

The AMERICAN ACADEMY of HIV MEDICINE

# HIV

## SPECIALIST

PATIENT CARE, PRACTICE MANAGEMENT & PROFESSIONAL  
DEVELOPMENT INFORMATION for HIV CARE PROVIDERS

July 2014 Volume 6 No. 2

[www.aahivm.org](http://www.aahivm.org)

# Positively Serving

HIV and  
the VA

18

Depression and  
ART Adherence

26

Time to Quit  
Smoking

30

Updated  
HIV Testing

34

# Start or Switch: Consider the possibilities

For adults with no ARV treatment history and with HIV-1 RNA  $\leq 100,000$  copies/mL at the start of therapy or to replace current ARV therapy in certain stably suppressed adults with no history of virologic failure and no resistance to COMPLERA



## INDICATION

COMPLERA is indicated as a complete regimen for the treatment of HIV-1 infection in adults with no ARV treatment history and with HIV-1 RNA  $\leq 100,000$  copies/mL at the start of therapy; and in certain virologically suppressed (HIV-1 RNA  $< 50$  copies/mL) adults on a stable ARV regimen at the start of therapy to replace their current regimen, efficacy was established in patients who were virologically suppressed on a stable ritonavir-boosted protease inhibitor-containing regimen. Additional monitoring of HIV-1 RNA and regimen tolerability is recommended after replacing therapy to assess for potential virologic failure or rebound. COMPLERA is not recommended for patients  $< 18$  years of age.

- **Prescribing considerations in adults with no ARV treatment**

**history:** Virologic failure (HIV-1 RNA  $\geq 50$  copies/mL) was higher in subjects with baseline HIV-1 RNA  $> 100,000$  copies/mL

and in subjects with baseline CD4 cell count  $< 200$  cells/mm<sup>3</sup> (regardless of baseline HIV-1 RNA levels). Compared to efavirenz, virologic failure in rilpivirine-treated subjects conferred a higher rate of overall resistance and cross-resistance to the NNRTI class and more subjects developed tenofovir and lamivudine/emtricitabine associated resistance

- **Prescribing considerations in virologically suppressed adults:** Patients must have no history of virologic failure, be stably suppressed (HIV-1 RNA  $< 50$  copies/mL) for  $\geq 6$  months prior to switching therapy, currently be on their first or second ARV regimen prior to switching therapy, and have no current or past history of resistance to any component of COMPLERA

Please see additional Important Safety Information and Brief Summary of full Prescribing Information, including **BOXED WARNING**, on the following pages.

ARV=antiretroviral; NNRTI=non-nucleoside reverse transcriptase inhibitor.

**References:** 1. COMPLERA Prescribing Information. Gilead Sciences, Inc; June 2014. 2. US Department of Health and Human Services, Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. <http://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf>. Accessed May 5, 2014.





Visit [complera.com/hcp](http://complera.com/hcp)

#### DHHS-Recommended

in adults with no ARV treatment history with pretreatment HIV-1 RNA <100,000 copies/mL and with CD4 count >200 cells/mm<sup>3</sup>.<sup>2</sup>



## IMPORTANT SAFETY INFORMATION

**BOXED WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B**

- Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate (tenofovir DF), a component of COMPLERA, in combination with other antiretrovirals
- COMPLERA is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of COMPLERA have not been established in patients coinfecting with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfecting with HBV and HIV-1 and have discontinued emtricitabine or tenofovir DF, which are components of

COMPLERA. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are coinfecting with HIV-1 and HBV and discontinue COMPLERA. If appropriate, initiation of anti-hepatitis B therapy may be warranted

### Contraindications

- **Coadministration:** COMPLERA should not be coadministered with drugs that induce CYP3A or increase gastric pH as this may lead to loss of virologic response and possible resistance to COMPLERA or the NNRTI class. Use of the following drugs with COMPLERA is contraindicated: carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, proton pump inhibitors (e.g., esomeprazole, lansoprazole, dextansoprazole, omeprazole, pantoprazole, rabeprazole), systemic dexamethasone (>1 dose) and St. John's wort



**COMPLERA®**

emtricitabine 200mg/rilpivirine 25mg/  
tenofovir disoproxil fumarate 300mg tablets

## IMPORTANT SAFETY INFORMATION (CONT)

### Warnings and Precautions

- **New onset or worsening renal impairment:** Cases of acute renal failure and Fanconi syndrome have been reported with the use of tenofovir DF. In all patients, assess estimated creatinine clearance (CrCl) prior to initiating and during therapy. In patients at risk for renal dysfunction, additionally monitor serum phosphorus, urine glucose, and urine protein. Do not administer COMPLERA in patients with CrCl <50 mL/min. Avoid concurrent or recent use with a nephrotoxic agent. Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after initiation of high dose or multiple NSAIDs in patients with risk factors for renal dysfunction; consider alternatives to NSAIDs in these patients. Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function
- **Drug interactions:** Use COMPLERA with caution when given with drugs that may reduce the exposure of rilpivirine or when coadministered with a drug with known risk of Torsades de Pointes. Supratherapeutic doses of rilpivirine have been shown to prolong the QTc interval of the electrocardiogram (ECG) in healthy subjects
- **Depressive disorders:** The incidence of depressive disorders (depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, suicidal ideation) reported in clinical trials (N=686) was 9% (most were mild or moderate in severity); and Grades 3 and 4 depressive disorders (regardless of causality) was 1%. Suicidal ideation was reported in 4 subjects and suicide attempt was reported in 2 subjects. Patients with severe depressive symptoms should seek immediate medical evaluation and the risks of continued therapy should be determined
- **Hepatotoxicity:** Hepatic adverse events have been reported, including cases of hepatic toxicity in patients without pre-existing hepatic disease or other identifiable risk factors. Patients with underlying hepatitis B or C, or those with marked elevations in liver-associated tests may be at increased risk. Appropriate laboratory testing and monitoring before and during therapy is recommended in patients with underlying hepatic disease or in patients with marked elevations in liver-associated tests prior to treatment initiation; consider testing and monitoring in patients without pre-existing hepatic dysfunction or other risk factors
- **Bone effects:** Decreases in bone mineral density (BMD) and mineralization defects, including osteomalacia, have been seen in patients treated with tenofovir DF. Consider monitoring BMD in patients with a history of pathologic fracture or risk factors for bone loss. In patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms, hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered
- **Antiviral products:** COMPLERA is a complete regimen for the treatment of HIV-1 infection. Do not coadminister with other antiretrovirals including products containing any of the same active components (unless needed for dose adjustment); products containing lamivudine; or with adefovir dipivoxil

- **Fat redistribution** and accumulation has been observed in patients receiving ARV therapy
- **Immune reconstitution syndrome**, including the occurrence of autoimmune disorders with variable times to onset, has been reported

### Adverse Reactions

- **In adults with no ARV treatment history:** Common adverse reactions reported in clinical studies (incidence  $\geq 2\%$ , Grades 2-4) were depressive disorders (2%), insomnia (2%) and headache (2%)
- **In virologically suppressed adults:** No new types of adverse reactions to COMPLERA were identified in stable, virologically suppressed patients switching to COMPLERA from a regimen containing a ritonavir-boosted protease inhibitor; however, the frequency of adverse reactions increased by 20% after switching to COMPLERA

### Drug Interactions

- **CYP3A inducers:** Drugs that induce CYP3A may decrease rilpivirine plasma concentrations which may lead to loss of virologic response and possible resistance to COMPLERA or the NNRTI class
- **CYP3A inhibitors:** Drugs that inhibit CYP3A may increase rilpivirine plasma concentrations
- **Drugs increasing gastric pH** may significantly decrease rilpivirine plasma concentrations and lead to loss of virologic response and possible resistance to COMPLERA or the NNRTI class
  - Use of proton pump inhibitors with COMPLERA is contraindicated
  - Antacids should be administered  $\geq 2$  hours before or  $\geq 4$  hours after COMPLERA
  - $H_2$  receptor antagonists should be administered  $\geq 12$  hours before or  $\geq 4$  hours after COMPLERA
- **Drugs affecting renal function:** Coadministration of COMPLERA with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of emtricitabine and tenofovir
- **Prescribing information:** Consult the full Prescribing Information for COMPLERA for more information on potentially significant drug interactions, including clinical comments

### Pregnancy and Breastfeeding

- **Pregnancy Category B:** There are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if potential benefits justifies the potential risk. An Antiretroviral Pregnancy Registry has been established
- **Breastfeeding:** Emtricitabine and tenofovir have been detected in human milk. Because of both the potential for HIV transmission and the potential for serious adverse reactions in nursing infants, mothers should be instructed not to breastfeed

### Dosage and Administration

**Adults:** One tablet taken orally once daily with food.

**Renal Impairment:** Do not use in patients requiring dose reduction including in patients with estimated CrCl <50 mL/min.

**Rifabutin coadministration:** Additional rilpivirine 25 mg taken once daily with a meal is recommended.

Please see Brief Summary of full Prescribing Information, including **BOXED WARNING**, on the following pages.



**COMPLERA®**  
emtricitabine 200mg/rilpivirine 25mg/  
tenofovir disoproxil fumarate 300mg tablets

**COMPLERA® (emtricitabine 200 mg, rilpivirine 25 mg, tenofovir disoproxil fumarate 300 mg) tablets, for oral use**

**Brief Summary of full Prescribing Information. See full Prescribing Information. Rx Only.**

**WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B**

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate (tenofovir DF), a component of COMPLERA, in combination with other antiretrovirals [See Warnings and Precautions].

COMPLERA is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of COMPLERA have not been established in patients coinfecting with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfecting with HBV and human immunodeficiency virus-1 (HIV-1) and have discontinued emtricitabine or tenofovir DF, which are components of COMPLERA. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are coinfecting with HIV-1 and HBV and discontinue COMPLERA. If appropriate, initiation of anti-hepatitis B therapy may be warranted [See Warnings and Precautions].

**INDICATIONS AND USAGE:**

COMPLERA is indicated as a complete regimen for the treatment of HIV-1 infection in adults with no antiretroviral (ARV) treatment history and with HIV-1 RNA  $\leq 100,000$  copies/mL at the start of therapy; and in certain virologically suppressed (HIV-1 RNA  $< 50$  copies/mL) adults on a stable ARV regimen at the start of therapy to replace their current regimen, efficacy was established in patients who were virologically suppressed on a stable ritonavir-boosted protease inhibitor-containing regimen. Additional monitoring of HIV-1 RNA and regimen tolerability is recommended after replacing therapy to assess for potential virologic failure or rebound. COMPLERA is not recommended for patients  $< 18$  years of age.

**Prescribing considerations when initiating therapy with COMPLERA in adults with no ARV treatment history:**

- More rilpivirine-treated subjects with HIV-1 RNA  $> 100,000$  copies/mL at the start of therapy experienced virologic failure (HIV-1 RNA  $\geq 50$  copies/mL) compared to rilpivirine-treated subjects with HIV-1 RNA  $\leq 100,000$  copies/mL.
- Regardless of HIV-1 RNA level at the start of therapy, more rilpivirine-treated subjects with CD4+ cell count  $< 200$  cells/mm<sup>3</sup> experienced virologic failure compared to rilpivirine-treated subjects with CD4+ cell count  $\geq 200$  cells/mm<sup>3</sup>.
- The observed virologic failure rate in rilpivirine-treated subjects conferred a higher rate of overall treatment resistance and cross-resistance to the NNRTI class compared to efavirenz.
- More subjects treated with rilpivirine developed tenofovir and lamivudine/emtricitabine associated resistance compared to efavirenz.

**Prescribing considerations that should be met when replacing current ARV regimen with COMPLERA in virologically suppressed adults:**

- Patients should have no history of virologic failure.
- Patients should have been stably suppressed (HIV-1 RNA  $< 50$  copies/mL) for  $\geq 6$  months prior to switching therapy.
- Patients should currently be on their first or second ARV regimen prior to switching therapy.
- Patients should have no current or past history of resistance to any component of COMPLERA.

**DOSAGE AND ADMINISTRATION:**

See **Warnings and Precautions**, **Adverse Reactions**, and **Use in Specific Populations** for additional information.

**Adult Dosage:** One tablet taken orally once daily with food.

**Renal Impairment:** Do not use in patients with estimated creatinine clearance (CrCl)  $< 50$  mL/min.

**Rifabutin Coadministration:** Additional rilpivirine 25 mg taken once daily with a meal during rifabutin coadministration.

**CONTRAINDICATIONS:**

**Coadministration:** Do not use with drugs that induce CYP3A or increase gastric pH as significant decreases in rilpivirine plasma concentrations may occur leading to loss of virologic response and possible resistance to COMPLERA or to the class of NNRTIs [See Drug Interactions].

- Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- Antimycobacterials: rifampin, rifapentine
- Proton pump inhibitors: esomeprazole, lansoprazole, dexlansoprazole, omeprazole, pantoprazole, rabeprazole
- Systemic glucocorticoid: dexamethasone ( $> 1$  dose)
- Herbal product: St. John's wort

**WARNINGS AND PRECAUTIONS:**

**Lactic Acidosis/Severe Hepatomegaly with Steatosis:** Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir DF, a component of COMPLERA, in combination with other antiretrovirals. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Particular caution should be exercised when administering nucleoside analogs to any patient with known risk factors for liver disease; however, cases have also been reported in patients with

no known risk factors. Treatment with COMPLERA should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

**Patients Coinfected with HIV-1 and HBV:** All patients with HIV-1 should be tested for chronic HBV before initiating ARV therapy. COMPLERA is not approved for the treatment of chronic HBV infection and the safety and efficacy of COMPLERA have not been established in patients coinfecting with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfecting with HBV and HIV-1 and have discontinued emtricitabine or tenofovir DF, two of the components of COMPLERA. In some patients infected with HBV and treated with emtricitabine, the exacerbations of hepatitis B were associated with liver decompensation and liver failure. Patients who are coinfecting with HIV-1 and HBV should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment with COMPLERA. If appropriate, initiation of anti-hepatitis B therapy may be warranted.

**New Onset or Worsening Renal Impairment:** Renal impairment, including acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with tenofovir DF. Assess estimated CrCl in all patients prior to initiating therapy and as clinically appropriate during therapy with COMPLERA. In patients at risk of renal dysfunction, including patients who have previously experienced renal events while receiving adefovir dipivoxil, it is recommended that estimated CrCl, serum phosphorus, urine glucose, and urine protein be assessed prior to initiation of COMPLERA, and periodically during COMPLERA therapy. COMPLERA should be avoided with concurrent or recent use of a nephrotoxic agent (e.g., high dose or multiple NSAIDs) [See Drug Interactions]. Cases of acute renal failure after initiation of high dose or multiple NSAIDs have been reported in HIV-infected patients with risk factors for renal dysfunction who appeared stable on tenofovir DF. Some patients required hospitalization and renal replacement therapy. Alternatives to NSAIDs should be considered in patients at risk for renal dysfunction. Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function in at-risk patients. Do not use COMPLERA in patients with estimated CrCl  $< 50$  mL/min.

**Drug Interactions:** Caution should be given when prescribing COMPLERA with drugs that may reduce the exposure of rilpivirine or when coadministered with a drug with a known risk of Torsade de Pointes. In healthy subjects, supratherapeutic doses of rilpivirine (75 mg once daily and 300 mg once daily) have been shown to prolong the QTc interval of the electrocardiogram (ECG) [See Contraindications and Drug Interactions].

**Depressive Disorders:** Depressive disorders (depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, suicidal ideation) have been reported with rilpivirine. Through 96 weeks in Phase 3 trials (N=686), the incidence of depressive disorders (regardless of causality, severity) was 9% (most events were mild or moderate in severity). Grades 3 and 4 depressive disorders (regardless of causality) was 1%, and discontinuation due to depressive disorders was 1%; suicidal ideation was reported in 4 subjects and suicide attempt was reported in 2 subjects. Patients with severe depressive symptoms should seek immediate medical evaluation to assess the possibility that the symptoms are related to COMPLERA, and if so, to determine whether the risks of continued therapy outweigh the benefits.

**Hepatotoxicity:** Hepatic adverse events have been reported with rilpivirine. Patients with underlying hepatitis B or C, or marked elevations in liver-associated tests prior to treatment may be at increased risk for worsening or development of liver-associated tests elevations with use of COMPLERA. A few cases of hepatic toxicity have been reported in patients receiving a rilpivirine containing regimen who had no pre-existing hepatic disease or other identifiable risk factors. Appropriate laboratory testing prior to initiating therapy and monitoring for hepatotoxicity during therapy with COMPLERA is recommended in patients with underlying hepatic disease such as hepatitis B or C, or in patients with marked elevations in liver-associated tests prior to treatment initiation. Liver-associated test monitoring should also be considered for patients without pre-existing hepatic dysfunction or other risk factors.

**Bone Effects of Tenofovir DF: Bone mineral density (BMD):** In clinical trials in HIV-1 infected adults, tenofovir DF was associated with decreases in BMD and increases in biochemical markers of bone metabolism, suggesting increased bone turnover relative to comparators. Serum parathyroid hormone levels and 1,25 Vitamin D levels were also higher in subjects receiving tenofovir DF. For more information, please consult the VIREAD (tenofovir DF) full Prescribing Information. The effects of tenofovir DF-associated changes in BMD and biochemical markers on long-term bone health and future fracture risk are unknown. Consider assessing BMD in patients with a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. Although the effect of supplementation with calcium and Vitamin D was not studied, such supplementation may be beneficial. If bone abnormalities are suspected, appropriate consultation should be obtained. **Mineralization defects:** Cases of osteomalacia associated with proximal renal tubulopathy manifested as bone pain or pain in extremities and which may contribute to fractures, have been reported in association with the use of tenofovir DF. Arthralgias and muscle pain or weakness have also been reported in cases of proximal renal tubulopathy. Hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered in patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms while receiving products containing tenofovir DF.

**Coadministration with Other Products:** COMPLERA should not be administered concurrently with other products containing any of the same active components (emtricitabine, rilpivirine or tenofovir DF) unless needed for dose adjustment; with products containing lamivudine; or with adefovir dipivoxil.

**Fat Redistribution:** Redistribution/accumulation of body fat including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, facial wasting, breast enlargement, and "cushingoid appearance" have been observed in patients receiving ARV therapy. The mechanism and long-term consequences of these events are unknown. A causal relationship has not been established.

**Immune Reconstitution Syndrome (IRS):** IRS has been reported in patients treated with combination ARV therapy, including the components of COMPLERA. During the initial phase of combination ARV treatment, patients whose immune system responds may develop an inflammatory response to indolent or residual opportunistic infections (e.g., *Mycobacterium avium* infection, cytomegalovirus, *Pneumocystis jirovecii* pneumonia [PCP], or tuberculosis), which may necessitate further evaluation and treatment. Autoimmune disorders (e.g., Graves' disease, polymyositis, and Guillain-Barré syndrome) have also been reported to occur in the setting of immune reconstitution, however, the time to onset is more variable, and can occur many months after initiation of treatment.

#### ADVERSE REACTIONS:

See **BOXED WARNING** and **Warnings and Precautions** for additional serious adverse reactions.

#### In HIV-1 Infected Subjects with No ARV Treatment History:

The safety assessment of rilpivirine, used in combination with other antiretrovirals, is based on the week 96 pooled data from two Phase 3 trials in ARV treatment-naïve HIV-1 infected adults. A total of 686 subjects received rilpivirine in combination with other antiretrovirals as background regimen; 550 of whom received emtricitabine/tenofovir DF. The median duration of exposure for subjects was 104 weeks.

**Adverse Reactions:** Treatment emergent adverse reactions (Grades 2-4) reported in ≥2% of subjects receiving rilpivirine + emtricitabine/tenofovir DF (N=550) through week 96 were: depressive disorders (2%); includes depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, and suicidal ideation), headache (2%), and insomnia (2%). Frequencies of adverse reactions are based on all Grades 2-4 treatment emergent adverse reactions assessed to be related to study drug. No new adverse reactions were identified between weeks 48 and 96. The adverse reactions observed in this subset of subjects were generally consistent with those seen for the overall patient population [for additional information, consult the Edurant (rilpivirine) full Prescribing Information]. Two percent of subjects discontinued treatment with rilpivirine + emtricitabine/tenofovir DF due to adverse reactions (regardless of severity). The most common adverse reactions leading to discontinuation were psychiatric disorders (9 [1.6%] subjects); rash led to discontinuation in 1 (0.2%) subject. **Rilpivirine adverse reactions:** Treatment emergent adverse reactions (≥Grade 2) occurring in <2% of subjects receiving rilpivirine (N=686) were (grouped by Body System): vomiting, diarrhea, abdominal discomfort, abdominal pain, fatigue, cholecystitis, cholelithiasis, decreased appetite, somnolence, sleep disorders, anxiety, glomerulonephritis membranous, glomerulonephritis mesangioproliferative, and nephrolithiasis.

**Laboratory Abnormalities:** Treatment emergent laboratory abnormalities (Grades 1, 2, 3, and 4, respectively) occurring in subjects receiving rilpivirine + emtricitabine/tenofovir DF (N=550) through week 96 were: increased creatinine (6%, 1%, <1%, 0%), increased AST (16%, 4%, 2%, 1%), increased ALT (19%, 5%, 1%, 1%), increased total bilirubin (6%, 3%, 1%, 0%), increased fasting total cholesterol (14%, 6%, <1%, 0%), increased fasting LDL cholesterol (13%, 5%, 1%, 0%), and increased fasting triglycerides (0%, 1%, 1%, 0%).

**Adrenal Function:** Mean changes from baseline in basal cortisol and ACTH-stimulated cortisol at week 96 (N=686) were -19.1 nmol/L (95% CI: -30.9; -7.4) and +18.4 ± 8.36 nmol/L, respectively; both values were within normal range. Effects on adrenal function were comparable by background N(t)RTIs. No serious adverse reactions, deaths, or treatment discontinuations were attributed to adrenal insufficiency.

**Serum Creatinine:** Mean change from baseline in serum creatinine at week 96 (N=686) was 0.1 mg/dL (range: -0.3 mg/dL to 0.6 mg/dL); most increases occurred within the first four weeks of treatment. Observed serum creatinine increases were similar among subjects with baseline mild or moderate renal impairment and subjects with baseline normal renal function; increases were comparable by background N(t)RTIs. No changes were considered to be clinically relevant and no subject discontinued treatment due to serum creatinine increases.

**Serum Lipids:** Mean changes from baseline in fasting serum lipids at week 96 were: total cholesterol: +2 mg/dL (N=430; baseline 162 mg/dL); HDL-cholesterol: +4 mg/dL (N=429; baseline 42 mg/dL); LDL-cholesterol: -1 mg/dL (N=427; baseline 97 mg/dL); and triglycerides: -14 mg/dL (N=430; baseline 123 mg/dL). The change from baseline is the mean of within-patient changes from baseline for patients with both baseline and week 96 values. Subjects receiving lipid lowering agents during treatment were excluded from these lipid analyses.

**Subjects Coinfected with Hepatitis B and/or Hepatitis C Virus:** In patients coinfecting with hepatitis B or C virus receiving rilpivirine, the incidence of hepatic enzyme elevation was higher than in subjects receiving rilpivirine who were not coinfecting. The pharmacokinetic exposure of rilpivirine in coinfecting subjects was comparable to that in subjects without coinfection.

#### In Virologically Suppressed HIV-1 Infected Subjects:

No new types of adverse reactions to COMPLERA were identified in stable, virologically suppressed subjects switching to COMPLERA from a regimen containing a ritonavir-boosted protease inhibitor; however, the frequency of adverse reactions increased by 20% after switching to COMPLERA.

**Consult the respective full Prescribing Information for each individual component of COMPLERA for additional information regarding adverse reactions, including laboratory abnormalities and postmarketing events.**

#### DRUG INTERACTIONS:

See **Contraindications** for additional serious drug interactions.

COMPLERA is a complete regimen for the treatment of HIV-1 infection and should not be administered with other antiretrovirals. Information regarding potential drug interactions with other antiretrovirals is not provided.

**Drugs Inducing or Inhibiting CYP3A:** Rilpivirine is primarily metabolized by CYP3A, thus drugs that induce or inhibit CYP3A may affect the clearance of rilpivirine. Coadministration of rilpivirine and drugs that induce CYP3A may result in decreased plasma concentrations of rilpivirine leading to loss of virologic response and possible resistance to rilpivirine or to the class of NNRTIs. Coadministration of rilpivirine and

drugs that inhibit CYP3A may result in increased plasma concentrations of rilpivirine. Rilpivirine at a dose of 25 mg once daily is not likely to have a clinically relevant effect on the exposure of drugs metabolized by CYP enzymes.

**Drugs Increasing Gastric pH:** Coadministration of rilpivirine with drugs that increase gastric pH may decrease plasma concentrations of rilpivirine leading to loss of virologic response and possible resistance to rilpivirine or to the class of NNRTIs.

**Drugs Affecting Renal Function:** Because emtricitabine and tenofovir are primarily eliminated by the kidneys through a combination of glomerular filtration and active tubular secretion, coadministration of COMPLERA with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of emtricitabine, tenofovir, and other renally eliminated drugs, which may increase the incidence of adverse reactions [See **Warnings and Precautions**].

**QT Prolonging Drugs:** There is limited information available on the potential for a pharmacodynamic interaction between rilpivirine and drugs that prolong the QTc interval of the ECG. In a study of healthy subjects, supratherapeutic doses of rilpivirine (75 mg once daily and 300 mg once daily) have been shown to prolong the QTc interval of the ECG. COMPLERA should be used with caution when coadministered with a drug with a known risk of Torsade de Pointes.

**Established and Other Potentially Significant Drug Interactions:** The drug interactions described are based on studies conducted with individual components of COMPLERA or are predicted drug interactions that may occur with COMPLERA; no drug interaction studies have been conducted using COMPLERA as a fixed-dose combination tablet. The list includes potentially significant interactions but is not all inclusive. For additional information, consult the Edurant, EMTRIVA (emtricitabine) or VIREAD full Prescribing Information. **An alteration in dose or regimen may be recommended when the following drugs are coadministered with COMPLERA:**

- Antacids: aluminum, magnesium hydroxide, calcium carbonate. Antacids should be taken ≥2 hours before or ≥4 hours after COMPLERA.
- Antimycobacterials: rifabutin. Give additional rilpivirine 25 mg once daily with a meal during rifabutin coadministration.
- Azole Antifungals: fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole. No dose adjustment required; monitor for breakthrough fungal infections.
- H<sub>2</sub>-Receptor Antagonists: cimetidine, famotidine, nizatidine, ranitidine. H<sub>2</sub>-receptor antagonists should be taken ≥12 hours before or ≥4 hours after COMPLERA.
- Macrolide/Ketolide Antibiotics: clarithromycin, erythromycin, telithromycin. Consider alternatives (e.g., azithromycin) when possible.
- Narcotic Analgesic: methadone. No dose adjustment required at therapy initiation; monitor during treatment; methadone maintenance dose may need adjustment.

**Consult the full Prescribing Information prior to and during treatment with COMPLERA for potential drug interactions; this list is not all inclusive.**

#### USE IN SPECIFIC POPULATIONS:

**Pregnancy:** COMPLERA is Pregnancy Category B; however, there are no adequate and well-controlled studies in pregnant women. COMPLERA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Antiretroviral Pregnancy Registry:** To monitor fetal outcomes of pregnant women exposed to COMPLERA, an Antiretroviral Pregnancy Registry has been established. Healthcare providers are encouraged to register patients by calling 1-800-258-4263.

**Nursing Mothers:** The Centers for Disease Control and Prevention recommend that HIV infected mothers not breastfeed their infants to avoid risking postnatal transmission of HIV. Studies in rats have demonstrated that rilpivirine and tenofovir are secreted in milk. Emtricitabine and tenofovir have been detected in human milk; it is not known if rilpivirine is secreted in human milk. Because of both the potential for HIV transmission and the potential for serious adverse reactions and/or drug resistance in nursing infants, **mothers should be instructed not to breastfeed if they are receiving COMPLERA.**

**Pediatric Use:** COMPLERA is not recommended for patients <18 years of age because not all the individual components of COMPLERA have safety, efficacy and dosing recommendations available for all pediatric age groups.

**Geriatric Use:** Clinical studies of emtricitabine, rilpivirine, or tenofovir DF did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for the elderly patients should be cautious, keeping in mind the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

**Renal Impairment:** COMPLERA should not be prescribed for patients with moderate, severe or end stage renal impairment (CrCl <50 mL/min) or patients who require dialysis [See **Warnings and Precautions**].

**Hepatic Impairment:** No dose adjustment of COMPLERA is required in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. COMPLERA has not been studied in patients with severe hepatic impairment (Child-Pugh Class C).

#### OVERDOSAGE:

If overdose occurs the patient must be monitored for evidence of toxicity. Treatment of overdose with COMPLERA consists of general supportive measures including monitoring of vital signs and ECG (QT interval) as well as observation of the clinical status of the patient.

COMPLERA, EMTRIVA, and VIREAD are trademarks of Gilead Sciences, Inc., or its related companies. All other trademarks referenced herein are the property of their respective owners.

202123-GS-006 June 2014



COMPLERA, the COMPLERA Logo, EMTRIVA, GILEAD, the GILEAD Logo, GSI, HEPSERA, STRIBILD, TRUVADA, and VIREAD are trademarks of Gilead Sciences, Inc., or its related companies. ATRIPIA is a trademark of Bristol-Myers Squibb & Gilead Sciences, LLC. All other marks referenced herein are the property of their respective owners.

©2014 Gilead Sciences, Inc. All rights reserved. CPAP0139 7/14

# HIV SPECIALIST

PATIENT CARE, PRACTICE MANAGEMENT & PROFESSIONAL  
DEVELOPMENT INFORMATION for HIV CARE PROVIDERS

VOLUME 6 / NUMBER 2 • JULY 2014

## CHAIR/BOARD OF DIRECTORS

**DONNA ELAINE SWEET, MD, MACP, AAHIVS**

## EXECUTIVE DIRECTOR

**JAMES FRIEDMAN, MHA**

## DIRECTOR OF MARKETING & COMMUNICATIONS

**AMBER McCracken**

## EDITOR

**ROBERT GATTY**

G-Net Strategic Communications  
e: bob@gattyedits.com

## PUBLICATION DESIGN AND ART DIRECTION

**BONOTOM STUDIO, INC.**

p: 703-276-0612  
e: info@bonotom.com

## ADVERTISING

**JANE DEES RICHARDSON, President**

Ad Marketing Group, Inc.

p: 703-243-9046 ext. 102

e: jrichardson@admarketinggroup.com

## PUBLISHER

## THE AMERICAN ACADEMY OF HIV MEDICINE

1705 DeSales St., NW, Suite 700  
Washington, D.C. 20036

p: 202-659-0699 • f: 202-659-0976

e: info@aahivm.org • w: www.aahivm.org

## EDITORIAL ADVISORY GROUP

### CHAIR

**JEFFREY T. KIRCHNER, DO, FAAP, AAHIVS**

Medical Director

Comprehensive Care Medicine for HIV  
Lancaster General Hospital, Lancaster, PA

**JOSEPH S. CERVIA,**

MD, MBA, FACP, FAAP, FIDSA, AAHIVS

Clinical Professor of Medicine and Pediatrics,  
Hofstra North Shore-LIJ School of Medicine;  
Regional Medical Director, HealthCare  
Partners, IPA & MSO, Garden City, NY

**D. TREW DECKARD, PA-C, MHS, AAHIVS,**

Steven M. Pounders, MD, PA

Dallas-Fort Worth, TX

**TERESA MACK, MD**

St. Lukes—Roosevelt Hospital

New York, NY

**RICHARD C. PROKESCH, MD, FACP, FIDSA, AAHIVS**

Infectious Diseases Associates, Riverdale, GA

**JEFFREY T. SCHOUTEN, MD, AAHIVE,**

Attorney at Law

Director HIV/AIDS Network Coordination  
(HANC) Project, Fred Hutchinson Cancer  
Research Center, Seattle, WA

**SAMI SHAFIQ, PharmD, CPH, AAHIVE**

Lead HIV/AIDS Clinical Pharmacist

Walgreens Pharmacy

Miami, FL

**CARL STEIN, MHS, PAC, AAHIVS**

Owen Medical Group

San Francisco, CA

**SHARON VALENTI, NP, AAHIVS**

St. John Hospital and Medical Center

Grosse Point Woods, MI

# CONTENTS

## FEATURES

COVER: MARIA AREFYEVA/THINKSTOCK

July 2014 Volume 6 No.2

www.aahivm.org

## 11 POSITIVELY SERVING + HIV in the Military

BY BOB GATTY, EDITOR

## 12 POSITIVELY SERVING + SOLDIER: What Happens with an HIV+ Diagnosis?

BY ROBERT J. MATYAS II, MD, AAHIVS

## 18 POSITIVELY SERVING + HIV & the VA

HIV Program, Policies, and Infrastructure

BY MARISSA MAIER, MD AND MAGGIE CHARTIER, PSY.D., MPH

## 26 Impact of Depression on ART Adherence and Retention in Care

BY GLENN J. TREISMAN, MD, PHD

## 30 TIME to QUIT

CDC anti-smoking campaign emphasizes  
importance of HIV patients avoiding tobacco

BY JOHN T. BROOKS, MD AND TIM MCAFFEE, MD



## DEPARTMENTS

## 6 LETTER FROM THE DIRECTOR

About Military Health, the VA and HIV

BY JAMES M. FRIEDMAN, MHA

## 8 IN THE NEWS

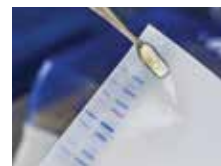
CDC campaign inspires HIV conversations,  
HIV accepts HIV therapy drug applications,  
new research reports, and more.

## 34 BEST PRACTICES

Where's My  
Western Blot?

What HIV  
Specialists Need  
to Know about  
Updated HIV  
Testing Recommendations

BY BERNARD M. BRANSON, M.D.



Copyright 2014® by the American Academy of HIV Medicine (AAHIVM). All rights reserved. Reproduction in whole or in part without written permission from AAHIVM is prohibited. *HIV Specialist*® is published quarterly by AAHIVM. For library subscriptions and re-production information, please call 202-659-0699 or write AAHIVM, 1705 DeSales St., NW, Suite 700, Washington, D.C. 20036. Persons depicted on the cover and within the articles of this publication are models. Any and all depictions of individuals are for illustrative purposes only. Depictions of individuals in this publication do not in any way certify, imply or otherwise confirm any relation to or engagement in subjects such as contraception; sexual or implied sexual activity; sexual preferences; dating services; chat lines; substance abuse; physical or mental abuse; violence; poverty; homelessness; dysfunctional family matters; alcohol; tobacco; HIV/AIDS; cancer; or other serious physical or mental ailments, disabilities or serious physical or mental disease, or any diagnostic test for same.

## About Military Health, the VA and HIV

**T**HIS ISSUE of the magazine focuses on HIV care in the military and through the Veterans Administration (VA). I have had some substantial, though very different, experiences with both.

I served four years in the U.S. Air Force during the Vietnam conflict. On several occasions, I came in contact with military healthcare, both in the U.S. and overseas from a variety of perspectives. Both of my sons were born in the military system. The physicians I saw for the most part were bright and committed. While I was in the U.S. Public Health Service, I took a two-month mid-career assignment working for the Defense Department's Assistant Secretary for Health in the Pentagon.

This issue includes an excellent article by Dr. Robert Matyas, an HIV Special-



ist practicing in Hawaii. Before accepting his current position as Director of HIV Services for the

Hawaii Region of Kaiser Permanente, he served as a flight surgeon for a Marine Corps helicopter squadron. In his article, he describes the experiences of three Marines who found out they were HIV-positive while in the military. We appreciate his willingness to contribute to this issue, both as an author and an advisor.

While I was in the U.S. Public Health Service, I had the opportunity to work with both Bopper Deyton and Ron Valdiserri before they moved to take leadership roles in managing HIV care in the VA. I met with both of them again just after I became executive director of the Academy. The VA is the largest provider of HIV

services in the United States. Dr. Amy Justice, who has helped the Academy with our AIDS and Aging initiative, has compiled some of the best statistics regarding HIV care for the elderly in the VA.



James M. Friedman

As I write this, the VA is receiving some well-deserved negative attention because of the delay in getting many veterans into care. But at the same time, once in care, veterans are quite pleased with the care they receive. It is also useful to note that over one-half of U.S. physicians receive at least some of their training in VA facilities.

Both the VA and Military Health confront very difficult medical, political, bureaucratic and budgetary environments. It is a testament to the commitment and quality of the practitioners in these systems that they succeed as well as they do.

Finally, while I was at the ACTHIV Conference this past May, I had the opportunity to talk to a number of VA HIV practitioners. My major concern was how the HIV-positive soldier was tracked when he/she leaves the military (by the way, the HIV infected soldier does not have to leave the military) and becomes eligible for care from the VA. The troubling answer was not very well. There is no formal transfer mechanism from one system to the other. If it happens at all, it is on an ad hoc basis. The transfer should be both timely and seamless—and not just for HIV patients. **HIV**

*James M. Friedman*

A TIP FROM A  
**FORMER  
SMOKER**

**HIV alone  
didn't cause the  
clogged artery  
in my neck.  
Smoking with  
HIV did.**

*Brian, age 45, California*

*Brian had his HIV under control with medication. But smoking with HIV caused him to have serious health problems, including a stroke, a blood clot in his lungs and surgery on an artery in his neck. Smoking makes living with HIV much worse. You can quit.*

**CALL 1-800-QUIT-NOW.**



U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention  
[CDC.gov/tips](https://www.cdc.gov/tips)

#CDCTips



## Study Shows Differences Between Treated and Untreated People Living with HIV

ViiV Healthcare announced in June new survey data that provide important insights that may help explain why HIV treatment rates remain low in the United States.

Findings from the online survey, conducted by Harris Interactive in 2013, reveal gaps in knowledge about HIV and its treatment among diagnosed but untreated people living with HIV (PLWHIV), as well as misperceptions about HIV prescription medicine and fewer positive perceptions of well-being compared to PLWHIV treating their disease.

Both the U.S. Centers for Disease Control and Prevention and the Department of Health and Human Services recommend early treatment, but many PLWHIV do not initiate therapy at the time of diagnosis, if at all. In fact, only 33 percent of the 1.1 million Americans living with HIV take the medicines they need.

The survey findings point to four poten-

tial barriers to treatment use by comparing the reported perceptions and experiences of HIV-positive adults (aged 18+) who had never taken a prescription medicine to treat their HIV ("untreated patients") to those who had begun taking a prescription medicine to treat their HIV in the past five years ("treated patients"):

**Limited disease-specific knowledge.** Untreated patients are less knowledgeable about HIV and its potential effects than treated patients.

**Limited treatment-specific knowledge.** Untreated patients also have limited treatment-specific knowledge and cite reasons for not using HIV prescription medicine that are inconsistent with available data or current treatment guidelines.

**Misperceptions regarding treatment use.** The reported perceptions of HIV prescription medicine among untreated patients were

somewhat negative and inconsistent with the reported experiences of treated patients.

**Fewer positive perceptions of overall well-being.** Untreated patients are less likely than treated patients to agree that their disease is well controlled (84 percent vs. 91 percent) and less likely to agree they will live a full life despite their HIV (72 percent vs. 83 percent).iv

The survey was conducted online within the United States by Harris Interactive on behalf of ViiV Healthcare from May 16 to June 14, 2013, among 251 U.S. adults (aged 18+) who had been diagnosed with HIV and either had never taken HIV prescription medicine ("untreated patients") or were, at that time, taking prescription medicine and had begun treatment within the past five years ("treated patients"). The majority of respondents were male, aged 18 to 44. **HIV**

## PrEP Urged to Prevent Infection in Those at Risk of HIV

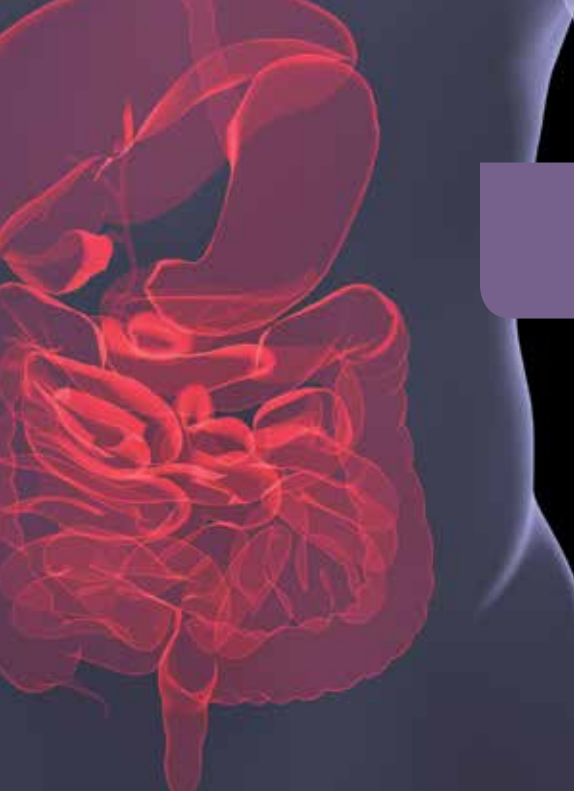
**H** EALTHY PEOPLE AT RISK OF HIV are advised to take daily medication that reduce the odds of infection by more than 90 percent, U.S. health officials said in recommending use of the drugs as a preventative.

The U.S. Centers for Disease Control (CDC) urged people with HIV- infected partners and those who inject illicit drugs and share equipment, or have been in treatment programs for injection medicine use to use the medication. Gilead Sciences Inc.'s anti-AIDS pill Truvada has been approved as a preventative medicine for HIV.

Also advised to take the medicines are heterosexual men or women who don't always use condoms with at-risk partners and gay or bisexual men who have sex without a condom or aren't in mutually exclusive relationships with partners testing HIV- negative, the agency said.

"PrEP has the potential to alter the course of the epidemic," said Jonathan Mermin, director of the CDC's national center for HIV/AIDS, Hepatitis, STD and TB prevention, told *The Washington Post*. "Having these guidelines come out now will hopefully prevent thousands of people from getting and spreading a potentially fatal disease."

**HIV**



SHUTTERSTOCK

## Dr. David Holtgrave Named Vice Chair of Presidential Advisory Council On HIV/Aids

DAVID HOLTGRAVE, PHD, professor and chair of the Department of Health, Behavior and Society at the Johns Hopkins Bloomberg School of Public Health, has recently been appointed to the newly created position of Vice Chair of the Presidential Advisory Council on HIV/AIDS (PACHA).



Dr. Holtgrave, who has served on PACHA since 2010, will work closely with PACHA's chairperson, Nancy Mahon, Senior Vice President, M·A·C Cosmetics and Global Executive Director, M·A·C AIDS Fund. PACHA provides advice, information and recommendations to the Secretary of HHS and the White House regarding programs and policies intended to improve the U.S. response to the HIV/AIDS epidemic—including to promote effective prevention of HIV and improved delivery of HIV care, treatment and housing services—and to advance research on HIV/AIDS.

PACHA also provides recommendations on how to effectively implement the National HIV/AIDS Strategy and monitors implementation of the Strategy. Dr. Holtgrave is one of 24 members who serve on the council, which is comprised of a diverse group of researchers, service providers, and community leaders from around the country, including people living with HIV.

HIV

## Early HIV Treatment May Limit Inflammation, Gut Damage

**S**TARTING ANTIRETROVIRAL (ARV) THERAPY immediately after HIV infection may both limit the virus's toll on the gut lining and also lower the body's overall chronic inflammatory state, *HIVandHepatitis* reports.

Researchers, who studied 34 people with acute HIV infection, presented their findings at the Conference on Retroviruses and Opportunistic Infections (CROI) in Boston.

Out of 53,000 screened samples, 13 participants were identified in Fibig stage I (FI), the first acceleration of viral replication following infection. An additional 21 of the participants were diagnosed at FIII. The study also included various matched controls: five HIV-negative participants and nine treatment-naïve people who had been living with the virus for six to 12 months.

The participants underwent initial gut tissue biopsies and again six and 24 months after beginning ARVs. Those who started therapy during FI maintained a proportion of Th17 cells, which are key to maintaining the gut lining, similar to that of HIV-negative people at the six- and 24-month reads.

While progressing through the Fibig stages apparently led to a drop in Th17 cell proportion, the introduction of ARVs prevented additional cell loss. Nevertheless, HIV therapy did not reverse this loss in those who started treatment during FIII. Those in FI at the study's outset displayed signs of an increased inflammatory state in both the gut and in peripheral blood, while those in FIII showed much greater signs of inflammation.

Starting HIV treatment at FI reduced the inflammatory state to that of HIV-negative people. If treatment didn't begin until FIII, there was still evidence of an elevated inflammatory state after six and 24 months. HIV-related chronic inflammation is believed to lead to an increased risk for cardiovascular disease and cognitive impairment.

HIV

## Obamacare Increases Primary Care Providers' HIV Caseload

**PRIMARY CARE PROVIDERS** who provide clinical HIV care (HIV PCPs) are experiencing rising HIV caseloads from newly insured patients under the Patient Protection and Affordable Care Act (PPACA), according to a national survey released in May by HealthHIV.

Forty percent of those surveyed say the number of providers treating HIV in their area is inadequate for the demand. Half of HIV PCPs say their HIV caseloads have grown, a trend likely to continue as health reform steers patients to primary care settings.

*HealthHIV's Third Annual State of HIV Primary Care National Survey* report shows that a majority of HIV PCPs are female, 54 percent are physicians, and 55 percent are over the age of 50. They primarily work in urban or metropolitan areas and are more likely to treat

underserved populations, including racial and ethnic minorities, homeless, and immigrant populations.

"We compared the PPACA enrollment numbers with the number of PCPs added and needed to treat the newly insured," said HealthHIV Executive Director Brian Hujdich. "This comparison shows that, as the demand for health care increases through enrollment in health care plans, the workforce supply continues to decrease, creating a shortfall of 8,000 PCPs to treat the newly insured."

Nearly half (49 percent) of PCPs surveyed do not provide clinical HIV care, with the lack of knowledge about HIV treatment preventing them from providing care. A similar number (48 percent) say they need more clinical training to fully integrate HIV care into their practice.

HIV

# IN THE NEWS

## CDC campaign inspires HIV conversations

Safer-Sex Chat Cheat Sheet

**THE CENTERS FOR DISEASE CONTROL AND PREVENTION** has launched *Start Talking. Stop HIV.*, a new national communication campaign encouraging gay and bisexual men to talk openly with their sexual partners about HIV risk and prevention strategies.

Although research suggests that open communication leads to behaviors that can help reduce risk, such as HIV testing and status disclosure, studies have found that important discussions about HIV do not occur within many relationships.

"Given the range of HIV prevention options available today, talking about HIV prevention has never been more important for gay and bisexual men," said Jonathan Mermin, M.D., M.P.H., director of CDC's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. "Only after having open and honest conversations can partners make informed choices about which strategies will work for them. *Start Talking. Stop HIV.* urges gay and bisexual men to break the silence and take control of their health."

**Make conversation before you make out.**



Protect yourself and your partner. Talk about **testing**, your **status**, **condoms**, and new options like **medicines** that prevent and treat HIV. Get the facts and tips on how to start the conversation at [cdc.gov/ActAgainstAIDS/StartTalking](http://cdc.gov/ActAgainstAIDS/StartTalking).

**Start Talking. Stop HIV.**

Follow us online at: [facebook.com/StartTalkingHIV](https://www.facebook.com/StartTalkingHIV) @TalkHIV

The campaign, created in consultation with more than 500 gay and bisexual men, is designed to reach gay and bisexual men of all races and ethnicities in all types of relationships, from casual to long-term. Featuring real-world individuals and couples, the campaign—which includes online and print advertisements, as well as social media outreach and online videos—encourages gay and bisexual men to talk to their sexual partners about HIV testing and their HIV status; safer sex, including using condoms and engaging in lower risk sexual behaviors; medicines that can prevent and those that can successfully treat HIV; and healthy relationships.

The *Start Talking. Stop HIV.*

campaign website features information and resources as well as practical tips for starting conversations about safe sex and HIV. The campaign will also be featured at gay pride events and other community activities across the country.

For more information about *Start Talking. Stop HIV.*, please visit <http://www.cdc.gov/actagainstaids/campaigns/starttalking/index.html>. **HIV**

## FDA Accepts Gilead's Applications for Cobicistat and Elvitegravir for HIV Therapy

GILEAD SCIENCES, INC. announced that the FDA has accepted the company's refiling of two New Drug Applications (NDA) for cobicistat, a pharmacoenhancing or "boosting" agent that increases blood levels of the protease inhibitors atazanavir and darunavir to enable once-daily dosing of these medicines in HIV therapy, and elvitegravir, an integrase inhibitor for the treatment of HIV-1 infection in treatment-experienced adults.

FDA has set target review dates under the Prescription Drug User Fee Act (PDUFA) of

October 3, for cobicistat and October 4, for elvitegravir. Gilead said it submitted NDAs for cobicistat and elvitegravir in June 2012.

Cobicistat is approved under the tradename Tybost and elvitegravir is approved under the tradename Vitekta in Europe, Canada and Australia.

Cobicistat is a cytochrome P450 3A (CYP3A) inhibitor. It boosts blood levels of the HIV protease inhibitors atazanavir and darunavir by suppressing CYP3A, an enzyme that metabolizes these drugs in the body. Cobicistat

acts only as a pharmacokinetic enhancer and has no antiviral activity.

Elvitegravir was licensed by Gilead from Japan Tobacco Inc. (JT) in March 2005. Under the terms of Gilead's agreement with JT, Gilead has exclusive rights to develop and commercialize elvitegravir as a single agent in all countries of the world, excluding Japan, where JT retains rights.

Cobicistat and elvitegravir are investigational products in the United States and their safety and efficacy have not yet been established. **HIV**

# POSITIVELY SERVING +



## HIV in the Military

BY BOB GATTY

WHAT WOULD IT BE LIKE TO BE A SOLDIER, far from home, perhaps afraid of what might lie ahead, only to learn that you have HIV, or even AIDS.

Think of that.

A young man or woman, training for or going into combat, risking literally everything. Worried about loved ones back home. Scared that the next trash can on the corner or pothole in the road might explode in your face and maim and disfigure you for the rest of your life.

Or worse.

Then you receive that devastating news, which in some people's mind, might even be worse than any injury that a bomb or bullet could cause.

Think, too, about what you as an HIV Specialist would do if asked to treat and care for such a soldier, whether on active duty or as a returning veteran. What special treatment would be required? What resources would you be able to use?

What would you do?

In active military service, HIV shows no favorites. It does not stay away because someone is in uniform. It is not afraid of stripes on the sleeve or bars, eagles or stars on the collar. It strikes in the very same way as it does in our civilian population, and it requires the same care, but even more.

The military has its own structure, its own way of dealing with all manner of injuries and illnesses. But there also are the practical implications of rank, of requirements for promotion, and yes, of stigma. It is tough enough for a young man or woman to acknowledge sexual status outside the "norm." We need not recount the battle over elimination of "Don't Ask, Don't Tell," and the political demagoguery that accompanied that long debate.

Now put yourself in the boots of a soldier who not only has had the courage to "come out," but also must acknowledge that the reason for his or her frequent medical visits is because of HIV.

What happens to the soldier's psyche? How does he or she cope with that? How do the medical team, the counselors, the chaplain—all of whom most likely rank far above this individual—respond effectively?

And then, when those soldiers return home having been discharged, how do the Veterans Administration and other health care agencies respond? Are there concerted efforts, coordinated programs and effective policies in place to provide the specialized care that is required?

That is what the following two articles are about.

"Soldiers: What Happens with an HIV Diagnosis?" examines the cases of three soldiers who discovered they were HIV-positive, the challenges they faced, and how their providers stepped in to provide the care they need. The author, Dr. Robert Matyas II, an HIV Specialist practicing in Hawaii, is a former Marine flight surgeon and has extensive experience treating military HIV patients. Dr. Matyas served as a co-editor, counselor and expert for this issue and we very much appreciate his insight and direction on this important topic.

"HIV & the VA" details the many services, policies and procedures in place to assist the returning HIV-positive soldier. It covers the VA's HIV care infrastructure, treatment, management of co-infection, screening, prevention, and more. Written by the VA's Maggie Chartier, Psy.D., M.P.H. and Marissa Maier, M.D., the article is filled with facts and solid information helpful to any HIV patient or provider who needs to assist HIV+ veterans.**HV**



SHUTTERSTOCK, THINKSTOCK/ JORGE VILLALBA

# SOLDIER

## What Happens with an HIV+ Diagnosis?

BY ROBERT J. MATYAS II, MD, AAHIVS

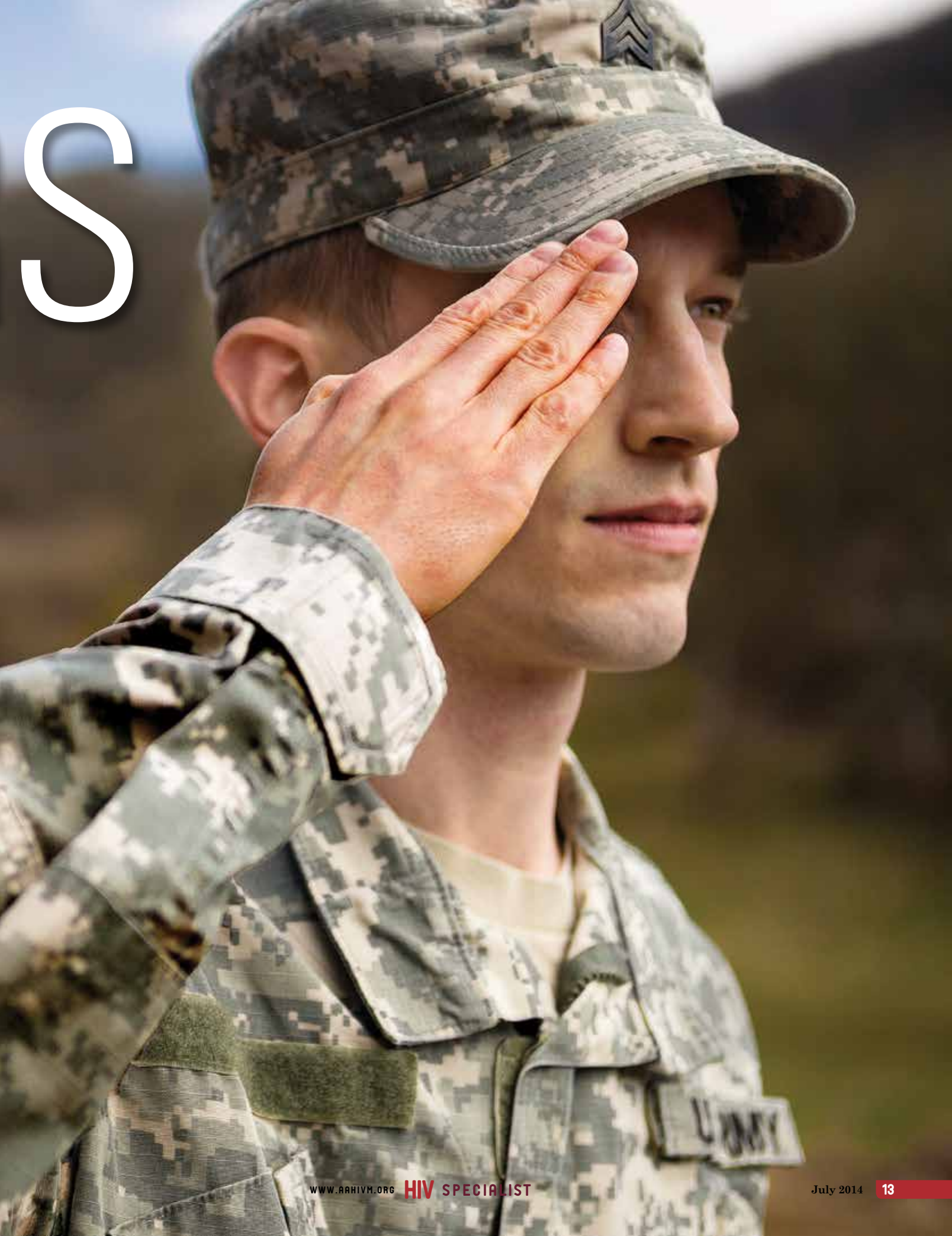
**I**T IS NO SECRET that we owe much of our freedom to the brave men and women serving in the United States Military. The image most of us have when picturing our military members is of healthy, strong-bodied, mentally-focused soldiers ready to swing into action on command. And that is indeed the case. The U.S. military has established a medical system dedicated to keeping service members in top physical shape.

However, few realize that HIV infection rates are higher among members of the military compared with the general population, and incidence rates dramatically increase during times of conflict.<sup>1</sup> Currently, there are approximately 1.4 million active soldiers in the US armed forces, and 2009 estimates suggest that 0.15-0.20 per 1,000 active duty personnel are infected with HIV.<sup>2,3</sup>

Whether you're a new recruit trying to endure a grueling boot camp in Paris Island, a seasoned soldier in the middle of your first deployment to Kuwait, or an experienced Staff Sergeant serving at your post in Georgia, hearing that you might be HIV positive in the armed forces is undoubtedly a very difficult thing to cope with and will change your military life forever.

For the following three soldiers, all at different points in their military careers, coming face-to-face with the diagnosis was one challenge they never expected when they enlisted.

# S



## Battling More Than Boot Camp

It was 1989 and Private First Class (PFC) “JP” was in Paris Island, South Carolina trying to survive yet another day of boot camp, the prerequisite rite of initiation when any enlisted soldier enters the military. Endless pushups, pull-ups, and sit ups. Hours of marching in brand new boots until the blisters on your heels are large, raw and causing excruciating pain with every step. Yes, this was boot camp and for PFC JP, he loved it.

“I wanted to be a Marine, a diehard Marine since I was 16,” explained JP. “This was my lifelong dream because we all know the Marines are the best!”

However, halfway through boot camp, his training was interrupted when he was ordered to report to base medical only to find out he was HIV positive.

Like any other recruit, PFC JP went through the typically battery of questionnaires and screening blood work at the time of his enlistment, but somehow his positive HIV lab test was missed.

“Several weeks into boot camp, I had to go see their head doctor” said JP. “He sat me down and told me you have AIDS and that because of the risk we cannot put the other recruits in jeopardy because of this. He said, ‘You can’t really be in the military because of this. We have to send you home. I can’t have you around the other recruits if blood splatters or if there’s bloodshed. You’ll be spreading the disease and endangering the other recruits.’ I felt like my whole world crumbled.”

PFC JP was sent to ‘casual,’ for recruits that got badly hurt and couldn’t make it through boot camp, or if their medical condition didn’t allow them to go through boot camp, and there they told him he was going home.

While devastated, PFC JP began to utilize the resources of the Department of Veterans Affairs (VA) for his HIV care. The VA system is the nation’s largest provider of HIV-related care, and reports show that the VA treats nearly 25,000 HIV-positive veterans. For PFC JP, transition of care from active duty to VA care occurred easily and efficiently. With over 1,700 hospitals, clinics and medical facilities in the U.S., there is excellent access to care. While PFC JP’s military career ended almost before it began, he remains undetectable and very well controlled as a patient in the VA over 25 years later.

## The Kuwait Connection

Stationed in Kuwait, Corporal (Cpl) “MS” was just wrapping up a typical 12-hour duty in the 110 degree desert heat. He was excited at the opportunity to talk to his partner back in the states and, like many other soldiers deployed overseas, it was the thought of hearing a loving, familiar voice that kept him going. After endless failed attempts at a phone connection, he ultimately got through to his partner. However, what his partner said to him when he answered was completely unexpected. It was that day that Cpl MS was told that his partner had just seroconverted and that he should be tested for HIV right away.

At the same time Cpl MS was receiving his diagnosis, HIV Specialist Lieutenant Colonel (LTC) Ida Stewart was reporting back to her fellow HIV practitioners in the U.S. about her new role as a primary care doctor serving in the Army Reserve based in Kuwait.

“This deployment to Kuwait was my first time overseas in the Middle East,” said LTC Stewart. “Back home, I was part of a busy practice caring for over 500 HIV positive patients. But in the desert of Kuwait, my role was to function solely as a primary care doctor because there was no need for an HIV Specialist overseas.”

As per army regulation, soldiers who receive OCONUS (Outside the Contiguous United States) assignments must have tested negative for HIV within six months prior to departure. Any positive test precludes the soldier from being allowed to deploy. The reason for this policy is in part driven by the lack of HIV experts to manage care OCONUS, especially if a service member’s immune system becomes compromised. Soldiers often don’t have access to multi-specialty clinics in the field and there are only a handful of military MTFs (Medical Treatment Facilities) that manage HIV care for active duty members within the U.S.

Despite these screenings, there are occasions where the screening test comes back negative, but the soldier is in the window period of seroconversion or is exposed to HIV directly before the deployment. As LTC Stewart explains, all members have two weeks of leave just prior to the deployment date. This period can be a particularly high risk period as some “cut-loose” right before their year long period of abstinence, sobriety and duty.

When Cpl MS entered LTC Stewart’s medical clinic about to ask for an HIV test, he was very nervous.

“He was really concerned,” said LTC Stewart. “His last HIV test was in January, but there were a few months between the last test and his possible seroconversion.”

Getting an HIV test overseas was no easy task for LTC Stewart.

“I had to send out for the HIV test from Kuwait on a plane to Landstuhl, Germany,” explained LTC Stewart. “From there it went to Walter Reed in Bethesda, Maryland, then back to Landstuhl, then back to Kuwait. HIV testing would take over a month if you were deployed, and I thought this is totally ridiculous!”

With just one week left in her deployment LTC Stewart, wasn’t able to even give Cpl MS his result, but she was able to counsel him about HIV and make him feel much better about what was happening.

LTC Stewart admits, “It was like divine intervention that I should be here for this.”

Upon giving several talks to other physicians in the military, she was surprised to learn that some practitioners didn’t even know that HIV-positive members could still stay in the military and that it does still exist.

After their encounter, Cpl MS took the time to write LTC Stewart an e-mail thanking her for making him feel



**His CO was silent as they walked inside and waited in the lobby to be called. Looking around, SSGT R started to see several brochures on STDs and HIV. Knowing that he was waiting for his HIV test results from the week prior, he immediately thought, “OK, I have AIDS. This is the worst case scenario.”**

so comfortable. For LTC Stewart it was validation why she remained in the reserves.

“I felt so good because I was really making a difference there,” she said.

### **A Difficult Diagnosis**

Christmas Eve is generally a very exciting day for most active duty service members as they prepare to fly home for the holidays. However, for a Staff Sergeant (SSGT) stationed in southern Georgia, it was anything but.

“SSGT R” was sitting next to his unit commander when he said, “Let’s go for a ride.”

Generally, it was only if a soldier had done something exceptional or if a soldier was to be reprimanded to the severest degree that he was asked to join his commanding officer (CO), so SSGT R was quite nervous. They pulled him into a building that he had never been to with a sign out front labeled “Preventive Medicine Services.”

His CO was silent as they walked inside and waited in the lobby to be called. Looking around, SSGT R saw several brochures on STDs and HIV and knowing that he was waiting

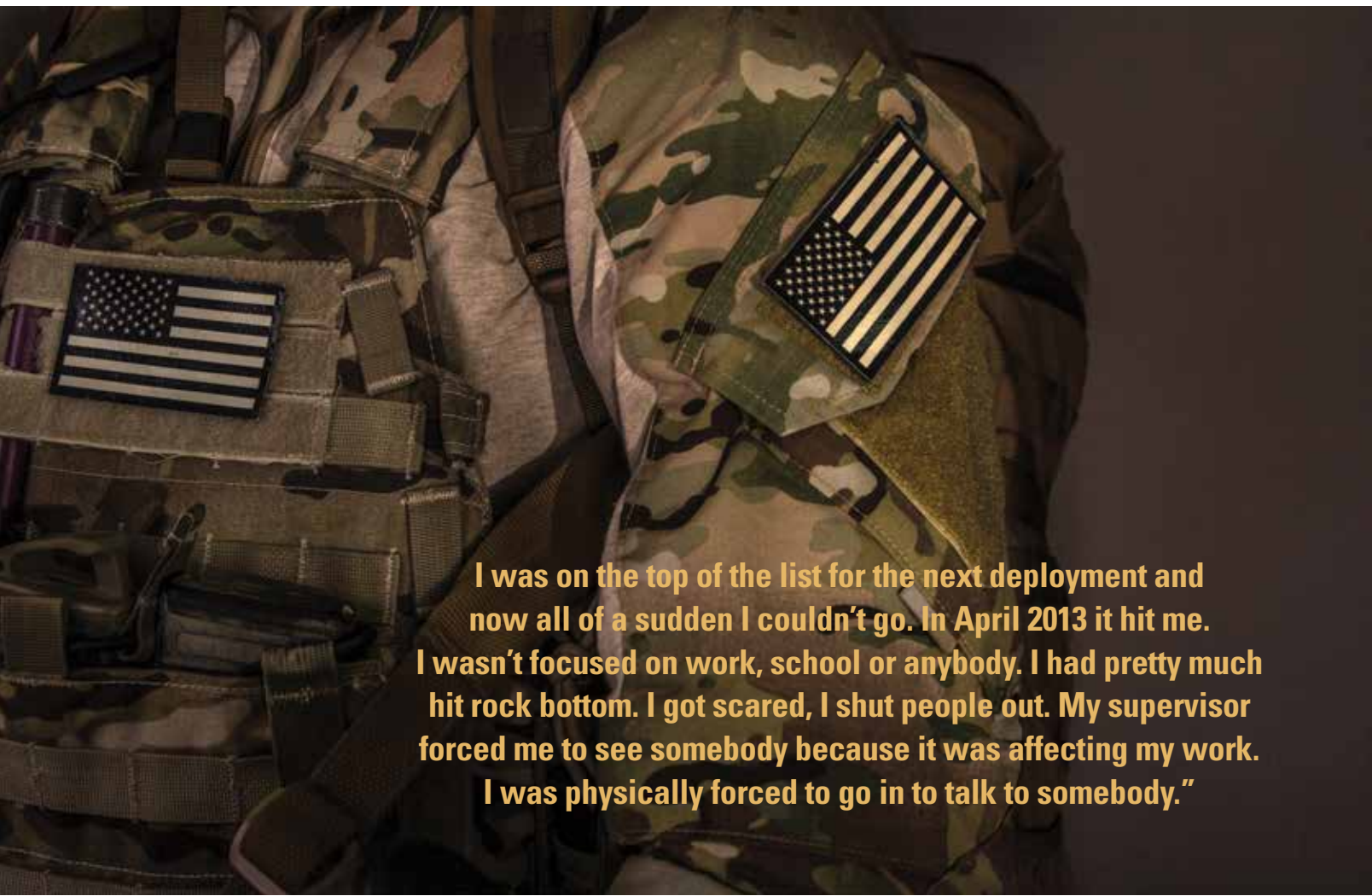
for his HIV test results from the week prior, he immediately thought, “OK, I have AIDS. This is the worst case scenario.”

With boot camp a thing of the distant past and with several deployments already under his belt, SSGT R was a well-seasoned Marine who joined the military in 2003 in part because he wanted to travel, see the world and do something different with his life. He started his military career as part of the National Guard, but quickly discovered through overseas deployments that he really liked the Army, so in 2007 he formally enlisted.

“At first it was great,” stated SSGT R. “I got to work as artillery and shoot cannons and I worked as Infantry when I was deployed for a year to Kuwait.”

SSGT R enjoyed his deployments, even the more difficult ones like his deployment to Iraq, just outside of Balad, where he took fire and lost about 25 guys in his unit. While he never was formally diagnosed with PTSD, he said it was a big transition for six months after he got home.

“I had an Iraq mentality and was careful of things like trash on the side of the road,” continued SSGT R. “In Iraq, these often contained IEDs (improvised explosive devices) common in ambushing troops.”



**I was on the top of the list for the next deployment and now all of a sudden I couldn't go. In April 2013 it hit me. I wasn't focused on work, school or anybody. I had pretty much hit rock bottom. I got scared, I shut people out. My supervisor forced me to see somebody because it was affecting my work. I was physically forced to go in to talk to somebody."**

Despite these adversities, SSGT R had not yet faced his greatest challenge.

"In July of 2012 I was raped, admitted SSGT R. "I was jumped by two active duty servicemen outside base while running late one night. It's hard to say, sometimes."

The incident was reported to the base medical center where fluid samples were obtained. After DNA sampling was performed on the fluids, both men were caught. Thinking he had closure on the incident, he tried to put the entire event behind him and move on—until he was notified that one of the two soldiers was HIV-positive and that even though initial screening was negative, he would have to wait three months for the follow-up antibody screening to be performed.

A Lieutenant Colonel (LTC) physician working in the lobby of the Preventative Services building finally called his name and brought him into a room. Reporting HIV test results is somewhat different in the military, as a member's HIV status may have a direct impact on the unit as a whole. Any positive HIV antibody test is reported to the unit's commanding officer. While the CO is not authorized to inform the soldier of the diagnosis, they generally escort them to the physician for the results. The LTC told him that he was HIV-positive.

"I didn't react," recalled SSGT R. "I was like a robot. I didn't feel anything. I thought it would be just like a sickness that could be cured, like diabetes."

The support that he received after being told was typical for any active duty service member. There were multiple people standing by to help counsel him, including nurse practitioners, case managers, the base chaplain and behavioral health specialists. But finding the courage to discuss HIV with your superiors can be challenging, as many of these counselors are officers, many rank higher than the soldier. This can be intimidating, especially if the discussions include same-sex relations. While the "Don't Ask, Don't Tell" policy was formally repealed in 2011, there is still quite a bit of stigma associated with being gay in the military.

"At that time, since I didn't *feel* anything," said SSGT R. "I refused all the help." Since he was the healthiest guy in his unit, having frequent medical appointments raised suspicion.

"My immediate supervisor, an enlisted sergeant one rank higher than me, was shocked because of all of these appointments I had to go to," explained SSGT R. "He asked a lot of questions and I didn't know what to say. I told him that I had a medical issue and I'm good."

Further, while his medical record was kept confidential, it was kept in a public office space within the unit—and contained a red flag that read “non-deployable.” It is standard military policy that any member diagnosed with HIV while active duty may not be deployed OCONUS. Since he was formally changed to a “non-deployable soldier,” people wondered why.

“People in my unit thought—he’s not limping, and there isn’t anything obviously wrong with this guy, but there’s something about him that makes him non-deployable,” said SSGT R. “I think people figured it out.”

Being assigned to an overseas deployment, such as serving in Kuwait or Iraq, is highly desirable for someone joining the military. For many, it is why they enlisted. It earns them respect among their peers. It gives them invaluable experience. It’s *the* item that gets most brought up when your résumé is reviewed for a future civilian job interview.

“I was looking forward to my deployments” said SSGT R. “In my unit, only one of us can be deployed at a time to places like Honduras, Kuwait or Belgium. I was on the top of the list for the next deployment and now all of a sudden I couldn’t go. In April 2013 it hit me. I wasn’t focused on work, school or anybody. I had pretty much hit rock bottom. I got scared, I shut people out. My supervisor forced me to see somebody because it was affecting my work. I was physically forced to go in to talk to somebody.”

Because of the direct supervision and rank structure of the military, when an active duty member isn’t performing to the best of his or her ability, the supervisors are notified and actions are quickly taken to intervene. Unlike the civilian sector where things like poor performance and depression can often go unnoticed for a significant period of time, these things generally are more readily addressed and dealt with quickly in the military.

“I spoke to a civilian behavioral health specialist,” SSGT R explained. “I was her first HIV positive soldier and she helped me a lot.”

The problems surrounding a soldier’s medications constitute yet another challenge of being HIV positive in the military.

“I was first placed on a drug that made me so groggy that I couldn’t wake up until noon the next day,” said SSGT R.

These decisions are important when the bugle plays Reveille at 0500 (5 a.m.) every morning and your day needs to start promptly. There’s no time to adjust for grogginess. Also, some medications require administration with a full meal. SSGT R would eat dinner every day with his fellow soldiers and he didn’t want them to see him taking a medication every day as this might raise suspicion, on top of everything else.

So, SSGT R would go home and schedule in an extra meal just to take his meds. While these types of schedule adjustments can be difficult for any individual, in the military, where most of your time is accounted for, it becomes even more of a challenge.

Overall SSGT R believes he received good HIV care in the military. However, the support structure from fellow HIV positive service members is often absent. This must be sought out by the individual.

Many HIV-positive service members don’t wish to discuss their status with others, partly because of the stigma associated with HIV, but also because many automatically associate being HIV-positive with being gay, and this can lead to further stigmatization.

“I have acquaintances that are HIV-positive in the military, friends of friends, but I haven’t really talked to them,” he admitted.

Being diagnosed as HIV-positive when you’re active duty undoubtedly changes your career path. While it doesn’t directly affect a soldier’s ability to get promoted, there are indirect impacts.

“The only thing killing me at this point is that I can’t get stationed overseas, so if there’s a position overseas that would get me promoted faster, being HIV-positive acts as a barrier,” he stated.

Relationships can also present a challenge.

“I’m so scared of telling people that I’m HIV-positive,” SSGT R admitted. “I don’t think I’m ready unless I really do trust them with my life.”

When thinking about his HIV status and his experiences thus far in the military, SSGT R said, “It’s hard to forget what happened. This is part of me. This is who I am. The past is the past. I just need to move on. Since then, I did a lot of things I didn’t think I would be able to. I achieved a lot of my goals. I see life from a different perspective now than before. I could say that I am healthier than before I was diagnosed, but it did change my military plans.”

**HIV**



#### ABOUT THE AUTHOR:

**Robert J. Matyas II, MD, AAHIVS** is the Director of HIV Services for the Hawaii Region of Kaiser Permanente. He works at the Honolulu Clinic on Oahu and manages a practice of approximately 500 HIV patients. After his first year of medical school, he joined the U.S. Navy, and upon finishing medical school, he completed a Family Medicine Internship at the Naval Hospital Bremerton in Washington. He served as the Flight Surgeon for the Marine Corps helicopter squadron HMM-362 at the Marine Corps base in Oahu, then completed a seven month tour in Iraq, receiving a Marine Corps Commendation Award for exemplary service. Following his service, Dr. Matyas moved to Los Angeles to finish a residency in Family Medicine at the Kaiser Los Angeles Medical Center.

Dr. Matyas began treating HIV positive patients in 2004 when he started his military career. He has earned his HIV Specialist certification through AAHIVM and became Director of HIV Services for Kaiser Permanente in the Hawaiian Islands. Dr. Matyas also practices Family Medicine and launched a Transgender Care Clinic in 2013 to provide comprehensive care and meet the diverse and often complex primary care needs of Hawaii’s transgender patient population in an environment devoid of prejudice, judgment or bias.

 POSITIVELY  
SERVING

# HIV & VA THE





# DEPARTMENT OF VETERANS AFFAIRS: HIV Program, Policies, and Infrastructure

MARISSA MAIER, M.D. AND MAGGIE CHARTIER, PSY.D., M.P.H.

**T**HE VETERANS HEALTH ADMINISTRATION (VHA) of the Department of Veterans Affairs (VA) is a comprehensive federal health care system serving eligible, enrolled veterans who have served in the United States Armed Forces, but are no longer in active duty.

The largest provider of integrated civilian health care in the United States, VHA is organized into 21 regional Veterans Integrated Service Networks (VISNs), each of which oversees the administrative and clinical functions within its geographic area of operations.

The 21 VISNs contain 151 regional health care systems called Stations, each of which include numerous medical facilities. There are currently 152 hospitals (VA Medical Centers or VAMCs), and almost 1,400 community-based outpatient clinics, skilled nursing facilities, Vet Centers, rehabilitation centers, hospices, and domiciliaries in the United States and its territories.<sup>1</sup>

## The VA HIV Care Infrastructure

The HIV, Hepatitis, and Public Health Pathogens Program (HHPHP) within VHA's Office of Public Health/Clinical Public Health (OPH/CPH) guides HIV care within VHA. HHPHP is dedicated to providing state-of-the-art clinical public health services in the areas of HIV, viral hepatitis, and public health pathogens.

In addition to developing national policy on HIV care within VHA, it analyzes the quality of HIV care in VHA, identifies and disseminates evidence-based quality improvement interventions, facilitates Veteran and provider input on the provision of HIV-related health care and policies, and monitors trends in HIV infection prevalence and its clinical sequelae.

HHPHP advocates for veterans with HIV infection and the VHA clinical providers who serve them. To carry out its mission, HHPHP collaborates with multiple stakeholders within VHA, such as the Office of Public Health/Population Health, the National Center for Health Promotion and Disease Prevention (NCP), the Office of Specialty Care, and the Primary Care Office.

It also collaborates with non-VHA stakeholders, such as the U.S. Centers for Disease Control and Prevention (CDC), Department of Health and Human Service (HHS), National Office of HIV/AIDS Policy (ONAP) professional societies, and HIV patient advocates.

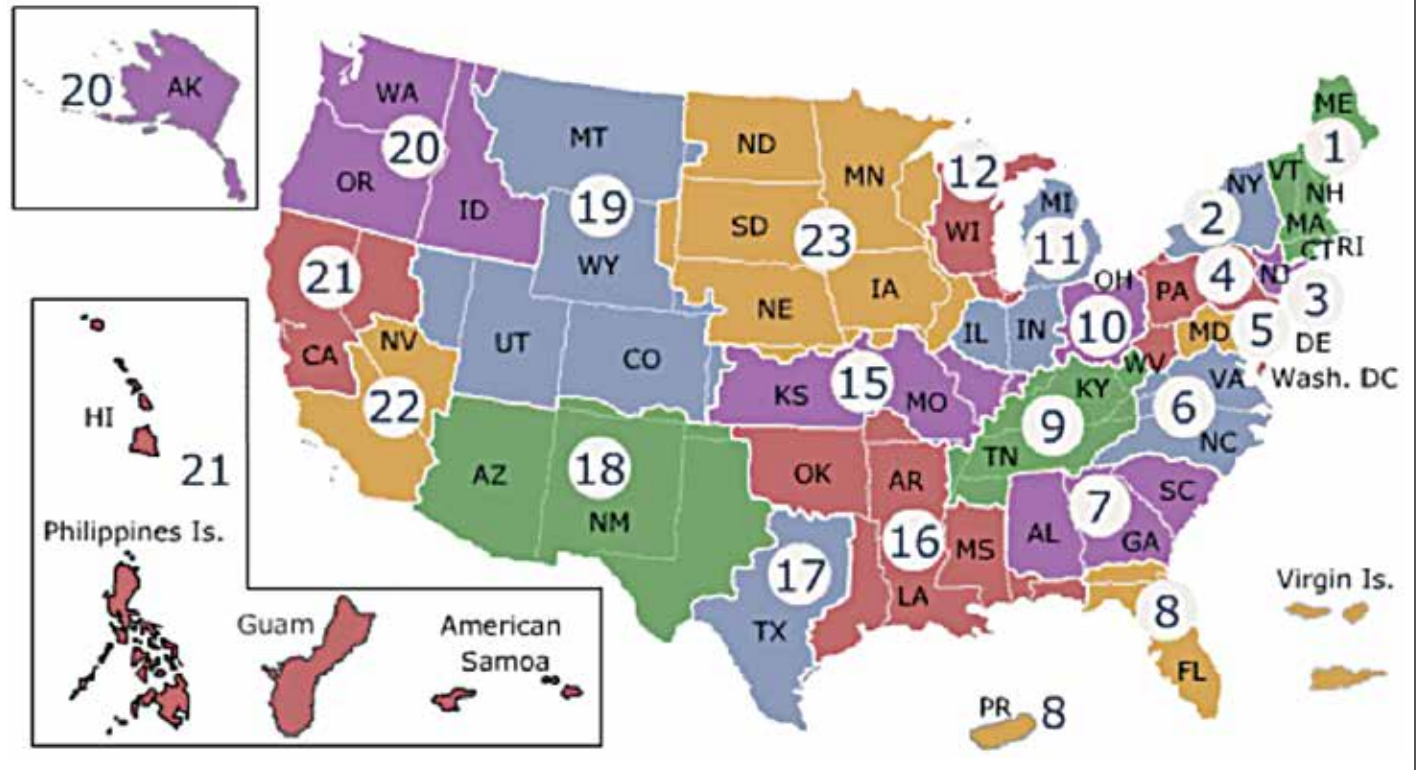
HHPHP's goal is for veterans with or at risk of HIV infection to receive the highest-quality health care services. Led by HHPHP and carried out by providers at VHA medical facilities across the country, the program promotes excellence across the HIV Care Continuum as mandated by the President's National HIV/AIDS Strategy.

## Policy and planning

The National HIV Program within HHPHP is charged with developing policy guidance for VHA regarding best practices in clinical care for HIV infection; advocating for the development, maintenance, and restructuring of the resources (personnel, expertise, equipment, and funds) necessary to ensure high-quality care for Veterans with HIV; and supporting VHA providers by removing barriers to diagnosis and care.

To ensure appropriate patient and provider input into national policy and programmatic initiatives, HHPHP supports two formal advisory groups. One comprises HIV-positive veterans who receive their medical care through VHA (the HIV Community Advisory Board); the other comprises VHA health care providers who serve HIV-positive Veterans (the HIV Technical Advisory Group). These groups, convened on a regular basis, provide an opportunity for HHPHP staff to seek advice and obtain feedback on issues related to HIV patient care throughout the nation.

**Figure 1: The 21 VISNs of the VHA health care system**



### Structure of clinical care

HIV-positive veterans in VHA care primarily receive their care locally, at a community-based outpatient clinic or medical center. In some rural areas, veterans may receive their primary care from a local outpatient clinic and their HIV care from a regional clinic or medical center.

Some veterans receive primary care from a primary care provider and their HIV care from an infectious diseases or HIV specialist, while others receive both their primary care and HIV care from an infectious diseases or HIV specialist. Efforts are under way nationwide through the Specialty Care Access Network-Extension for Community Healthcare Outcomes (SCAN-ECHO) training program to increase the capacity of rural primary care providers to also provide HIV care, thereby decreasing the need for rural veterans to travel long distances to receive high-quality HIV care.

Each HIV clinic is led by a director, who ensures timely linkage to care, evaluates retention in care, and monitors quality-of-care indices such as virologic suppression and immunization.

Each Medical Center also has a designated HIV lead clinician, who often also serves as the HIV clinic director. These individuals often serve as a local resource and advocate for promoting routine HIV screening within their facility and catchment area. They serve as point personnel for communications to and from HHPHP regarding issues such as

HIV testing, pre-exposure prophylaxis (PrEP), engagement in and linkage to care, addressing medical and mental health comorbidities, and disseminating analytic reports summarizing performance on standardized quality indices to pertinent providers and staff members.

### Educational resources and training

In addition to the advisory groups, HHPHP supports regularly scheduled teleconference seminars pertaining to active issues in HIV care within VHA. These conference calls are a platform for rapidly disseminating policy or programmatic changes to HIV providers and HIV clinics nationwide, and for educating providers about important advances in HIV clinical knowledge.

Veterans with HIV/AIDS have high rates of mental health and substance use disorder (MH/SUD) treatment needs that are critical to address to facilitate access and linkage to care, efficacy of medical treatment, and disease management.

Evidence shows that providing MH/SUD services in integrated care settings results in improved medical outcomes for these populations. HHPHP is therefore supporting a postdoctoral training fellowship for psychologists in hepatitis C and HIV clinical care.

The expansion of this fellowship has educated mental health and liver providers about the high prevalence of mental health and substance use comorbidities among veterans with HIV,

as well as augmented the national availability of psychology professionals with dedicated training in evidence-based psychotherapy and integrated care for HIV-infected individuals.

Another important resource is the HIV Clinical Consultation Service, or “Warmline.” This is a nationwide, cost-free telephone service providing confidential expert clinical advice on HIV care for VHA clinicians of any experience level. It is an important additional clinical and educational resource for all providers, but particularly those who work in rural environments or urgent care settings.

### Surveillance of HIV in VHA

The Office of Public Health/Population Health maintains the HIV Clinical Case Registry (HIV-CCR) (Backus, et al.; 2009), a national database of HIV-infected Veterans in the United States receiving medical care at any VHA facility.

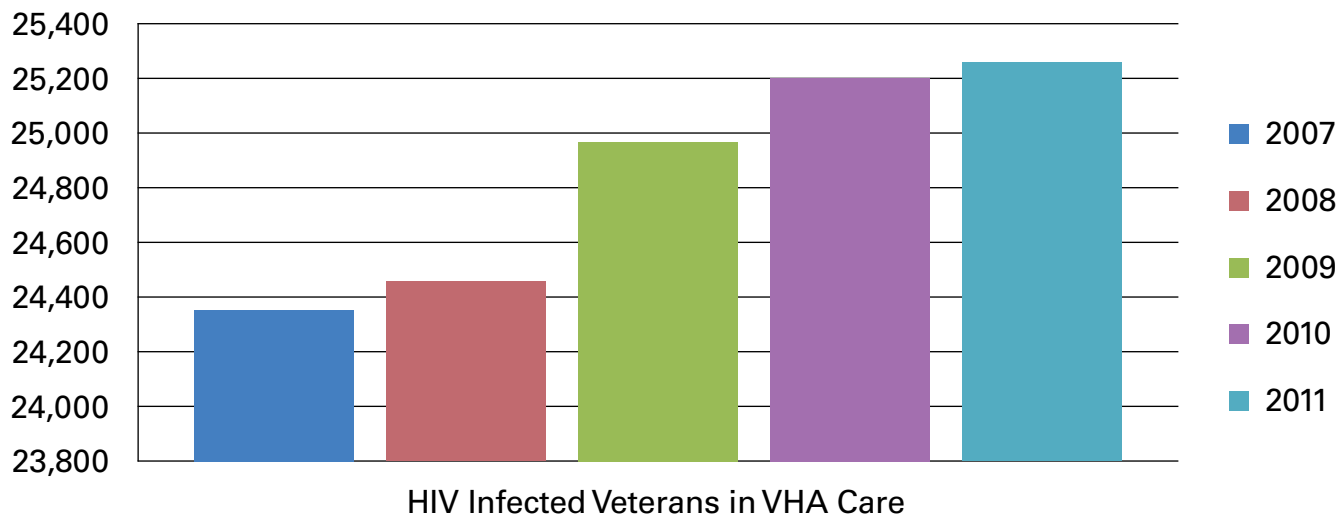
Designated HIV-CCR coordinators at all VHA medical centers manually verify all new diagnoses of HIV infection based on laboratory results and ICD-9 diagnostic codes, and upload verified patients to the CCR. After confirmation of HIV infection, clinical, laboratory, and administrative data on patients at each local VHA medical facility are electronically transmitted nightly to the national HIV-CCR using secure messaging.

The HIV-CCR data facilitates the National HIV Program/HHPHP’s efforts to monitor the epidemiology of HIV infection within VHA, monitor clinical outcomes and crucial quality-of-care indices, and ensure appropriate linkage to care. The data are also used by local facilities and providers to monitor caseloads, and provide immediate accurate local data about important care parameters, such as virologic suppression. HHPHP uses CCR data to develop evidence-based, system-wide quality improvement interventions.

**Veterans with HIV/AIDS have high rates of mental health and substance use disorder (MH/SUD) treatment needs that are critical to address to facilitate access and linkage to care, efficacy of medical treatment, and disease management. Evidence shows that providing MH/SUD services in integrated care settings results in improved medical outcomes for these populations.**



**Figure 2: Number of HIV-positive Veterans in care: 2007–2011**



### **The epidemiology of HIV infection within VHA**

Nationally, 25,271 HIV-infected veterans were in VHA care in 2011. The number of HIV-positive veterans in the various VISNs ranged from 343 (VISN 2) to 3,389 (VISN 8). One half of the VISNs had more than 1,000 HIV-positive veterans in care during the year.

Between 2007 and 2011, the number of HIV-positive veterans in care increased 3.8 percent. Between 2007 and 2011, the number of HIV-positive veterans in VHA care increased from 24,350 to 25,271 individuals.

Between 2007 and 2011, the number of veterans with HIV decreased in the East and increased in the South and Central United States. In 2011, 35 percent of the Veteran population with HIV in VHA care received care in the South, 28 percent received care in the East, 22 percent in the Central part of the country, and 22 percent in the West. This regional distribution of veterans with HIV in care mirrors the distribution of new HIV cases in the United States in 2007.

### **Sex**

The majority of HIV-positive veterans in VHA care are men (97 percent); however, VHA provides care to over 600 HIV-infected women. This contrasts with the United States as a whole, where approximately one quarter of HIV-positive individuals are women (CDC, HIV Among Women; 2014). The proportion of female HIV-infected veterans in care remained stable between 2007 and 2011.

### **Race and ethnicity**

The majority of HIV-positive veterans in VHA care are veterans of color. In 2011, African-Americans comprised nearly half of the VHA HIV-positive population (48%), while white veterans represented 40 percent. Seven percent of veterans

infected with HIV identified themselves as Hispanic or Latino. Less than 1 percent were American Indian, Alaskan Native, Asian, Native Hawaiian, or Pacific Islander.

### **Age**

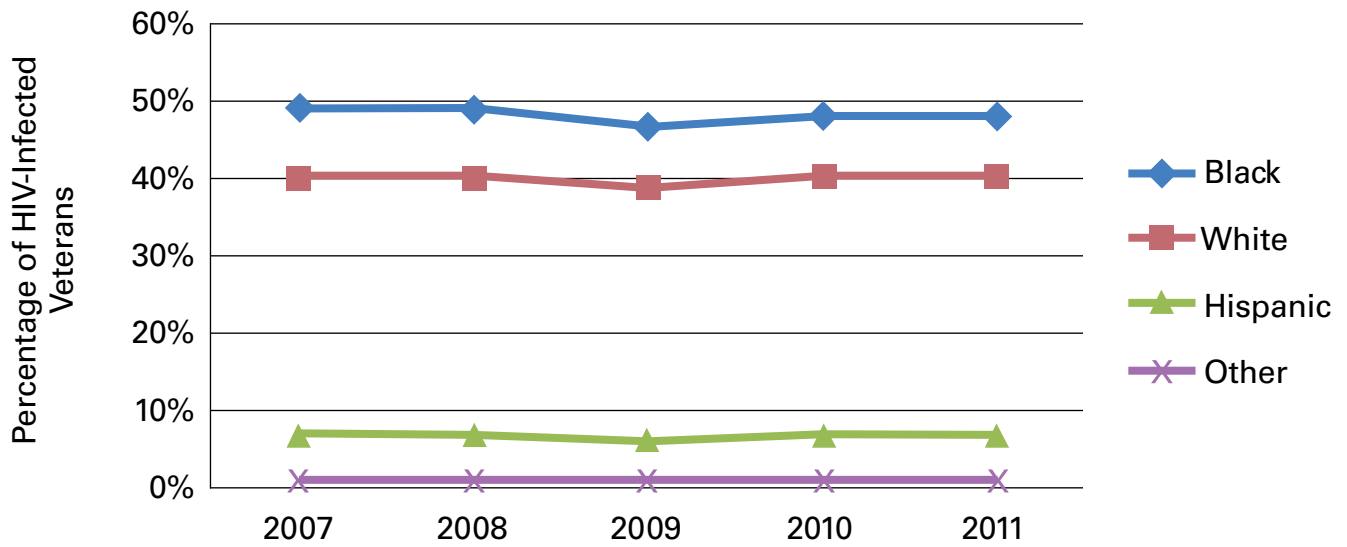
The majority (66 percent) of HIV-positive veterans in VHA care are between the ages of 50 and 69. Between 2007 and 2011, the mean age of HIV-positive veterans increased from 51.6 to 54. The proportion of HIV-positive veterans in VHA care over the age of 50 rose from 60 percent in 2007 to 70% in 2011. The increase in the number of persons aged 50 and older living with HIV in VHA is partially due to widespread use of combination antiretroviral therapy (cART), which has transformed HIV into a chronic infection for most patients.

### **Comorbid conditions**

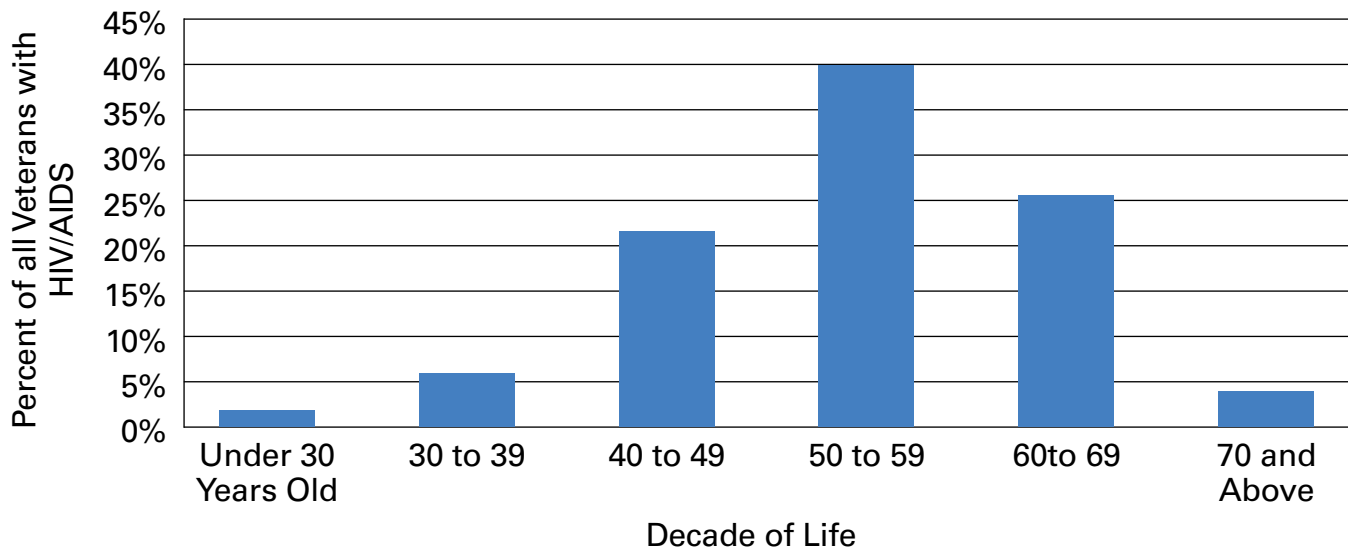
Comorbid medical and mental health conditions contribute to the complex health needs of veterans with HIV. HHPHP, in conjunction with the Population Health group, collects and reports rates of comorbid conditions in HIV-positive veterans in VHA care. These data help VHA prioritize resources for high-prevalence comorbid conditions, align staffing to address comorbid conditions, anticipate workload, and make budget projections.

For example, the level of health care utilization for an otherwise healthy Veteran with HIV infection may be very different than for a Veteran with depression, diabetes, and hypertension as well as HIV. In 2011, the most common comorbid conditions among HIV-positive veterans in VHA care were: depression (55 percent), hypertension (53 percent), dyslipidemia (50 percent), anemia (30 percent), anxiety disorders (30 percent), chronic hepatitis C virus infection (26 percent), and diabetes mellitus (18 percent).

**Figure 3: Race and ethnicity of HIV-positive Veterans: 2007-2011**



**Figure 4: Age by decade of life among HIV-positive Veterans in care: 2011**



Other important clinical conditions impacting HIV care include post-traumatic stress disorder (16 percent), chronic obstructive pulmonary disease (13 percent), history of hepatitis B virus infection (12 percent), ischemic heart disease (12 percent), and chronic renal failure (11 percent).

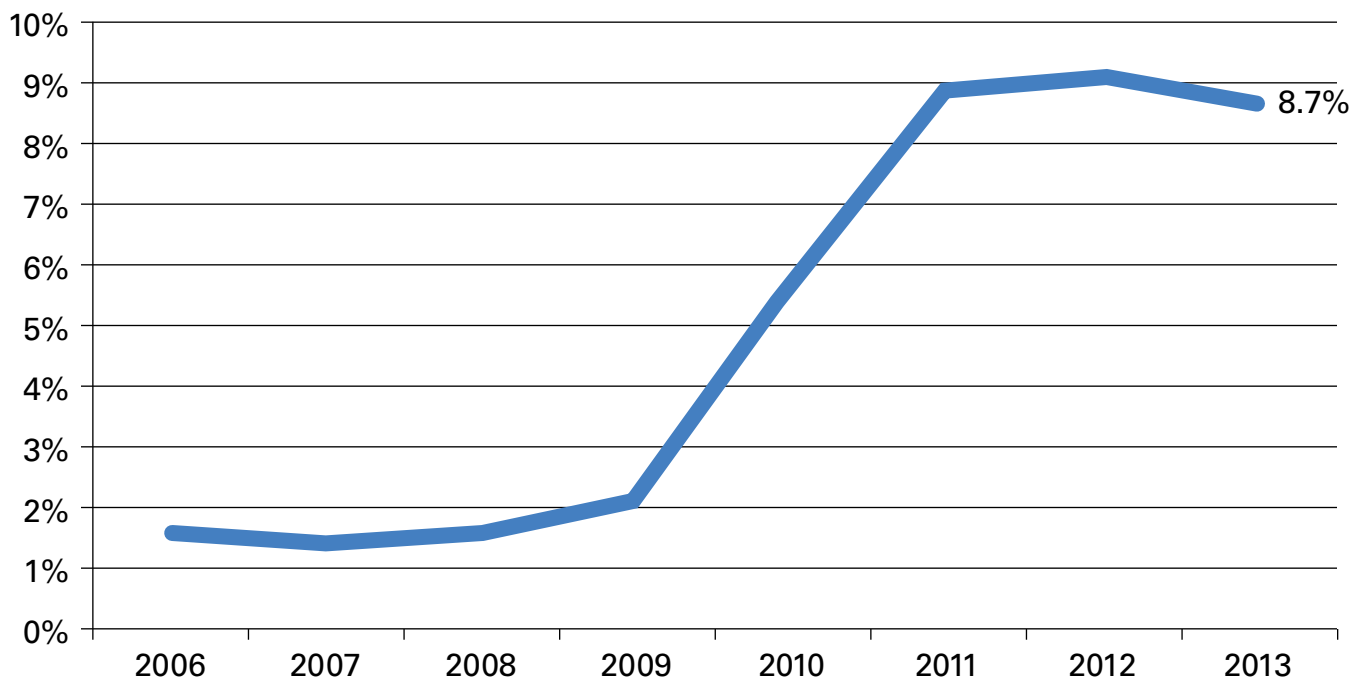
Substance use is quite prevalent in the HIV-positive Veteran population, with 34 percent reporting a history of alcohol abuse, 15 percent reporting a history of cannabis use, and 26 percent reporting a history of cocaine use in 2011.

### **The management of HIV infection within VHA**

Potent combinations of antiretroviral medications have transformed HIV from an illness with uniformly high rates of fatality to a chronic infection for most patients. VHA follows the recommendations of HHS on prescribing antiretroviral therapy. In VHA, all Food and Drug Administration (FDA)-approved antiretroviral medications are available to HIV-positive veterans.

Antiretroviral medications are prescribed at all local VHA

**Figure 5: HIV screening rates in Veterans eligible for one-time screening in care in the year\***



\* DATA PROVIDED BY LISA BACKUS, MD, PHD, OFFICE OF PUBLIC HEALTH, VHA. PERSONAL COMMUNICATION 5/2014.

health care systems, and uptake of newly introduced anti-retroviral medications is generally rapid across the system. In 2011, 93 percent of HIV-infected veterans had ever filled an outpatient prescription for an antiretroviral medication. Between 2007 and 2011, the proportion of veterans ever prescribed antiretroviral medication rose from 78 percent to 93 percent.

### **Virologic suppression**

Virologic suppression is the final step in the HIV Care Continuum. The National Quality Forum has endorsed an HIV viral load of less than 200 copies/mL at last viral load test as a primary performance measure for HIV (National Quality Forum; 2014).

Among HIV-positive veterans in VHA in 2011, 74 percent had achieved virologic suppression. This statistic takes into account all veterans in VHA care, not just the veterans who qualify for antiretroviral therapy according to HHS guidelines.

### **General medical care**

Beyond ensuring routine access to antiretrovirals and achieving high rates of virologic suppression, VHA HIV health care encompasses all aspects of HIV-related medical care, with multiple care indices closely monitored.

For example, 98 percent of HIV-positive veterans in VHA care in 2011 had been screened for hepatitis B virus infection,

and 98 percent of HIV-positive veterans meeting National Quality Forum visits in 2011 had been screened for hepatitis C virus infection. Additional quality-of-care indices that are routinely evaluated include rates of influenza and pneumococcal vaccination, tuberculosis screening, syphilis screening, tobacco use screening, and screening for hypercholesterolemia. As part of its emphasis on high-quality general medical care, VHA supports programs such as the West Haven VA Medical Center, which has a long-standing program to train infectious diseases fellows to provide hepatitis C virus infection care.

### **HIV Screening within the Veterans Health Administration**

The diagnosis of HIV is the crucial first step in the HIV care continuum. CDC estimates that approximately one fifth (16 percent) of all HIV-positive Americans do not know they are infected (CDC, Basic Statistics; 2014).

VHA is committed to identifying these individuals, and engaging them in care. As a reflection of this commitment, in August 2009, VHA made significant changes in its HIV screening policy.

Prior to this policy update, providers were required to obtain and document written informed consent, in addition to performing pre-test and post-test counseling, before screening a Veteran for HIV. This created an undue burden on providers, and limited the uptake of regular testing.

Since August 2009, VHA has required only documentation of verbal consent before screening a Veteran for HIV. In addition to updating policy on how screening should be performed, the 2009 revision aligned VHA with CDC recommendations on who should be screened. It introduced the requirement for routine one-time screening of all adult veterans (rather than previous risk-based screening), with annual screening recommended among high-risk populations.

As a result of these policy changes, and vigorous promotion of routine HIV testing nationwide, HIV testing rates in the United States have increased dramatically. In 2009, only 9.2 percent of all veterans in VHA care had been tested for HIV; in 2011, just two years after the policy change, this increased to 20 percent (Czarnagorski, et al. 2013). Screening rates among veterans eligible for one-time screening in a calendar year increased from under 2 percent in 2009 to almost 9 percent by 2011 (Figure 5).

## HIV prevention

VHA is committed to the prevention of HIV transmission and supporting the dissemination of best practices in evidence-based clinical care that informs policy and programmatic initiatives.

For example, in May 2014, CDC released its first clinical guidelines outlining the appropriate use of PrEP for the prevention of HIV (CDC, 2014), which is available nationwide at VHA facilities or through VHA health care providers. Condoms are also free and available across the system to promote safer sex.

Research has demonstrated the importance of HIV “treatment as prevention,” with markedly reduced rates of heterosexual transmission of HIV when antiretrovirals are used (Cohen and the HPTN 052 Study Team, 2011). VHA’s success in promoting the broad use of antiretrovirals is demonstrated in the 93 percent of veterans in care in 2011 who have ever been prescribed antiretrovirals, and the 74 percent of veterans with virologic suppression.

Finally, VHA and its providers are keenly aware of the comorbid substance use diagnoses that place veterans at risk of HIV transmission and acquisition (including intravenous drug use), and the complex interplay between mental health and substance use disorders. The co-location of mental health care within HIV clinics is strongly supported, both in terms of training psychologists in this specialty area and advocating for increased integration of mental health and substance use services into HIV clinical care across the system.

## Conclusion

VHA is the nation’s largest integrated health system, and the single largest provider of HIV care within the United States. It strives for excellence at every step of the HIV Care Continuum, from diagnosis to virologic suppression with a focus on access and linkage to care. Through data monitoring, collaboration with external and internal stakeholders, and communication

across its network of HIV care providers and patients, VHA will continue to proactively and dynamically set policy and promote programmatic initiatives to maintain high-quality HIV care.

HIV



### ABOUT THE AUTHORS:

**Marissa Maier, M.D.** received her Doctor of Medicine from the University of California, San Francisco School of Medicine. She serves as an Infectious Diseases staff physician at the Portland VA Medical Center, and as an Assistant Professor at Oregon Health and Sciences University in Portland, Oregon. She is the Senior Medical Officer for the HIV, Hepatitis, and Public Health Pathogens Program in the Office of Public Health, Veterans Health Administration.



**Maggie Chartier, Psy.D., M.P.H.** received her Master of Public Health from the University of Washington and her Doctor of Psychology from the PGSP-Stanford University Consortium. She serves as a staff psychologist at the San Francisco VA Medical Center, and as an Assistant Clinical Professor at the University of California, San Francisco Department of Psychiatry. She is the National Public Health Clinical Psychologist for the HIV, Hepatitis, and Public Health Pathogens Program in the Office of Public Health, Veterans Health Administration.

## Endnotes

1 <http://www.va.gov/health/findcare.asp>

## References

- Backus, LI, and S Gavrilov. “Clinical case registries: simultaneous local and national disease registries for population quality management.” *Journal of the American Medical Informatics Association* 16, no. 6 (n.d.): 775-783.
- Centers for Disease Control and Prevention. *Preexposure prophylaxis for the prevention of HIV infection in the United States- 2014*. May 2014. <http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf> (accessed May 27, 2014).
- Cohen, M S, T R Fleming, and HPTN 052 Study Team. “Prevention of HIV-1 infection with early antiretroviral therapy.” *New England Journal of Medicine* 365, no. 6 (August 2011): 493-505.
- Czarnagorski, M, et al. “Expanded HIV testing in the US Department of Veterans Affairs, 2009-2011.” *Am J Public Health* 103, no. 12 (December 2013): e40-5.
- Forum, National Quality. National Quality Forum. May 5, 2014. <http://www.qualityforum.org/QPS/QPSTool.aspx?projectActivityId=478#qpsPageState=%7B%22TabType%22%3A1,%22TabContentType%22%3A2,%22SearchCriteriaForStandard%22%3A%7B%22TaxonomyIDs%22%3A%5B%5D,%22SelectedTypeAheadFilterOption%22%3Anull,%22Keyword%22%3A%22%22> (accessed May 23, 2014).
- Prevention, Centers for Disease Control and. Basic Statistics. February 12, 2014. <http://www.cdc.gov/hiv/basics/statistics.html> (accessed May 22, 2014).
- Center for Disease Control and Prevention. *HIV Among Women*. March 6, 2014. <http://www.cdc.gov/hiv/risk/gender/women/facts/index.html> (accessed May 22, 2014).

# IMPACT OF DEPRESSION

## on ART Adherence and Retention in Care

BY GLENN J. TREISMAN, MD, PHD

**I**n HIV-infected persons, depression can refer to the understandable psychological reaction to loss that results from the diagnosis (the Diagnostic and Statistical Manual of Mental Disorders [DSM] refers to this as an “Adjustment Disorder,” but we will use the term “demoralization”). It also can refer to an organically-based syndrome (the DSM term is “Major Depression”) with a combined prevalence as high as 57 percent. [American Psychiatric Association 2013; Treisman 2012; Treisman 2007; Harris 2008]

Left untreated, depression can complicate or compromise successful HIV treatment and prevention. Distinguishing between demoralization and major depression is important for successful treatment. Major depression, in particular, may be underdiagnosed in HIV-infected patients because symptoms such as decreased energy, weight change, sleep problems, or neurocognitive disturbance are similar to those of HIV infection, AIDS-related medical complications, and the adverse effects of some antiretroviral therapy (ART) medications. [Treisman 2012]

In addition, providers may mistake a patient’s major depression for demoralization as a result of their HIV diagnosis and not pursue treatment options. Even when HIV providers correctly diagnose major depression, referral to a psychiatrist is not always an option. This article discusses: 1) the impact of depression on HIV-infected persons, 2) the diagnosis of demoralization and major depression in HIV-infected patients, and 3) the approach to treatment of depression by HIV providers.

## Impact on ART Adherence

### ***How does depression affect ART adherence and retention in care in HIV-infected patients?***

Both major depression and demoralization can complicate or compromise HIV care. Patients with untreated depression are less likely to adhere to medications and keep medical appointments [Treisman 2012; Achappa 2013]; are more likely to discontinue ART [Kim 2007], drop out of HIV care [Pecararo 2013], and engage in high-risk sexual behavior and substance use [Treisman 2012; Wilson 2014; Taniguchi 2014]; and are more likely to experience greater morbidity and mortality with poor health care and poor health outcomes. [Ickovics 2001; Olatunji 2006] In particular, the severity of depressive symptoms in HIV-infected patients has been independently and significantly associated with lower CD4 counts. [Taniguchi 2014]

### **How to identify and differentiate depression in HIV-infected patients**

*Major depression*, sometimes referred to as biological or organic depression, is characterized primarily by persistent low mood accompanied by complaints of sadness or flatness of emotional tone, decreased energy, feelings of helplessness or despair, poor sleep with early-morning awakening and fatigue, poor concentration, memory impairment, other cognitive problems, and anhedonia (the inability to experience pleasure or satisfaction from things or activities that ordinarily would produce such responses). [Angelino 2001]

Anhedonia is the most sensitive and specific diagnostic indicator of major depression. [Treadway 2011] Major depression has been defined in the DSM as lasting at least two weeks with depressed mood. [American Psychiatric Association 2013; Treisman 2012] HIV providers can elicit these clinical

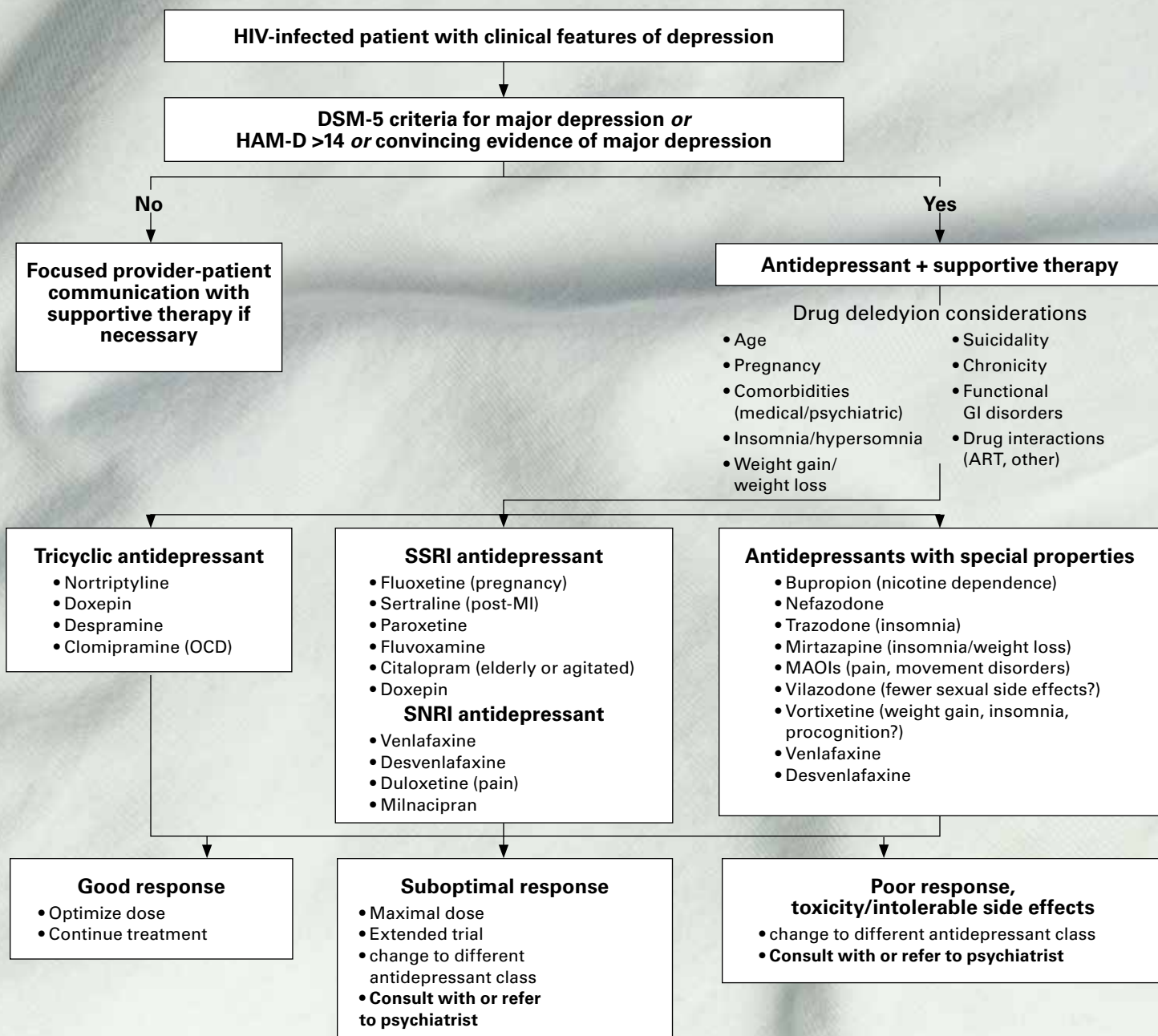
indicators of depression from patients during regular visits by asking about the following:

- Has your mood, energy, or feeling of being healthy changed?
- Has the pleasure, enjoyment, or satisfaction that you get from activities changed?
- Has the pattern of your sleep, level of energy, or ability to concentrate changed?
- Do you ever feel like a burden to others, have thoughts about death, or even wished you did not have to go on?

The psychiatric criteria for diagnosis of major depressive disorder have not changed from DSM-IV-TR to DSM-5, although “dysthymia” has been replaced by “persistent depressive disorder.” [American Psychiatric Association 2013] Persistent depressive disorder includes: 1) a depressed mood for most of the day, for more days than not, as indicated either by subjective account or observation by others, for at least two years, and 2) the presence while depressed of at least two of the following criteria: poor appetite or overeating, insomnia or hypersomnia, low energy or fatigue, low self-esteem, poor concentration or difficulty making decisions, and feelings of hopelessness for at least two months at a time. [American Psychiatric Association 2013]

*Demoralization* is a psychological reaction to life stresses. In contrast with major depression, demoralization generally presents with sadness that is specifically related to a particular event or circumstance, although some of the symptoms of major depression can be present, which can make it difficult to differentiate between them. In general, however, patients with demoralization report feeling fairly normal when distracted from thinking about the event or circumstance causing their distress, but, when reminded, they experience a welling up of sadness and overwhelming grief. Demoralization is a predictable response to an HIV diagnosis [Houston-Hamilton 2013] and tends to be transitory or intermittent. [American Psychiatric Association 2013]

Note that depressive symptoms can also be caused by some medical conditions including hypothyroidism, hypogonadism, CNS infections or neoplasms, HIV dementia, and substance use/dependence. In addition, certain medications such as efavirenz, raltegravir, interferon, beta-blockers, and steroids can cause depressive symptoms and thus may need to be changed or discontinued unless absolutely necessary for care. [Treisman 2012; Harris 2008].



Algorithm for treatment of depression in HIV-infected patients. Reprinted with permission, as adapted, from Watkins CC, Pieper AA, Treisman GJ (2011). Safety considerations in drug treatment of depression in HIV-positive patients. *Drug Safety*. 2011;34:623-639. Granted by Springer Special Licensing Department, April 7, 2014.

Screening tools and rating scales, such as the Hamilton Depression (HAM-D) Rating Scale, Beck Depression Inventory, Zung Depression Scale, Montgomery-Asberg Depression Rating Scale, and Patient Health Questionnaire-9, have proven useful for determining the level of depression before, during, and after antidepressant treatment and can be useful in screening patients for depression. The HAM-D can be administered by a psychiatric nurse or other provider with specific skills in this area and probes symptoms such as depressed mood, guilty feelings, suicidal ideations, sleep disturbances, anxiety levels and weight loss. The interview and scoring take only about 15 minutes. The HAM-D Rating Scale is available online at <https://outcometracker.org/library/HAM-D.pdf>.

## Treatment of depression in HIV-infected patients

Treatment of depression in HIV-infected patients is important and can improve ART adherence and retention in care, thus leading to better health outcomes for HIV patients. [Treisman 2012] In a meta-analysis of 29 studies, which included 12,243 persons living with HIV/AIDS, treatment of depression significantly improved ART adherence ( $P < 0.001$ ); the odds of adherence were 83 percent better among patients who were treated for depression. [Sin 2013] In addition, depression is associated with dropping out of HIV care; thus receiving mental health treatment for depression could lead to improved retention in HIV care. [Pecoraro 2013] HIV providers can initiate a course

of antidepressant therapy, possibly with cognitive behavioral and interpersonal therapies, for patients presenting with major depression. [Treisman 2007] All antidepressants have an approximately 60 percent response rate and appear to be equally effective, so antidepressant selection in HIV-infected patients should be based mainly on side effect profiles and drug-drug interactions. [Treisman 2012] Patients who do not respond can be referred for psychiatric evaluation.

It is important to differentiate between major depression and demoralization so that interventions with the greatest benefit can be selected for treatment. [Treisman 2007]

The primary requisite for implementing effective psychiatric treatment of major depression is the ability to recognize its characteristic signs and symptoms, which are often masked by those associated with other comorbidities commonly present in HIV-infected patients. Pharmacotherapy is the mainstay of treatment. [Watkins 2011]

Studies have shown that treatment of major depression with antidepressant medication increases viral suppression among HIV-infected persons, which is likely attributable to improved adherence to a continuum of HIV care, including increased uptake of and adherence to ART. [Tsai 2010] Antidepressant therapy has also been shown to improve adherence to ART directly in depressed HIV-infected patients. [Kumar 2009] In addition, antidepressant medication can be used to evaluate a depressed HIV-infected patient's readiness to begin and adhere to an ART regimen. An algorithm for the treatment of depressed HIV-infected patients is shown in the Figure. [Watkins 2011] This algorithm summarizes the

suitability of antidepressant classes and individual agents in different clinical settings.

In contrast, the greatest benefit for HIV-infected patients with demoralization will be derived from encouragement, supportive psychotherapy, and/or coaching, with referral to such services if necessary. [Treisman 2007]

## Conclusion

Major depression and demoralization are highly prevalent in HIV-infected patients. Accurate diagnosis and successful treatment of depression can improve ART adherence and retention in care, leading to better outcomes for HIV patients. Additional resources on depression for HIV providers include

- Depression and Mania in Patients with HIV/AIDS. October 2010. National Guideline Clearing House. Agency for Healthcare Research and Quality. U.S. Department of Health and Human Services. Available at: <http://www.guideline.gov/content.aspx?id=34265>
- Primary Care of Veterans with HIV. Depression. Neurology, Psychiatry, and Pain. April 2009. Available at: <http://www.hiv.va.gov/provider/manual-primary-care/depression.asp>.
- HIV & Mental Health. In: HIV Specialist. December 2013. Available at: [http://www.aahivm.org/HIV\\_Specialist/upload/FINAL%20PDF2.pdf](http://www.aahivm.org/HIV_Specialist/upload/FINAL%20PDF2.pdf)

HIV



### ABOUT THE AUTHOR:

**Glenn J. Treisman, MD, PhD** is Director of AIDS Psychiatry Services and Professor, Department of Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Baltimore, MD.

## References

- Achappa B, Madi D, Bhaskaran U, et al. Adherence to antiretroviral therapy among people living with HIV. *N Am J Med Sci*. 2013;53:220-223.
- American Psychiatric Association. Highlights of changes from DSM-IV-TR to DSM-5. 2013. American Psychiatric Publishing. Available at: <http://www.dsm5.org/Documents/changes%20from%20dsm-iv-tr%20to%20dsm-5.pdf>.
- Houston-Hamilton AH. Trauma & HIV. *HIV Specialist*. 2013;5:14-17.
- Harris M, Larsen G, Montaner JS. Exacerbation of depression associated with starting raltegravir: a report of four cases. *AIDS*. 2008;22:1890-1892.
- Ickovics R, Hamburger ME, Vlahov D, et al. Mortality, CD4 cell count decline, and depressive symptoms among HIV-seropositive women: longitudinal analysis from the HIV Epidemiology Research Study. *JAMA*. 2001;285:1466-1474.
- Kim TW, Palepu A, Cheng DM, et al. Factors associated with discontinuation of antiretroviral therapy in HIV-infected patients with alcohol problems. *AIDS Care*. 2007;19:1039-1047.
- Kumar V, Encinosa A. Effects of antidepressant treatment on antiretroviral regimen adherence among depressed HIV-infected patients. *Psychiatr Q*. 2009;80:131-141.
- Olatunji BO, Mimiaga MJ, O'Leary C, Safren SA. A review of treatment studies of depression in HIV. *Top HIV Med*. 2006;14:112-124.
- Pecoraro A, Royer-Malvestuto C, Rosenwasser B, et al. Factors contributing to dropping out from and returning to HIV treatment in an inner city primary care HIV clinic in the United States. *AIDS Care*. 2013;25:1399-1406.
- Sin NL, Dimatteo MR. Depression treatment enhances adherence to antiretroviral therapy: a meta-analysis. *Ann Behav Med*. 2013 Nov 14. [Epub ahead of print]
- Taniguchi T, Shacham E, Onen NF, et al. Depression severity is associated with increased risk behaviors and decreased CD4 cell counts. *AIDS Care*. 2014 Jan 30. [Epub ahead of print]
- Treadway MT, Zald DH. Reconsidering anhedonia in depression: lessons from translational neuroscience. *Neurosci Biobehav Rev*. 2011;35:537-555.
- Treisman GJ, Angelino AF, Hsu J. Depression. In: Gallant JE, ed. *Johns Hopkins HIV Guide 2012*. Burlington, MA; Jones & Bartlett Learning. 2012:124-127. [Available at: [http://books.google.com/books?id=nooCC0\\_5F0AC&pg=PA127&lpg=PA127&dq=Treisman+GJ,+Angelino+AF,+Hsu+J,+Depression.&source=bl&ots=e0QYiBSkKl&sig=ZC-y2HHm58aOrqJtWWChf66coaw&hl=en&sa=X&ei=mmHqUs-ZK8TQyAG-loGQDg&ved=0CDEQ6AEwAg#v=onepage&q=Treisman%20GJ%2C%20Angelino%20AF%2C%20Hsu%20J.%20Depression.&f=false](http://books.google.com/books?id=nooCC0_5F0AC&pg=PA127&lpg=PA127&dq=Treisman+GJ,+Angelino+AF,+Hsu+J,+Depression.&source=bl&ots=e0QYiBSkKl&sig=ZC-y2HHm58aOrqJtWWChf66coaw&hl=en&sa=X&ei=mmHqUs-ZK8TQyAG-loGQDg&ved=0CDEQ6AEwAg#v=onepage&q=Treisman%20GJ%2C%20Angelino%20AF%2C%20Hsu%20J.%20Depression.&f=false)]
- Treisman G, Angelino A. Interrelation between psychiatric disorders and the prevention and treatment of HIV infection. *Clin Infect Dis*. 2007;45(suppl 4):S313-S317.
- Tsai AC, Weiser SD, Petersen ML, et al. A marginal structural model to estimate the causal effect of antidepressant medication treatment on viral suppression among homeless and marginally housed persons with HIV. *JAMA Psychiatry*. 2010;67:1282-1290.
- Watkins CC, Pieper AA, Treisman GJ. Safety considerations in drug treatment of depression in HIV-positive patients. *Drug Saf*. 2011;34:623-639.
- Wilson PA, Stadler G, Boone MR, Bolger N. Fluctuations in depression and well-being are associated with sexual risk episodes among HIV-positive men. *Health Psychol*. 2014 Jan 27. [Epub ahead of print]

BY JOHN T. BROOKS, MD AND TIM McAFEE, MD

# TIME TO QUIT

**CDC anti-smoking campaign emphasizes importance of HIV patients avoiding tobacco**

**T**HIS MONTH CDC features an HIV-infected smoker as part of its highly successful anti-smoking campaign, “Tips From Former Smokers” which tells the stories of real people harmed by smoking ([www.cdc.gov/tips](http://www.cdc.gov/tips)).

At age 43, Brian, a smoker with well-controlled HIV infection and few other cardiovascular disease risk factors, experienced an ischemic stroke from severe carotid stenosis that required endarterectomy. “It took a stroke for me to actually stop smoking,” Brian told us. For months after the stroke, Brian had trouble speaking and reading. He couldn’t work or even dress himself. Today, his right hand remains weak so he can no longer work as a waiter or teach pottery classes.

Smoking is among the most prevalent problems affecting HIV-infected patients. CDC estimates that in 2009, 42 percent of HIV-infected Americans in care smoked cigarettes,<sup>1</sup> one of the highest rates reported for any subgroup. Smoking poses a special hazard to persons living with HIV infection. It inhibits effective CD4<sup>+</sup> T lymphocyte function<sup>2,3</sup> increasing susceptibility to infectious diseases, especially pulmonary infections.<sup>4,5</sup>

Additionally, emerging science finds that even in persons with well-controlled HIV infection, HIV also stimulates chronic immune activation.<sup>6</sup> This inflammatory state increases risk for a set of illnesses for which smoking is a well-established risk and that appear to be on the rise. These illnesses include cardiovascular disease, chronic obstructive pulmonary disease, low bone mineral density and associated fragility fracture, and a variety of non-AIDS-defining cancers of infectious etiology, notably of the lung, liver, anus, and oropharynx.<sup>7-11</sup> In other words, HIV infection adds to the risk for smoking-related illnesses, while smoking adds to the injury caused by HIV infection.

## Life Saving Care Squandered

For HIV-infected smokers, antiretroviral therapy shifts the risk of death dramatically away from HIV and towards smoking-related causes.<sup>12-14</sup> The hard-earned life-years gained from effective HIV treatment are squandered on cigarettes at great personal and societal cost. In this context, smoking cessation should be a priority for HIV-infected persons; in addition to achieving effective antiretroviral therapy, smoking

cessation could likely produce the greatest increase in quality and length of life.

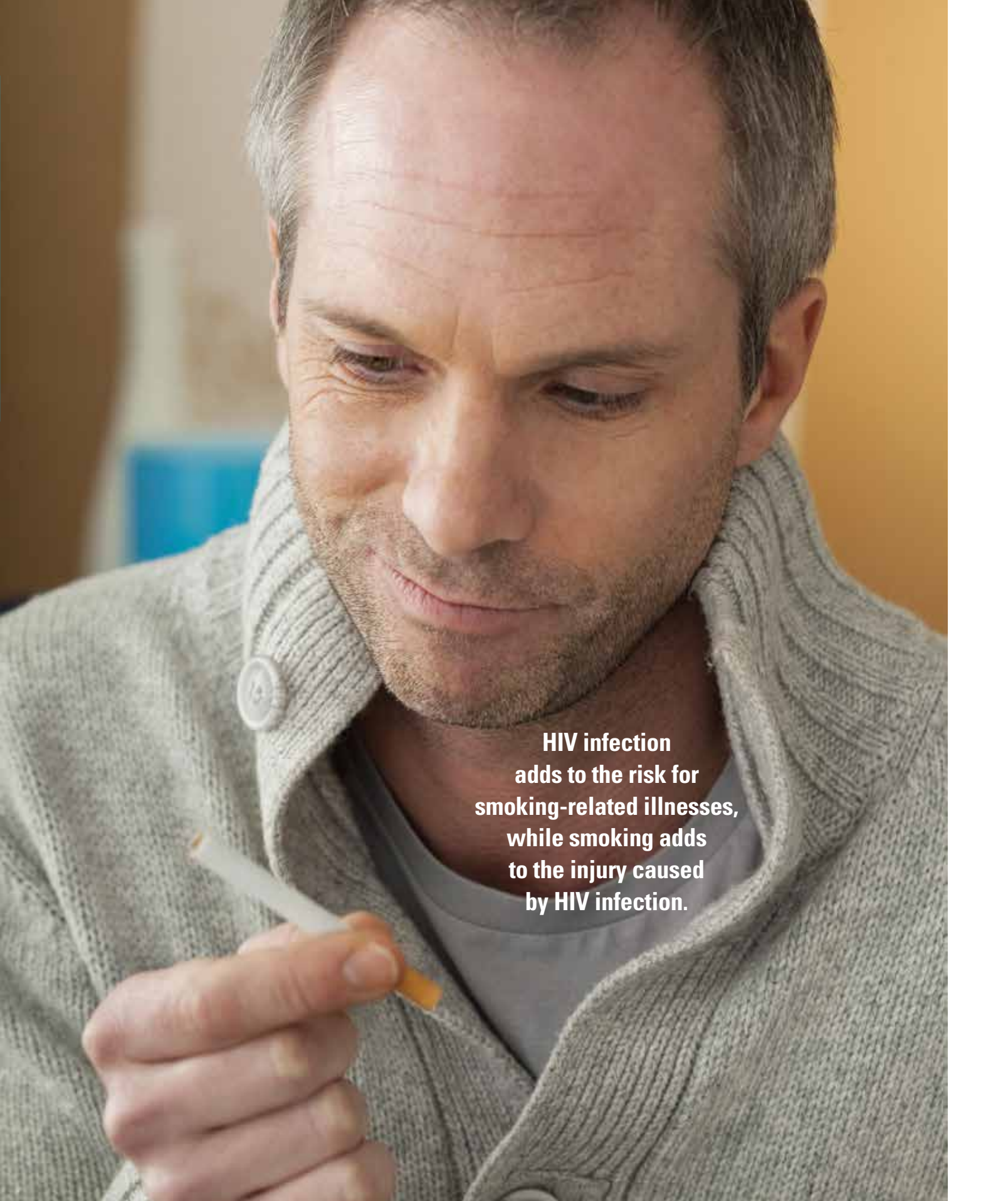
With the increased life expectancy now afforded by remarkable advances in care, the need and opportunity to address smoking cessation have grown. Smoking cessation has long been a cornerstone of primary care practice. We can take this extensive experience and build on it by tailoring interventions to the unique needs of HIV-infected



smokers. Progress has been mostly modest<sup>15</sup> but recent success with novel strategies<sup>16-18</sup> promises effective cessation programs for HIV-infected smokers are possible.

The current care model and work force for HIV infection are well suited to address smoking cessation. The frequency of care-related visits necessitated by HIV infection creates repeated opportunities to address smoking cessation, which benefits from repeated interventions and quit attempts.

HIV specialists have experience administering behavioral interventions, such as adherence and risk-reduction counseling, which is directly applicable to smoking cessation. For primary



**HIV infection  
adds to the risk for  
smoking-related illnesses,  
while smoking adds  
to the injury caused  
by HIV infection.**

care practitioners, who in the changing healthcare landscape are expected to take on more of routine management of HIV infection, smoking cessation is already part of basic good clinical practice. Reassuringly, the pharmacologic interventions available for smoking cessation are generally safe to use with antiretrovirals.

HIV-infected smokers may be more ready and willing to quit than we expect. In various surveys, 84 percent have expressed an interest in quitting, 40-60 percent have

contemplated quitting, and 70 percent have made at least one quit attempt.<sup>19,20</sup> After quitting, HIV-infected smokers

experience not only significant reduction in risk for pulmonary and cardiovascular diseases,<sup>21-23</sup> but significant improvement in HIV-related symptoms.<sup>24</sup>

There are multiple resources to help busy clinical practices help their patients quit, including a specific handbook for HIV-infected smokers produced by the Veterans Administration. ([http://www.va.gov/vhapublications/ViewPublication.asp?pub\\_ID=2826](http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2826))

For more information about the CDC stop smoking campaign and available resources, please visit [www.cdc.gov/tips](http://www.cdc.gov/tips).

The bad news is that markedly high rates of smoking are a major cause of excess morbidity and mortality in our HIV-infected patients. The good news is that there are straightforward clinical interventions that can help our patients successfully quit if we practice them systematically in the context of delivering care for HIV.

HIV



**Smoking cessation should be a priority for HIV-infected persons; in addition to achieving effective antiretroviral therapy, smoking cessation could likely produce the greatest increase in quality and length of life.**

## References

- 1 Mdofo, R., et al. *Cigarette smoking among HIV-infected adults: Medical Monitoring Project, US, 2009*. in *20th Conference on Retroviruses and Opportunistic Infections*. 2013. Atlanta, GA.
- 2 Wewers, M.D., et al., *Cigarette smoking in HIV infection induces a suppressive inflammatory environment in the lung*. *Am J Respir Crit Care Med*, 1998. 158(5 Pt 1): p. 1543-9.
- 3 Valiathan, R., et al., *Tobacco smoking increases immune activation and impairs T-cell function in HIV-infected patients on antiretrovirals: a cross-sectional pilot study*. *PLoS One*, 2014. 9(5): p. e97698.
- 4 Miguez-Burbano, M.J., et al., *Increased risk of Pneumocystis carinii and community-acquired pneumonia with tobacco use in HIV disease*. *Int J Infect Dis*, 2005. 9(4): p. 208-17.
- 5 Gordin, F.M., et al., *Pneumonia in HIV-infected persons: increased risk with cigarette smoking and treatment interruption*. *Am J Respir Crit Care Med*, 2008. 178(6): p. 630-6.
- 6 Hunt, P.W., *HIV and inflammation: mechanisms and consequences*. *Curr HIV/AIDS Rep*, 2012. 9(2): p. 139-47.
- 7 Crothers, K., et al., *HIV infection and risk for incident pulmonary diseases in the combination antiretroviral therapy era*. *Am J Respir Crit Care Med*, 2011. 183(3): p. 388-95.
- 8 Young, B., et al., *Increased rates of bone fracture among HIV-infected persons in the HIV Outpatient Study (HOPS) compared with the US general population, 2000-2006*. *Clin Infect Dis*, 2011. 52(8): p. 1061-8.
- 9 Miller, C.J., et al., *Adjudicated morbidity and mortality outcomes by age among individuals with HIV infection on suppressive antiretroviral therapy*. *PLoS One*, 2014. 9(4): p. e95061.
- 10 Wang, C.C., M.J. Silverberg, and D.I. Abrams, *Non-AIDS-defining malignancies in the HIV-infected population*. *Curr Infect Dis Rep*, 2014. 16(6): p. 406.
- 11 Hearps, A.C., et al., *Inflammatory comorbidities in HIV+ individuals: learning lessons from healthy ageing*. *Curr HIV/AIDS Rep*, 2014. 11(1): p. 20-34.
- 12 Lifson, A.R., et al., *Smoking-related health risks among persons with HIV in the Strategies for Management of Antiretroviral Therapy clinical trial*. *Am J Public Health*, 2010. 100(10): p. 1896-903.
- 13 Helleberg, M., et al., *Mortality attributable to smoking among HIV-1-infected individuals: a nationwide, population-based cohort study*. *Clin Infect Dis*, 2013. 56(5): p. 727-34.
- 14 Helleberg, M., et al. *Impact of smoking on life expectancy among HIV-infected individuals: The ART cohort collaboration*. in *21st Conference on Retroviruses and Opportunistic Infections*. 2014. Boston, MA.
- 15 Moscou-Jackson, G., et al., *Smoking-cessation interventions in people living with HIV infection: a systematic review*. *J Assoc Nurses AIDS Care*, 2014. 25(1): p. 32-45.
- 16 Vidrine, D.J., et al., *The influence of HIV disease events/stages on smoking attitudes and behaviors: project STATE (Study of Tobacco Attitudes and Teachable Events)*. *BMC Public Health*, 2014. 14: p. 149.
- 17 Vidrine, D.J., et al., *Efficacy of cell phone-delivered smoking cessation counseling for persons living with HIV/AIDS: 3-month outcomes*. *Nicotine Tob Res*, 2012. 14(1): p. 106-10.
- 18 Browning, K.K., et al., *Tobacco use and cessation in HIV-infected individuals*. *Clin Chest Med*, 2013. 34(2): p. 181-90.
- 19 Burkhalter, J.E., et al., *Tobacco use and readiness to quit smoking in low-income HIV-infected persons*. *Nicotine Tob Res*, 2005. 7(4): p. 511-22.
- 20 Benard, A., et al., *Tobacco addiction and HIV infection: toward the implementa-*



## Smoking Cessation Counseling Fundamentals

These effective counseling fundamentals to help patients stop smoking have been validated in numerous clinic-based trials over decades:

- Ensure that tobacco use status is routinely collected at clinic visits as a “vital sign”;
- Provide brief advice to patients encouraging quitting, ideally with tailoring to their circumstances;
- Determine interest in quitting, and if interested, provide assistance either in-office or by referral to community resources. Assistance can include brief counseling and cessation medications. If in-house resources are not available or acceptable, consider referring to 1-800-QUITNOW, which provides phone counseling in all 50 states as well as community referrals. If not interested, explore reasons for lack of interest. Regularly remind patients as needed that smoking adds to the harm caused by HIV, undermining the benefits of antiretroviral treatment; and
- As with other key aspects of HIV treatment, track smoking or quit status at follow-up visits, and provide support based on patient characteristics.

tion of cessation programs. *ANRS CO3 Aquitaine Cohort*. *AIDS Patient Care STDS*, 2007. 21(7): p. 458-68.

21 Lipodystrophy and dyslipidemia among patients taking first-line, World Health Organization–recommended highly active antiretroviral therapy regimens in western India. *Journal of Acquired Immune Deficiency Syndromes*. 39(2): p. 199-202.

22 Petoumenos, K., et al., *Rates of cardiovascular disease following smoking cessation in patients with HIV infection: results from the D:A:D study*(<sup>®</sup>). *HIV*

*Med*, 2011. 12(7): p. 412-21.

23 De, P., et al., *Systematic review and meta-analysis: influence of smoking cessation on incidence of pneumonia in HIV*. *BMC Med*, 2013. 11: p. 15.

24 Vidrine, D.J., R.C. Arduino, and E.R. Gritz, *The effects of smoking abstinence on symptom burden and quality of life among persons living with HIV/AIDS*. *AIDS Patient Care STDS*, 2007. 21(9): p. 659-66.

**DISCLAIMER:** *The findings and conclusions of this paper are those of the authors*

*and do not necessarily represent the views of the Centers for Disease Control and Prevention.*



#### ABOUT THE AUTHORS:

**John T. Brooks, MD** and



**Tim McAfee, MD** work in the Division of HIV/AIDS Prevention and the Office of

Smoking and Health, respectively, at the Centers for Disease Control and Prevention, Atlanta GA.

# Where's My Western Blot?

## What HIV Specialists Need to Know about Updated HIV Testing Recommendations

**O**N JUNE 26, 2014, CDC issued new guidelines, "Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations" (available at <http://www.cdc.gov/hiv/testing/lab/guidelines/index.html>). The new testing strategy represents a complete overhaul of the diagnostic algorithm for HIV testing in the United States.

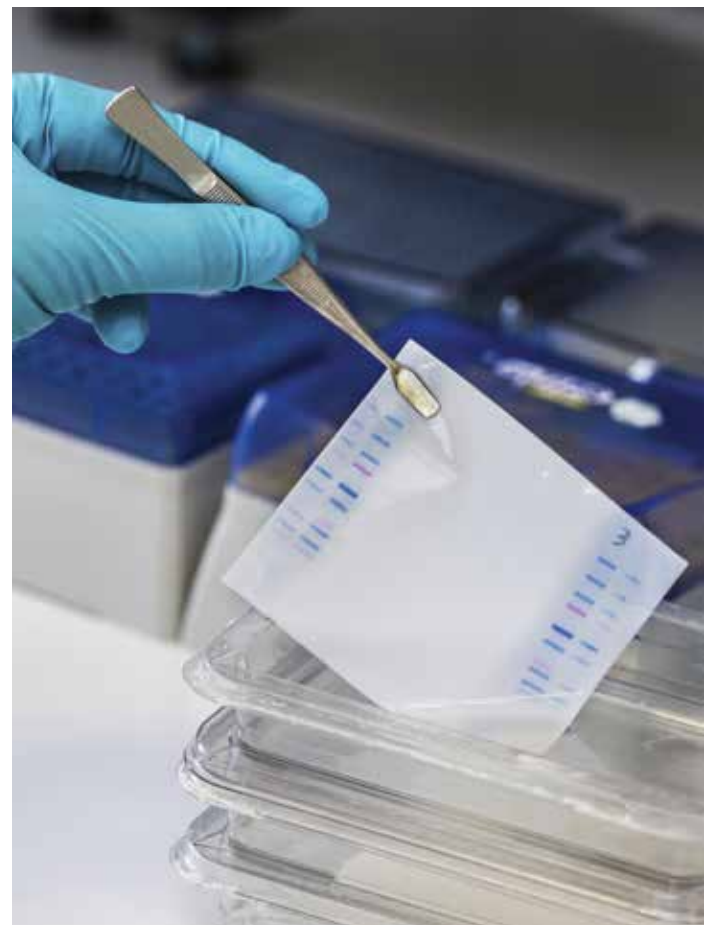
Since 1989, the diagnostic standard for serum or plasma specimens relied on initial screening with an antibody enzyme immunoassay, followed by validation of repeatedly reactive results using a more specific test such as HIV-1 Western blot or immunofluorescence assay (IFA). Clinicians often consider the Western blot to be the gold standard for HIV diagnosis, but many are not aware that the Western blot and IFA are both 1st generation assays that detect only IgG antibodies against HIV proteins.

All laboratories now screen for HIV with 3rd generation immunoassays, which detect IgM and IgG antibodies, or 4th generation immunoassays (available since 2010) which detect p24 antigen in addition to IgM and IgG antibodies. These immunoassays may become reactive as many as 25 days before the Western blot.<sup>1</sup> Thus, the Western blot is no longer adequate to confirm all specimens with true HIV infection. The HIV-1 Western blot also misclassifies as HIV-1 more than 60 percent of specimens from persons with HIV-2 infection.<sup>2,3</sup> Although HIV-2 is uncommon in the United States, its accurate identification is important, because first-line therapies for HIV-1 (including non-nucleoside reverse transcriptase inhibitors and some protease inhibitors) are ineffective against HIV-2.<sup>4</sup>

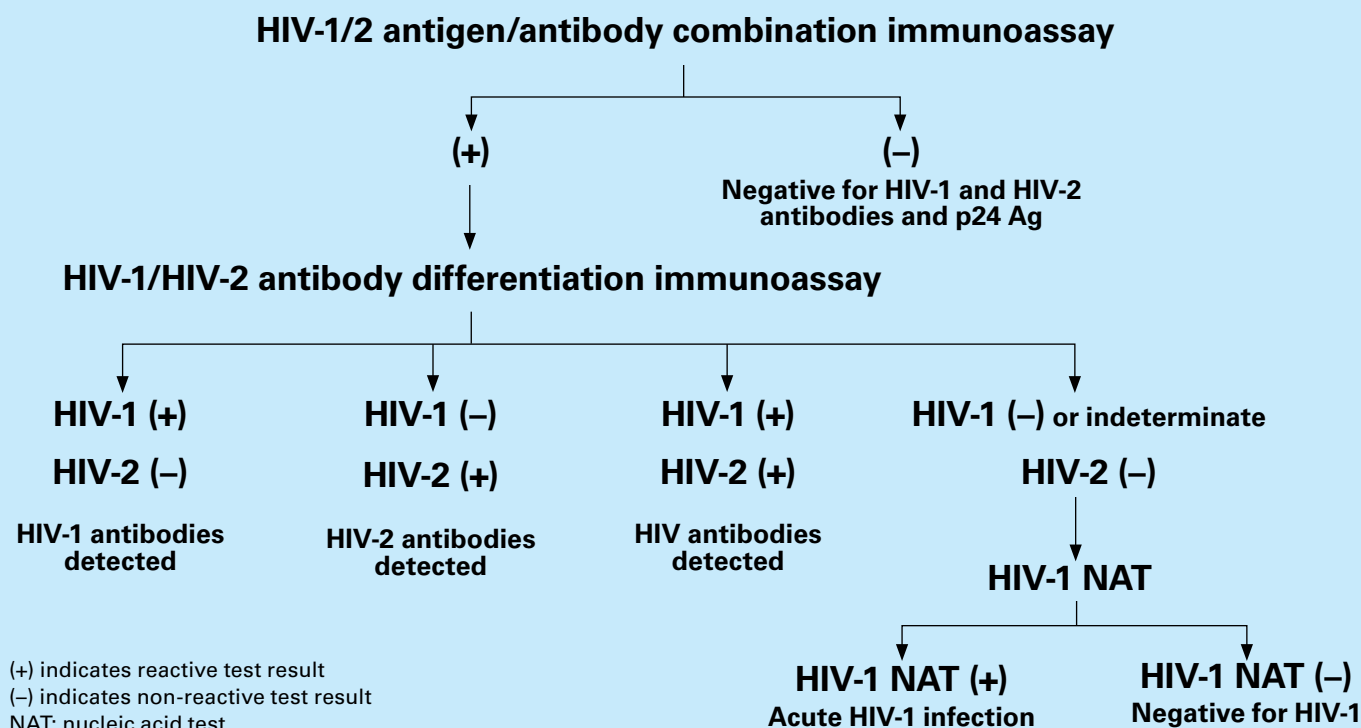
### The Updated Testing Algorithm

The new testing algorithm (Figure) begins with a combination 4th generation immunoassay that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen. All specimens reactive on this initial assay undergo supplemental testing with an immunoassay that differentiates HIV-1 from HIV-2 antibodies. Reactive results on both assays indicate HIV-1 or HIV-2 antibodies are present. Specimens that are reactive on the initial immunoassay and nonreactive or indeterminate on the second, antibody differentiation assay proceed to HIV-1 nucleic acid (RNA) testing.

Detectable HIV-1 RNA indicates acute HIV-1 infection; negative RNA results indicate that the initial immunoassay result was false-positive. The new diagnostic algorithm, developed and validated by CDC and the Association of Public Health Laboratories, no longer includes the Western blot.



# Updated Diagnostic Testing Algorithm for the Diagnosis of HIV Infection



It offers several advantages over previously recommended testing approaches, including:

- more accurate laboratory diagnosis of acute HIV-1 infection with equally accurate diagnosis of established HIV-1 infection,
- more accurate diagnosis of HIV-2 infection,
- fewer indeterminate results, and
- faster turnaround time for most test results.

## What Clinicians Need to Know

- As of June 27, 2014, the FDA has approved two 4th generation antigen/antibody combination assays (*Abbott Architect HIV Ag/Ab Combo* and *Bio-Rad GS HIV Ag/Ab Combo EIA*) and one HIV-1/HIV-2 antibody differentiation assay (*Multispot HIV-1/HIV-2 Rapid Test*) that are already used by many laboratories. Some laboratories offer both 3rd generation antibody-only assays (e.g., *Advia Centaur*, *Bio-Rad GS Plus O*, *Ortho Vitros*) and the 4th generation antigen/antibody combination assays. It is important to know which test your laboratory performs. Check the laboratory's specific ordering codes or procedures to obtain the recommended tests.
- Some laboratories have not yet adopted the updated algorithm and screen specimens with 3rd generation antibody assays followed by *Multispot*, HIV-1 Western blot, or IFA. The 3rd generation assays detect IgM antibodies, but *Multispot*,

Western blot, and IFA detect only IgG antibodies. Thus, if the initial antibody test is reactive and the second (antibody) test is negative or indeterminate, it is important to test for HIV RNA to rule out the possibility of acute HIV infection.

- Some 4th generation assays produce test results in as little as 30 minutes. The *Multispot* differentiation assay is a rapid test that can be performed by most laboratories in 30 minutes or less. Therefore, turnaround time for positive antibody test results will likely be much faster than with the Western blot. If RNA testing is necessary, the time to definitive results will be longer. Some labs request an additional specimen for RNA testing in the small number of specimens with discordant 4th generation (reactive) and *Multispot* (negative) test results.
- Current FDA-approved 4th generation assays do not distinguish whether antigen or antibody is causing the reactive result. Laboratories might also report reactive results on the initial (4th generation) immunoassay and negative *Multispot* antibody test results before RNA test results are available. This pattern might indicate the possibility of acute HIV infection, but it will more often represent a false-positive result from the initial immunoassay. The specificities of 4th generation HIV assays are >99.6%—which means that as many as 40 per 10,000 test results may be false-positive. In most populations of persons testing for HIV, the prevalence of acute HIV infection is 2 per 10,000 persons tested or less.

Thus, the frequency of false-positive immunoassay results usually far exceeds the prevalence of acute HIV infection.

- Currently, only one RNA assay, the *Aptima HIV-1 RNA Qualitative Assay*, is FDA-approved for HIV diagnosis, but it is available in far fewer laboratories than quantitative HIV-1 (viral load) RNA assays. To facilitate prompt diagnosis of acute HIV infection when faced with discordant screening and supplemental antibody test results, clinicians can order a viral load test to differentiate acute HIV-1 infection from false-positive initial immunoassay results.

Due to extensive cross-reactivity between HIV-1 and HIV-2 antibodies, a small number of specimens will produce *Multispot* results that are reactive for both HIV-1 and HIV-2 antibodies. Dual infection with HIV-1 and HIV-2 is very rare, and even in populations where HIV-2 is endemic, the majority of dually reactive specimens represent HIV-1 infection.<sup>5</sup> However, if the HIV-1 viral load conducted as part of the initial medical evaluation is undetectable, repeat antibody testing on a different specimen or further investigation of HIV-2 (with HIV-2 nucleic acid testing) might be warranted. Because HIV-2 RNA is undetectable in at least half of HIV-2 infected patients, testing for proviral HIV-2 DNA may be required for definitive diagnosis. No tests for HIV-2 RNA or DNA are FDA-approved, but such tests may be available from commercial laboratories, city or state public health laboratories, or CDC.

- The *Alere Determine Combo*, a rapid, single-use, combination antigen/antibody assay has also received FDA approval. Studies with plasma seroconversion panels suggest its sensitivity during early infection is similar to that of 3rd generation antibody assays (more sensitive than other currently available rapid tests, but less sensitive than laboratory-based 4th generation assays).<sup>6</sup> CDC recommends that specimens submitted after a preliminary positive rapid test (including the *Determine Combo* or *Multispot*, if it is used as an initial rapid test) be tested according to the updated algorithm (i.e., start with a 4th generation immunoassay and not an HIV-1 Western blot). Specimens that are negative on the initial laboratory 4th generation antigen/antibody combination immunoassay should be considered negative and require no further testing.

No test or testing algorithm can be completely accurate in all cases of HIV infection. Rare instances have been reported of persons who remained persistently negative for antibodies despite detectable HIV RNA. False-positive results have been attributed to specimen mix-up, mislabeling, and to autoimmune disorders. RNA is undetectable in approximately 3% to 5% of specimens submitted for testing that are antibody positive by Western blot.<sup>7,8</sup> Inconsistent or conflicting test results should be investigated with follow-up testing on a newly collected specimen—the test of time.

The new testing algorithm marks the beginning of a new era in HIV testing. The Western blot has been a stalwart for HIV diagnosis, but several evaluations have shown that the new algorithm detected more infections and produced

substantially fewer indeterminate results than testing based on the Western blot. Clinicians can download the updated recommendations with the rationale and review of the evidence upon which they are based, a 2-page quick reference guide, and suggested language for reporting of laboratory results at <http://www.cdc.gov/hiv/testing/lab/guidelines/index.html>. **HIV**

## Endnotes

- 1 Masciotra S, McDougal JS, Feldman J, Sprinkle P, Wesolowski L, Owen SM. Evaluation of an alternative HIV diagnostic algorithm using specimens from seroconversion panels and persons with established HIV infections. *J Clin Virol*. 2011;52 (Suppl 1):S17-22. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21981983>.
- 2 CDC. HIV-2 Infection Surveillance—United States, 1987-2009. *MMWR Morb Mortal Wkly Rep*. 2011;60:985-8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21796096>.
- 3 Torian LV, Eavey JJ, Punsalang AP, et al. HIV type 2 in New York City, 2000-2008. *Clin Infect Dis*. 2010;51:1334-42. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21039219>.
- 4 Ntemgwa ML, d'Aquin Toni T, Brenner BG, Camacho RJ, Wainberg MA. Antiretroviral drug resistance in human immunodeficiency virus type 2. *Antimicrob Agents Chemother*. 2009;53:3611-9. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19470514>.
- 5 Bonney EY, Sackey ST, Brandful JA. Laboratory diagnosis of dual HIV-1/HIV-2 infection in Ghanaian patients. *East Afr Med J*. 2008;85:537-43. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19413206>.
- 6 Masciotra S, Luo W, Youngpairoj AS, et al. Performance of the Alere Determine HIV-1/2 Ag/Ab Combo Rapid Test with specimens from HIV-1 seroconverters from the US and HIV-2 infected individuals from Ivory Coast. *J Clin Virol*. 2013;58 Suppl 1:e54-8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23911678>.
- 7 Owen SM, Yang C, Spira T, et al. Alternative algorithms for human immunodeficiency virus infection diagnosis using tests that are licensed in the United States. *J Clin Microbiol*. 2008;46:1588-95. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18322061>.
- 8 Patel P, Mackellar D, Simmons P, et al. Detecting acute human immunodeficiency virus infection using 3 different screening immunoassays and nucleic acid amplification testing for human immunodeficiency virus RNA, 2006-2008. *Arch Intern Med*. 2010;170:66-74. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20065201>.

**DISCLOSURE:** The findings and conclusions in this article are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention. Trade names are used for identification purposes only, and do not represent an endorsement by the Department of Health and Human Services or the Centers for Disease Control and Prevention.



### ABOUT THE AUTHOR:

**Bernard M. Branson, M.D.** is Associate Director for Laboratory Diagnostics in the Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention at the Centers for Disease Control and Prevention in Atlanta, Georgia.



# Letter from the CDC

MAY 14, 2014

**Dear Health Care Provider,**

**T**HIS LETTER is to communicate that CDC and the U.S. Public Health Service today released new clinical guidelines recommending health care providers consider prescribing pre-exposure prophylaxis (PrEP) for patients at substantial risk for HIV. The strategy of providing daily oral antiretroviral drugs continuously to uninfected individuals prior to HIV exposure, known as PrEP, has been shown to reduce HIV acquisition among all populations at high risk.

The new guidelines were developed by CDC in close partnership with health care providers like you, public health experts, community leaders and other federal agencies. The guidelines recommend that providers consider PrEP as a prevention option for patients who meet specified risk criteria. They also underscore the importance of counseling that covers adherence and HIV risk reduction and recommend regular monitoring of HIV status, side effects and toxicities, and risk behaviors.

More specifically, the guidelines recommend PrEP for HIV-uninfected patients with any of the following indications:

- Is in an ongoing relationship with an HIV-infected partner.
- Is not in a mutually monogamous relationship with a partner who recently tested HIV-negative, and who is:
  - A gay or bisexual man who has had sex without a condom or been diagnosed with a sexually transmitted infection within the past six months.
  - A heterosexual man or woman who does not regularly use condoms when having sex with partners known to be at risk for HIV (for example, injecting drug users or bisexual male partners of unknown HIV status) or whose partners are from communities with high rates of HIV infection.
- Has injected illicit drugs within the past six months and has shared equipment or been in drug treatment within the past six months.

For sexually-active people, since no prevention strategy is 100% effective, the guidelines also recommend that physicians encourage patients to use PrEP with other proven prevention strategies such as condoms to provide even greater protection than when used alone.

CDC issued interim guidance in 2011, 2012 and 2013 as trial results on PrEP within various populations became available. These new guidelines replace the interim guidance and are the first to offer detailed and comprehensive clinical guidance on PrEP for both sexual and injecting drug use.

The new guidelines also include a providers' supplement with additional materials and tools for clinicians who prescribe PrEP. Materials include a checklist for providers to use in discussions with patients, fact sheets to help providers and patients increase their knowledge about PrEP and a risk assessment tool.

The guidelines published today are an important step forward in the fight against HIV as they give health care providers on the front lines of this epidemic the information needed to effectively deliver this powerful new prevention tool. With 2.7 million new infections estimated to occur each year worldwide—and approximately 50,000 in the United States—safe and effective new approaches to prevent HIV are urgently needed.

PrEP has the potential to alter the course of the U.S. epidemic, if targeted to populations in need and used as directed. In fact, CDC estimates that as many as 275,000 uninfected gay men and 140,000 discordant heterosexual couples could benefit from this intervention.

Ultimately the role of PrEP in preventing new HIV infections will depend on: its acceptability to users; how effectively it is delivered by health care providers, including support for patients to achieve high medication adherence and prevent increases in risk behavior; and access to the drug by those at substantial risk of HIV.

As a clinician, you play a critical role in helping to realize the promise of PrEP for HIV prevention in the United States. Research shows that the doctor-patient relationship is a powerful one—what you say to your patients can have a great impact on their behaviors and health care choices.

Starting today, there are several key steps you can take to help expand uptake of PrEP and help address some of the practical issues for its effective delivery. These include:

- Prescribing PrEP to those patients with indications for its use
- Increasing awareness of this safe and effective HIV prevention intervention
- Creating an open dialogue with patients to screen for behaviors that may result in HIV acquisition, communicate prevention messages and reinforce safer behaviors
- Communicating to patients in HIV-discordant relationships that PrEP is an available option for the HIV-negative partner

The new guidelines and clinical providers' supplement are published in full at <http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf> and <http://www.cdc.gov/hiv/pdf/guidelines/PrEPProviderSupplement2014.pdf>.

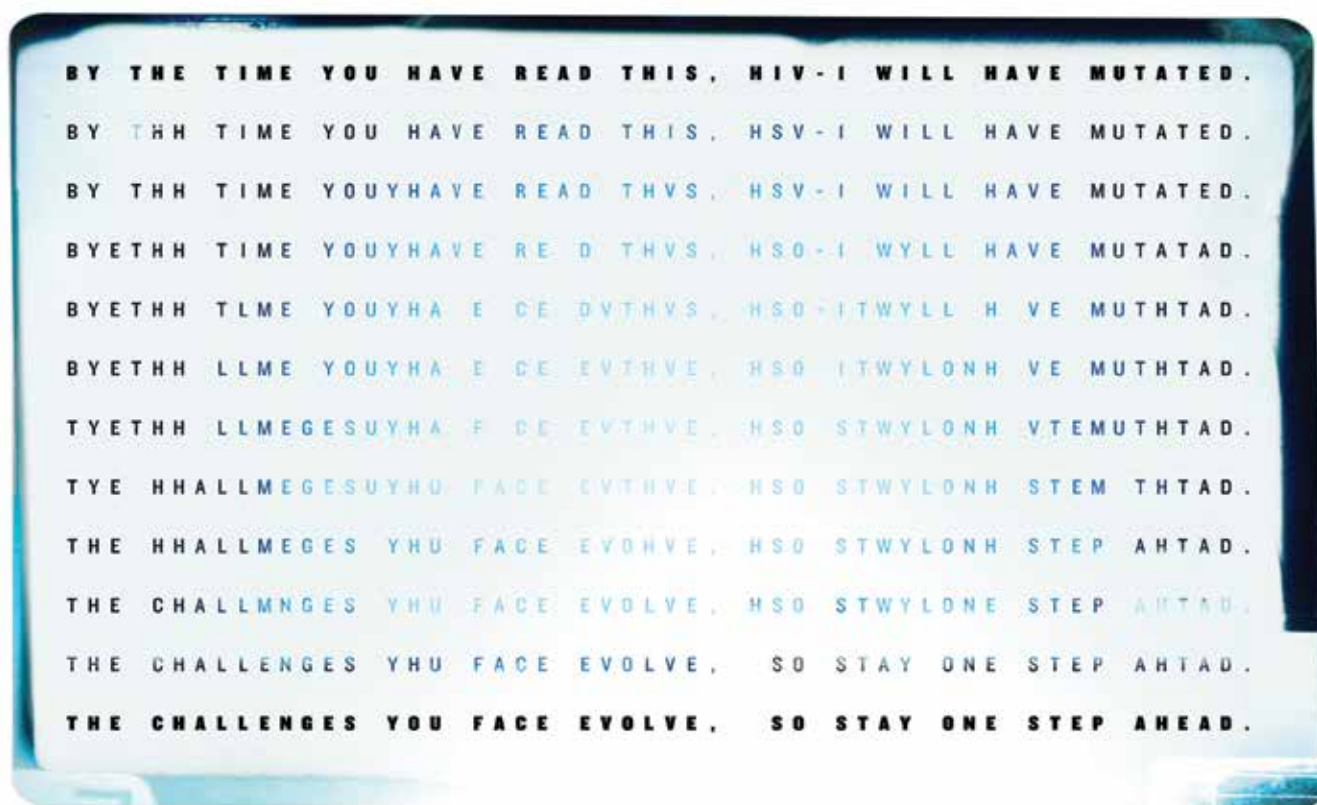
For more information on efforts around PrEP implementation in the United States, visit [www.cdc.gov/hiv/prevention/research/prep/](http://www.cdc.gov/hiv/prevention/research/prep/). CDC will also present Public Health Grand Rounds on PrEP for Prevention of HIV on Tuesday, May 20 at 1:00 PM EDT.

Your role in ensuring PrEP is delivered effectively is crucial. We trust that these guidelines will give you the information and confidence you need to prescribe and support PrEP use for patients who meet the risk criteria.

Sincerely,

**RAHM KENNETH G. CASTRO, M.D.**  
Commanding Flag Officer,  
CDC/ATSDR Commissioned Corps  
Acting Director, Division of HIV/AIDS Prevention  
NCHHSTP  
Centers for Disease Control and Prevention

**AMY LANSKY, PH.D., M.P.H.**  
Deputy Director for Surveillance,  
Epidemiology and Laboratory Sciences  
Division of HIV/AIDS Prevention  
National Center for HIV/AIDS  
Viral Hepatitis, STD, and TB Prevention  
Centers for Disease Control and Prevention



Rapidly mutating HIV-1 virus can continue to evade quantification with a single target viral load assay. The innovative Dual Target HIV-1 assay from Roche Molecular Diagnostics measures two unique regions of the HIV-1 genome, which are not subject to selective drug pressure. Therefore, drug-induced mutations should not impact the assay's ability to detect and quantify the virus accurately. In turn, more accurate results drive better decisions for a positive impact on patients' lives.

Visit us at <http://molecular.roche.com> and ask for more information about the COBAS® AmpliPrep/ COBAS® TaqMan® HIV-1 Test, v2.0.