Background:
Vaccination is the most important preventive strategy against influenza, however post-vaccination antibody responses are often suboptimal especially among HIV-infected (HIV+) persons. Vitamin D deficiency is prevalent among HIV+ adults, and low 25-hydroxyvitamin D (25(OH)D) levels may adversely affect vaccine immunogenicity. We evaluated the association between 25(OH)D levels and post-influenza vaccination responses. We conducted a prospective cohort study evaluating the immunogenicity of monoclonal influenza A (H1N1) vaccine among HIV+ and HIV- adults (18-50 years of age) during the 2009-2010 influenza season. Antibody titers were evaluated at baseline, day 28, and month 6 after vaccination. GMTs at day 28 (269 vs. 80, p=0.0045) and 6 months (113 vs. 20, p=0.0002) post-vaccination were significantly higher among uninfected persons compared with HIV+ persons. GMTs among HIV+ persons decreased with increasing BMI but not among HIV- persons. Hence, this study found that use of vitamin D supplementation at the time of vaccination for any subsequent vaccination may improve immune responses. Three studies have examined vitamin D and influenza vaccine responses. In two studies, no significant relationship between baseline 25(OH)D levels and vaccine antibody responses were found [10,11]. A third study that used vitamin D supplementation at the time of influenza vaccination had no effect on post-vaccination antibody levels [12]. Since only one of these studies had a HIV-negative group, each involved differing influenza seasons, and none evaluated long-term post-vaccination responses (responses were measured at 3-6 weeks), further research is needed.

Methods:
Study Design:
The study evaluated vitamin 25(OH)D levels among HIV-infected and HIV-uninfected adults and the potential relationship with influenza vaccine immunogenicity. The study was conducted at the Naval Medical Research Center, Silver Spring, MD USA; The Institute of Human Virology, University of Maryland School of Medicine, Baltimore, MD USA; the University of Miami, Miami, FL USA; and the Department of Defense Medical Research and Development Program, Silver Spring, MD USA. Study Procedures:
Serum samples were collected at baseline (day 0, just prior to vaccination), day 28 (± 4 days), and 6 months (+/- 2 weeks) post-vaccination for influenza-specific antibody responses. The inclusion criteria were: aged 18-50 years, HIV-infected (World Health Organization stage 3-4, Karnofsky performance status >80), uninfected, BMI >18, ≤36, no active infection or malignancy, and no history of influenza vaccination within the past 6 months. The primary outcome was the GMTs at day 28 and month 6 for the hemagglutination inhibition (HAI) test.

Statistical Analyses:
Baseline characteristics (Table 1) were compared among the HIV-infected and HIV-uninfected groups using Student’s t-tests for continuous variables and χ2 tests for categorical variables. Baseline characteristics were adjusted for age and BMI using linear and regression models, respectively. The association between baseline 25(OH)D levels and GMTs at day 28 and month 6 was assessed using linear regression analyses. Regression analyses for each outcome were conducted in two models: without and with adjustment for BMI. A p-value <0.05 was considered statistically significant. This study was conducted at the Naval Medical Research Center, Silver Spring, MD USA. Acknowledgments: This work was supported by the Intramural Research Development Program (IRDP). G.S. is an intramural employee of the Intramural Research Program. A. B. is a principal investigator at the National Institute of Allergy and Infectious Diseases. The authors are grateful to the staff at the participating institutions for collecting biological samples and coordinating the research activities. The data reported here have not been subjected to Department of Defense, Department of Health and Human Services, or public health review. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the US Department of Health and Human Services, the US Department of Defense, or the views of the Army, Air Force, or Navy. This study has been funded by grants or contracts from the National Institute of Allergy and Infectious Diseases, the Department of Defence, and the Department of Health and Human Services. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.