Decision Memo for Screening for the Human Immunodeficiency Virus (HIV) Infection (CAG-00409N)

Decision Summary

The Centers for Medicare and Medicaid Services (CMS) has determined that the evidence is adequate to conclude that screening for HIV infection, which is recommended with a grade of A by the U.S. Preventive Services Task Force (USPSTF) for certain individuals, is reasonable and necessary for early detection of HIV and is appropriate for individuals entitled to benefits under Part A or enrolled under Part B.

Therefore CMS will cover both standard and U.S. Food and Drug Administration (FDA)-approved HIV rapid screening tests for:

1. Annual voluntary HIV screening of Medicare beneficiaries at increased risk for HIV infection per USPSTF guidelines:

   - Men who have had sex with men after 1975;
   - Men and women having unprotected sex with multiple [more than one] partners;
   - Past or present injection drug users;
   - Men and women who exchange sex for money or drugs, or have sex partners who do;
   - Individuals whose past or present sex partners were HIV-infected, bisexual or injection drug users;
   - Persons being treated for sexually transmitted diseases;
   - Persons with a history of blood transfusion between 1978 and 1985;
   - Persons who request an HIV test despite reporting no individual risk factors, since this group is likely to include individuals not willing to disclose high-risk behaviors; and

2. Voluntary HIV screening of pregnant Medicare beneficiaries when the diagnosis of pregnancy is known, during the third trimester, and at labor.

We are deleting the following reference to non-coverage of HIV screening from the coverage manual, Section 190.14: "However, in the absence of a documented AIDS defining or HIV-associated disease, an HIV-associated sign or symptom, or documented exposure to a known HIV-infected source, the testing is considered by Medicare to be screening and thus is not covered by Medicare (for example, history of multiple blood component transfusions, exposure to blood or body fluids not resulting in consideration of therapy, history of transplant, history of illicit drug use, multiple sexual partners, same-sex encounters, prostitution, or contact with prostitutes)."

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Decision Memo

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SUBJECT: Coverage Decision Memorandum for Screening for the Human Immunodeficiency Virus (HIV) Infection

DATE: December 8, 2009

I. Decision

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II. Background

Infection with HIV is a continuing worldwide pandemic described by the World Health Organization as "the most serious infectious disease challenge to global public health".[1,2] Acquired immunodeficiency syndrome (AIDS) is diagnosed when an HIV-infected person's immune system becomes severely compromised and/or a person becomes ill with an HIV-related opportunistic infection.[3,4] Without treatment, AIDS usually develops within 8-10 years after a person's initial HIV infection. While there is presently no cure for HIV, an infected individual can be recognized by screening; and subsequent access to skilled care plus vigilant monitoring and adherence to continuous antiretroviral therapy (ART) may delay the onset of AIDS and increase quality of life for many years.

Significantly, more than half of new HIV infections are estimated to be sexually transmitted from infected individuals who are unaware of their HIV status.[5] Consequently, improved secondary disease prevention and wider availability of screening linked to HIV care and treatment would not only delay disease progression and complications in untested or unaware older individuals, but could also decrease the spread of disease to those living with or partnered with HIV-infected individuals.

Despite such intentions, however, whether due an overall lack of understanding of HIV/AIDS, individuals' reluctance to disclose high-risk behaviors – or physicians' competing priorities and lack of reimbursement[6] – current risk-based screening methods based upon known or suspected HIV exposure still fail to identify a large percentage of infected individuals. In the U.S., for example, there are estimated to be more than one million persons living with HIV, including more than a quarter million who remain undiagnosed.[7, 8] When a life-threatening infectious disease without an effective vaccine, such as HIV, cannot be primarily prevented via combined behavioral strategies[9] and educational interventions, wider availability of screening – preliminary testing for persons without apparent signs and symptoms of the infection – may be the next best preventive strategy.

From an epidemiological perspective, HIV infection disproportionately impacts identifiable racial, gender and ethnic groups, and thus requires sensitivity to cultural and linguistic barriers to screening and access to medical care. By transmission category, while a growing proportion of HIV infections are now attributed to heterosexually acquired infections in women and persons of color, men who have sex with men remain the most affected group in the U.S., accounting for about half of Americans living with HIV. Globally, however, most HIV infections now result from heterosexual transmission; and most HIV infections in U.S. women are heterosexually acquired, including a 4.1% increase per year between 1999 and 2004 among women older than 60 years of age.[10]

Until 2007, there were no comprehensive, population-based data informing physicians about the well-being, sexual norms and sexual problems of older, community-dwelling Americans. Based on representative data from the National Social Life, Health, and Aging Project (NSHAP), it is now known that a majority of older adults regard sexuality as an important part of life and that many are sexually active, including 53% among those respondents 65-74 years of age and 26% among respondents 75 -85 years of age. Overall, only 38% of men and 22% of women in the NSHAP survey reported having discussed sex with a physician since 50 years of age; thus much high-risk behavior may go unrecognized. Frequent reasons noted for such poor communication included unwillingness of older patients and their physicians to initiate such discussions, sex and age differences between patients and physicians, as well as individual and societal attitudes inhibiting discussion about sexuality at older ages.[11]

In March 2009, based upon new authority to cover additional preventive services for Medicare beneficiaries and the publication of updated HIV screening guidelines, CMS initiated this national coverage analysis to evaluate the existing evidence on HIV screening and determine if the body of evidence is sufficient for Medicare coverage. Except to make a conforming change about HIV screening in NCD 190.14, this analysis does not address the use of HIV antibody testing as a diagnostic test (for example, confirmatory western blot or immunofluorescent assay in a seropositive patient), but rather focuses on the balance of benefits and harms, individually as well as from the public health perspective, of screening for HIV infection.

III. History of Medicare Coverage

Over the past 25 years, Congress added coverage of specific preventive and screening services to the voluntary Medicare Part B program, e.g., Pap smear, screening pelvic exams, screening mammography, colorectal cancer screening tests and diabetes screening tests.

Effective January 1, 2009, under Section 101(a) of the Medicare Improvements for Patients and Providers Act of 2008 (MIPPA) (Public Law 110-275), CMS may add coverage of "additional preventive services" if certain statutory requirements are met.[12] Under our rules implementing this statute, 42 CFR 410.64, this benefit allows the coverage of preventive services not otherwise described in Title XVIII of the Act.[13] Specifically, this regulation provides:

§410.64 Additional preventive services

(a) Medicare Part B pays for additional preventive services not otherwise described in this subpart that identify medical conditions or risk factors for individuals if the Secretary determines through the national coverage determination process (as defined in section 1869(f)(1)(B) of the Act) that these services are all of the following:

(1) Reasonable and necessary for the prevention or early detection of illness or disability.
(2) Recommended with a grade of A or B by the United States Preventive Services Task Force.
(3) Appropriate for individuals entitled to benefits under part A or enrolled under Part B.

(b) In making determinations under paragraph (a) of this section regarding the coverage of a new preventive service, the Secretary may conduct an assessment of the relation between predicted outcomes and the expenditures for such services and may take into account the results of such an assessment in making such national coverage determinations.[14]

IV. Timeline of Recent Activities

March 12, 2009	CMS initiates this national coverage analysis for screening for the HIV infection.
April 13, 2009	Initial 30-day public comment period closed.
September 9, 2009	Proposed decision memorandum posted; 30-day comment period begins.

V. FDA Status

HIV antibody testing first became available in 1985. These commonly used, FDA-approved HIV antibody screening tests – using serum or plasma from a blood draw – are known as EIA (enzyme immunoassay) or ELISA (enzyme-linked immunosorbent assay) tests. Laboratory results of EIA or ELISA antibody tests may not be available for a week or more.

Developed for point-of-care testing using alternative samples, six rapid HIV-1 and/or HIV-2 antibody tests – using fluid obtained from the oral cavity or using whole blood, serum or plasma from a blood draw or finger stick – were approved by the FDA from 2002-2006.[15, 16] Results can be available within approximately 20 minutes.

VI. General Methodological Principles

When making national coverage determinations concerning additional preventive services, CMS applies the statutory criteria in §1861(ddd) of the Social Security Act and evaluates relevant clinical evidence to determine whether or not the service is reasonable and necessary for the prevention or early detection of illness or disability, is recommended with a grade of A or B by the USPSTF, and is appropriate for individuals entitled to benefits under part A or enrolled under Part B of the Medicare program.

Public comments sometimes cite published clinical evidence and give CMS useful information. Public comments that give information on unpublished evidence such as results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. Public comments that contain personal health information will not be made available to the public. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

VII. Evidence

A.Introduction

Consistent with §1861 (ddd)(1)(A) and 42 CFR 410.64(a)(1), additional preventive services must be reasonable and necessary for the prevention or early detection of illness or disability. With respect to evaluating whether screening tests conducted on asymptomatic individuals are reasonable and necessary, the analytic framework involves consideration of different factors compared to either diagnostic tests or therapeutic interventions. Evaluation of screening tests has been largely standardized in the medical and scientific communities, and the "value of a screening test may be assessed according to the following criteria:

i. *Simplicity*. In many screening programmes more than one test is used to detect one disease, and in a multiphasic programme the individual will be subjected to a number of tests within a short space of time. It is therefore essential that the tests used should be easy to administer and should be capable of use by para-medical and other personnel.

ii. *Acceptability*. As screening is in most instances voluntary and a high rate of co-operation is necessary in an efficient screening programme, it is important that tests should be acceptable to the subjects.

iii. *Accuracy*. The test should give a true measurement of the attribute under investigation.

iv. *Cost*. The expense of screening should be considered in relation to the benefits resulting from the early detection of disease, i.e., the severity of the disease, the advantages of treatment at an early stage and the probability of cure.

v. *Precision (sometimes called repeatability)*. The test should give consistent results in repeated trials.

vi. *Sensitivity*. This may be defined as the ability of the test to give a positive finding when the individual screened has the disease or abnormality under investigation.

vii. *Specificity*. This may be defined as the ability of the test to give a negative finding when the individual screened does not have the disease or abnormality under investigation."[17]

As Cochrane and Holland (1971) further noted, evidence on health outcomes, i.e., "evidence that screening can alter the natural history of disease in a significant proportion of those screened", is important in the consideration of screening tests since individuals are asymptomatic and "the practitioner initiates screening procedures". The USPSTF has also integrated consideration of these factors in their assessments and recommendations.

B. United States Preventive Services Task Force (USPSTF) Recommendations 2007

According to the USPSTF, individual high-risk behaviors or those individuals at increased risk (as determined by prevalence rates) include:

- Men who have had sex with men after 1975
- Men and women having unprotected sex with multiple partners
- Past or present injection drug users
- Men and women who exchange sex for money or drugs, or have sex partners who do
- Individuals whose past or present sex partners were HIV-infected, bisexual or injection drug users
- Persons being treated for sexually transmitted diseases
- Persons with a history of blood transfusion between 1978 and 1985
- Persons who request an HIV test despite reporting no individual risk factors, since this group is likely to include individuals not willing to disclose high-risk behaviors[18]

USPSTF Summary of Recommendations on Screening for HIV (2007):

- "The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians screen for human immunodeficiency virus (HIV) all adolescents and adults at increased risk for HIV infection.

  Rating: ‘A’ Recommendation[19]

  Rationale: The USPSTF found good evidence that both standard and U.S. Food and Drug Administration (FDA)-approved rapid screening tests accurately detect HIV infection. The USPSTF also found good evidence that appropriately timed interventions, particularly highly active antiretroviral therapy (HAART), lead to improved health outcomes for many of those screened, including reduced risk for clinical progression and reduced mortality. Since false-positive test results are rare, harms associated with HIV screening are minimal. Potential harms of true-positive test results include increased anxiety, labeling, and effects on close relationships. Most adverse events associated with HAART, including metabolic disturbances associated with an increased risk for cardiovascular events, may be ameliorated by changes in regimen or appropriate treatment. The USPSTF concluded that the benefits of screening individuals at increased risk substantially outweigh potential harms."

- "The USPSTF makes no recommendation for or against routinely screening for HIV adolescents and adults who are not at increased risk for HIV infection.

  Rating: ‘C’ Recommendation[20]

  Rationale: The USPSTF found fair evidence that screening adolescents and adults not known to be at increased risk for HIV can detect additional individuals with HIV, and good evidence that appropriately timed interventions, especially HAART, lead to improved health outcomes for some of these individuals. However, the yield of screening persons without risk factors would be low, and potential harms associated with screening have been noted (above). The USPSTF concluded that the benefit of screening adolescents and adults without risk factors for HIV is too small relative to potential harms to justify a general recommendation."

- "The USPSTF recommends that clinicians screen all pregnant women for HIV.

  Rating:'A' Recommendation[21]

  Rationale: The USPSTF found good evidence that both standard and FDA-approved rapid screening tests accurately detect HIV infection in pregnant women and fair evidence that introduction of universal prenatal counseling and voluntary testing increases the proportion of HIV-infected women who are diagnosed and are treated before delivery. There is good evidence that recommended regimens of HAART are acceptable to pregnant women and lead to significantly reduced rates of mother-to-child transmission. Early detection of maternal HIV infection also allows for discussion of elective cesarean section and avoidance of breastfeeding, both of which are associated with lower HIV transmission rates. There is no evidence of an increase in fetal anomalies or other fetal harm associated with currently recommended antiretroviral regimens (with the exception of efavirenz). Serious or fatal maternal events are rare using currently recommended combination therapies. The USPSTF concluded that the benefits of screening all pregnant women substantially outweigh potential harms."

USPSTF Amendment (April 2007)

"In September 2006, the Centers for Disease Control and Prevention (CDC) published revised guidelines recommending that all individuals between 13 and 64 years of age be screened for HIV regardless of recognized risk factors [Branson 2006]. In making this recommendation, the CDC considered a number of factors, including research published subsequent to the completion of the systematic evidence report on which the 2005 HIV screening recommendations of the USPSTF are based. In November 2006, the USPSTF assessed this new research using established methods for evaluating the quality and strength of the evidence [Harris 2001]. Based on this review [Chou 2007], the USPSTF confirmed its 'C' recommendation for screening non-pregnant adolescents and adults who are not at increased risk for HIV infection."[22]

USPSTF Grade Definitions Prior to May 2007 (parentheses and brackets are the USPSTF's)

"The U.S. Preventive Services Task Force (USPSTF) grades its recommendations according to one of five classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms).

The USPSTF has updated its definition of the grades it assigns to recommendations. The definitions below (of USPSTF grades and quality of evidence ratings) were in use prior to the update and apply to recommendations voted on by the USPSTF prior to May 2007.

'A' – Strongly Recommended: The USPSTF strongly recommends that clinicians provide [the service] to eligible patients. The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.

'B' – Recommended: The USPSTF recommends that clinicians provide [the service] to eligible patients. The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.

'C' – No Recommendation: The USPSTF makes no recommendation for or against routine provision of [the service]. The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.

'D' – Not Recommended: The USPSTF recommends against routinely providing [the service] to asymptomatic patients. The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.

'I' – Insufficient Evidence to Make a Recommendation: The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. Evidence that the [service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined."[23]

C. Literature Search

In addition to the prerequisite USPSTF recommendations, CMS must consider not only whether an additional preventive service is reasonable and necessary for the prevention or early detection of illness or disability, but whether the service is appropriate for individuals entitled to benefits under part A or enrolled under part B of the Medicare program.

To facilitate these determinations, we searched PubMed from 2004 to 2009 for clinical research studies, reviews and guidelines for HIV screening and disparities in older or elderly adults, as well as pregnant patients (to include disabled female Medicare beneficiaries < 65 years of age). Since most recent studies focused primarily on test characteristics – and have not considered outcomes such as survival – articles and reviews relating to HIV care and outcomes were also included. Studies of cost and cost-effectiveness were likewise included, as §1861(ddd)(2) expressly authorizes the agency to "conduct an assessment of the relation between predicted outcomes and the expenditures for such services". Studies must have been published in peer-reviewed English language journals, and abstracts were excluded.

Using these general parameters, CMS identified one new clinical guideline (addressing both non-pregnant and pregnant individuals) plus 18 relevant articles and reviews.

D. Discussion of evidence reviewed

1. Evidence Questions

Our discussion focuses upon the adequacy of the evidence to draw conclusions about the risks and benefits of HIV screening for Medicare patients. CMS analyzed the following questions:

- *Is the evidence sufficient to determine that HIV screening is recommended with a grade of A or B by the USPSTF for any indications?*
- *Is the evidence sufficient to determine that HIV screening is reasonable and necessary for the prevention or early detection of illness or disability?*
- *Is the evidence sufficient to determine that HIV screening is appropriate for Medicare beneficiaries?*

2. External technology assessments and systematic reviews

No new external technology assessment or systematic review was identified.

3. Internal technology assessment

Winningham, et al. (2004)

Winningham and colleagues, acknowledging that African-American women ≥ 50 years of age are disproportionately affected by the HIV/AIDS epidemic and account for > 65% of HIV cases among older women, conducted a cross-sectional survey (N = 181) in three rural South Carolina counties – using the AIDS Risk Reduction Model (ARRM) as a conceptual framework – and investigated HIV risk behavior among older rural African American women (mean age = 58 years; range = 50-81 years). Results showed most (67%) of the women had at least one sex partner in the past five years, and of those, more than half (59.5%) reported at least one sexual risk behavior. High-risk behavior was associated with less education, lower condom use self-efficacy, more peers who discussed HIV-related risk behavior and less comfort communicating with partners about sex. Winningham, *et al.* concluded that a significant proportion of older African American women living in rural counties are at increased risk for HIV infection; that delivering HIV prevention is challenging, particularly when the messages have to reach populations that do not believe they are at risk and therefore do not seek prevention services; and that integrating HIV prevention with other medical services already in place may be effective for this hard-to-reach older female population.[24]

Burke, et al. (2007)

Burke and colleagues conducted a review of both the published and unpublished literature on HIV testing barriers at the provider level and summarized their current understanding of why U.S. physicians do not offer HIV testing. The barriers identified in the studies were then summarized separately for the three practice settings and compared. Results identified 41 testing barriers in 17 studies; but many reviewed studies exhibited high refusal rates and there were substantial methodological limitations, low peer-reviewed publication rates, and (as noted by commenters) no references regarding survey reliability or validity. Eight testing barriers, i.e., insufficient time, burdensome consent process, lack of knowledge and/or training, lack of patient acceptance, pretest counseling requirements, competing priorities and inadequate reimbursement, were identified in all three settings (prenatal, emergency department and other medical settings). Burke, *et al.* concluded that physicians experience many policy-based (consent process, pretest counseling requirements and inadequate reimbursement), logistical (insufficient time, competing priorities and language barriers) and educational (lack of patient acceptance and lack of physician knowledge/training) barriers to HIV testing which included substantial overlap across different practice settings.[25]

Espinoza, et al. (2007)

Recognizing that a growing proportion of cases of heterosexually acquired HIV infections occur in women and in persons of color, Espinoza and colleagues retrospectively analyzed data from 29 states reporting confidential name-based HIV/AIDS cases to the CDC to calculate estimated annual percentage change in number of actual diagnoses, followed by multiple-variable logistic regression analysis to determine the association between race/ethnicity and whether diagnoses of HIV and AIDS were made concurrently – while adjusting for covariates which included delays in reporting and absence of information about HIV risk factors. Results showed that from 1999 to 2004 diagnoses of heterosexually acquired HIV were made for 52,569 persons in 29 states, of which 33,554 (64%) were women. Among men and women, 38,470 (73%) were non-Hispanic black; 7,761 (15%) were non-Hispanic white; and 5,383 (10%) were Hispanic. The number of persons with heterosexually acquired HIV significantly increased, including a 6.1% increase among Hispanic men (95% CI = 2.7, 9.7) and a 4.5% increase among Hispanic women (95% CI = 1.8, 7.3). Concurrent late HIV and AIDS diagnoses were slightly more common for non-Hispanic whites (23%) and Hispanics (23%) than for non-Hispanic blacks (20%), and the proportion of concurrent late HIV/AIDS diagnoses increased with age, which the authors posited may be explained by HIV disease progression tending to occur more rapidly in older persons or that older persons are not assumed to be at risk and therefore not the focus of testing programs. Espinoza, *et al.* concluded that, to decrease the incidence of heterosexually acquired HIV infections in particularly Hispanic and non-Hispanic black populations who historically have had less access to treatment and prevention services, new strategies are needed to remove barriers to access. Because concurrent late AIDS/HIV diagnoses imply missed opportunities for early treatment of HIV, the authors suggested facilitation of earlier diagnosis and entry into care to improve prognosis and survival rates; and that since access to HIV testing does not necessarily imply access to care, knowledge of HIV status be linked to care and treatment.[26]

Ostermann, et al. (2007)

Ostermann and colleagues, noting that increasing testing rates for groups not usually perceived as being at high risk has been advanced as a primary strategy to combat HIV, conducted a pooled cross-sectional data analysis of 146,868 participants aged 18-64 years in the 2000-2005 National Health Interview Surveys to determine trends in testing rates and differences between planned and actual testing across demographic and risk groups in the U.S. Multivariable logistic models were estimated to assess correlates of perceived risk for HIV, as well as for planned and actual HIV testing. Difference-in-differences models, said to cancel out biases that equally affected the compared groups, examined how differences between planned and actual testing varied with demographic characteristics, perceived risk, alcohol consumption, depression, health behaviors and access. Results showed that rates of testing remained relatively unchanged from 2000-2005 (mean rates for lifetime and past year, respectively, 37% and 10%), but that rates of HIV testing varied substantially by sex and race, with females and minorities (nonwhite) more likely to get tested. Rates were higher in individuals reporting greater risks of HIV infection, but among respondents reporting medium or high risks of contracting HIV, < 25% reported an HIV test in the previous year. Those with higher perceived HIV risk, more alcohol consumption and more depressive symptoms had higher rates of both planned and actual testing, but demonstrated the greatest deficit of actual testing versus planned testing. Ostermann, *et al.* concluded that testing rates in the U.S. remain low, both nationally and in high-risk populations; that low HIV testing rates contribute to a substantial number of undiagnosed cases of HIV; and that while compelling arguments are focused upon general population testing, considerable potential likely still exists to increase HIV testing rates in higher risk populations needing ensured access to and utilization of testing in alcohol and mental health treatment sites.[27]

Owens, et al. (2007a)

Owens and colleagues conducted a retrospective cohort analysis of 13,991 at-risk patients and evaluated practice patterns for HIV identification from 1995-2000 at four large VA health care centers having an estimated HIV prevalence ranging from 0.5-2.1%. The study reviewed 1,100 medical records of tested patients and assessed HIV testing rates for at-risk patients, rationale for HIV testing, and predictors of HIV testing and of HIV infection. Patients were defined at risk for HIV if records contained ICD-9 codes for substance use (alcohol, amphetamine, barbiturate, cannabis, cocaine, opioid, hallucinogen or other drug use, and unspecified and drug psychosis), hepatitis B, hepatitis C, all viral hepatitis (other than hepatitis B or C) or sexually transmitted disease at any visit during the study period. At the time when testing was performed, guidelines recommended risk-based testing; regulations required consent for testing and counseling; but documentation of consent and counseling was variable. Rationale for testing was documented if patients had an ICD-9 risk factor defined as above; if the provider documented a risk factor or clinical presentation suggestive of HIV, including opportunistic infection, hepatitis B, hepatitis C, or sexually transmitted diseases; or if the patient requested HIV testing. Sensitivity analyses used the most restrictive definition, including only cocaine, opiate or amphetamine use. Of 13,991 patients considered at risk for HIV, results showed that only 36% had been tested for HIV. The authors acknowledged being unable to determine whether patients had been tested in non-VA facilities or had been offered testing and refused, but considered it rare for patients to be tested elsewhere and refuse testing at the VA. HIV prevalence ranged from 1-20% among tested patients at the four sites, and 90% of patients tested had a documented reason to test. Owens, *et al.* concluded that one-half to two-thirds of patients identified at risk for HIV (based on ICD-9 diagnoses of substance abuse, hepatitis or sexually transmitted diseases) had not been tested for HIV within a five year period at the selected VA sites; noted that a critical opportunity to provide early therapy and risk-reduction counseling for HIV-infected patients may have been missed; questioned whether there are barriers to testing, including time required for informed consent and counseling; and while unable to determine which barriers were responsible for low HIV testing rates, believed that pretest and posttest counseling methods should be reexamined.[28]

Gandhi, et al. (2007)

Gandhi and colleagues conducted a retrospective observational study of HIV positive (N = 4368) patients entering HIV care from 1998-2002 at VA medical centers nationwide. Outcomes of interest were the AIDS rates in year of presentation, the duration of VA utilization before HIV presentation, and the presence of clinical triggers signaling greater risk of HIV infection before presentation. Results showed that 51% (N = 2211) of patients presented with CD4 counts < 200 cells/mm^3; and that 39% (N = 1697) of patients used other VA services before presentation for HIV care, with median duration of 3.6 years [interquartile range (IQR) 25–75: 2.2 to 5.1 year] and six physician visits (IQR 25–75: 2–18 visits) between first utilization and HIV presentation. No difference existed in the percentage of patients presenting with CD4 counts < 200 cells/ mm^3 in those with and without prior VA healthcare (50% versus 51%, P = 0.76), and only 13% of patients with prior VA healthcare demonstrated a clinical trigger before HIV presentation. Gandhi and colleagues concluded that more than half of veterans entered HIV care with an AIDS diagnosis at presentation regardless of whether they previously established healthcare in the VA; that access to care did not seem to be the primary cause of delayed HIV presentation; and that widespread screening is needed to improve rates of early HIV detection.[29]

Owens, et al. (2007b)

In 2007 Owens and colleagues additionally conducted a blinded, anonymous HIV serological survey (reported to be the preferred method for obtaining an unbiased prevalence estimate for a population) in order to determine HIV prevalence in both inpatient and outpatient settings of six geographically diverse VA healthcare sites. Sites were selected to represent the range within the VA of documented HIV prevalence – defined as number of HIV positive cases among patients with a documented negative or unknown test result. Logistic regression, including inpatient or outpatient status, age group, site, race/ethnicity and multiple comorbid conditions as independent variables, was utilized to determine predictors of documented and undocumented HIV infection. The study tested 4,500 unique outpatient blood specimens and 4,205 unique inpatient specimens, stratified into 5 age categories (25–44, 45–54, 55–64, 65–74, and 75 years or older) with ≥10% more than the required number of specimens for each group per the CDC's recommendations for oversampling. A standard HIV-1 enzyme immunoassay (EIA) test was used to individually test all specimens; positive specimens underwent repeat EIA testing; and those positive after repeat testing underwent an HIV-1 Western blot confirmatory test. For study purposes, samples were defined as positive if positive according to both EIA and Western blot testing. Results showed that 326 (3.7%) patients tested positive for HIV. HIV prevalence ranged from 1.2-6.9% among inpatients and from 0.9-8.9% among outpatients; the percentage of HIV infections that had not been documented within the VA varied substantially between sites from 3-44%; and predictors of undocumented infection were age, race/ethnicity, site and history of pneumonia. Prevalence of previously undocumented HIV infection varied from 0.1-2.8% among outpatients and from 0.0-1.7% among inpatients. Compared to known HIV patients, undocumented HIV-infected patients were more likely older (> 55 years; P = 0.006) and less likely to have comorbidities (OR = 0.3; 95% CI = 0.15, 0.60; P < 0.001). For patients 65 -74 years of age with previous unknown test results, HIV prevalence was 0.5% (95% CI = 0.2, 1.2) for outpatients and 0.4% (95% CI = 0.1, 1.0) for inpatients. Owens, *et al.* concluded that prevalence of undocumented HIV infection was sufficiently high for routine screening to be cost-effective in each of the VA sites evaluated and that many VA health systems should consider expanded routine voluntary HIV screening.[30]

Patterson, et al. (2007)

Patterson and colleagues compared immunological reconstitution and virological response in the first six months of a first HAART regimen by both sex and age (≥ 50 versus < 50 years old) in two observational HIV-infected cohorts from the Johns Hopkins University and the University of North Carolina. A total of 246 individuals (28% women) were studied, with 63 cases (≥ 50 years old) and 183 controls (< 50 years old). Results showed that more than two-thirds of patients had HIV RNA levels < 400 HIV-1 RNA copies/mL and that CD4 count increased ≥ 50 cells/μL at six months from therapy initiation. There were no significant differences in immunological reconstitution across age and sex strata, or in virological suppression, even after adjusting for type of HAART or restricting the analysis to women only. Patterson, *et al.* concluded these results suggest that younger and older women and men may have similar short-term initial HAART outcomes, and that further evaluation of longer term response to initial HAART regimen based on sex and age is indicated with more efficacious and simplified regimens.[31]

Silverberg, et al. (2007)

Silverberg and colleagues reported on the growing, older adult, HIV-infected population's response to and tolerability of highly active antiretroviral therapy (HAART). Changes in HIV clinical markers after HAART initiation were compared among 2259 patients aged 18-39 years (controls), 1834 patients aged 40-49 years and 997 patients ≥ 50 years enrolled in an integrated health care system. Results showed that patients ≥ 50 years were more likely to achieve HIV RNA levels of < 500 copies/mL within one year of HAART initiation (hazard ratio [HR], 1.15; P = 0.009), but adjustment for adherence attenuated this finding (HR, 1.03; P = 0.59). Subsequent HIV RNA level rebound to ≥ 1000 copies/mL was less likely among patients aged 40-49 years (HR, 0.81; P = 0.01), which persisted after adjustment for adherence (HR, 0.79; P = 0.004). In year one of HAART, younger patients had larger CD4 T-cell count increases (131.8, 121.3, and 111.8 CD4 T cells/μL per year among patients aged 18-39, 40-49 and ≥ 50 years, respectively; P = 0.046). In years 2-6, older patients had larger CD4 T-cell count increases (4.5, 11.6, and 9.7 CD4 T cells/μL per year among patients aged 18-39, 40-49 and ≥ 50 years, respectively; P = 0.04). After adjustment for adherence, age differences in CD4 cell count changes remained in year one (P = 0.02) but not in years 2-6 (P = 0.08). Comorbidities had no effect on study results, but metabolic (glucose and lipids), hematologic (absolute neutrophils and hemoglobin) and renal (creatinine) abnormalities were more likely in older patients. Silverberg, *et al.* concluded that, despite higher risk of adverse events, patients ≥ 50 years sustained high therapy adherence to maintain improved virological outcomes and compensate for early blunted CD4 cell count response as compared to younger patients.[32]

Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group (2007)

The DAD group is an international collaboration of 11 investigator groups prospectively following 23,437 HIV-1 infected individuals during outpatient clinic visits at 188 clinics in 21 countries in Europe, the U.S. and Australia since enrollment from December 1999-April 2001. Writing for DAD, Friis-Møller and colleagues analyzed the association of cumulative exposure to protease inhibitors (PIs) and nonnucleoside reverse-transcriptase inhibitors (NNRTIs) with the risk of myocardial infarction (MI) and reported on data collected through February 2005. Data including sociodemographics, clinical findings, treatment (antiretroviral and other medications received before and after enrollment) plus laboratory results were collected at enrollment and at least every eight months thereafter. Median age at enrollment was 39 years (IQR, 34-45 years) and 24.1% of patients were female. MIs were categorized and coded without knowledge of the patients' ART history; incidence rates of MI during follow-up were calculated; and associations between MI and exposure to PIs or NNRTIs were determined. Results showed that 345 patients had an MI during 94,469 person-years of observation. The incidence of MI increased from 1.53 per 1000 person-years in those not exposed to PIs to 6.01 per 1000 person-years in those exposed to PIs for more than six years. When adjusted for exposure to the other drug class and known cardiovascular risk factors (excluding lipid levels), the relative rate of MI per year of PI exposure was 1.16 (95% CI, 1.10-1.23), whereas relative rate per year of exposure to NNRTIs was 1.05 (95% CI, 0.98-1.13). Adjustment for serum lipid levels reduced the effect of exposure to each drug class to 1.10 (95% CI, 1.04-1.18) and 1.00 (95% CI, 0.93-1.09), respectively. Friis-Møller, *et al.* concluded increased exposure to PIs is associated with increased risk of MI that is partly explained by dyslipidemia and found no evidence of association for NNRTIs, but the number of person-years of observation for exposure to NNRTIs was less than that for exposure to PIs.[33]

Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group (2008)

Since PIs are usually prescribed in combination with ART drugs from the nucleoside reverse transcriptase inhibitor (NRTI) class and it was unclear whether NRTIs increase risk of MI in HIV-infected individuals, the DAD Study Group also used regression models to quantify the relationship between cumulative, recent and past use of zidovudine, didanosine, stavudine, lamivudine and abacavir and development of MI in 33,347 patients followed by investigators at 212 clinics in the DAD group. Results showed that over 157,912 person-years, 517 patients had an MI, but that there were no associations between rate of MI and cumulative or recent use of zidovudine, stavudine or lamivudine. By contrast, recent but not cumulative use of abacavir or didanosine was associated with an increased rate of MI, compared with those with no recent use of the drugs, RR 1.90, 95% CI 1.47–2.45 [P = 0.0001] with abacavir and RR 1.49, 1.14–1.95 [P = 0.003] with didanosine. Rates of MI were not significantly increased in those who stopped these drugs more than six months previously compared with those who never received these drugs. After adjustment for predicted ten year risk of coronary heart disease, recent use of didanosine and abacavir remained associated with increased rates of MI (1.49, 1.14-1.95 [P = 0.004] with didanosine; 1.89, 1.47-2.45 [P = 0.0001] with abacavir). The DAD study group concluded increased risk of MI exists for patients exposed to abacavir and didanosine within the prior six months, but that the excess risk did not seem to be explained by underlying established cardiovascular risk factors and was not present beyond six months after drug cessation.[34]

Greenbaum, et al. (2008)

Noting conflicting results in prior studies examining responses to HAART between younger and older patients, Greenbaum and colleagues performed a retrospective analysis of an observational cohort of 906 HAART-naïve patients enrolled from February 1989-January 2006. Virologic and immunologic response, plus progression to AIDS and mortality were compared in 670 younger patients (< 40 years) versus 149 older patients (≥ 50 years). To evaluate virologic suppression, HIV-1 RNA levels were used from all clinic visits following treatment initiation, and plasma HIV-1 RNA was categorized as undetectable (≤ 400 copies/ml) or detectable (> 400 copies/ml). Immunologic response was measured by change in CD4 cell count from baseline using cell count at HAART initiation and at 6, 12 and 24 months after treatment initiation; time to increase in CD4 cell count was days from HAART initiation to laboratory test date when the cell count had increased by 50 cells/ml or more; disease progression was examined as time to new opportunistic infections (OIs) after HAART initiation; and survival was analyzed based on the death registry database. Results showed that older rather than younger patients were more likely to be on nonnucleoside reverse transcriptase inhibitor (NNRTI) regimens versus protease inhibitor (PI) regimens (42% versus 29%, P < 0.01). Time to HIV-1 RNA virologic suppression was less in older than in younger patients (3.2 versus 4.4 months, P < 0.01), but immunologic response did not differ by age. Older patients had fewer AIDS-defining OIs (22% versus 31%, P < 0.01) but higher mortality (36 versus 27%, P = 0.04) and shorter survival (25th percentile survivor function 36.2 versus 58.5 months, P = 0.02) than younger patients. Older age was associated with more rapid virologic suppression [adjusted hazard ratio = 1.33 (1.09–1.63)] and earlier mortality [adjusted hazard ratio = 1.56 (1.14–2.14)]. NNRTI regimens had more rapid virologic suppression [adjusted hazard ratio = 1.22 (1.03-1.44)]. Greenbaum, *et al.* concluded that new studies were needed to examine long-term outcomes of HAART therapy – including impact of comorbidities on HIV disease progression, potential drug-drug interactions and potential differences in drug toxicity profiles in older adults – as well at that age-specific HIV treatment guidelines may be warranted which include HAART initiation at higher CD4 cell count for older patients.[35]

Collaboration of Observational HIV Epidemiological Research Europe (COHERE) Study Group (2008)

COHERE, a collaboration of 33 observational cohort studies in 30 European countries, followed 49,921 antiretroviral-naive individuals starting combination antiretroviral (cART) from 1998-2006. Outcome measures included the time from cART initiation to HIV RNA < 50 copies/ml (virological response) and CD4 increase of > 100 cells/ml (immunological response). Ten age strata were chosen: < 2, 2-5, 6-12, 13-17, 18-29, 30-39 (reference group), 40-49, 50-54, 55-59 and ≥ 60 years; and patients ≥ 6 years were included in multivariable analyses. The three oldest age groups had 2693, 1656 and 1613 individuals; and despite more advanced disease at treatment initiation (possibly due to later presentation for HIV care), results showed older patients were more likely than younger patients to demonstrate good initial virological response to cART. Specifically, the probability of virological response was higher in those aged 50–54 (adjusted hazard ratio: 1.24), 55–59 (1.24) and ≥ 60 (1.18) years. Probability, however, of immunological response was reduced in those ≥ 60 years, and patients 55–59 and ≥ 60 years had poorer clinical outcomes after adjusting for latest CD4 cell count. The COHERE group concluded that better virological responses but poorer immunological responses, together with low pre-cART CD4 cell counts, may place older patients at increased risk of HIV disease progression and other clinical events, including both traditional HIV-associated events as well as comorbidities that may occur more frequently in older individuals.[36]

Strategies for Management of Antiretroviral Therapy (SMART) Study Group (2008)

In a follow-on publication from El Sadr, *et al's* 2006 SMART study demonstrating that episodic antiretroviral therapy (ART) guided by CD4 cell count did not reduce the risk of adverse events associated with ART, the SMART group in 2008 reported a comparison of two ART strategies – drug conservation (DC) and viral suppression (VS) – in 5472 HIV-infected patients with CD4 cell counts > 350 cells/μL. Rates and predictors of opportunistic disease or death (OD/death) and the relative risk (RR) in the DC versus VS groups according to the latest CD4 cell count and HIV RNA level were reported. During follow-up (mean = 16 months), results showed that the DC patients spent more time with a latest CD4 cell count < 350 cells/μL (for DC versus VS, 31% versus 8%) and with a latest HIV RNA level > 400 copies/mL (71% versus 28%) and had higher rate of OD/death (3.4 versus 1.3/100 person-years) than VS patients. For follow-up periods with CD4 cell count < 350 cells/μL, rates of OD/death were increased but similar in the two groups (5.7 versus 4.6/100 person-years), whereas rates were higher in the DC versus VS patients (2.3 versus 1.0/100 person-years; RR 2.3 [95% CI, 1.5-3.4]) for periods with the latest CD4 cell count ≥ 350 cells/μL, an increase said to be explained by the higher HIV RNA levels in the DC group. The SMART group concluded higher risk of OD/death in DC patients was associated with more follow-up time with relative immunodeficiency, as well as living longer with uncontrolled HIV replication at higher CD4 cell counts; and that ongoing HIV replication at a given CD4 cell count placed patients at an excess risk of OD/death. The SMART group also concluded that, because deaths from causes other than OD dominate among HIV-infected patients receiving ART, the findings supported considering ART initiation before even moderate levels of immunodeficiency develop, though definitive information to guide such an approach awaits a new randomized trial [enrolling asymptomatic treatment-naïve patients] approaching the scale of SMART.[37]

Lichtenstein, et al. (2008)

Noting that U.S. clinical guidelines recommend deferring initiation of HAART for most patients with CD4 counts > 350 cells/mm^3 in part due to concerns about ART toxicity, Lichtenstein and colleagues analyzed incidence rates in the HIV Outpatient Study (HOPS) for three comorbidities (peripheral neuropathy, anemia and renal insufficiency) in multivariate Cox proportional hazards models by CD4 cell counts at HAART initiation. HOPS is an ongoing, prospective, cohort study of HIV-infected patients receiving care in nine participating HIV clinics in eight U.S. cities since March 1993. Within a total cohort of 2165 patients followed more than 3 years (mean), a nested cohort of 895 patients restricted to those who did or did not start HAART in a CD4 cell count stratum were also compared. In all analyses, > 80% of the patients were male, > 60% were non-Hispanic whites, and approximately two thirds entered the HOPS from 1995-2001 with baseline CD4 cell counts ≥ 200 cells/mm3. Results showed that the incidence and risks of all three comorbidities decreased with initiation of HAART at CD4 counts > 200 cells/mm^3 versus < 200 cells/ mm^3. The incidence and risks of renal insufficiency were similar with HAART initiation at CD4 counts ≥ 350 cells/ mm^3 versus 200-349 cells/ mm^3, but the risk of peripheral neuropathy and anemia were further decreased in persons starting HAART at a CD4 count ≥ 350 cells/mm^3. The incidence of the conditions was highest during the first six months of treatment at any CD4 cell count and declined up to 19-fold with further therapy. Lichtenstein, *et al.* concluded that initiating HAART at CD4 cell counts ≥ 200 cells/mm^3 reduced incidence and risk of peripheral neuropathy, anemia and renal insufficiency, as well as reduced incidence and risk for anemia and peripheral neuropathy by starting at CD4 counts ≥ 350 cells/mm^3; and that the incidence of the comorbid conditions decreased rapidly and remained low with increasing time on HAART.[38]

Sanders, et al. (2008)

Utilizing a lifetime time horizon and societal perspective to examine costs and benefits of HIV screening in older patients, Sanders and colleagues developed a Markov model for patients aged 55-75 years with unknown HIV status and compared a screening program to current practice. Outcomes included life-years, quality-adjusted life-years (QALYs), costs and incremental cost-effectiveness. For a 65-year-old, results showed screening using traditional counseling costs $55,440 per QALY compared with current practice when the prevalence of HIV was 0.5% and the patient did not have a sexual partner at risk. For sexually active patients, results showed the incremental cost-effectiveness ratio was $30,020 per QALY. At a prevalence of 0.1%, results showed that HIV screening cost was < $60,000 per QALY for patients < 75 years of age with a partner at risk if less costly streamlined counseling was used. Overall, the results of sensitivity analysis showed cost-effectiveness of HIV screening depended on HIV prevalence, age of the patient, counseling costs and whether the patient was sexually active. Discussion of additional sensitivity analyses (appendix) described that recurrent screening became more economically favorable as HIV incidence increased. Acknowledged study limitations included that effects of age on toxicity and efficacy of HAART were uncertain, but sensitivity analyses exploring those variables did not qualitatively affect the final results. Based on the results of their analyses, the data available on prevalence and the relatively high rates of sexual activity for persons age > 55 years, Sanders, *et al.* recommended one-time voluntary screening with streamlined counseling on a routine basis for all persons age 55-64 years and one-time screening on a targeted basis for sexually active persons age 65-74 years if HIV prevalence is greater than 0.1%. The authors concluded that advanced age alone should not preclude HIV screening for HIV. Rather, cost-effectiveness of HIV screening for older people is within range of other accepted interventions.[39]

Kitahata, et al. (2009)

Kitahata and colleagues conducted two parallel analyses involving 17,517 asymptomatic HIV patients in the U.S. and Canada who received care from 1996-2005. Data for this study were collected as part of the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of the International Epidemiological Databases to Evaluate AIDS project, involving 22 research groups representing more than 60 sites. No patient had undergone prior antiretroviral therapy (ART), and study patients were stratified according to their CD4+ count (351-500 cells/mm^3 or > 500 cells/mm^3) at the initiation of ART. In each group, the relative risk (RR) of death was compared for patients who initiated therapy when the CD4+ count was above each of the two thresholds of interest (the early therapy group) with that of patients who deferred therapy until the CD4+ count fell below the thresholds (the deferred therapy group). In the first analysis involving 8,362 patients, results showed that 2,084 patients (25%) initiated therapy at a CD4+ count of 351-500 cells/mm^3 and 6,278 patients (75%) deferred therapy. After adjustment for calendar year, patient cohort, plus demographic and clinical characteristics, among patients in the deferred-therapy group there was an increase in risk of death of 69%, as compared to patients in the early-therapy group (RR 1.69; 95% CI, 1.26 to 2.26; P < 0.001). In the second analysis involving 9,155 patients, results showed that 2,220 patients (24%) initiated therapy at a CD4+ count of more than 500 cells/mm^3 and 6,935 patients (76%) deferred therapy. Among patients in the deferred-therapy group, there was an increase in risk of death of 94% (RR 1.94; 95% CI, 1.37-2.79; P < 0.001). While optimal time for ART initiation in asymptomatic patients with HIV infection remains uncertain compared with deferred therapy, Kitahata, *et al.* reported early ART initiation before the CD4+ count fell below the study's two prespecified thresholds significantly improved patient survival and that "significant advances in our understanding of the role of HIV infection in inflammation and immune activation resulting in potentially irreversible immune-system and end-organ damage have renewed the impetus for earlier treatment of HIV."[40]

Gebo and Justice (2009)

Over the past decade, Gebo and Justice noted that the percentage of HIV cases in patients ≥ 50 years of age increased to more than 17% and that the increase in HIV prevalence in middle-aged and older persons is expected to continue over the next decade. Compared to younger persons, older individuals may be more likely to develop drug toxicities and are more likely to have serious comorbidities including cardiovascular disease, renal disease, diabetes, bone loss, and obesity that complicate HAART utilization. Concerned that a balance be found between the potentially greater risk of cumulative drug toxicity and the need to treat older individuals earlier to sustain immune function and potentially reduce development or progression of comorbidities, Gebo and Justice reviewed the available literature and described the growing need to determine the ideal regimen and timing for HAART initiation in older patients. Notable among papers of major importance was the 2008 COHERE report of nearly 50,000 ART naïve European patients (the largest study of the impact of HIV and aging, but not differences in response by HAART class) which found that probability of virologic response was higher in persons > 50 years old but that probability of immunologic response was lower in persons > 60 years old. In their conclusions section, Gebo and Justice stated that HAART is "effective at reducing HIV disease progression and mortality and should be used in older patients. For the older patient, other concomitant drugs used for comorbidities should be explored; nephrotoxic and hepatotoxic drugs should be avoided if possible; and side effects of other drugs, especially in patients with insulin resistance, dyslipidemia, and cardiovascular disease, must be considered when selecting a HAART regimen." Summarizing, the authors noted that while HAART has been effective in reducing morbidity and mortality, clinical improvements "may be tempered by development of resistant HIV and toxicities from antiretroviral therapy, particularly in older patients… Therefore, research to evaluate the impact of age on clinical outcomes and adverse drug events in HIV-infected patients overall and by antiretroviral therapy class is needed, and likely will improve our understanding of the role of age in clinical care of HIV infection."[41]

4.MEDCAC

No Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) was convened for this screening issue.

5.Clinical Guidelines

United States Preventive Services Task Force (USPSTF) 2007 *(see Section VII.B. above)*

Centers for Disease Control (CDC) 2006

The CDC's Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings (September 2006) included the following recommendations:[42]

Screening for HIV Infection: The CDC recommends that screening for HIV infection should be performed routinely for all patients aged 13-64 years. This includes all patients initiating treatment for tuberculosis (TB)or seeking treatment for sexually transmitted diseases (STDs), including all patients attending STD clinics.

CDC recommends that health-care providers should subsequently test all persons likely to be at high risk for HIV at least annually. Persons likely to be at high risk include injection-drug users and their sex partners, persons who exchange sex for money or drugs, sex partners of HIV-infected persons, and MSM or heterosexual persons who themselves or whose sex partners have had more than one sex partner since their most recent HIV test.

Consent and Pretest Information: Screening should be voluntary and undertaken only with the patient's knowledge and understanding that HIV testing is planned. Patients should be informed orally or in writing that HIV testing will be performed unless they decline (opt-out screening). Oral or written information should include an explanation of HIV infection and the meanings of positive and negative test results, and the patient should be offered an opportunity to ask questions and to decline testing. With such notification, consent for HIV screening should be incorporated into the patient's general informed consent for medical care on the same basis as are other screening or diagnostic tests; a separate consent form for HIV testing is not recommended. Easily understood informational materials should be made available in the languages of the commonly encountered populations within the service area. The competence of interpreters and bilingual staff to provide language assistance to patients with limited English proficiency must be ensured. If a patient declines an HIV test, this decision should be documented in the medical record.

Recommendations for Pregnant Women: These guidelines reiterate the recommendation for universal HIV screening early in pregnancy but advise simplifying the screening process to maximize opportunities for women to learn their HIV status during pregnancy, preserving the woman's option to decline HIV testing, and ensuring a provider-patient relationship conducive to optimal clinical and preventive care. All women should receive HIV screening consistent with the recommendations for adults and adolescents. HIV screening should be a routine component of preconception care, maximizing opportunities for all women to know their HIV status before conception. In addition, screening early in pregnancy enables HIV-infected women and their infants to benefit from appropriate and timely interventions (e.g., antiretroviral medications, scheduled cesarean delivery, and avoidance of breastfeeding [To eliminate the risk for postnatal transmission, HIV-infected women in the United States should not breastfeed. Support services for use of appropriate breast milk substitutes should be provided when necessary. In international settings, UNAIDS and World Health Organization recommendations for HIV and breastfeeding should be followed]. These recommendations are intended for clinicians who provide care to pregnant women and newborns and for health policy makers who have responsibility for these populations.

American College of Physicians (ACP) and HIV Medicine Association (HIVMA) 2009

The new ACP and HIVMA clinical practice guideline was derived from an appraisal of available guidelines on HIV screening using the AGREE (Appraisal of Guidelines Research and Evaluation) instrument to evaluate both the current USPSTF and CDC guidelines. Two guidance statements were provided:

ACP recommends that clinicians adopt routine screening for HIV and encourage patients to be tested.

"The goal of screening for HIV is to identify patients with undiagnosed HIV so that timely treatment is provided and transmission is prevented. Our guidance to perform routine screening of all patients is based on the following rationale and evidence. First, early identification and treatment for HIV provides substantial health benefit by extending the length of life of the person identified as having HIV. Modeling studies suggest that identification and successful treatment also probably reduce HIV transmission, both through changes in risk behavior and from suppression of viral load through treatment, although the magnitude of the risk reduction has not been assessed directly.

Second, risk-based screening has failed to identify a substantial proportion of people with HIV early in disease. Although risk-based screening has been recommended for more than 15 years, evidence from the CDC and Veterans Affairs indicate that almost half of patients are identified late in the course of disease, when they will no longer receive the maximum benefit from antiretroviral therapy. A retrospective analysis of approximately 14,000 Veterans Affairs patients found that even when risk factors were clearly identifiable from the medical record, only about one third of at-risk patients were tested. In addition, 10% to 25% of people testing positive report no high-risk behaviors. Thus, the effectiveness of risk-based screening has been limited because providers seldom actually perform risk assessments, and even if providers did such assessments in all patients, a substantial proportion of people with HIV would still be missed because they either are unaware that they are at increased risk or do not wish to disclose risk behaviors.

Third, routine opt-out screening (screening all individuals unless they decline to be tested) has been widely implemented and highly successful for prenatal HIV screening. Acceptance among women has been high, and mother-to-child transmission has been nearly eliminated in the United States. Whether specific informed consent for HIV testing is required varies by state, and clinicians should be aware of requirements in their practice setting.

Finally, strong evidence indicates that screening is cost-effective, even when the prevalence of HIV is low. When the benefit from transmission is considered, a study found screening to be cost-effective at a prevalence of 0.05%, and another analysis found screening to be cost-effective at a prevalence of 0.2%, with favorable assumptions about the reduction in HIV transmission.

The CDC recommends that patients age 13 to 64 years be screened for HIV. Less evidence is available on screening older patients, but nationally, approximately 20% of patients with HIV are older than 50 years. A recent cost-effectiveness analysis found that screening patients up to age 75 years met conventional cost-effectiveness thresholds if screening was done with streamlined counseling, patients were sexually active, and the prevalence of HIV in the population was greater than 0.1%. Although data on prevalence in older patients are limited, evidence from a Veterans Affairs population indicates a prevalence of 0.5% among male outpatients 65 to 75 years of age."

ACP recommends that clinicians determine the need for repeat screening on an individual basis.

"The importance of repeated HIV screening depends on whether patients have ongoing risk for HIV infection. Higher-risk patients should be retested more frequently than lower-risk patients. The USPSTF does not make recommendations about the frequency of screening. The CDC guideline recommends that providers screen patients at high risk for HIV at least annually. The CDC defines persons likely to be at high risk as injection drug users and their sexual partners, persons who exchange sex for money or drugs, sexual partners of HIV-infected persons, men who have sex with men, and heterosexual persons who have had or whose sexual partners have had more than one sexual partner since their most recent HIV test."[43]

6. Professional Society Position Statements

American College of Obstetricians and Gynecologists (ACOG) 2008

The ACOG noted that women of color (primarily African-American and Hispanic women) comprise most new cases (> 80%) of HIV occurring in U.S. females, and that older women represent an increasing proportion of those new HIV diagnoses, including a 4.1% increase per year between 1999 and 2004 among women older than 60 years.

The ACOG recommended that "safe-sex practices, especially consistent condom use, must be emphasized for all women, particularly women of color" and that combined "testing, education and brief behavioral interventions can help reduce the rate of HIV infection and its complications among women of color."[44]

HIV Medicine Association (HIVMA) of the Infectious Diseases Society of America and the American College of Physicians (ACP) 2009

The latest collaborative HIVMA and ACP HIV Policy paper emphasized public health and clinical imperatives for earlier identification of persons with HIV infection, urgent need to expand access to state-of-the-art care and treatment for HIV infected individuals, plus needed access to comprehensive prevention and education for persons living with and at risk for HIV infection.

Included among the ten positions advocated for by the HIVMA and ACP are government support for routine HIV testing as a covered preventive service under Medicare, promotion of evidence-based interventions to minimize risk of HIV transmission, education regarding behaviors that put individuals at risk for HIV infection and other sexually transmitted infections, access to HIV care and services provided by or in consultation with clinicians skilled in providing the standard of care for HIV/AIDS, plus protection of confidentiality and privacy of persons living with HIV.[45]

7. Public Comments

During the initial 30-day public comment period (03/13/2009 - 04/12/2009), CMS received 34 comments, a summary of which is provided in the proposed decision memorandum.

During the final 30-day comment period (09/09/2009 - 10/09/2009)following publication of our proposed decision, CMS received 30 comments from individuals and groups, including 10 physicians, 17 other health professionals, and 3 from the general public. Of these 30 comments, 29 generally agreed with the proposed decision to add Medicare coverage for HIV screening, and many individuals or organizations strongly endorsed or supported the agency’s efforts.

One commenter appreciated our "informative in-depth review"; a second commenter stated that it "applauds CMS for taking this important and significant step, which will benefit Medicare beneficiaries across the nation"; and a third commenter indicated that "we commend CMS for selecting HIV screening as the first expanded preventive service coverage as provided by the Medicare Improvements for Patients and Providers Act of 2008." A fourth commenter wrote that "testing for HIV is a great/smart preventative service to offer Medicare and Medicaid patients", and a fifth commenter stated that "we strongly support the proposal outlined in CAG-00409N to cover HIV screening using a Food and Drug Administration-cleared HIV antibody test on an annual basis, in Medicare beneficiaries at increased risk for HIV infections, as defined in the U.S. Preventive Services Task Force (USPSTF) guidelines, and voluntary screening of pregnant Medicare beneficiaries."

Among the 29 of 30 commenters who supported CMS's efforts to add coverage of screening for HIV, 22 commenters encouraged the agency to provide even broader coverage than described in the proposed decision – even though some of them acknowledged that CMS's authority was limited by the plain terms of the statute that requires a grade of A or B from the USPSTF. The suggestions or recommendations which were offered dealt mostly with beneficiary eligibility and the frequency and types of HIV screening tests that commenters believed should be covered in our final decision.

In the paragraphs below, general comment themes are summarized followed by CMS responses in italics.

Comments with New Evidence

No commenters cited new peer-reviewed medical literature.

Comments without New Evidence

Cost of HIV Screening

One commenter believed that cost should not be a factor CMS considers in making national coverage determinations.

Response

As described under paragraph (b) within "Section III. History of Medicare Coverage" of our coverage decision memorandum, statute and regulations permit this consideration in making determinations regarding the coverage of a new preventive service.[46]

Types of HIV Screening Tests

Several commenters stated coverage of only FDA-approved EIA, ELISA or rapid HIV antibody tests was too limited. One commenter thought there was no basis for excluding HIV screening tests from coverage simply because they are performed using laboratory-developed tests.

Response

CMS agrees and has decided to broaden the coverage of HIV screening tests, based in part upon the USPSTF Summary of Recommendations on Screening for HIV (2007):

- *"The USPSTF found good evidence that both standard and U.S. Food and Drug Administration (FDA)-approved rapid screening tests accurately detect HIV infection."*
- *"The USPSTF found good evidence that both standard and FDA-approved rapid screening tests accurately detect HIV infection in pregnant women."*[47]

According to the USPSTF (2007), "the standard test for diagnosing HIV infection, the repeatedly reactive enzyme immunoassay followed by confirmatory western blot or immunofluorescent assay, is highly accurate (sensitivity and specificity ≥ 99%). Rapid HIV antibody testing is also highly accurate; can be performed in 10 to 30 minutes; and, when offered at the point of care, is useful for screening high risk patients who do not receive regular medical care (e.g., those seen in emergency departments), as well as women with unknown HIV status who present in active labor." The USPSTF review also "found that standard testing for HIV infection has a sensitivity and specificity greater than 99% and that false-positive test results are rare, even in low risk settings. While indeterminate results may occur a little more frequently among parous and pregnant women, the diagnostic accuracy of standard HIV testing is thought to be similar for pregnant women and non-pregnant women and men. Alternative FDA-approved screening technologies are also highly accurate and may increase testing acceptability. Compared with standard HIV testing, the reported sensitivities of rapid tests on blood specimens range from 96% to 100%, with specificities greater than 99.9%. Reported sensitivities and specificities of oral fluid HIV tests are also high (> 99%), although the diagnostic accuracy of urine tests appears lower than that of standard testing."[48]

Further, as discussed in our analysis section, Paltiel, et al's (2006) decision model estimated the costs of HIV screening using same-day rapid HIV antibody testing, and Sanders, et al's (2008) model incorporated the costs of HIV testing utilizing a serum enzyme-linked immunosorbent assay in patients age 55-75 years with unknown HIV status.[49,50] *The known low cost and high sensitivity and specificity of these commonly used HIV screening tests were thus important considerations in this coverage determination.*

Therefore, in accordance with the USPSTF's latest recommendations, CMS believes that statute and regulations permit – and that it is reasonable and appropriate to cover - both standard and FDA-approved HIV rapid screening tests.

Frequency of HIV Screening

Commenters made various recommendations for revision of the covered frequency of HIV screening, including that for pregnant Medicare beneficiaries CMS should cover up to three HIV screening tests for each pregnancy.

For nonpregnant Medicare beneficiaries at increased risk for HIV infection, several commenters agreed with our proposed annual limit for HIV screening. Other commenters suggested revision of the covered frequency of HIV screening ranging from removal of the word "annual" to coverage for HIV screening up to two times a year, three times per year, multiple times per year, at each visit for a new complaint, or any time a patient requests an HIV test.

Response

Regarding the recommended frequency of HIV screening for pregnant women, we appreciate the comment from the American College of Obstetricians and Gynecologists (ACOG), which particularly supports our decision to cover voluntary HIV screening for pregnant Medicare beneficiaries. In addition, the 2008 ACOG Committee Opinion No. 418 recommends HIV screening for all pregnant women as early as possible in each pregnancy, repeat testing in the third trimester for women living in areas with high HIV prevalence and women know to be at high risk for acquiring HIV infection, and testing at labor and delivery for women with undocumented HIV status.[51] As stated in the ACOG comment, "early diagnosis and treatment of HIV not only improves chances of survival, it also enables women who are infected with HIV to take steps to avoid unintended pregnancy, protect their sexual partners, and reduce the likelihood of mother-to-child transmission for women who are pregnant".

The CDC's 2006 Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings also recommends HIV screening early in pregnancy as part of a routine panel of prenatal screening tests for all pregnant women, repeat HIV testing in the third trimester for all women in areas with elevated HIV or AIDS incidence, and rapid HIV testing for all women in labor who do not have documentation of results from an HIV test during pregnancy.[52]

Importantly, childbirth is clearly imminent for pregnant beneficiaries; and early detection of HIV infection can dramatically decrease the rate of vertical transmission from mother-to-child. Repeat HIV screening up to three times during each pregnancy is thus appropriate because rapid initiation of treatment can decrease HIV transmission from approximately 25% to less than 2% via antiretroviral treatment early in pregnancy, as well as scheduled cesarean delivery, avoidance of breastfeeding and neonatal antiretroviral prophylaxis. CMS will therefore cover voluntary HIV screening for pregnant Medicare beneficiaries as soon as the diagnosis of pregnancy is known, during the third trimester for women who may be at increased risk for HIV infection, and at labor for any woman with undocumented or unknown HIV status, if ordered by the woman's clinician.

However, for nonpregnant beneficiaries who are at increased risk for HIV infection, knowledge of one's serostatus following HIV screening does not necessarily reduce horizontal transmission from person-to-person; and some HIV positive patients delay entry into care and do not receive medical care or interrupt their treatment.[53]Similarly, despite models that assume all individuals identified by annual voluntary universal screening programs as HIV positive will receive ART, "individuals frequently are diagnosed to have HIV in settings apart from those where they ultimately will receive treatment, and significant barriers impede the efficient movement of a patient infected with HIV from diagnosis to care. These include the lack of health insurance, homelessness, substance abuse, mental illness, and denial by the individuals of their newly diagnosed HIV status."[54] Furthermore, identification and enrollment of elderly HIV-infected individuals with multiple comorbidities into pivotal studies investigating optimal ART initiation strategies – such as the new Strategic Timing of AntiRetroviral Treatment(START) trial[55] – are essential to inform clinical guidelines of whether, and possibly in which subgroups, ART should be initiated in persons who are still in the early stages of HIV infection.[56]

Therefore, since current guideline recommendations[57] suggest testing all persons aged 13-64 years likely to be at high risk for HIV at least annually, CMS does not believe it is appropriate to remove the word "annual" or make other changes to the covered frequency of repeat HIV screening in nonpregnant Medicare beneficiaries who are at increased risk for HIV infection.

Routine screening

Several comments requested coverage of routine HIV testing for all individuals, including persons at low risk for HIV infection, regardless of risk, based on more recent data, or based upon the C rating of the USPSTF.

Response

Our statute and regulations only permit coverage of additional preventive services which have been recommended with a grade of A or B by the USPSTF and do not permit coverage of such services for groups that are rated C, specifically "adolescents and adults who are not at increased risk for HIV infection."

Number of Partners

In the USPSTF criteria for individuals at increased risk for HIV infection, one commenter noted that having unprotected sex with multiple partners implies multiple concurrent partners and alternatively suggested using the phrase "having unprotected sex with a new partner".

Response

Our statute and regulations only permit coverage of additional preventive services that identify medical conditions or risk factors for individuals, such as voluntary HIV screening, which have been recommended with a grade of A or B by the USPSTF.[58] In our coverage decision, the phrase "multiple partners" is clarified to mean "multiple [more than one] partners". The word "concurrent" was not used or implied.

Screening of New Medicare Beneficiaries

One commenter suggested that HIV testing "be offered as part of the Initial Preventive Physical Exam (IPPE), also known as the ‘Welcome to Medicare’ exam."

Response

CMS notes that while voluntary HIV screening cannot be added as a mandatory part of the IPPE benefit (developed through a separate rulemaking process), eligible new Medicare beneficiaries will be able to obtain coverage of the test based on a referral from a qualified physician or a qualified nonphysician obtained during the IPPE effective with this final national coverage determination.

Screening of Donors and Recipients

One commenter stated that CMS should also cover HIV testing for both hematopoietic transplant donors and recipients.

Response

CMS notes that this suggested testing is not considered screening but rather a part of pre-operative testing, which is outside of the scope of this analysis.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under title XVIII of the Social Security Act §1869(f)(1)(B). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Since January 1, 2009, CMS is authorized to cover "additional preventive services" (see Section III above) if certain statutory requirements are met as provided under §1861(ddd) of the Social Security Act and our regulations at 42 CFR 410.64:

(a) Medicare Part B pays for additional preventive services not otherwise described in this subpart that identify medical conditions or risk factors for individuals if the Secretary determines through the national coverage determination process (as defined in section 1869(f)(1)(B) of the Act) that these services are all of the following:

(1) Reasonable and necessary for the prevention or early detection of illness or disability.
(2) Recommended with a grade of A or B by the USPSTF.
(3) Appropriate for individuals entitled to benefits under part A or enrolled under Part B.

(b) In making determinations under paragraph (a) of this section regarding the coverage of a new preventive service, the Secretary may conduct an assessment of the relation between predicted outcomes and the expenditures for such services and may take into account the results of such an assessment in making such national coverage determinations.[59]

USPSTF

Is the evidence sufficient to determine that HIV screening is recommended with a grade of A or B by the USPSTF for any indications?

USPSTF Summary of Recommendations on Screening for HIV (2007):

- "The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians screen for human immunodeficiency virus (HIV) all adolescents and adults at increased risk for HIV infection. Rating: 'A' Recommendation [strongly recommended]"
- "The USPSTF makes no recommendation for or against routinely screening for HIV adolescents and adults who are not at increased risk for HIV infection. Rating: 'C' Recommendation [no recommendation]"
- "The USPSTF recommends that clinicians screen all pregnant women for HIV. Rating: 'A' Recommendation [strongly recommended]"[60]

We conclude that HIV screening of all adolescents and adults at increased risk for HIV infection and HIV screening of all pregnant women are recommended with a grade of A or B by the USPSTF.

Reasonable and Necessary for Prevention

Is the evidence sufficient to determine that HIV screening is reasonable and necessary for the prevention or early detection of illness or disability?

HIV screening is a simple test using either a small amount of fluid obtained from an oral swab or a small amount of blood, serum or plasma from a venous blood draw or finger stick – which is acceptable to many persons and has high accuracy and precision, plus excellent sensitivity and specificity. While sensitivity and specificity of currently available FDA-approved HIV antibody tests exceed 99%, the positive predictive value of these screening tests – the proportion of tested individuals with a reactive preliminary positive result who have HIV infection – decreases as prevalence of HIV decreases in the population screened.

In 2007, Paltiel and Walensky commented: "Rapid HIV tests have similar sensitivity and specificity to standard antibody tests. They provide results within 20 minutes, eliminating the high rate of failure to return for results (25% in persons testing HIV-positive and 33% in persons testing HIV-negative at publicly funded U.S. clinics). However, unlike standard antibody tests, rapid testing allows positive results to be reported to the patient before they can be confirmed by repeated tests and Western blots. The tradeoff is clear: Wait one or two weeks, knowing that up to one third of cases will be lost to follow-up, or report preliminary results to patients and link them to care, knowing that this may cause short-term distress in a small percentage of those tested. We find that the benefits of rapid testing more than offset the risks, even when we assume a low-specificity test and assign large economic and quality-of-life costs to false-positive findings."[61]

The prevalence of HIV is thus a key determinant of the usefulness of screening, and the 2006 CDC guidelines for HIV screening recommend one-time screening in all health care settings unless the prevalence of undiagnosed HIV infection is documented to be < 0.1%.[62]

Based on results of their cost-effectiveness analyses, currently available data on HIV prevalence and the relatively high rates of sexual activity in people > 55 years of age, Sanders, *et al.* (2008) recommended one-time HIV screening on a targeted basis to sexually active persons age 65-74 years if HIV prevalence is greater than 0.1%. Whereas Paltiel, *et al's* (2006) analysis utilized a decision model to estimate cost effectiveness of same-day rapid HIV antibody testing, Sanders and colleagues' (2008) model incorporated standard HIV testing using a serum enzyme-linked immunosorbent assay (ELISA) followed by confirmatory Western blot analysis and explored the effects of streamlined counseling (abbreviated pretest counseling requirements as recommended by the CDC) on HIV screening in their sensitivity analyses.[63,64] For persons age 65-74 years without a partner at risk, Sanders, *et al.* calculated that screening costs $50,000-$100,000 per QALY gained where HIV prevalence is between 0.1% and 0.5%. "Thus, screening is more expensive if the person is not sexually active, but it is still a reasonable option, particularly if prevalence approaches 0.5%." Additional sensitivity analyses also described that recurrent HIV screening becomes more economically favorable when the incidence of HIV increases, as would be the case for individuals with high-risk behaviors.

While unbiased estimates for the elderly have been difficult to obtain, Owens, *et al's* (2007b) blinded, anonymous HIV serological survey of six geographically diverse VA health care sites reported that undocumented HIV-infected patients were more likely to be older (> 55 years); and for patients 65-74 years of age with previous unknown test results, prevalence of HIV was 0.5% among outpatients and 0.4% among inpatients.[65] Based on these best available estimates, HIV screening appears reasonable for Medicare beneficiaries, especially for beneficiaries with high-risk behaviors for whom there is a corresponding high incidence of HIV. As noted, however, by Walensky and colleagues (2007) in their review of cost-effectiveness of HIV testing and treatment in the U.S, simply asserting that screening for HIV is cost-effective does not imply that it is cost saving. What actually determines the cost-effectiveness of a testing program is not the cost[66] of the HIV test itself, which is relatively inexpensive, but rather future costs of care for persons identified and treated for HIV infection, medical care that typically includes combination ART with three different agents from at least two different drug classes, prophylaxis and treatment of associated opportunistic infections, as well as outpatient, inpatient and laboratory expenditures.[67]

Equally important, while comprehensive guidelines are needed to address secondary preventive measures in older HIV-infected patients with multiple comorbid conditions, compliance with medical therapy is essential since patient adherence to continuous HAART effectively decreases an infected individual's viral load and can also subsequently reduce the spread of HIV in the population. Moreover, reports from the completed SMART study[68] reinforced that the benefits of antiretroviral therapy (ART) may extend well beyond viremia control, i.e., comorbidities themselves may be mitigated due to the decreased inflammatory process of uncontrolled viremia. In other words, according to Hughes and Ribaudo (2008):

"The SMART study was important because it showed that the serious morbidity that was considered a priori to be related to ART might, in fact, be beneficially affected by ART, perhaps because such morbidity is a consequence of chronic HIV infection or because some adverse effects of ART might be less frequent when ART is initiated at higher $CD4^+$ cell counts (Lichtenstein*, et al.* 2008). Because a major argument against ART initiation at higher $CD4^+$ cell counts has concerned the risk-benefit ratio for ART when the notion of benefit tended to focus upon AIDS-defining events and mortality, results from the SMART study emphasized the need to look at serious morbidity more broadly in a when-to-start trial, either as a set of coprimary endpoints or as a composite endpoint."[69]

Regarding enrollment in such studies, CMS believes it is essential that a representative number of older adults and elderly patients with typical comorbidities be included in all new randomized controlled clinical trials, well-designed prospective observational cohort studies and comparative effectiveness research investigating patient-related outcomes, guidelines and ART strategies.

Beginning that process of obtaining critical new data, amidst the worldwide trend toward earlier initiation of antiretroviral therapy[70,71,72], Kitahata and colleagues (2009) recently reported that ART can extend the healthy life of persons living with HIV/AIDS. Notably, the early initiation of ART before patients' $CD4^+$ count fell below prespecified thresholds, i.e., treatment initiation at $CD4^+$ cell count of 351-500 cells/mm^3 versus deferred (or at > 500 cells/mm^3 versus deferred) significantly improved survival as compared to deferred therapy. Or phrased conversely, the strikingly increased risk of death in the two deferred ART groups was, respectively, 69% and 94%.[73] Stressing the need for continued research, however, an accompanying NEJM editorial, argued that Kitahata and colleagues' results were not yet definitive and that HIV patients who began ART earlier may have differed from those who waited in ways that improved survival.[74]

Pursuing still further outcomes research regarding potential usefulness of earlier ART initiation, the NIH's new Strategic Timing of AntiRetroviral Treatment (START) study began recruiting the first 900 participants of its pilot phase in March 2009.[75] The purpose of this randomized trial is to determine whether immediate ART initiation is superior to ART deferral until $CD4^+$ cell count declines < 350 cells/mm^3, in terms of morbidity and mortality, in HIV-infected persons who are antiretroviral naive with $CD4^+$ cell count > 500 cells/mm^3. START's inclusion criteria include patient age $\geq$ 18 years with a perceived life expectancy of at least 6 months, and the new START study's primary outcome measure is to determine whether early ART is superior to deferred ART in delaying occurrence of a composite outcome consisting of AIDS, non-AIDS or death from any cause. As stated in Lundgren, *et al's* (2009) response to a review[76] of when to begin ART:

"Once completed, the START study will inform guidelines of whether – and possibly in which subgroups – ART should be initiated in persons who are still in the early stages of HIV infection. If the START study finds a favorable benefit-to-risk ratio for early use of ART, then, when applied, this strategy of early use of ART will likely further reduce the reservoir of infectious persons."[77]

Coverage of annual voluntary HIV screening for Medicare beneficiaries at increased risk for HIV infection would enable the identification and enrollment of elderly individuals in such pivotal studies investigating optimal ART initiation strategies. And looking forward, age-stratified results from the START trial would assuredly aid in developing treatment guidelines for elderly HIV-infected patients.

Additionally, the USPSTF (2007) concluded that "the benefits of screening all pregnant women substantially outweigh potential harms."[78] And voluntary HIV screening for pregnant Medicare beneficiaries would , as recommended by the CDC (2006), "maximize opportunities for women to learn their HIV status during pregnancy, preserving the woman's option to decline HIV testing, and ensuring a provider-patient relationship conducive to optimal clinical and preventive care" for disabled, young and middle-aged, female Medicare beneficiaries.[79]

Regarding normal aging and common comorbidities affecting older Medicare beneficiaries, early symptoms of HIV/AIDS can at times be mistakenly attributed to one or more manifestations of chronic diseases and/or aging such as weight loss, loss of bone and muscle mass, increased pain, decreased glomerular filtration rate (kidney function), memory loss and immunosenescence. Accordingly, several groups[80,81,82,83] have reviewed the literature and addressed the astute, multidisciplinary team required to care for the growing population of HIV-infected older adults. In concluding their most recent review of HIV infection in elderly adults, Gebo and Justice (2009) thus stated that:

"Clinicians taking care of older patients should ask all patients about high-risk behaviors and educate them on the risks of HIV. The presentation and natural history of HIV in the older patient may be different than in younger patients with worse immune suppression at diagnosis and more rapid disease progression. Older adults have a more severe HIV course, more opportunistic illnesses and malignancies, shortened survival, and shorter AIDS free intervals than younger patients. In the HAART era [1996 to present], rapid initiation of antiretroviral treatment when indicated is particularly important to reduce HIV disease progression and HIV-associated mortality. Although more rapid HIV progression could occur because of comorbidities in older patients, immunosenescence, and the adverse effects of medications, research is needed to determine the differences in immune reconstitution in older and younger patients.

Current HAART therapy is effective at reducing HIV disease progression and mortality and should be used in older patients. For the older patient, other concomitant drugs used for comorbidities should be explored; nephrotoxic and hepatotoxic drugs should be avoided if possible; and side effects of other drugs, especially in patients with insulin resistance, dyslipidemia, and cardiovascular disease, must be considered when selecting a HAART regimen. Management of comorbidities is complicated and may require triaging conditions by level of importance."[84]

Regarding the control of viremia and age differences in therapeutic response, while the goal of current medical therapy is virologic suppression in all patients, Silverberg and colleagues (2007) interestingly found that:

"Older patients [age ≥ 50 years] had better virological responses to HAART compared with younger patients and, despite blunted initial immunological responses, had similar CD4 T-cell counts by three years. Higher HAART adherence was the key factor for older patients, who must overcome potential obstacles to a robust response, including an increased risk of adverse events, a higher comorbidity burden, and possible age-related immune senescence."

But as more recently stated regarding therapeutic responses of elderly HIV-infected individuals, while HAART is effective at reducing HIV viral load and improving CD4 lymphopenia, existing "data regarding the clinical, immunologic, and virologic benefit in older patients treated with HAART have been mixed." Furthermore, Gebo and Justice noted that studies by Patterson, *et al.* (2007) and Greenbaum, *et al.* (2008), the only two HIV studies to have examined the impact of regimen type on clinical outcomes by age, had relatively small sample sizes and "future studies that are adequately powered to address the impact of specific antiretroviral therapy regimens are needed to further answer the question of most appropriate treatment type for older patients."[85]

Regarding the side effects of antiretroviral therapy, according to the Data Collection on Adverse Events of Anti-HIV Drugs (DAD) group, the harmful cardiovascular effects of HAART vary according to antiretroviral drug class, and cumulative exposure to protease inhibitors (PIs) but not non-nucleoside reverse-transcriptase inhibitors (NNRTIs) is associated with an increased risk of myocardial infarction.[86] Additionally, compared to other nucleoside reverse transcriptase inhibitors (NRTIs), conflicting reports about excess risk of myocardial infarction associated with abacavir in combination ART have also been published by large international cohort studies and manufacturer-sponsored trials.[87,88,89] But as recommended by reviewers in May 2009, "further studies comparing the rates of CVD [cardiovascular disease] in HIV-infected older patients to age-matched HIV seronegative controls with similar demographic profiles are needed to examine the overlapping issues of age, HIV infection, and HAART therapy in an older HIV cohort."[90]

After careful review of the available body of evidence, we conclude that voluntary HIV screening is reasonable and necessary for the prevention or early detection of illness or disability for individuals at increased risk for HIV infection as well as for pregnant women when the diagnosis of pregnancy is known, during the third trimester and at labor.

Appropriateness

Is the evidence sufficient to determine that HIV screening is appropriate for Medicare beneficiaries?

Voluntary consent for screening typically invokes one of two assumptions regarding a patient's willingness to undergo testing, commonly known as "opt-in" or "opt-out" testing, and we have adopted definitions from a recent national consensus conference.[91]

Opt-in screening (asking asymptomatic persons if they would like to be tested for HIV) may be declined by individuals who value privacy or are concerned regarding personal disclosure, feel uncomfortable discussing such matters with an unfamiliar or new physician, or worry that their personal physician might negatively perceive them as engaging in high-risk behaviors.

Opt-out screening (informing patients they will be screened for HIV unless they decline or defer) may minimize perceived prejudice or rejection, and may more efficiently screen individuals who do not consider themselves at risk or who do not wish to discuss whether they have ever or are now engaging in high-risk sexual or drug use behaviors.

Regardless of the type of voluntary screening performed, however, screening represents only a snapshot or preliminary finding; and the meaning of HIV test results should be thoroughly and confidentially communicated to those screened. Further testing is always required to confirm a reactive preliminary positive screening test result. "A simple message to convey this information could be 'Your preliminary test result is positive, but we won't know for sure if you are infected with HIV until we get the results from your confirmatory test. In the meantime, you should take precautions to avoid transmitting the virus.'"[92]

Nevertheless, HIV screening may be declined or deferred due to a perceived lack of risk; and Brown and colleagues' (2008) survey of emergency room patients confirmed that an individual's perception that "I don't think I am at risk for getting HIV" was indeed the number one reason for declining rapid HIV testing.[93]

Additionally, as elucidated by Burke and colleagues (2007), "U.S. physicians experience many policy-based, logistical and educational barriers to HIV testing", and some physicians may not adequately identify or test older at-risk persons. Barriers to preventive services for HIV thus exist at both the patient and provider levels; and while individuals may be generally accepting of screening when offered by their physician, failure to expand testing despite published national guidelines from the CDC may also in part stem from physicians' hesitancy to test for HIV.[94] Consequently, declined or delayed HIV screening, regardless of whether due to patient or physician reluctance, may ultimately negatively impact an HIV-infected elderly person's, as well as their spouse's and/or partners', long-term survival and quality of life.

Notably, of new HIV infections in the U.S., more than half are estimated to be acquired from the 25% of infected individuals who are unaware of their serologic status.[95] But due to diminished horizontal HIV transmission to their sexual and drug use partners, treatment benefits accruing to infected Medicare beneficiaries, who undergo screening and become aware of their HIV status, may extend more generally to individuals partnered with that HIV-infected person.[96] However, while early detection and timely access to medical care can substantially improve the course of disease among HIV-infected persons, "whether they also reduce the risk for transmitting the virus to others is not clear because survival gains from ART prolong infectious lifetimes and may lead to complacency toward HIV risk behavior. Recent studies report increases in HIV infections, other sexually transmitted diseases, and sexual risk behaviors in vulnerable populations; [and] access to effective ART may also be associated with sexual risk-taking."[97]

Lubinski and colleagues (2009) reiterated that knowledge of one's HIV serostatus does not necessarily reduce disease transmission and that – while screening, early diagnosis, treatment and counseling can reduce spread of HIV in the population – some HIV positive patients may delay entry into care, not receive medical care or interrupt their treatment. "Although some studies have suggested that there is a decrease in high-risk behavior following knowledge of one's HIV status, the finding is not consistent across all populations; and others have reported that initial decrease in high-risk behavior may wane over time, suggesting that prevention messages for HIV positive individuals needs to be reinforced throughout their lifetime."[98]

Further, as described by Dieffenbach and Fauci (2009), despite models that assume all persons identified by annual voluntary universal screening programs as HIV positive will receive ART, "individuals frequently are diagnosed to have HIV in settings apart from those where they ultimately will receive treatment, and significant barriers impede the efficient movement of a patient infected with HIV from diagnosis to care. These include the lack of health insurance, homelessness, substance abuse, mental illness, and denial by the individuals of their newly diagnosed HIV status. As with voluntary testing, a public health-systems research agenda will be needed to define efficient and effective means of entering and retaining patients in care."[99]

Informative also regarding the early identification and treatment of HIV infected individuals, Espinoza and colleagues (2007) added that concurrent late HIV and AIDS diagnoses imply missed opportunities for early HIV treatment; and in Owens, *et al's* (2007) large observational study of persons entering HIV care at VA Medical Centers nationwide, 51% of those veterans had AIDS with baseline CD4 counts < 200 cells/ml, despite the fact that those who previously accessed VA healthcare had a median of 6 physician visits over 3.7 years before presenting for HIV care. Noting that such patients were likely not identified earlier because they did not manifest signs and symptoms suggesting an increased risk for HIV infection, Owens' group posited that were access to care the major barrier preventing timely initiation of treatment for HIV, eligible veterans should be expected to present earlier (at higher CD4 cell counts) than non-veterans because the VA provides comprehensive healthcare benefits. Similarly, Gandhi and colleagues (2007) concluded that more than half of veterans entered HIV care with an AIDS diagnosis at presentation irrespective of whether they had previously established healthcare in the VA; that access to care did not seem to be the primary cause of delayed HIV presentation; and that widespread HIV screening is needed to improve rates of early HIV detection.[100]

However, while the VA is the largest provider of HIV care in the U.S. and access to care may not necessarily be a barrier to care for veterans, the latest policy paper from the HIVMA and ACP explained that in 2004 the Institute of Medicine (IOM) "conducted a Congressionally mandated study of the financing and delivery of HIV care and treatment for low-income uninsured and underinsured individuals with HIV disease. They [IOM] issued a report finding that nearly 50% of individuals with HIV infection have no access or limited access to HIV care and that [overall] the fragmentation of coverage from multiple funding sources was impeding sustained access to HIV care."[101]

Regarding existing guidelines, since 2005 the USPSTF has given an "A" recommendation for screening all adults at increased risk for HIV infection and a "C" recommendation neither for nor against routinely screening those without high-risk behaviors. In response to Beckwith, *et al's* comments[102] describing HIV testing strategies dependent on risk assessment as inadequate and urging that opt-out HIV testing be routinely offered in primary care, inpatient, urgent care and emergency departments, Calonge (USPSTF Chair) and Petitti (Vice Chair) clarified that the Task Force left the decision of whether to screen non-high-risk persons to the primary care clinician's discretion. According to the Task Force's pre-May 2007 definitions, a "C" recommendation indicated that the USPSTF had found at least fair evidence that HIV screening can improve health outcomes but had concluded that the balance of benefits and harms associated with screening were too close [at that time] to justify a general recommendation. For non-high-risk patients, the "C" recommendation thus allowed a clinician "to give lower priority to this service and to make the decision on an individualized basis, in collaboration with his or her patient."[103]

However, there are estimated to be more than one million persons living with HIV, including greater than a quarter million who remain undiagnosed; and since the USPSTF's 2007 update, considerable new clinical evidence – as detailed in this national coverage analysis – has been published which supports expanding screening efforts and access to care for persons with HIV. Although risk-based screening methods based upon known or suspected HIV exposure fail to identify a moderate percentage of infected individuals – and routine screening recommended by the ACP (2009) clinical guidelines and CDC recommendations might better identify a larger proportion of HIV-infected individuals – CMS believes that statute and regulations only permit expanded coverage of additional preventive services that identify medical conditions or risk factors for individuals, such as voluntary HIV screening, which have been recommended with a grade of A or B by the USPSTF.

After careful review of the available body of evidence, we conclude that voluntary HIV screening is appropriate for the prevention or early detection of illness or disability for Medicare beneficiaries at increased risk for HIV infection as well as for pregnant women when the diagnosis of pregnancy is known, during the third trimester and at labor.

Disparities in HIV/AIDS

As related in detail by the CDC, the greatest HIV prevalence (i.e., the number of people living with HIV with or without a diagnosis of AIDS at any specific point in time) is among African-Americans, who comprise 12% of the U.S. population but who represent nearly half of all Americans living with HIV. Moreover, African-American men bear the greatest burden of HIV with six times the prevalence rate for white men. Additionally, HIV prevalence for black women is 18 times the rate for white women, and HIV prevalence for Hispanic/Latino women is four times the rate for white women.[104]

Significantly, Espinoza and colleagues (2007) concluded that – in order to decrease the incidence of heterosexually acquired HIV infections in particularly the Hispanic and non-Hispanic black populations who historically have had less access to treatment and prevention services – new strategies are needed to remove barriers to access. In their study of heterosexually acquired HIV infections in 29 states, the proportion of concurrent late HIV and AIDS diagnoses was increased with age, which Espinoza, *et al.* thought could be explained by HIV disease progression tending to occur more rapidly among older persons or that older individuals are not assumed to be at risk and are therefore not the focus of screening programs.[105]

Further, as noted by Winningham and colleagues, delivering HIV prevention can be challenging, especially when attempting to reach older African-American women who do not believe they are at risk. Integrating HIV prevention with existing medical services may be a particularly effective method for screening such hard-to-reach older women.[106]

CMS believes that coverage of voluntary HIV screening will not only improve identification of infected individuals and enhance understanding of HIV/AIDS but – in conjunction with the availability of combination HAART and medical care for HIV-infected individuals provided by skilled clinicians– will simultaneously reduce disparities by providing access to HIV recognition, antiretroviral treatment and care for older men and women regardless of their race, gender, ethnicity or socioeconomic status.

Summary

Having carefully evaluated newly published articles, reviews, guidelines and cost-effectiveness studies, CMS believes that there is now adequate evidence that voluntary HIV screening, which is approved with a grade of A or B by the USPSTF for all adolescents and adults at increased risk for HIV infection as well as for all pregnant women, is reasonable and necessary for early detection of HIV and is appropriate for Medicare beneficiaries.

Specifically, CMS believes that both standard and FDA-approved rapid HIV screening tests – simple, acceptable, accurate, cost-effective screening tests, exhibiting high sensitivity and high specificity, plus reactive preliminary positive/false positive rates, which are capable of being clinically managed by confirmatory testing and access to care – are appropriate for HIV screening and reasonable to be covered for Medicare beneficiaries.

Therefore, CMS encourages physicians to provide annual voluntary HIV screening to Medicare beneficiaries who are at increased risk for HIV infection or who request an HIV test despite reporting no individual risk factors, as well as to provide voluntary HIV screening to pregnant Medicare beneficiaries up to three times during each pregnancy, i.e., as soon as the diagnosis of pregnancy is known, during the third trimester for women who may be at increased risk for HIV infection, and at labor for any woman with undocumented or unknown HIV status, if ordered by the woman's clinician.

IX. Conclusion

The Centers for Medicare and Medicaid Services (CMS) has determined that the evidence is adequate to conclude that screening for HIV infection, which is recommended with a grade of A by the U.S. Preventive Services Task Force (USPSTF) for certain individuals, is reasonable and necessary for early detection of HIV and is appropriate for individuals entitled to benefits under Part A or enrolled under Part B.

Therefore CMS will cover both standard and FDA-approved rapid HIV screening tests for:

1. Annual voluntary HIV screening of Medicare beneficiaries at increased risk for HIV infection per USPSTF guidelines:

   - Men who have had sex with men after 1975;
   - Men and women having unprotected sex with multiple [more than one] partners;
   - Past or present injection drug users;
   - Men and women who exchange sex for money or drugs, or have sex partners who do;
   - Individuals whose past or present sex partners were HIV-infected, bisexual or injection drug users;
   - Persons being treated for sexually transmitted diseases;
   - Persons with a history of blood transfusion between 1978 and 1985;
   - Persons who request an HIV test despite reporting no individual risk factors, since this group is likely to include individuals not willing to disclose high-risk behaviors; and

2. Voluntary HIV screening of pregnant Medicare beneficiaries when the diagnosis of pregnancy is known, during the third trimester, and at labor.

We are deleting the following reference to non-coverage of HIV screening from the coverage manual, Section 190.14: "However, in the absence of a documented AIDS defining or HIV-associated disease, an HIV-associated sign or symptom, or documented exposure to a known HIV-infected source, the testing is considered by Medicare to be screening and thus is not covered by Medicare (for example, history of multiple blood component transfusions, exposure to blood or body fluids not resulting in consideration of therapy, history of transplant, history of illicit drug use, multiple sexual partners, same-sex encounters, prostitution, or contact with prostitutes)."

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1 http://data.unaids.org/pub/EPISlides/2007/2007_epiupdate_en.pdf (December 2007)

2 http://www.who.int/hiv/pub/priority_interventions_chap1.pdf (August 2008)

3 "HIV infection can weaken a person's immune system to the point that it has difficulty fighting off certain infections. These types of infections are known as opportunistic infections [OIs] because they take the opportunity a weakened immune system gives to cause illness. Some examples of opportunistic infections are *Pneumocystis carinii* pneumonia (PCP) and Kaposi's sarcoma (KS). Opportunistic infections are CDC-defined AIDS indicator illnesses, which means that an HIV-infected person receives a diagnosis of AIDS after the development of one of them." (http://www.cdc.gov/hiv/topics/surveillance/resources/guidelines/epi-guideline/la_supp/glossary.htm)

4 http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5804a1.htm?s_cid=rr5804a1_e (April 2009)

5 Marks, *et al.* (2006)

6 Burke, *et al.* (2007)

7 Hall, *et al.* (2008)

8 Bartlett, *et al.* (2008)

9 Coates, *et al.* (2008)

10 Espinoza, *et al.* (2007)

11 Lindau, *et al.* (2007)

12 §1861(ddd) of the Social Security Act

13 73 FR 69726, 69869 (November 19, 2008)

14 42 CFR 410.64

15 http://www.cdc.gov/hiv/topics/testing/rapid/rt-comparison.htm

16 Globally, most HIV infections are caused by HIV-1, and if unspecified the type of virus referred to is HIV-1. The relatively uncommon HIV-2 type is infrequently reported in the U.S. and is predominantly found in West Africa.

17 Cochran and Holland (1971)

18 http://www.ahrq.gov/clinic/uspstf05/hiv/hivrs.htm (USPSTF Recommendation Statement, 2007)

19 "Strongly Recommended" (USPSTF Grade Definitions Prior to May 2007)

20 "No Recommendation" (USPSTF Grade Definitions Prior to May 2007)

21 "Strongly Recommended" (USPSTF Grade Definitions Prior to May 2007)

22 http://www.ahrq.gov/clinic/uspstf05/hiv/hivrs.htm (USPSTF Recommendation Statement, 2007)

23 http://www.ahrq.gov/Clinic/uspstf/gradespre.htm (USPSTF Grade Definitions Pre-May 2007)

24 Winningham, *et al.* (2004)

25 Burke, *et al.* (2007)

26 Espinoza, *et al.* (2007)

27 Ostermann, *et al.* (2007)

28 Owens, *et al.* (2007a)

29 Gandhi, *et al.* (2007)

30 Owens, *et al.* (2007b)

31 Patterson, *et al.* (2007)

32 Silverberg, *et al.* (2007)

33 Friis-Møller, *et al.* (The DAD Study Group) 2007

34 Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group (2008)

35 Greenbaum, *et al.* (2008)

36 Collaboration of Observational HIV Epidemiological Research Europe (COHERE) Study Group (2008)

37 Strategies for Management of Antiretroviral Therapy (SMART) Study Group (2008)

38 Lichtenstein, *et al.* (2008)

39 Sanders, *et al.* (2008)

40 Kitahata, *et al.* (2009)

41 Gebo and Justice (2009)

42 http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm

43 Qaseem, *et al.* (2009)

44 American College of Obstetricians and Gynecologists, Committee Opinion Number 414 (2008)

45 Lubinski, *et al.* (2009)

46 42 CFR 410.64

47 http://www.ahrq.gov/clinic/uspstf05/hiv/hivrs.htm (USPSTF Recommendation Statement, 2007)

48 http://www.ahrq.gov/clinic/uspstf05/hiv/hivrs.htm (USPSTF Recommendation Statement, 2007)

49 Paltiel, *et al.* (2006)

50 Sanders, *et al.* (2008)

51 ACOG Committee Opinion Number 414 (2008)

52 http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm

53 Lubinski, *et al.* (2009)

54 Dieffenbach and Fauci (2009)

55 ClinicalTrials.gov Identifier: NCT00867048 (Ongoing 2009 START trial)

56 Lundgren, *et al.* (2009)

57 http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm (CDC Revised Recommendations, 2006)

58 http://www.ahrq.gov/clinic/uspstf05/hiv/hivrs.htm (USPSTF Recommendation Statement, 2007)

59 *42 CFR 410.64*

60 http://www.ahrq.gov/clinic/uspstf05/hiv/hivrs.htm (USPSTF Recommendation Statement, 2007)

61 Paltiel and Walensky (2007)

62 Branson, *et al.* (2006)

63 Paltiel, *et al.* (2006)

64 Sanders, *et al.* (2008)

65 Owens, *et al.* (2007b)

66 http://www.cdc.gov/hiv/topics/testing/rapid/rt-comparison.htm

67 Walensky, *et al.* (2007)

68 ClinicalTrials.gov Identifier: NCT00027352 (Completed SMART study)

69 Hughes and Ribaudo (2008)

70 Braithwaite, *et al.* (2008)

71 Wilkin and Gulick (2008)

72 Hammer, *et al.* (2008)

73 Kitahata, *et al.* (2009)

74 Sax and Baden (2009)

75 ClinicalTrials.gov Identifier: NCT00867048 (Currently recruiting, new START study)

76 Wilkin and Gulick (2008)

77 Lundgren, *et al.* (2009)

78 http://www.ahrq.gov/clinic/uspstf05/hiv/hivrs.htm

79 http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm

80 Luther and Wilkin (2007)

81 Nguyen and Holodniy (2008)

82 Martin, *et al.* (2008)

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