*Chronic Obstructive Pulmonary Disease in HIV and Aging

- In the absence of data on the treatment of chronic obstructive pulmonary disease (COPD) specifically in the setting of HIV infection, current therapy of COPD in HIV-infected persons should follow the management guidelines proposed for HIV-uninfected patients. HIV-infected persons have an increased risk for several non-infectious pulmonary conditions including chronic obstructive pulmonary disease (COPD). COPD can present at younger ages in HIV-infected compared to HIV-uninfected patients (Crothers et al. 2011). HIV infection, particularly in the presence of a high viral load, appears to be associated with COPD (Drummond et al. 2011), and lung function decline may be accelerated in patients with high viral load and low CD4 cell counts (Drummond et al. 2013). As in HIV- uninfected persons, cigarette smoking is a major risk factor for COPD among HIV- infected individuals. However, HIV infection is associated with an increased risk for COPD independent of smoking, drug abuse, and opportunistic infections (Crothers et al. 2006; Diaz et al. 2000).

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According to the Global Initiative for Chronic Obstructive Lung Diseases, COPD is "characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases" (GOLD 2014) The major risk factor for COPD is cigarette smoking, but occupational and environmental exposures also contribute. Prior bacterial pneumonia and Pneumocystis pneumonia are associated with airflow obstruction on pulmonary function testing (Morris et al. 2000), and may play an important role in the risk and progression of COPD in HIV-infected persons.

COPD can occur at any CD4 cell count or HIV viral load in HIV-infected persons. However, the risk of COPD was increased in HIV-infected persons with a high viral load (>200,000 copies/ml) after adjusting for antiretroviral therapy (ART) use (Drummond et al 2012). COPD may progress more rapidly in HIV-infected persons with poorly controlled HIV. Amongst HIV-infected injection drug users, the rate of decline in the forced expiratory volume in one second (FEV1) and the forced vital capacity (FVC) was accelerated in patients with high HIV viral load (defined as >75,000 copies/ml) and with low CD4 cell count (defined as <100 cells/µl), when compared to patients with better controlled HIV disease and to those without HIV infection (Drummond et al, 2013).

The diagnosis of COPD should be suspected in patients who have chronic cough or sputum production, dyspnea, and/or exposure to risk factors for the disease (GOLD 2014). The diagnosis of COPD requires spirometry, preferably with bronchodilator testing to demonstrate fixed airflow obstruction; the definition of fixed airflow obstruction requires that the ratio of

the forced expiratory volume in one second (FEV1) to the forced vital capacity (FVC) be less than 70%, or less than 95% of the lower limit of normal, in association with an FEV1 of less than 80% of predicted (GOLD 2014). Among older patients, using a threshold of the FEV1/FVC of less than 95% of the lower limit of normal is preferred, as this results in fewer false-positive diagnoses of COPD (Hankinson et al. 1999). Screening spirometry to detect COPD in asymptomatic populations is generally not recommended (Lin et al. 2008), although studies have not addressed screening in HIV-infected populations.

In HIV-infected patients with chronic respiratory symptoms, health care providers should obtain spirometry. Complete pulmonary function testing including measurement of diffusing capacity should also be considered, as HIV-infected patients may be particularly likely to have a decrease in diffusing capacity despite relatively normal spirometry (Gingo et al. 2010). Indeed, HIV-infected persons have an increased risk of a low diffusing capacity, defined as <60% predicted normal, compared to uninfected persons after adjusting for smoking and other risk factors (Crothers et al. 2013, Fitzpatrick et al. 2013). A decreased diffusing capacity suggests the presence of emphysema or other disease processes that interfere with normal gas exchange within the lung.

In the absence of data on the treatment of COPD specifically in the setting of HIV infection, current therapy of COPD in HIV- infected persons should follow the management guidelines proposed for HIV- uninfected patients (GOLD 2014, Qaseem et al. 2011). In general, therapy is initiated for symptomatic COPD patients with inhaled bronchodilators. For patients who have regular symptoms and an FEV1<60% of predicted, monotherapy with a long acting inhaled beta-agonist or anticholinergic is recommended; combination therapy may also be considered (Qaseem et al. 2011). Inhaled steroids are generally reserved for patients with more severely impaired lung function (FEV1 less than 50% predicted) and who also have frequent yearly exacerbations (Qaseem et al. 2011).

Special consideration should be given to a few key aspects of COPD management for HIV-infected patients. As with HIV- uninfected patients, smoking cessation should be prioritized. HIV-infected patients should also be monitored for potential complications and interactions between COPD medications and antiretroviral therapy. Protease inhibitors, particularly ritonavir, have been reported to increase systemic levels of inhaled or intranasal fluticasone. Cushing's syndrome or adrenal suppression may result when corticosteroids are tapered (Soldatos et al. 2005; St Germain et al. 2007). The use of high-dose inhaled corticosteroids also requires careful monitoring, as inhaled corticosteroids are associated with increased risk of oral candidiasis, bacterial pneumonia, (Calverley et al. 2007, Drummond et al. 2008) and tuberculosis (Brassard et al. 2011). The regular use of systemic steroids should preferably be avoided. Given the potential complications associated with steroids, additional studies on the efficacy and/or effectiveness and safety of these medications in HIV-infected persons with COPD are needed.

In addition, COPD is associated with several comorbidities that may particularly complicate care of elderly patients. These include cardiovascular disease, muscle wasting, osteoporosis, malnutrition, depression, anxiety and lung cancer (Nazir & Erbland, 2009). Providers should review vaccination records with their HIV-infected patients to ensure that all patients have

received the recommended pneumococcal and yearly influenza vaccine.

HIV-infected patients with COPD should be considered for participation in pulmonary rehabilitation programs. Lung disease may be an important determinant contributing to poor physical function in HIV-infected persons. Among HIV-infected Veterans, chronic obstructive lung disease (COPD and/or asthma) was among the top comorbid conditions independently associated with self-reported increased physical disability (Oursler et al. 2006). Airflow limitation, as reflected by a low FEV1 is also associated with decreased 6-minute walk distance in HIV-infected patients (Campo et al. 2014, in press)8.

In studies of HIV-uninfected patients with COPD, physical functioning is significantly improved with participation in pulmonary rehabilitation programs (Nici et al. 2006). In general, pulmonary rehabilitation programs should be prescribed in COPD patients who are symptomatic with an FEV1<50% predicted (Qaseem et al. 2011). Studies support the safety and potential benefit of exercise training in HIV-infected patients (O'Brien et al. 2010) although further studies are needed to determine the role and optimal type of exercise training in HIV- infected patients, particularly older patients with concomitant comorbid diseases such as COPD.

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