deficiency [115].

#### **Pregnancy Testing**

##### **Recommendation**

41. All persons of childbearing potential should have a pregnancy test upon initiation of care or reengagement in care.

##### **Evidence Summary**

The pregnancy status of all persons of childbearing potential should be assessed at the initial visit. In addition, the intent to have children, intent or ability to use consistent birth control, and timing of potential conception should be discussed. Because a higher rate of neural tube defects has been associated with use of dolutegravir at the time of conception, these issues may impact the choice of ART and discussions about therapy [116]. The DHHS perinatal guidelines provide ART recommendations for pregnant individuals [117]. The DHHS ART guidelines provide recommendations for individuals who are planning to conceive or those unable to use reliable contraception [32] (see Sections III and IV).

#### **Serum Testosterone Level**

##### **Recommendations**

42. Morning serum testosterone levels are recommended in adult cisgender men with decreased libido, erectile dysfunction, reduced bone mass or low trauma fractures, hot flashes, or sweats.
43. Obtaining testosterone levels in women at baseline in nonresearch settings is not recommended.

##### **Evidence Summary**

Cisgender men with HIV, especially those with advanced disease, are at risk for hypogonadism. Interpretation of testosterone values must be made in clinical context, as all currently available assays (including measures of total, free, and bioavailable testosterone) are associated with technical issues that may result in significant variability. Testing should be performed on a specimen obtained in the morning (ideally before 10:00 AM) and confirmed with repeat testing if the result is below the lower limit of normal. Recommendations differ regarding the optimal assay to use for initial testing in the setting of HIV. Because testosterone circulates primarily bound to plasma proteins (including sex hormone-binding globulin and albumin), if total testosterone is used for initial testing, a determination of sex hormone-binding globulin and/or free testosterone is strongly recommended when alterations of binding proteins are suspected (eg, patients with cirrhosis and hepatitis, hyper- or hypothyroidism, nephrotic syndrome). Free testosterone may be obtained by equilibrium dialysis (most reliable but most expensive) or determined using the free online testosterone calculator, developed by the Hormonology Department, University Hospital of Ghent, Belgium [118].

So-called direct free testosterone (analogue) assays are unreliable and should not be used. If a diagnosis of hypogonadism is established, measurement of luteinizing hormone and follicle-stimulating hormone is recommended to determine whether the source of dysfunction is primary (testicular) or central (pituitary or hypothalamic) in origin. Hypogonadism should be treated by clinicians familiar with monitoring patients on androgen replacement therapy (see Section IV).

#### **Tests Not Recommended for General Screening Purposes**

##### **Recommendations**

44. Routine testing for herpes simplex virus (HSV) IgG, cytomegalovirus (CMV) IgG, toxoplasma IgG, and biomarkers of inflammation is not recommended.
45. Testing for serum cryptococcal antigen may be considered in persons with CD4 cell count  $<100$  cells/mm<sup>3</sup> or in symptomatic patients.

##### **Evidence Summary**

Routine screening for HSV is not recommended [119]. Routine screening for CMV IgG is not generally useful because CMV seroprevalence is extremely high and generally not actionable [85]. Testing for CMV IgG may be considered, however, if blood transfusion is contemplated in a person at low risk for CMV exposure. The identification of seronegativity would prompt the use of CMV-negative or leukocyte-reduced blood products when transfusions are needed, thus reducing the risk of iatrogenic infection. Testing for toxoplasmosis should be reserved for patients with advanced immunodeficiency with suggestive clinical findings or if prophylaxis is being considered. Testing for serum cryptococcal antigen may be considered in persons with CD4 cell count  $<100$  cells/mm<sup>3</sup>. There are no data supporting the use of inflammatory biomarkers for risk assessment of comorbidities [120].

### **III. ROUTINE HEALTHCARE MAINTENANCE CONSIDERATIONS FOR PEOPLE WITH HIV**

Effective HIV primary care requires regular health maintenance in addition to HIV monitoring, including HIV RNA viral load testing (Table 5).

#### **HIV-specific Monitoring Following the Initial Assessment**

##### **Recommendations**

46. After initiation of ART, HIV RNA should be rechecked after 2 to 4 weeks but no later than 8 weeks and then every 4 to 8 weeks until suppression is achieved. Afterward, viral load should be monitored every 3 to 4 months to confirm maintenance of suppression below the limit of assay detection. This interval may be prolonged to every 6 months for adherent patients whose viral load has been suppressed for more than 2 years and whose clinical and immunologic status is stable. Viral load should be monitored more

**Table 5. Routine Healthcare Maintenance for People With Human Immunodeficiency Virus After Initial Assessment**

Intervention	Recommendation	Comments
<b>HIV-specific monitoring</b>		
HIV RNA	Should be performed every 4–6 weeks after initiation of ART until <50 copies/mL and then every 3–4 months. In patients with consistent viral suppression and stable CD4 cell count for more than 2 years, can be measured every 6 months [35].	
CD4 cell count	Every 3–6 months for the first 2 years after starting ART, or if viremia develops, or if CD4 cell count <300/mm <sup>3</sup> . If CD4 cell count 300–500/mm <sup>3</sup> and HIV RNA suppressed for 2 years, can be measured every 12 months. If CD4 cell count >500/mm <sup>3</sup> and HIV RNA suppressed for 2 years, measurement is optional [35].	
<b>Screening for mental health and substance use issues</b>		
Depression screening	Perform at least annually and when clinically appropriate	Use standard depression screening tool such as Personal Health Questionnaire-9 (PHQ-9) or Generalized Anxiety Disorder 2-item (GAD-2) [74, 75]
Substance use screening	General messages regarding risk reduction should be provided at all healthcare encounters, regardless of risk behaviors reported by the patient or perceived risk on the part of the healthcare provider. Such messages can be delivered by the provider, by others in the healthcare setting, or via educational materials (eg, pamphlets, posters, and videos) in the healthcare setting.	
<b>Screening for and monitoring of metabolic disorders (also see Section IV)</b>		
Blood pressure screening	Perform at every visit	
Weight measurement	Perform at every visit	
Screening for hyperlipidemia	Lipid profile: perform every 5 years if normal; more frequently if abnormal or other cardiovascular risk factors present (every 6–12 months); if abnormal, repeat fasting	Follow the atherosclerotic cardiovascular disease risk calculator [248]. Consider testing 1–3 months after starting or changing ART. See Section IV for further discussion [63].
Screening for diabetes mellitus and glucose intolerance	Serum glucose: perform annually; if abnormal, obtain fasting glucose. Hemoglobin A1C should be obtained prior to initiation of ART, if possible.  In persons with diabetes, repeat at least every 6 months (more frequently if clinically indicated). Urine microalbumin or urine protein/creatinine ratio: in patients with diabetes, repeat at least every 6 months (more frequently if clinically indicated).	Consider testing 1–3 months after starting or changing antiretroviral medications. Hemoglobin A1c is not used to diagnose diabetes in persons on ART. It may be used for screening and monitoring. Consider threshold cutoff of 5.8%. See Section IV for further discussion [64].
Screening for bone mineral density	Baseline bone densitometry by dual-energy X-ray absorptiometry (bone densitometry) should be performed in all postmenopausal women and men aged ≥50 years.	See Section IV for further discussion.
<b>Screening and vaccination for infectious diseases</b>		
Syphilis screening	Perform at least annually in asymptomatic persons; repeat every 3–6 months in asymptomatic persons if risk of acquisition is high	Acquisition risk depends on sexual activities, use of barrier protection, and local prevalence.
Gonorrhea and chlamydia screening	Perform at least annually in asymptomatic persons; can repeat every 3–6 months in asymptomatic persons if risk of acquisition is high	Screening using NAAT at all sites of sexual contact (rectal, oropharyngeal, vaginal, urine/urethral) is recommended for all sexually active persons with HIV. Acquisition risk depends on sexual activities, use of barrier protection, and local prevalence.
Trichomoniasis screening	Perform annually for persons having vaginal sex	Screen using NAAT testing
Hepatitis A, B, and C screening	Hepatitis C: in sexually active, HCV negative men having sex with men, transgender women, and people who inject drugs. Screen annually.	In those with new abnormal liver function test, check for acute hepatitis A, B, and C virus.
Tuberculosis screening	Perform annually in patients at risk for tuberculosis	Either tuberculin skin test or interferon-γ release assay [249]
Vaccinations	Pneumococcus (PCV13 and PCV23): repeat PCV23 once every 5 years after first vaccination. All patients with HIV should receive 1 dose of PCV13. If not vaccinated previously, this should be the first dose. If never vaccinated, 1 dose of PCV13 at least 1 year after PCV23.	
For most current vaccination recommendations, consult current vaccination schedules [94, 121], 250]	Influenza: administer annually	Avoid live influenza vaccine if CD4 cell count <200/μL
	Tetanus-diphtheria-whooping cough: administer Tdap once followed by tetanus toxoid, reduced diphtheria toxoid, or Tdap every 10 years and as indicated for wound management	
	Meningococcal vaccine (series of serogroup A, C, W, and Y meningococcal vaccine) × 2 doses; booster every 5 years depending on risk	
	Hepatitis A and B: administer if not immune	Check Hepatitis B Surface antibody 1–2 months or next scheduled visit after completion of series Administer hepatitis A and B boosters based on immune status

**Table 5. Continued**

Intervention	Recommendation	Comments
	HPV vaccine: administer if aged $\leq 26$ years. Consider administering if aged 27–45 years and unvaccinated or inadequately vaccinated.	HPV vaccine now recommended for persons up to age 45 years
	Varicella zoster: Shingrix vaccine $\times 2$ doses if aged $>50$ years and CD4 cell count $>200/\mu\text{L}$	The Advisory Committee on Immunization Practices has not made a recommendation for CD4 cell count $\leq 200/\mu\text{L}$ .
Screening for and prevention of cancer		
Smoking	Recommend cessation (if presently smoking) at every visit	Provide resources per local guidelines, including classes, agents that facilitate smoking cessation
Low-dose chest computed tomography scan	Recommended for smokers with 30+ pack-years smoking or have quit in last 15 years	Patients aged between ages 55 and 80 years who have 30 pack-years of smoking and are current smokers or have quit in the last 15 years should have an annual low-dose computed tomography scan of their lungs until smoking has been discontinued for 15 years.
Prostate cancer screening	Digital rectal exam: considered primary evaluation before PSA screening; consider for men aged 55–69 PSA screening: Age 50–69 years: discuss risks and potential benefits with patient Age $\geq 70$ years: PSA screening is not recommended	The impact of HIV on prostate cancer risk is not yet known. African Americans and people with a relative with prostate cancer have a higher burden of prostate cancer. Clinicians should follow US Preventative Services Task Force or American Cancer Society guidelines and consider patient wishes [251, 252].
Colon cancer screening	Age 50–75 years: screen using Perform starting at age 45–50 years at average risk. Age 76–85 years: individualize screening based on overall health and prior screening. Consider screening earlier if first-degree relatives diagnosed with colon cancer prior to age 50 years.	Screening tests include stool-based screening (guaiac-based fecal occult blood testing, fecal immunochemical test, fecal immunochemical test–DNA) every year, or colonoscopy every 10 years if normal, or more frequently if polyps are identified. Begin screening in those patients who are high-risk (first degree relatives of a patient with a diagnosis of colorectal cancer at age $\leq 50$ years) 10 years prior to age at which the relative was diagnosed with cancer [253].
Breast cancer screening	Age 50–75 years: mammography performed at least every 2 years [122]	Age 40–49 years: inform the patient of the potential risks and benefits of screening and offer screening every 2 years. See Section IV for further discussion.
Cervical cancer screening	Age $<21$ years: Pap within 1 year of sexual activity, no later than age 21 Age 21–29 years: Pap at diagnosis of HIV, repeat yearly $\times 3$ , then if all normal, Pap every 3 years Age $<30$ years: no HPV testing unless abnormalities are found on Pap test Age $\geq 30$ years: Pap only, same as 21–29 years or Pap with HPV testing, if both negative then Pap with HPV every 3 years. Note: In general, continue screening past 65 years.	Abnormal Pap and/or HPV follow-up similar to general population [94]. See Section II for further discussion.
Anal cancer screening	Digital anorectal exam: perform at least annually if asymptomatic. Anal pap: there are no national guidelines at this time. Some experts recommend anal cytology for persons with HIV who have receptive anal sex, but only if high-resolution anoscopy is available.	Abnormal anal Pap should prompt referral for high-resolution anoscopy.
Hepatocellular carcinoma screening	Alpha-fetoprotein and liver ultrasound every 6 months	For patients with cirrhosis for any cause or with chronic hepatitis B
Other healthcare maintenance		
Complete blood count and chemistry panel	Perform as needed based upon underlying conditions and need for toxicity management for ART and other medications	
Contraceptive management	All persons with HIV should be asked about their reproductive desires. Persons capable of bearing children should be routinely asked about their plans and desires regarding pregnancy.	Plans for conception may influence the choice of ART. See Section IV for further discussion.
Oral health examination	All persons with HIV should have oral health examinations semiannually.	
Patient education	Provide regularly for all patients, particularly sexual risk reduction to prevent STIs (and HIV transmission if not virally suppressed) and importance of medication adherence for personal health and to eliminate HIV transmission to sexual partners.	General messages regarding sexual risk reduction should be provided at all HIV primary care encounters, including need for maximal viral control to improve personal health and eliminate HIV transmission to others (Undetectable = Untransmittable). Those patients who report high-risk behaviors or those who present with repeated STIs should be offered brief counseling and tailored interventions to reduce their subsequent risk. Attempts should also be made to refer the patient to programs that offer a more extensive intervention program.

Abbreviations: ART, antiretroviral therapy; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HPV, human papillomavirus; NAAT, nucleic acid amplification test; PCV, pneumococcal conjugate vaccine; PSA, prostate-specific antigen; STI, sexually transmitted infection; Tdap, tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis.



frequently after initiation or change in ART, preferably within 2 to 4 weeks, with repeat testing every 4 to 8 weeks until viral load becomes undetectable.

47. CD4 cell count should be monitored to determine the need for prophylaxis against opportunistic infections. CD4 cell counts should generally be monitored every 3 to 6 months for the first 2 years or if the virus is not suppressed. For patients on suppressive ART regimens with CD4 cell counts 300–500/ $\mu\text{L}$ , CD4 cell count can be monitored every 12 months unless there are changes in the patient's clinical or virologic status. If the CD4 cell count rises above 500 cells/ $\mu\text{L}$ , CD4 monitoring is optional.

#### **Evidence Summary**

Frequency of HIV RNA monitoring depends on the response to therapy and duration and consistency of viral suppression. Once ART has been initiated, HIV RNA is monitored to confirm response to therapy and attainment of viral suppression. After HIV RNA has become undetectable, monitoring is approximately quarterly but can be every 6 months for persons with at least 2 years of continuous suppression and stable clinical and immune status. Measurement of CD4 cell count is initially helpful to assess the need for opportunistic infection prophylaxis as well as to choose ART. Once ART is initiated and sustained virologic suppression is achieved, CD4 cell count can be monitored less frequently. Once the virus is suppressed for at least 2 years and CD4 cell count rises above the levels associated with risk for opportunistic diseases, monitoring can occur annually or not at all if  $>500/\mu\text{L}$  [32]. The recommended frequency of HIV RNA and CD4 monitoring is not the only determinant of how frequently patients should be seen for overall healthcare needs. Patients with concurrent medical conditions may need to be seen more frequently, as may those needing ancillary services, such as treatment adherence counseling, mental health and substance use treatment services, STI screening, HIV education, case management services, or harm reduction counseling.

#### **Screening for Mental Health and Substance Use Issues Recommendations**

48. Screening for substance use should be done at all healthcare encounters.
49. Screening for depression using validated screening tools should be conducted at least annually and as needed.

#### **Evidence Summary**

People with HIV should be screened for drug and alcohol use [123, 124]. Self-reported substance use screening tools can be incorporated into electronic health records [125]. Those who are found to have substance misuse or substance use disorder should be offered treatment. Co-location of substance use treatment with HIV care is ideal [126]. Brief interventions that include use of motivational interviewing can be provided by trained healthcare personnel [127]. Screening for depression should include the use of validated screening tools such as PHQ-9 and GAD-2 [71, 72].

#### **Screening and Vaccination for Infectious Diseases: Screening for Chlamydia, Gonorrhea, Trichomonas and Syphilis Recommendations**

50. Screening for syphilis, chlamydia, and gonorrhea in asymptomatic persons should be repeated at least annually after initial screening or every 3–6 months depending on sexual activities, presence of other STIs in the patient or their partner, and local community STI prevalence.
51. All persons who have vaginal sex should be screened for trichomonas annually.
52. Tailored messages are critical for patients who report persistent high-risk behavior or who have symptoms or signs of STIs. In nearly all situations, the provider should offer brief counseling. In general, persons who exhibit ongoing risk behaviors should be referred to programs capable of offering more extensive interventional treatment.

#### **Evidence Summary**

Periodic follow-up screening for chlamydia, gonorrhea, trichomonas, and syphilis in asymptomatic persons should follow CDC guidelines [86]. Screening should occur at least annually. The frequency of screening should take into account the patient's reported sexual activities, past history of STIs, and community STI prevalence. For example, more frequent STI screening (ie, at 3- to 6-month intervals) is indicated for persons who have multiple or anonymous partners, who have had recent past STIs, or who live in an area with a high STI prevalence within their demographic group. In addition, persons who have sex in conjunction with drug use (particularly methamphetamine use) or whose sex partners participate in these activities should be screened more frequently [86]. Sexually active gay and bisexual men and transgender women with HIV should be screened every 3 months [89, 128, 129]. Routine serologic screening for syphilis is recommended at least annually for sexually active women with HIV, with more frequent screening (every 3 to 6 months) in those with multiple partners, a history of condomless intercourse, a history of sex in conjunction with drug use including methamphetamine use, or for sexual partners who participate in such activities [86].

#### **Screening and Vaccination for Other Infectious Diseases Recommendations**

53. Tuberculosis screening should be performed annually for persons at risk for infection (see Section II).
54. Repeat testing is recommended in patients with advanced HIV disease who initially had negative TST or IGRA results but subsequently experienced an increase in the CD4 cell count to  $>200$  cells/ $\mu\text{L}$  on ART and who may thus have developed sufficient immunocompetence to mount a positive reaction.
55. Vaccinations for pneumococcal infection, influenza, tetanus-diphtheria-whooping cough, and meningococcus

should be offered according to CDC Opportunistic Infection and ACIP guidelines.

56. Asymptomatic persons with CD4 cell count  $>200$  cells/mm<sup>3</sup> who travel internationally should receive required vaccinations, including live vaccines.

#### *Evidence Summary*

Annual testing should be considered for those who have negative results by TST but are at ongoing risk for exposure [85, 93]. A TST or IGRA should be performed any time there is concern of a recent exposure or after an increase of CD4 cell count to  $>200$  cells/ $\mu$ L following initiation of ART. Routine cutaneous anergy testing is not recommended as previously discussed. The likelihood of a response to any vaccine is greatest in patients with higher CD4 cell counts and in patients who receive suppressive ART. Persons with HIV should be immunized against pneumococcus upon diagnosis, regardless of age, with both 13- and 23-valent vaccines. Initial and periodic revaccination should follow ACIP guidelines [130]. Persons with HIV should receive annual influenza vaccinations, but live influenza virus vaccine is not recommended. Recommendations for tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis (Tdap) are the same as for the general population. Individuals who are pregnant should receive Tdap during each pregnancy between 26 and 37 weeks' gestation [130]. Adults with HIV should receive a 2-dose primary series of serogroup A, C, W, and Y meningococcal vaccine at least 2 months apart and be revaccinated every 5 years. Serogroup B meningococcal vaccine is not routinely recommended but may be given to persons aged 16–23 years in certain circumstances [85]. Live virus vaccines may pose a risk to persons with HIV who have advanced immunosuppression, defined as CD4 cell count  $<200$  cells/mm<sup>3</sup> or an AIDS-defining illness, and should be discussed with an expert before administration [131].

#### **Hepatitis A and B (HAV, HBV)**

##### *Recommendations*

57. Those who are susceptible to infection should be vaccinated against HBV. For those whose HBsAb levels are negative or  $<100$  mIU/mL after a primary vaccine series, a second series is recommended using higher doses or an additional dose. Ideally, revaccination should be attempted after suppression of HIV viral load and improvement in CD4 cell count.
58. Vaccination should be recommended for nonimmune sexual partners of patients who are positive for HBsAg.
59. Patients who are negative for HBsAg and HBsAb but positive for HBeAb should receive vaccination.
60. Vaccination for HAV is recommended for all nonimmune individuals especially those with indications for hepatitis A vaccine (eg, PWID, those unstably housed, those with current or prior incarceration, gay and bisexual men or

transgender persons with chronic liver disease, travelers to countries with high endemicity, or persons who are infected with hepatitis B and/or C). HAV IgG antibody testing should be repeated 1–2 months or at the next scheduled visit after the second vaccine to assess for immunogenicity. A repeat vaccine series is recommended in those who remain seronegative.

#### *Evidence Summary*

Responses to both HAV and HBV vaccines are reduced in patients with CD4 cell count  $<200$  cells/ $\mu$ L and detectable HIV RNA level. Decisions to delay HAV and HBV vaccination until immunologic and virologic response on ART should be individualized based on the potential benefits of the vaccine weighed against the patient's risk of exposure to HAV and HBV infection. Persons without immunity to HBV should receive Recombivax HB 40  $\mu$ g per dose, Enerix-B 20  $\mu$ g per dose (both require a 3-dose series over 6 months), or Heplisav-B 20  $\mu$ g per dose (2-dose series over 1 month), similar to recommendations for other immunocompromised patients [130, 132]. HBsAb should be repeated 1 to 2 months or at the next scheduled visit after completion of the vaccine series to assess for immunogenicity. HBV vaccination should be administered to those persons who have a positive anti-HBc with a negative HBsAg and HBsAb [121]. Patients who fail to respond to HBV vaccine should be revaccinated with a complete series and after virologic suppression on ART. An additional dose might be administered if standard doses are used [85, 130, 133]. The measurement of HBV DNA may be misleading if below quantification limits. All infants born to HBsAg-positive women should receive hepatitis B immune globulin and hepatitis B immunization, preferably in the first 12 hours of life. Routine vaccination for HAV and HBV is recommended for all infants [77, 130, 132]. Serologic testing for viral hepatitis should be repeated if suspected exposure occurs or there are newly elevated transaminase levels.

#### **Human papillomavirus**

##### *Recommendation*

61. Persons aged between 9 and 26 years should be vaccinated against HPV and persons with HIV aged 27–45 years who were not vaccinated or inadequately vaccinated should be offered the vaccination series if appropriate.

#### *Evidence Summary*

A preventive 9-valent HPV vaccine (9vHPV) is routinely recommended in a 3-dose schedule for all persons aged 9–26 years. According to ACIP, catch-up vaccination can be offered to those aged 27–45 years based on shared decision-making [130, 134–140]. This preparation is safe and highly effective in preventing infection with the HPV subtypes associated with genital warts and those responsible for approximately 70% of cervical cancers and most anal cancers. Evidence shows a decrease in the

prevalence of HPV infections, anogenital lesions, and precancerous cervical neoplasia [140, 141]. Studies show safety of HPV vaccine in women, men, and children [142]. However, the data on HIV are limited, with one study showing no efficacy and others showing modest impact, perhaps due to immunogenicity [143–146]. The vaccine is not expected to impact the development of cancer in those already harboring oncogenic subtypes. All persons with HIV should receive 3 rather than 2 doses of vaccine, regardless of age [147].

#### *Varicella zoster virus*

##### **Recommendations**

62. Patients who are susceptible to VZV (those who have not been vaccinated, have no history of varicella or herpes zoster, or are seronegative for VZV) should receive postexposure prophylaxis with varicella zoster immune globulin (VariZIG) as soon as possible (but within 10 days) after exposure to a person with varicella or shingles.
63. Varicella primary vaccination may be considered in VZV-seronegative persons aged >8 years with CD4 cell counts >200 cells/ $\mu$ L and in children with HIV aged 1–8 years with CD4 cell percentages >15%.
64. Recombinant zoster vaccine, 2-dose series, should be given to those aged >50 years on ART with CD4 cell count >200 cells/ $\mu$ L to prevent herpes zoster.

##### **Evidence Summary**

Varicella vaccination may be considered (2 doses of single-antigen varicella vaccine, not measles/mumps/rubella/varicella, administered 3 months apart) for adults and adolescents with HIV with a CD4 cell count >200 cells/ $\mu$ L on suppressive ART who do not have evidence of immunity to varicella [130, 148, 149]. Children should also receive the vaccine if aged >8 years and with a CD4 percentage  $\geq$ 15% [101]. Persons without evidence of immunity who have no history of varicella or shingles and no history of vaccination against VZV and who are at risk of developing severe disease or complications should receive VariZIG within 10 days after exposure [101, 149, 150]. VariZIG can be obtained only under a treatment investigational new drug protocol (contact FFF Enterprises at 1-800-843-7477). VariZIG is not indicated for persons who received 2 doses of varicella vaccine and became immunocompromised later in life [101, 130, 149]. Recombinant zoster vaccine should be administered to adults aged >50 years using 2 doses 2 to 6 months apart for the prevention of herpes zoster [151, 152]. Studies in HIV have found the vaccine to be safe and immunogenic after 2 doses.

#### **Screening for and Prevention of Cancer**

##### **Recommendations**

65. All patients who smoke should be strongly encouraged to stop smoking and offered smoking cessation assistance.

Screening for smoking should be done at every healthcare encounter.

66. Screening for prostate, breast, lung, and colon cancer should be conducted according to the US Preventative Services Task Force (USPSTF) and American Cancer Society guidelines for the general population.
67. Biennial screening mammography is recommended for persons aged 50–74 years, as per USPSTF guidelines.
68. Persons with HIV aged between 21 and 29 years should have a cervical Pap test annually. If the results of 3 consecutive cervical Pap tests are normal, follow-up Pap screening should be in 3 years.
69. For persons aged 30 years or greater, cervical Pap tests should be done annually. If the results of 3 consecutive Pap tests without an HPV test are normal, a follow-up Pap should be performed in 3 years. If the Pap test is done with HPV testing and both the cytology and HPV testing are negative, follow-up cervical cancer screening can be done in 3 years after a single Pap smear.
70. Anal cancer screening: periodic anal cytology by anal Pap test should be performed if access to referral and high-resolution anoscopy is available.
71. Screening for hepatocellular carcinoma every 6 months by ultrasound with or without alpha-fetoprotein is recommended for those with cirrhosis from any cause.

##### **Evidence Summary**

Healthcare systems should maintain a record of current smoking status of patients. All clinicians should advise patients to stop smoking and document this message at least yearly in the health record. Referrals should be made for smoking cessation [153, 154]. Although persons with HIV have increased rates of certain cancers, recommendations for screening (prostate, breast, colon, lung) are not different than for the general population. Screening for hepatocellular carcinoma every 6 months by ultrasound with or without alpha-fetoprotein is recommended for those with cirrhosis from any cause [155]. Breast cancer is the second leading cause of cancer-related death in women in the United States after lung cancer [156]. It does not appear to be increased in prevalence among women with HIV, although unusual clinical presentations and rapid progression have been reported, suggesting that breast cancer may behave more aggressively in this setting (bilateral disease, poorly differentiated carcinoma, and early metastasis) [157]. At present, screening mammography in persons with HIV should follow standard USPSTF guidelines [158].

For persons aged between 21 and 29 years, cervical cancer screening should be performed within 1 year of sexual debut but not later than age 21 years or at the diagnosis of HIV. If the initial Pap smear is negative, some experts recommend a repeat Pap smear be performed within 6 to 12 months. If the results of 3 consecutive Pap tests are normal, a follow-up Pap test should

be performed at 3 years. The use of HPV cotesting in this age group is not recommended [113]. For persons aged >30 years, cervical cancer screening should commence at diagnosis and be continued throughout a women's lifetime and not stopped at age 65 as recommended for the general population. In this age group, Pap testing can be done with cytology alone or with the addition of HPV cotesting. Some experts recommend a repeat Pap test be done 6 months after the initial Pap test. If the results of 3 consecutive Pap tests are normal, a follow-up Pap test should be done in 3 years. If testing is done with Pap and HPV cotesting and if the results of both tests are normal, the next screening can occur in 3 years [85].

There are no national screening guidelines for the use of anal Pap tests in healthcare maintenance. Additional data are needed to prove whether identification and treatment of persons with a history of receptive anal intercourse or abnormal cervical Pap test results and all persons with genital warts should have a periodic anal Pap tests if access to appropriate referral for follow-up, including high-resolution anoscopy, is available [114].

The Centers for Medicare & Medicaid Services and the USPSTF recommend that adults aged between 55 and 77 years with a history of heavy smoking (>30 pack-years) receive a low-dose computed tomography (LDCT) if currently smoking or have quit in the last 15 years [68, 109]. Persons with HIV may receive the same mortality benefit from LDCT screening as those not living with HIV if the CD4 cell count is >500 cells/ $\mu$ L and the patient is ART-adherent [110].

#### **Other Healthcare Maintenance Recommendations**

72. Complete blood count and chemistry panels should be monitored on a regular basis as needed to assess medication toxicity and to monitor potential or existing comorbid conditions (eg, chronic kidney disease, hepatitis).
73. Urinalysis should be monitored annually among those at risk for kidney disease.
74. All persons with HIV should be asked about their reproductive desires. Persons capable of bearing children should be routinely asked about their plans and desires regarding pregnancy.
75. Patient education should be provided at every visit, tailored to the patient's current needs. In particular, the clinician should evaluate the need for education on optimizing sexual health and the importance of medication adherence to maximize personal health and to eliminate HIV transmission to sexual partners.
76. All persons with HIV should have semiannual oral health examinations.

#### **Evidence Summary**

The frequency of monitoring complete blood counts and chemistry panels depends on the presence of underlying

medical conditions and the need to monitor for ART toxicities, depending upon the regimens chosen. Chronic kidney disease is a common comorbidity in persons with co-occurring diabetes, hypertension, HCV, nephrotoxic medication, genetic predisposition, or advanced HIV disease [159]. Biannual monitoring for renal function and urinary abnormalities is warranted for patients who receive tenofovir [81] (see Section V for contraception management). Clinicians should engage in effective patient education for maintenance of physical, emotional, spiritual, and sexual health. Barriers to adherence and care engagement should be repeatedly assessed (see Section I).

#### **IV. METABOLIC AND OTHER NONCOMMUNICABLE COMORBIDITIES ASSOCIATED WITH HIV, ANTIRETROVIRAL THERAPY, AND AGING**

Now that approximately 50% of the global population with HIV is aged >50 years, concern has heightened about increased rates of common comorbidities associated with age [160, 161], including long-term cardiovascular morbidity, especially in those with traditional risk factors such as dyslipidemia, glucose intolerance or diabetes mellitus, hypertension, and smoking. The benefits of ART used in accordance with published guidelines outweigh the risks of cardiovascular disease and other comorbidities associated with long-term exposure [122]. Multiple guidelines are available to assist providers in the identification and management of lipid abnormalities, diabetes mellitus, and other comorbidities [162–165]. People with HIV also are at higher risk for loss of bone mineral density (BMD), hypogonadism, and neurocognitive disorders.

#### **Recommendations**

77. Lipid levels should be obtained prior to and within 1–3 months after starting ART. Patients with abnormal lipid levels should be managed according to the National Lipid Association Part 2 and 2018 Multispecialty Blood Cholesterol Guidelines.
78. Random or fasting blood glucose and hemoglobin A1c (HbA1c) should be obtained prior to starting ART. If random glucose is abnormal, fasting glucose should be obtained. After initiation of ART, only plasma glucose criteria should be used to diagnose diabetes. Patients with diabetes mellitus should have an HbA1c level monitored every 6 months with an HbA1c goal of <7%, in accordance with the American Diabetes Association Guidelines.
79. Baseline bone densitometry (DXA) screening for osteoporosis should be performed in postmenopausal women and men aged  $\geq$ 50 years. There is insufficient evidence to guide recommendations for bone density testing in transgender or nonbinary individuals. Screening for transgender people should follow national recommendations based

upon their sex at birth and individualized based on risk for osteoporosis.

80. Testosterone replacement therapy for cisgender men should be prescribed with caution and only in those with symptomatic hypogonadism given the long-term side effects. See Section VIII for discussion of hormone therapy for transgender men.

#### Evidence Summary

Dyslipidemia has been associated with traditional risk factors, HIV infection itself, and antiretroviral drugs (ARVs). HIV is now a recognized independent atherosclerotic cardiovascular disease (ASCVD) risk enhancer in the 2018 American College of Cardiology/American Heart Association (ACC/AHA) multispecialty cholesterol management guidelines. At this time, there are no validated cardiovascular risk assessment tools for use in persons with HIV, and the default is to use the pooled cohort equations from the 2013 ACC/AHA guidelines, understanding the limitations of such [127]. The frequency of follow-up testing and response to therapy should be based on the current National Lipid Association Recommendations for Patient-Centered Management of Dyslipidemia: Part 2 and the 2018 Multispecialty Blood Cholesterol Guidelines [162]. All patients should be assessed for ASCVD risk, and those with elevated low-density lipoprotein cholesterol and/or risk should be further evaluated and managed according to established guidelines.

Caution should be used when prescribing statins with PIs, cobicistat, and NRTIs due to potential serious drug–drug interactions (Table 6). Most PIs and cobicistat inhibit the metabolism of statins, thereby increasing the potential for statin toxicity. However, there are exceptions such as pitavastatin and pravastatin, which are metabolized by glucuronidation, thereby having little effect when coadministered with a PI or cobicistat. Pravastatin may adversely interact with darunavir, and dose modification may be needed. In addition, atorvastatin and rosuvastatin may be used in patients on a PI but should be initiated at low doses and titrated carefully according to tolerability and effect. Efavirenz induces statin metabolism, resulting in lowering of statin levels. Nevirapine, etravirine, and rilpivirine have not been extensively studied. Doravirine does not affect levels of atorvastatin [63, 165]. Cobicistat is expected to have similar interactions as ritonavir with statins; however, these interactions have not been fully studied. There may be other pathways that affect drug metabolism and lead to unexpected interactions, and it is advisable to refer to the package insert of the ARV before prescribing lipid-lowering agents.

HbA1c is no longer the preferred method for diagnosing diabetes among persons with HIV on ART given the impact of HIV treatment on the HbA1c levels [64, 65, 166–168]. The American Diabetes Association (ADA) established the diagnostic criteria of diabetes mellitus of a fasting plasma glucose level of  $\geq 126$  mg/dL (7.0 mmol/L) or a 2-hour plasma glucose

level of  $\geq 200$  mg/dL (11.1 mmol/L) during an oral glucose tolerance test conducted with a standard loading dose of 75 g or an HbA1c  $\geq 6.5\%$  [87]; however, the National Health and Nutrition Examination Survey endorses a cutoff of  $\geq 5.8\%$ , as it improves the sensitivity for diagnosis for patients with HIV on ART [88]. In the 2019 ADA Standards, the ADA recommends against the use of HbA1c to diagnose diabetes in persons with HIV on ART. Although data are lacking on the effects of integrase inhibitors on HbA1c, the NRTIs, NNRTIs, and PIs do affect HbA1c; therefore, combination therapy with an integrase inhibitor may also result in misleading HbA1c results. The ADA does state that in cases of HbA1c and fasting glucose discordance, the abnormal laboratory test should be repeated, and the diagnosis of diabetes should be made only if repeat testing is again above the diagnostic cut-point [78].

Random or fasting serum glucose and HbA1c should be obtained prior to starting ART. If random blood glucose is abnormal, fasting blood glucose should be obtained. After initiation of ART, only plasma glucose criteria should be used to diagnose diabetes. A random glucose  $>200$  mg/dL should prompt further testing with a fasting blood glucose. Therefore, either a random or fasting glucose should be obtained at entry to care and annually thereafter for screening of diabetes. Patients with diabetes mellitus should have their HbA1c level monitored every 6 months, with a HbA1c goal of  $<7\%$  in accordance with the ADA guidelines. Though controversial, the American College of Physicians recommends less stringent control, with an aim to achieve an HbA1c between 7% and 8% [169]. Given the potential for over- or underestimation of HbA1c in patients on ART, it is prudent to assess the correlation of blood glucose levels with HbA1c values on an individual basis in order to determine the appropriate HbA1c target.

Lifestyle intervention such as weight loss, increased exercise, and dietary modification remain the cornerstone to diabetes prevention and management. Incident diabetes was reduced by 27% in the lifestyle group and by 18% in the metformin group compared with placebo in the Diabetes Prevention Program Outcomes Study of more than 2700 individuals at risk for diabetes followed for 15 years [170]. However, if treatment is needed, insulin-sensitizing agents are preferred. Patients should be managed according to the ADA guidelines [78]. No data suggest that switching ARVs is beneficial in patients with impaired glucose tolerance associated with HIV infection itself or traditional risk factors.

Baseline bone densitometry by DXA should be performed in all postmenopausal women and men aged  $\geq 50$  years, based on expert opinion with limited supporting evidence [164, 171–175]. If the DXA demonstrates osteopenia or the patient has a history of fragility or fracture, intervention with vitamin D, calcium, and a bisphosphonate or other medical therapy may be warranted. A vitamin D level should be measured if the DXA reveals osteopenia or osteoporosis. Bisphosphonates appear

**Table 6. Effect of Protease Inhibitors and Nonnucleoside Reverse Transcriptase Inhibitors on Statins**

Statin	Protease Inhibitor	Nonnucleoside Reverse Transcriptase Inhibitor
Atorvastatin	Caution (moderately increase atorvastatin's AUC) Use lowest starting atorvastatin dose	Acceptable with appropriate dosing and monitoring; efavirenz [254] and etravirine [255] decrease atorvastatin's AUC; no data for nevirapine May need higher atorvastatin starting dose; doravirine does not affect levels of atorvastatin [166]
Fluvastatin	Not recommended with nelfinavir Use of other protease inhibitors is allowed with appropriate dosing and monitoring	Acceptable with appropriate dosing and monitoring Etravirine may increase fluvastatin's AUC [255]  May need lower fluvastatin starting dose with etravirine No data on doravirine
Lovastatin	Contraindicated (greatly increases lovastatin's AUC [256])	Acceptable with appropriate dosing and monitoring  Decreases simvastatin's AUC, so may need higher lovastatin starting dose No data on doravirine
Pitavastatin	Acceptable with appropriate dosing and monitoring No significant change in pitavastatin's AUC with lopinavir/ritonavir [257] Pitavastatin's mean AUC decreased 26% with darunavir [258]	No data for nonnucleoside reverse transcriptase inhibitors
Pravastatin	Acceptable with appropriate dosing and monitoring, except with darunavir Decrease in pravastatin's AUC, except with darunavir, which increases pravastatin's AUC by 81% [259]	Acceptable with appropriate dosing and monitoring  Efavirenz decreases pravastatin's AUC [254], but no change with etravirine [255]  No data for nevirapine, rilpivirine, doravirine May need higher pravastatin starting dose with efavirenz
Rosuvastatin	Acceptable with appropriate dosing and monitoring; lopinavir/ritonavir and tipranavir + ritonavir increase rosuvastatin's AUC [260] May need to start rosuvastatin at lower dose with lopinavir/ritonavir No dose adjustments with cobicistat; cobicistat increases peak concentration (C <sub>max</sub> ) 89% and AUC by 38% [261]	Acceptable with appropriate dosing and monitoring  No data on doravirine
Simvastatin	Contraindicated (greatly increases simvastatin's AUC [255])	Acceptable with appropriate dosing and monitoring  Efavirenz [254] and etravirine [255] decrease simvastatin's AUC; no data for nevirapine, doravirine; may need higher simvastatin starting dose

Abbreviation: AUC, area under the curve.

to be effective in improving BMD in small studies of persons with HIV, but the data are limited. It is important to exclude osteomalacia prior to initiating a bisphosphonate, as this could lead to increased fragility and fracture. Common reasons for osteomalacia in this population are tenofovir-induced renal phosphate wasting and vitamin D deficiency, which have been reported in 40%–80% of persons with HIV. The spectrum and severity of metabolic complications associated with vitamin D deficiency among adult persons with HIV remain to be better characterized. Patients with vitamin D deficiency and osteopenia by DXA should be treated with vitamin D and calcium without bisphosphonates until the vitamin D deficiency has resolved. A follow-up DXA should be repeated 1 year later to monitor the response to therapy.

There is insufficient evidence to guide recommendations for BMD testing specific to transgender or gender-diverse individuals.

In a meta-analysis that include 6 cross-sectional and 14 pre-post hormonal therapy studies, with a total of 487 transgender men and 812 transgender women, hormone therapy had a neutral effect on BMD at all body sites evaluated, except for the lumbar spine of transgender women, where a modest but significant increase was detected [176]. At this time, some programs recommend transgender people (regardless of birth-assigned sex) begin BMD screening at age 65. Screening between ages 50 and 64 years should be considered for those with established risk factors for osteoporosis. Transgender people (regardless of birth-assigned sex) who have undergone gonadectomy and have a history of at least 5 years without hormone replacement should also be considered for BMD testing, regardless of age. Transgender people without gonads who are not using hormone replacement should follow guidelines for agonadal or postmenopausal women, regardless of birth-assigned sex or gender identity [177].

Routine screening for vitamin D deficiency is not recommended given the lack of data among persons with HIV. The USPSTF concludes that the evidence on screening for vitamin D deficiency in asymptomatic adults to improve health outcomes is insufficient [178]. Patients, however, should be counseled about the health benefits of regular exercise and normal dietary calcium and vitamin D intake and the harmful risks of cigarette smoking and excessive alcohol consumption. Secondary causes of decreased BMD, such as hypogonadism, alcoholism, glucocorticoid exposure, and vitamin D deficiency, should be investigated and treated.

In persons with HIV, avascular necrosis (AVN) was reported to be associated with exposure to tenofovir for longer than 1 year in one study [179]. Other more common causes of AVN include moderate to high alcohol consumption, hyperlipidemia, and corticosteroid use [179, 180]. Routine radiographic monitoring for AVN in asymptomatic persons is not recommended. However, for patients who present with persistent hip pain who have normal standard radiologic studies, magnetic resonance imaging is the preferred method of diagnosis, and both sides should be imaged. Most patients with symptomatic AVN will ultimately require surgical intervention, including hip replacement [180, 181].

The prevalence of hypogonadism among cisgender men with HIV has been reported to be high prior to the introduction of ART; however, screening for hypogonadism is recommended only for men who have symptoms [182, 183]. In 2014, the FDA released safety alerts that warned of potential increased cardiac risk associated with testosterone replacement products [184–186]. Subsequently, a large systematic review and meta-analysis failed to demonstrate an increased risk of cardiac events; however, caution remains [187]. Although the Endocrine Society Guidelines recommend short-term testosterone replacement therapy (TRT) for cisgender men with HIV with low testosterone, many patients have remained on TRT long term. It is unclear whether those who were diagnosed with hypogonadism at the time of their HIV diagnosis need to remain on TRT after immune recovery on ART. Since the FDA advisory, the percentage of cisgender men overall using TRT has declined, but less so among those with HIV [188, 189]. As the population of men with HIV ages, clinicians should balance the benefits against the harms of continuing TRT that may no longer be indicated. TRT may result in testicular atrophy and permanent inability to produce natural hormone. Men may experience “withdrawal” when TRT is stopped given the steroidal effects of testosterone as well. Therefore, initiating TRT should be prescribed with caution and only in cisgender men with symptomatic hypogonadism given the long-term side effects.

Neurocognitive impairment is more common in older people with HIV than those not living with HIV [190]. HIV-associated neurocognitive disorder (HAND) encompasses

multiple neurocognitive effects of HIV and associated inflammation on the central nervous system, resulting in deficits that range from asymptomatic neurocognitive impairment to dementia [191]. While there are no specific treatments for HAND at this time, clinicians should be aware that some persons with HIV may experience neurocognitive decline that is out of proportion to their age and should provide an appropriate work-up when such symptoms present.

## V. SPECIAL CONSIDERATIONS FOR CISGENDER WOMEN AND TRANSGENDER MEN OF CHILDBEARING POTENTIAL AND FOR PREVENTION OF PERINATAL HIV TRANSMISSION

People with HIV who are of childbearing potential are living long, healthy lives, and the need for routine gynecological care has increased. They have the same reproductive health needs and concerns as those not living with HIV infection. As part of the initial assessment, a comprehensive gynecologic and obstetrical history should be obtained that consists of menstrual history, sexual practices, contraception history and current use, male or female condom use and consistency of use, previous STIs and other genital tract infections, prior abnormal Pap test results including subsequent evaluation and treatment, history of gynecologic conditions (ie, uterine fibroids, endometriosis, and infertility) or surgery, and current gynecologic symptoms (ie, abnormal vaginal discharge, abnormal vaginal bleeding, amenorrhea, and pelvic pain). Recommendations for care during menopause do not differ from those for persons not diagnosed with HIV.

### *Contraception and Preconception Care Recommendation*

81. All persons with HIV who are of childbearing potential should be asked about their plans and desires regarding pregnancy upon initiation of care and routinely thereafter. Clinicians should ensure that informed decisions are made about contraception to prevent unintended pregnancy and offer counseling if pregnancy is desired.

### *Evidence Summary*

Any patient encounter with a nonpregnant person with reproductive potential is an opportunity to counsel about wellness and healthy habits that may improve reproductive and obstetrical outcomes if they decide to reproduce [192]. An in-depth discussion about childbearing is indicated if the patient expresses the desire for future pregnancy, is not trying to conceive but is not using appropriate contraception, or expresses uncertainty about reproductive plans. Regardless of the patient's sex, the goal is to ensure that informed decisions are made about contraception with prevention of an unintended pregnancy and to offer counseling if pregnancy is desired. Patients should

explicitly be asked to communicate with their provider if their plans change, when they are ready to consider pregnancy, or when they have questions related to reproduction. In persons who are at risk for pregnancy (ie, are trying to conceive or are not using effective and consistent contraception), providers should carefully review all medications, including over-the-counter medications, and avoid drugs with potential reproductive toxicity. The time of greatest risk to the fetus is early in pregnancy, often before the pregnancy has been recognized. In these settings, choice of ART may be influenced by discussions about the association of dolutegravir with neural tube defects. Choice of ART in these circumstances is discussed in detail in DHHS ART guidelines [32].

Individuals who do not wish to become pregnant should be counseled on effective contraception. Combined estrogen–progestin hormonal contraceptives (birth control pill, transdermal patch, and vaginal ring) are one option but may have interactions with several antiretrovirals, resulting in decreased effectiveness or increased risk of adverse effects. Contraceptive implants, injectable contraception (depot medroxyprogesterone acetate), and intrauterine devices are other available options. Spermicides have been associated with an increased risk of HIV acquisition and are not recommended for use with partners who are not diagnosed with HIV [193].

Providers should be prepared to discuss conception among serodiscordant couples. The partner with HIV should always be started on ART and achieve sustained HIV RNA suppression to below the limits of detection prior to beginning efforts to conceive. With durable viral suppression, there is effectively no risk of sexual transmission. For couples that are using condoms and wish to limit their episodes of condomless sex, a discussion about sex during the time of peak fertility is appropriate. Prepregnancy administration of antiretroviral preexposure prophylaxis for the partner not diagnosed with HIV offers an additional means to reduce the risk of sexual transmission [193].

#### **Prevention of Perinatal Transmission Recommendations**

82. To prevent perinatal transmission, all pregnant persons with HIV should be treated with ART, regardless of their immunologic or virologic status. Therapy should be initiated as early as possible, preferably prior to conception.
83. Infants exposed to HIV in utero should be managed according to DHHS perinatal guidelines.

#### **Evidence Summary**

Perinatal transmission of HIV is preventable if pregnant persons are screened and identified through antenatal HIV testing and receive immediate ART according to DHHS perinatal guidelines [117]. In those who start ART before conception and maintain viral load suppression, there is essentially zero risk of perinatal transmission [194].

If an individual in labor presents for delivery without having antenatal HIV testing, and a rapid HIV test is positive, ART should be initiated immediately without waiting for confirmatory tests. Person who are pregnant and who have an HIV viral load that is unknown or >1000 copies/mL at or near delivery, independent of antepartum ART, should be counseled regarding the potential benefit of cesarean delivery and, if consenting, should be offered a scheduled cesarean delivery at 38 weeks' gestation to reduce the risk of perinatal transmission [117]. The use of postexposure prophylaxis in the neonate or a multidrug ART prophylactic regimen or empiric therapy based on the clinical assessment of risk should be instituted as soon as possible after delivery, ideally within 6 to 12 hours, to significantly decrease perinatal transmission [117]. An HIV expert should be consulted for persons who have difficulty controlling the virus.

#### **Breastfeeding Recommendation**

84. In the United States, persons with HIV should avoid breastfeeding.

#### **Evidence Summary**

Infant feeding should be discussed [117, 131]. In the United States, avoidance of breastfeeding is the standard recommendation for women with HIV due to the safety of the water supply [117]. There have been cases of HIV transmission through breastfeeding in the setting of an undetectable viral load on ART [117, 195]. As some women may face environmental, social, familial, and personal pressures to breastfeed despite the recommendation, consultation with an expert is strongly recommended regarding harm-reduction strategies to minimize transmission.

## **VI. SPECIAL CONSIDERATIONS FOR CHILDREN**

#### **Recommendations**

85. Infants diagnosed with HIV should undergo HIV resistance testing prior to administering ART and, because of the rapid progression of disease, ART should be initiated as early as possible regardless of CD4 cell count, HIV RNA level, or clinical status.
86. All children with HIV should initiate ART, regardless of CD4 cell count/percentage, HIV RNA level, or symptoms.
87. CD4 cell counts and HIV RNA should be monitored no less than every 3–4 months in infants and children.
88. Childhood vaccinations should be administered according to ACIP schedules for infants and children with HIV.
89. Infants and children with HIV should be managed by a specialist with knowledge of the unique therapeutic, pharmacologic, behavioral, psychosocial, and developmental issues associated with HIV.



### Evidence Summary

Neonates exposed to HIV should be managed according to DHHS perinatal guidelines [117]. All infants and children diagnosed with HIV, regardless of CD4 cell count, viral load, or symptoms, should be started on ART as soon after diagnosis as possible using regimens recommended by DHHS [11, 77]. Resistance testing should be performed, but ART can be initiated before results are available. Infants aged <12 months and those with CDC stage 3–defining conditions or CD4 cell count <500 cells/mm<sup>3</sup> are the highest priority for ART initiation [77]. All infants should also receive *Pneumocystis* prophylaxis in the first year of life, irrespective of CD4 cell count or percentage [101]. In general, infants with untreated perinatal-acquired HIV have higher viral loads than adults, and there are age-specific differences in CD4 cell counts, with infants having higher normal absolute lymphocyte counts than adults. In young children (aged <5 years), CD4 percentages are less variable than absolute counts. While assessing family readiness is essential to optimize understanding and adherence, it should not preclude prioritizing ART initiation [77].

Frequent clinical visits are required to ensure that growth and development are on schedule, that appropriate adjustment of dosages are made, and that the infant is tolerating ART. Vaccination status should be reviewed at each visit. Infants and children with HIV can safely receive most childhood vaccines, although effective response depends on the degree of immunosuppression. Varicella and MMR vaccines should not be administered to children with CD4 cell percentages <15%. All children with HIV should be vaccinated against pneumococcus and receive yearly quadrivalent inactivated influenza vaccine. Once a child's ART is stable, the frequency of laboratory testing is similar to that for adults.

Infants and children with undiagnosed HIV are more likely to present with common bacterial infections, chronic diarrhea with failure to thrive, or delays in development, than with category B or C conditions seen in adults [77, 196]. This population has higher rates of serious bacterial infections (such as pneumococcal disease,) herpes zoster, tuberculosis, asthma, and chronic lung and skin disease [197]. Up to 20% of perinatal infections present after age 6 years in populations that lack access to prenatal or newborn screening. These cases can present diagnostic challenges, presenting with immune thrombocytopenic purpura, anemia, recurrent parotitis, chronic diarrhea, encephalopathy, or stroke [198]. Unfortunately, HIV transmission attributable to sexual abuse occurs in children, so children with signs and symptoms of HIV should be tested for HIV even if initial testing as an infant was negative. Additionally, children who have been adopted from resource limited settings or who have arrived as immigrants or refugees from locations where transfusion and/or unsafe injection practices may exist in the setting of undertesting for HIV, should be screened for HIV infection.

## VII. SPECIAL CONSIDERATIONS FOR ADOLESCENTS

### Recommendations

90. Adolescents with HIV require an individual and developmental approach to therapy and care, ideally through an HIV specialist with expertise in this population.
91. Adolescents with HIV should have a coordinated, deliberate transition to adult care.
92. Vaccinations should be administered according to ACIP schedules for children with HIV.

### Evidence Summary

The care of adolescents with HIV, whether perinatally or nonperinatally acquired, presents many challenges [198–200]. The median age of the US cohort of children who acquired HIV perinatally is now in the mid-teens, and many have reached adulthood [201]. Youth with HIV, in addition to the biologic and psychosocial changes that normally occur in adolescence, often cope with stigma, disclosure, loss of family members, and negotiation of sexual activity. In many studies, rates of cognitive, psychiatric, and behavioral problems are higher in those with perinatally acquired infection [202, 203]. As a result of these challenges, many youth with perinatally acquired infection have poorer adherence to ART and may experience decreased engagement in care [198]. Disclosure of diagnosis can be overwhelming to caregivers but should occur early, in late childhood, as it has been correlated with better adjustment to illness, lower rates of depression, and improved adherence with care and ART [77, 199, 200]. Puberty can affect drug metabolism; thus, decisions regarding dosing should consider Tanner staging, with those with sexual maturity rating ≥4 dosed according to adult treatment guidelines [77, 203]. Long-term treatment from infancy may result in viral resistance, treatment fatigue, as well as increased end-organ toxicity and requires careful monitoring [204]. Special attention should be paid to attainment and maintenance of viral suppression, along with risk reduction counseling, STI prevention, and secondary HIV prevention in early or later adolescence [205, 206].

Youth who acquired HIV through sexual activity or injection drug use have issues that are similar to those for adults including high rates of substance use, STIs, psychiatric comorbidities, and social determinants that may present barriers to care. Sexual orientation and gender identity should be discussed in a nonjudgmental manner in order to understand sexual risk and diminish stigma [207]. Multidisciplinary teams that simultaneously address biological and psychosocial issues are critical in optimizing outcomes, including early initiation of therapy to maximize immune recovery and health and minimize transmission risk [208, 209]. ART should be prescribed according to established adult and adolescent treatment guidelines [77].

The transition of care from pediatric/adolescent to adult providers should be a deliberate, comprehensive, and coordinated youth-friendly process that involves the healthcare team and the patient [210–212]. Care must be given to attend to the diverse needs of the adolescent that extend beyond medical care, including employment, independent living, and intimate relationships. Over time, youth must learn to negotiate the healthcare system and assume increasing responsibility for their healthcare. The national AIDS Education and Training Centers provide a resource book on best practices for transition, as do several other sources [213–216].

### VIII. CONSIDERATIONS FOR TRANSGENDER AND GENDER DIVERSE POPULATIONS AGED AT LEAST 18 YEARS

#### Recommendations

93. Transgender and gender-diverse persons with HIV should have access to gender-affirming, nondiscriminatory, nonstigmatizing, and culturally sensitive care.
94. Intake forms, medical records, and other documentation should integrate gender-neutral language and include gender identity options rather than be limited to sex at birth.
95. Transgender persons should be offered medical and/or surgical therapy in order to achieve their desired gender characteristics, in accordance with the World Professional Association for Transgender Health (WPATH) standards of care. HIV care providers should be familiar with initial laboratory monitoring and gender-affirming hormone treatment or provide referral to a clinician or endocrinologist experienced in transgender care.
96. Cancer screening should be conducted based on guidelines for the organs and tissues present in the individual.

#### Evidence Summary

Transgender people identify with a gender that differs from the sex assigned at birth. It is important to use the appropriate terminology when talking with and about transgender persons. Many terms are used and often are confused with each other or used incorrectly (Table 7). Gender dysphoria refers to discomfort around a discrepancy between one's gender identity and sex assigned at birth. Not all transgender people experience gender dysphoria. When experienced, gender dysphoria can be treated through hormones and other therapies [70]. Stigma and discrimination are serious issues that threaten quality of care for transgender and gender-diverse persons, regardless of HIV status. Nearly half of transgender persons face family rejection, 40% report a history of suicide attempt, 30% live in poverty, 14% experience homelessness, 35% are bullied in school, 30% have experienced discrimination within the healthcare system, and 28% avoid the healthcare system due to fear of discrimination [217]. Global estimates show a pooled HIV prevalence of 19.1% among transgender women, with 49-fold higher odds of HIV prevalence than the general population [218]. Data for HIV prevalence among transgender men are inadequate, but estimates are between 0% and 10% [219]. Given the disproportionate impact of HIV on transgender individuals and the psychosocial barriers they face, health systems and healthcare providers should create more welcoming, accepting, and comfortable clinical environments for transgender persons. Clinic intake and registration forms should allow selection of gender identity and preferred pronouns that then should be used by staff [220]. Additionally, educational and health promotional materials designed for transgender individuals create a better sense of inclusion. Staff should undergo training on gender diversity and cultural sensitivity. This comprehensive approach with all staff may create a culture of gender-affirming care that

**Table 7. Terminology Associated with Gender Identity and Hormonal Therapy**

#### Gender Identity Terminology and Definitions

Gender/sex: broad terms describing the entire category of relevant biological characteristics, self-identification, and stereotypical behaviors that might be considered male, female, or some variation

Gender identity: the internal sense of being male, female, or neither

Transgender, transsexual, trans, gender nonbinary, gender diverse, gender incongruent, genderqueer: adjectives used to refer to persons whose gender identity does not align with their sex recorded at birth (the latter primarily based on visible physical anatomy)

Cisgender, nontransgender: adjectives used to refer to persons whose gender identity aligns with their sex recorded at birth

Gender expression: how a person communicates gender identity through appearance, dress, name, pronouns, mannerisms, and speech

Gender-affirming hormone treatment and surgeries: broad categories of medical interventions that transgender persons might consider to align their appearance and their gender identity

Gender transition, gender affirmation, gender confirmation: an overall process of alignment of physical characteristics and/or gender expression with gender identity

Gender dysphoria: discomfort felt by some persons due to lack of alignment between gender identity and the sex recorded at birth; not all transgender persons have dysphoria, but many US insurance companies require this diagnosis for payment for transgender medical and surgical interventions

Feminizing hormone therapy: the use of estrogens and often androgen blockers with the objective of inducing changes in physical characteristics to better match patient gender identity

Masculinizing hormone therapy: the use of testosterone with the objective of inducing changes in physical characteristics to better match patient gender identity

Adapted from [224].

is important for patient empowerment, care engagement, and viral suppression [221, 222]. A core set of principles for care of transgender and gender-diverse persons has been incorporated into WPATH standards. (Table 8)

In order to initiate gender-affirming medical therapy, the clinician should ascertain that the patient's gender identity is persistent and support the individual's capacity to make medical decisions. Many payers, however, require a referral letter from a mental health professional prior to gender-affirming genital reconstruction surgery. The Endocrine Society recommends that a team-based care approach include a mental health provider in the care of children and adolescents [223]. General preventive care and cancer screening should be conducted based on disease risk factors, risks that hormonal therapy may incur, and the anatomical structures present.

Transgender hormone therapy is safe when provided under medical supervision. Persons should be offered medical therapy according to published guidelines in order to achieve their desired gender characteristics [70, 223]. HIV care providers should be familiar with clinical and laboratory monitoring and gender-affirming hormone treatment or provide referral to a medical provider or endocrinologist experienced in transgender care. Patients should be provided information on expectations in terms of timeline for changes and types of changes associated with hormone therapy, as well as a balanced risk assessment of those therapies.

Transgender women who receive hormone therapy may be at increased risk of thrombosis and cardiovascular disease, and risks and benefits should be discussed. Smoking cessation should be encouraged. Nonoral estrogen formulations that avoid first pass metabolism may pose lower risk of thrombosis and should be considered. Androgen therapy may result in erythrocytosis. Prior to hormone therapy or any gender-affirming surgical procedure, individuals who may wish to conceive may consider sperm or oocyte preservation. For feminizing hormone therapy, estrogen and antiandrogen medications are generally the first line of therapy. In 6 to 18 months patients may experience breast growth, decreased muscle mass, softer skin, decreased sexual desire, and fewer erections [223]. Clinical evaluations with laboratory monitoring of estradiol and testosterone should

occur every 3 months for the first year and once to twice per year thereafter, with potassium monitoring at the same intervals for those on spironolactone. The exact monitoring interval for prolactin has not been determined, but periodic monitoring during ongoing hormone therapy should occur [70, 223]. Goal levels for testosterone are <50 ng/dL and for estradiol they are between 100 and 200 pg/mL. Oral conjugated estrogen formulations (eg, ethinyl estradiol) are not recommended due to increased risk of thromboembolic events [223].

For masculinizing hormone therapy, testosterone remains the mainstay treatment, with results seen in 3 to 6 months including cessation of menses, deepening of voice, increased muscle mass, and increased acne and sexual desire [224]. Clitoral enlargement and male hair pattern changes can occur in the longer term. For masculinizing therapy, hemoglobin/hematocrit and testosterone should be obtained at baseline and measured every 3 months for the first year and 1–2 times per year thereafter. The testosterone level goal is the normal physiologic male range [223].

All boosted PIs may decrease estradiol levels and increase testosterone levels. Some NNRTIs (efavirenz, etravirine, nevirapine) may decrease estradiol and testosterone levels. Rilpivirine and doravirine have no documented interactions with estradiol, but data on interactions with testosterone are lacking [225–227]. Cobicistat may decrease or increase estradiol and increase testosterone levels, so dose adjustments may be necessary. Detailed drug–drug interactions are available in the DHHS adult and adolescent guidelines [32]. It is important to provide patients accurate information on drug–drug interactions between their ART and hormone therapy, and to make dose adjustments as appropriate, as lack of communication around this concern may contribute to toxicities, lack of efficacy, and poor adherence to one therapy or the other. It is important to emphasize that ART will not have a deleterious effect on hormonal therapy [228].

## IX. CONSIDERATIONS FOR THE SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 PANDEMIC AND CORONAVIRUS DISEASE 2019 IN PERSONS WITH HIV

As of September 2020, limited knowledge exists about how the novel coronavirus severe acute respiratory syndrome

**Table 8. Standards of Care for the Health of Transsexual, Transgender, and Gender-diverse Persons**

- Exhibit respect for patients who are transgender and gender-diverse (do not pathologize differences in gender identity or expression)
- Provide care (or refer to knowledgeable colleagues) that affirms patients' gender identities and reduces the distress of gender dysphoria, when present
- Become knowledgeable about the healthcare needs of transsexual, transgender, and gender-nonconforming people, including the benefits and risks of treatment options for gender dysphoria
- Match the treatment approach to the specific needs of patients, particularly their goals for gender expression and need for relief from gender dysphoria
- Facilitate access to appropriate care
- Seek patients' informed consent before providing treatment
- Offer continuity of care
- Be prepared to support and advocate for patients within their families and communities (schools, workplaces, and other settings)

Adapted from [70].

coronavirus 2 (SARS-CoV-2) affects persons with HIV with regard to acquisition and clinical course of its disease, coronavirus disease 2019 (COVID-19). There is concern that persons with poorly controlled virus (high HIV RNA levels) and advanced immune suppression, as measured by CD4 cell count <200 cells/ $\mu$ L, may be at higher risk for serious COVID-19 outcomes, but data are lacking. Studies are ongoing to determine whether those with HIV are at increased risk for acquisition of infection or severe illness [229–232]. Persons with HIV may, however, have comorbidities that increase overall risk [229, 230]. While advanced HIV disease is a condition to consider when advising SARS CoV-2 testing, it is not specifically an indication for testing.

Two ARV drugs, lopinavir/ritonavir (LPV/r) and tenofovir (TDF), are undergoing clinical studies because of in vitro activity against some coronaviruses, including SARS-CoV-2 [233, 234]. An initial trial of LPV/r in advanced disease was disappointing, and other studies are ongoing, including a prevention trial with TDF for Spanish healthcare workers [233, 235]. Currently, there is no indication for changing ART in persons with HIV, including those with COVID-19 [32]. HIV viral suppression and improved immune recovery should benefit those with concurrent COVID-19 infection. Management of other comorbidities, including diabetes mellitus, should be beneficial and is encouraged [236].

During this pandemic, challenges to HIV care include access to HIV testing, care linkage, access to medication, and psychosocial stress and stigma [237, 238]. Community-based organizations, clinics, emergency rooms, and other healthcare delivery systems are adapting their operations to provide services for prevention, testing, pharmacy services, medical care, and counseling for persons with HIV and vulnerable populations at risk for HIV [239, 240]. Many health systems have increased the use of telemedicine among persons with HIV. While telemedicine cannot replicate some elements of the office visit, many aspects of the asymptomatic patient visit, including providing medical and HIV-related history, reviewing systems, ordering and reviewing laboratory results, renewing and reviewing medication side effects, and many other aspects of physical and behavioral health, can be accomplished with a telemedicine visit. Many private health insurers, Medicaid plans, and Medicare pay for telemedicine visits that incorporate elements of the regular office visit (other than the physical exam.) Many professional societies and the Agency for Healthcare Research and Quality are issuing guidance on how best to achieve a successful telemedicine visit. If feasible, a video-enabled visit may be more effective than one performed on the telephone alone. The provider should enable an in-person visit as needed to evaluate acute conditions or symptoms. In Chicago, a review of medical records showed that providers prioritized in-person over virtual visits for those with detectable viral loads to optimize clinical outcomes [241]. For the latest information, consult guidelines from the IDSA

for recommendations on testing, treatment, and prevention of COVID-19 and DHHS guidelines regarding ART [32, 242].

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