Multimorbidity Patterns in HIV-Infected Patients: The Role of Obesity in Chronic Disease Clustering

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Background: Increases in multimorbidity and obesity have been noted in HIV-infected populations in the current treatment era. Patterns of multimorbid disease clustering and the impact of obesity on multimorbidity are understudied in this population.

Methods: We examined obesity and multimorbidity patterns among 1844 HIV-infected patients in the UAB 1917 Clinic. Exploratory factor analysis was used to identify the underlying factor structure responsible for clustering. Patterns among the resulting morbidity factors by body mass index (BMI) category were explored. Multivariable logistic regression models were fit to identify predictors of multimorbidity cluster patterns.

Results: The prevalence of multimorbidity was 65% (1205/1844). Prevalence increased with progressive BMI categories from underweight (64%) to obese (79%). Three multimorbidity clusters were identified: "metabolic," including hypertension, gout, diabetes mellitus, and chronic kidney disease (range, 0.41–0.84; $P < 0.001$); "Behavioral," including mood disorders, dyslipidemia, chronic obstructive pulmonary disease, chronic ulcer disease, osteoarthritis, obstructive sleep apnea, and cardiac disorders (range, 0.32–0.57; $P < 0.001$); "Substance Use," including alcohol abuse, substance abuse, tobacco abuse, and hepatitis C (range, 0.53–0.89; $P < 0.001$). Obesity was associated with increased odds of multimorbidity (obese vs. normal BMI category: OR = 1.52, 95% CI: 1.15 to 2.00).

Conclusions: Three patterns of disease clustering were identified. Obesity was associated with a higher likelihood of multimorbidity. The management of multimorbidity and obesity will need to be addressed in future clinical practice guidelines to enhance long-term outcomes of HIV-infected patients in the current treatment era.

Key Words: multimorbidity, obesity, HIV, factor analysis, tetrachoric

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INTRODUCTION

Effective antiretroviral therapy (ART) has significantly prolonged the life expectancy of people living with HIV/AIDS.[1] Estimates indicate that by 2015, more than 50% of HIV-infected patients will be older than the age of 50 years.[2] Multimorbidity, defined as the co-occurrence of 2 or more chronic conditions, is increasingly common in the aging population. In non–HIV-infected populations, the presence of multimorbidity has significant clinical implications because of its association with decreased functional status and quality of life, and increased adverse drug events, medical costs, disability, and mortality.[3–7] Few studies have addressed the issue of multimorbidity in HIV-infected patients.

Another emerging and understudied issue in contemporary HIV care is obesity.[8] In our practice setting, we found that 45% of patients were either overweight [body mass index (BMI) of 25–29.9 kg/m^2] or obese (BMI >30 kg/m^2) before initiation of ART, consistent with results obtained from similar studies done in other demographic regions of the United

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States.[9] Overweight or obese status confers increased risks for chronic conditions, such as hypertension (HTN), cardiovascular disease, and diabetes, potentially adding significantly to the disease burden of an HIV-infected person.[8,10,11]

To explore the impact of obesity on multimorbidity and to determine its effect on disease clustering among HIV-infected patients, we sought to (1) use exploratory factor methods to identify patterns of multimorbidity in HIV-infected patients,[5] (2) characterize the resulting factor patterns by BMI category, and (3) determine the association between obesity and the likelihood of having conditions in more than one factor group (which for the purposes of this study was defined as "multimorbidity") while controlling for other sociodemographic and clinical variables. We hypothesized that multimorbidity disease clusters would be identified and that increasing BMI would be associated with a higher risk of multimorbidity.

METHODS

Data were obtained from the University of Alabama at Birmingham (UAB) 1917 HIV/AIDS Clinic Cohort Observational Database Project, an ongoing Institutional Review Board (IRB)–approved clinical cohort study. The UAB 1917 Clinic Cohort database includes detailed sociodemographic, psychosocial, and clinical information from more than 6000 HIV-infected patients dating back to 1988. Currently, more than 1900 patients receive primary and subspecialty HIV care at the clinic. The UAB 1917 Clinic uses a locally developed electronic health record (EHR) that imports all laboratory values from the central UAB laboratory, requires electronic prescription for all medications, and contains detailed provider encounter notes. The EHR and database are quality controlled, with all provider notes reviewed to ensure appropriate data capture regarding changes (additions or deletions) in diagnoses, allergies, and medications, including start and stop dates for antiretroviral and all other prescribed medications. New and ongoing diagnoses are maintained in patients' active problem lists, whereas resolved diagnoses discontinued by providers are removed from active problem lists and remain part of patients' electronic records. The UAB IRB approved this cross-sectional retrospective study nested in the UAB 1917 Clinic Cohort.

PARTICIPANTS

We retrieved data from 1844 HIV-infected patients who attended a primary HIV care visit at the 1917 Clinic between July 1, 2010 and June 30, 2011. Inclusion criteria were (1) aged 19 years or older, (2) currently receiving ART, with (3) plasma HIV viral load (VL), CD4 count, height, and weight measured between June 31, 2010 and July 1, 2011. All data were acquired through queries (MS SQL) of the electronic database.

GENERATION OF DIAGNOSIS LIST

An initial list of 28 common non-AIDS–related chronic conditions was compiled after review of contemporary multimorbidity literature in both the general and HIV-infected populations.[1,5,12] Three providers (M.J.M, J.L.R, and J.H.W) reviewed this initial list for relevance and clinical significance to HIV-infected patients. When possible, diagnoses were collapsed into related groups (eg, mania, bipolar disorder, and depression were collapsed under the term "mood disorders"). In addition, we combined individual diagnoses with a prevalence of less than 2% into groups (eg, chronic ischemic heart disease, cardiac insufficiency, and myocardial infarction were grouped as "cardiac disorders"). A patient was considered to have a condition if the diagnosis was ever entered in the EHR. Because empty cells adversely affect the factor modeling of correlations among categorical variables, conditions otherwise not collapsed into larger diagnosis groups were excluded from analyses if present in less than 2% of our study sample. Table 1 displays the final list of conditions (n = 15) included in the factor analysis model.

Independent Variables

Patient-level sociodemographic and laboratory information included age, gender, race (white, non-white), HIV transmission risk factor (heterosexual, men who have sex with men, or intravenous drug use), health insurance status (public, private, or uninsured), most recent plasma HIV VL, CD4 count, and BMI (weight in kilograms per height in square meters). Patients were grouped into 4 different BMI categories according to the National Institute of Health criteria: underweight (BMI <18.5 kg/m^2), normal weight (BMI = 18.5–24.9 kg/m^2), overweight (BMI = 25–29.9 kg/m^2), and obese (BMI ≥ 30 kg/m^2).[13] Race and gender were subsequently modeled as a 4-level interaction term (white males/females; non-white males/females).

TABLE 1. Prevalence of Conditions in Descending Order for 1844 HIV-Infected Patients Receiving Care at the UAB 1917 Clinic as of July 1, 2011

Condition	Prevalence (%)
Mood disorders*	48
Tobacco abuse/dependence	43
HTN	40
Dyslipidemia	36
Osteoarthritis	26
Substance abuse/dependence†	26
Alcohol abuse/dependence	15
Hepatitis C	12
Chronic Obstructive Pulmonary Disease	12
Ulcer disease‡	11
Diabetes mellitus	9
Chronic kidney disease	7
Cardiac disorders§	7
Obstructive sleep apnea	4
Gout	2

*Hypomania, mania, depression, cyclothymia, mood disorder, bipolar disorder, and dysthymia.

†Cocaine, heroin, methamphetamine, LSD, opioid abuse, and marijuana.

‡Gastroesophageal reflux disease, chronic duodenal ulcer, gastric ulcer, and peptic ulcer disease.

§Chronic ischemic heart disease, cardiac insufficiency, and myocardial infarction.

Dependent Variables

The primary outcome was multimorbidity, defined in our study as the presence of at least one condition in 2 or more disease clusters in addition to HIV infection.

Statistical Analysis

Descriptive statistics were used to calculate the distributions of all study variables and to ensure that assumptions of statistical tests were met. The term factor analysis encompasses a family of statistical methods used to investigate patterns of correlations. In this study, we used Exploratory Structural Equation Modeling, a recently developed variation of exploratory factor analysis to identify patterns of disease clustering among our patients. Eigenvalues were calculated to decide how many factors to extract in the overall factor analysis (first 5 results were 3.22, 2.60, 1.38, 1.04, and 0.98). Exploratory Structural Equation Modeling combines the advantages of both exploratory and confirmatory factor analysis. We used the Horn parallel test, Velicer minimum average partial criterion, and very simple structure complexity to determine that a 3-factor model fit the data best (see **Supplemental Digital Content**, http://links.lww.com/QAI/A356). Tetrachoric correlations were measured using weighted least square with mean and variance adjustment estimation and oblique rotation.[14] Adequacy of model fit was determined by the χ^2 test and several other descriptive models discussed in previous literature.[15] These analyses were completed with Mplus computer software (version 6)[16] and the module "psych" of the statistical package R.

A multivariable logistic regression model was fit to evaluate the association between obesity and the presence of multimorbidity while controlling for covariates. Statistical significance for all tests was defined as a 2-tailed P value < 0.05. Descriptive and logistic regression statistical analyses were performed using SAS software, version 9.2.

TABLE 2. Demographic Characteristics for 1844 HIV-Infected Patients Receiving Care at the UAB 1917 Clinic as of July 1, 2011

Characteristics	N (%)
Age (yrs), mean (SD)	44.3 (10.9)
Multimorbidity	1205 (65.3)
Race/gender*	
White male	725 (39.6)
White female	112 (6.1)
Non-white male	683 (37.3)
Non-white female	313 (17.1)
BMI category	
Underweight	73 (4.0)
Normal weight	567 (30.8)
Overweight	665 (36.1)
Obese	539 (29.2)
Insurance type	
Private	579 (31.4)
Public	684 (37.1)
Uninsured	581 (31.5)
CD4 count, cells/mm^3	
<200	221 (12.0)
200–350	310 (16.8)
>350	1313 (71.2)
VL: HIV RNA copies/mL	
<50	1231 (66.8)
≥50	613 (33.2)
HIV risk factor†	
IVDU	149 (8.8)
MSM	927 (54.5)
Heterosexual	625 (36.7)

*Data for 11 patients were missing; Racial distribution among non-whites (n = 996, 54.3%) is as follows: American Indian or Alaska Native (n = 2, 0.11%), Asian (n = 4, 0.22%), Black or African American (n = 963, 52.55%), Hispanic (n = 21, 1.14%), Multiracial (n = 3, 0.16%), Other (n = 3, 0.16%).

†Risk factor is missing for 143 patients.

MSM, men who have sex with men; IVDU, intravenous drug use.

RESULTS

Among 1833 patients meeting inclusion criteria, the mean age (±SD) was 44 ± 10.9 years, 46% were white (n = 837), 77% male (n = 1408), and men who have sex with men constituted the largest HIV transmission risk group (59%, n = 992). Most patients had a CD4 count >350 cells/mm^3 (71%, n = 1313) and 65% of patients had an elevated BMI (36% overweight, 29% obese). Multimorbidity, defined in our study as the presence of conditions in more than one cluster, was prevalent in 65% of the study sample (Table 2) and increased with each progressive BMI category: underweight (n = 41 of 73, 56%), normal weight (n = 351 of 566, 62%), overweight (n = 443 of 661, 67%), and obese (n = 370 of 536, 69%).

The overall prevalence of specific conditions ranged from a low of 2% (gout) to a high of 48% (mood disorders; Table 1). Results indicated that a 3-factor model provided the most interpretable solution for our data set (χ^2 test of goodness of fit, $P < 0.001$; root mean square error approximation, 0.020; Tucker-Lewis index, 0.957; and comparative fit index 0.974). Each of the 3 factors is comprised of a number of diagnoses that were grouped together by a data-driven computer model based on frequency of co-occurrence. To simplify nomenclature, we labeled each cluster of diagnoses based on the diagnosis that had the highest prevalence within each factor. In our case, the 3 most common conditions in our population were mood disorders (48%), tobacco dependence/abuse (43%), and HTN (40%). Factor 1, labeled "Metabolic," loaded HTN, gout, diabetes mellitus, and chronic kidney disease (range of standardized loadings: 0.41–0.84; $P < 0.001$); factor 2, labeled "Behavioral," loaded mood disorders, dyslipidemia, chronic obstructive pulmonary disease, peptic ulcer disease, osteoarthritis, obstructive sleep apnea, and cardiac disorders (range of standardized loadings: 0.32–0.57; $P < 0.001$); factor 3, labeled "Substance use," loaded alcohol abuse, substance abuse, tobacco abuse, and hepatitis C (range of standardized loadings: 0.53–0.89; $P < 0.001$).

Multimorbidity patterns showing overlapping distributions of factors stratified by BMI category are shown in Figure 1. The proportion of patients with a factor 1 (Metabolic) condition increased with BMI: underweight (22%), normal weight (33%), overweight (44%), and obese (61%).

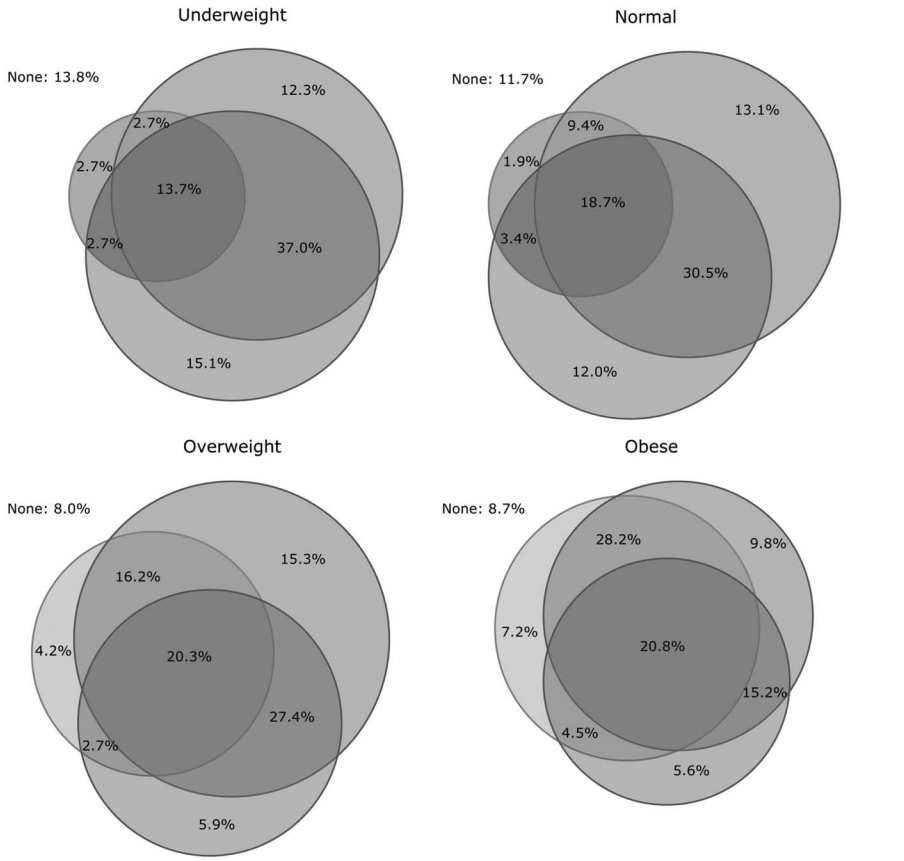

FIGURE 1. Multimorbidity patterns of 1844 HIV infected patients receiving care at UAB 1917 cliinic as of July 1, 2011, organized per BMI category.

The presence of factor 2 (Behavioral) conditions was roughly proportional across all BMI categories: underweight (66%), normal weight (72%), overweight (79%), and obese (74%). The frequency of factor 3 (Substance use) conditions decreased as BMI category increased: underweight (69%), normal weight (65%), overweight (56%), and obese (46%). Overall, overlap among factors increased with BMI category, with the most notable overlap occurring between factors 1 (Metabolic) and 2 (Behavioral): underweight (3%), normal weight (9%), overweight (16%), and obese (28%).

In the multivariable logistic regression model, obesity (obese vs. normal weight OR = 1.52, 95% CI: 1.15 to 2.00), white males (white male vs. non-white male OR = 1.60, 95% CI: 1.25 to 2.05), insurance status (public vs. private insurance OR = 2.06, 95% CI: 1.57 to 2.69; uninsured vs. private insurance OR = 1.34, 95% CI = 1.03 to 1.74), CD4 >350 (CD4 >350 vs. <200 OR = 1.62, 95% CI: 1.18 to 2.24), and increased age (per 10-year increase, OR = 1.81, 95% CI: 1.62 to 2.02) were associated with increased odds of multimorbidity (Table 3).

DISCUSSION

Our study represents one of the first efforts to characterize multimorbidity patterns in an HIV-infected population. Factor analysis and hierarchical item cluster analysis were used to take a data driven approach to how common chronic conditions clustered together based on frequency of co-occurrence alone, irrespective of mechanisms or shared similarities in pathophysiology. These factor groups or disease clusters were then stratified per BMI category in an effort to see how weight gain and obesity affected patterns of multimorbidity. In our study population, most patients (65%) met our criteria for multimorbidity overall, which required patients to have conditions in more than one of the 3 clusters that we described. In addition, our model of multimorbidity did not include 11% of the study sample that had multiple conditions within a single factor. Taken together, these data suggest our estimate of the association between multimorbidity and obesity in the present study is likely conservative.

In concordance with our hypothesis and consistent with existing literature,[6] obesity was associated with a significantly higher likelihood of multimorbidity (OR = 1.51, 95% CI: 1.15 to 1.99). In addition to increasing the odds of having conditions in multiple disease clusters, it is interesting to observe the impact of higher BMI categories on the patterns of disease clustering in our patients. For instance, the prevalence of overlap among conditions in both factor 1 (Metabolic) and factor 2 (Behavioral) was higher in obese patients compared with underweight patients (28.2% vs. 2.7%). In addition,

TABLE 3. Multivariable Logistic Regression Model Relationship Between Multimorbidity and Sociodemographic and Laboratory Values in 1844 HIV-Infected Patients Receiving Care at the UAB 1917 Clinic as of July 1, 2011

	Univariate, OR (95% CI)	Multivariable, OR (95% CI)
Age (per 10 yrs)	**1.93 (1.75 to 2.13)**	**1.81 (1.62 to 2.02)**
BMI category		
Normal weight	1.00	1.00
Obese	**1.35 (1.05 to 1.73)**	**1.51 (1.15 to 1.99)**
Overweight	1.23 (0.97 to 1.55)	1.14 (0.88 to 1.46)
Underweight	0.79 (0.48 to 1.29)	0.86 (0.50 to 1.50)
Race/Gender		
Non-white male	1.00	1.00
White male	**1.93 (1.54 to 2.41)**	**1.59 (1.24 to 2.04)**
Non-white female	1.26 (0.95 to 1.65)	0.82 (0.61 to 1.12)
White female	**1.82 (1.18 to 2.82)**	1.36 (0.85 to 2.17)
Insurance type		
Private insurance	1.00	1.00
Public insurance	**1.80 (1.41 to 2.29)**	**2.06 (1.58 to 2.70)**
Uninsured	**0.77 (0.61 to 0.98)**	**1.34 (1.03 to 1.74)**
CD4 value, cells/mm^3		
<200	1.00	1.00
200 to350	1.24 (0.87 to 1.76)	1.05 (0.72 to 1.53)
>350	**1.65 (1.24 to 2.21)**	**1.56 (1.12 to 2.18)**
VL: HIV RNA copies/mL		
<50	1.00	1.00
≥50	**0.63 (0.52 to 0.77)**	0.89 (0.71 to 1.12)

Values in bold indicate statistical significance.

underweight patients were 3 times as likely to have at least one factor 3 (Substance use)–related condition. Overall, the degree of overlap among all disease clusters was greater as BMI increased.

Conditions such as obesity and dyslipidemia, in particular, once considered to be a side effect of ART, are now observed as baseline conditions for treatment-naive HIV-infected patients[17,18] and play a key role in multimorbidity. In our practice setting, we found that 45% of patients were either overweight or obese before initiation of ART.[19] The prevalence of obesity among our patients (29.2%) is similar to the general population averages for Alabama (32%) and the United States (30%).[20] Thus, the issue of weight management must be stressed in longitudinal care to diminish its impact on multimorbidity among HIV-infected patients.

Older HIV-infected patients have higher odds of multimorbidity than older non–HIV-infected patients with similar baseline characteristics.[12] Consistent with existing medical literature,[21] we determined older age to be significantly associated with multimorbidity (OR = 1.81, 95% CI: 1.62 to 2.02 per 10 years) among our HIV-infected patients. Increased longevity among well-managed HIV-infected patients will likely contribute to higher rates of multimorbidity in the future and will play a key role in the evolving care needs of our patient population. Higher CD4 values increase the risk for multimorbidity. This finding is in concordance with previously published results and underscores the growing importance of non-HIV–related morbidities among those successfully treated for HIV.[22]

The impact of aging, obesity, and increasing prevalence of multimorbidity in the HIV-infected population will have far reaching implications. First, clinical practice guidelines are often based on results from clinical trials with strict entry criteria, that frequently exclude patients with significant comorbid disease and even more so those with multimorbidity. With such variability between patient populations in clinical trials and clinical practice, the applicability of data derived from prior and similarly exclusive future trial populations must be carefully considered. Looking beyond isolated comorbidity and accounting for multimorbidity in trial design will be an integral part of optimized HIV management in the future.[23] In addition, although guidelines often exist to address management of comorbid conditions in isolation (ie, hepatitis C infection or dyslipidemia), guidelines rarely address multimorbidity and its associated impact on drug–drug interactions, functional status, quality of life, and mortality for those managing the care of complex HIV-infected patients burdened with multiple chronic diseases.[24] As the health care needs of the HIV-infected population continue to evolve, our field will need to formally address this challenge.

LIMITATIONS

This study has several limitations. This article used exploratory factor analysis, a data driven approach, and different results may have been found using a different specification of the model, such as a rotational strategy. Replication would be important to assure generalizability of these findings in other study samples. There is no established list of diagnoses used to define multimorbidity and definitions of multimorbidity vary in the medical literature. Because it was not possible to include every potential diagnosis in the factor analysis model, we combined clinical judgment with statistical analysis to determine the conditions that best described our study population. Furthermore, we were guided by data from the general population where multimorbidity has been better defined.[25] Although the 1917 Clinic draws from a broad referral area, our study is composed of a sample from one site in the Southeastern United States. Because our region has historically seen a higher incidence of obesity and chronic diseases, our findings may not be generalizable to other HIV-infected populations. However, other studies have shown that the overweight/obese epidemic among HIV infected individuals is equally prevalent in other regions of the United States.[9] Finally, this study used a cross-sectional sample of adults who attended the UAB 1917 Clinic between June 2010 and July 2011 regardless of the duration of care or cumulative ART exposure. Therefore, it is difficult to characterize the role that such factors might have had on existing comorbidities in this cross-sectional study.

CONCLUSIONS

We are in the midst of several demographic shifts among people living with HIV/AIDS, with aging and obesity becoming

concomitantly more prevalent. In our analysis of HIV-infected patients, we determined both aging and obesity as risk factors for multimorbidity. Our attempt to characterize multimorbidity patterns and observe commonly co-occurring conditions will provide critical first steps in further defining the scope of the problem and inform interventions to address the management of multimorbidity in the context of HIV. Our focus as HIV care providers must extend beyond CD4 counts, VL, and traditional AIDS-defining illnesses to embrace HIV care as complex chronic disease management of multiple overlapping conditions within the context of primary care. Attention to these changing needs across the field, from trial design to guideline development will allow us to dynamically adapt to the changing care needs of people living with HIV/AIDS.

REFERENCES

1. Justice AC. HIV and aging: time for a new paradigm. *Curr HIV/AIDS Rep.* 2010;7:69–76.
2. Effros RB, Fletcher CV, Gebo K, et al. Aging and infectious diseases: workshop on HIV infection and aging: what is known and future research directions. *Clin Infect Dis.* 2008;47:542–553.
3. Fortin M, Hudon C, Haggerty J, et al. Prevalence estimates of multimorbidity: a comparative study of two sources. *BMC Health Serv Res.* 2010;10:111.
4. Salter ML, Lau B, Go VF, et al. HIV infection, immune suppression, and uncontrolled viremia are associated with increased multimorbidity among aging injection drug users. *Clin Infect Dis.* 2011;53:1256–1264.
5. Schafer I, von Leitner EC, Schon G, et al. Multimorbidity patterns in the elderly: a new approach of disease clustering identifies complex interrelations between chronic conditions. *PLoS One*. 2010;5:e15941.
6. van den Bussche H, Koller D, Kolonko T, et al. Which chronic diseases and disease combinations are specific to multimorbidity in the elderly? Results of a claims data based cross-sectional study in Germany. *BMC Public Health.* 2011;11:101.
7. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. *Arch Intern Med.* 2002;162:2269–2276.
8. Bogers RP, Bemelmans WJ, Hoogenveen RT, et al. Association of overweight with increased risk of coronary heart disease partly independent of blood pressure and cholesterol levels: a meta-analysis of 21 cohort studies including more than 300 000 persons. *Arch Int Med.* 2007;167:1720–1728.
9. IDSA. HIV-positive people now overweight like everyone else—as disease becomes a chronic condition, other health issues arise. Available at: http://www.medicalnewstoday.com/releases/84848.php. Accessed December 15, 2011.
10. Calle EE, Rodriguez C, Walker-Thurmond K, et al. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med.* 2003;348:1625–1638.
11. Sullivan PW, Morrato EH, Ghushchyan V, et al. Obesity, inactivity, and the prevalence of diabetes and diabetes-related cardiovascular comorbidities in the U.S., 2000-2002. *Diabetes Care*. 2005;28:1599–1603.
12. Goulet JL, Fultz SL, Rimland D, et al. Aging and infectious diseases: do patterns of comorbidity vary by HIV status, age, and HIV severity? *Clin Infect Dis.* 2007;45:1593–1601.
13. National Institutes of Health NHL. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report*. Bethesda, MD: National Institutes of Health; 1998.
14. Beauducel A, H YP. On the performance of maximum likelihood versus means and variance adjusted least squares estimation in CFA. *Struct Equ Modeling.* 2006;13:186–203.
15. Revelle W, R T. Very simple structure. An alternative procedure for estimating the optimal number of interpretable factors. *Multivariable Behav Res.* 1979;14:403–414.
16. Muthén B. A general structural equation model with dichotomous, ordered categorical, and continuous latent variable indicators. *Psychometrika*. 1984 49:115–132.
17. Feeney ER, Mallon PW. HIV and HAART-associated dyslipidemia. *Open Cardiovasc Med J.* 2011;5:49–63.
18. Palella FJ Jr, Baker RK, Buchacz K, et al. Increased mortality among publicly insured participants in the HIV Outpatient Study despite HAART treatment. *AIDS*. 2011;25:1865–1876.
19. Tate T, Willig A, Willig J, et al. HIV infection and obesity: where did all the wasting go? *Antivir Ther.* E-pub ahead of print: 2012.
20. Flegal KM, Carroll MD, Ogden CL, et al. Prevalence and trends in obesity among US adults, 1999-2000. *JAMA*. 2002;288:1723–1727.
21. Vance DE, Mugavero M, Willig J, et al. Aging with HIV: a cross-sectional study of comorbidity prevalence and clinical characteristics across decades of life. *J Assoc Nurses AIDS Care.* 2011;22:17–25.
22. Mocroft A, Reiss P, Gasiorowski J, et al. Serious fatal and nonfatal non-AIDS-defining illnesses in Europe. *J Acquir Immune Defic Syndr.* 2010; 55:262–270.
23. O'Kelly FD, Bury G. An analysis of the effects of HIV infection in a cohort of intravenous drug users. *Ir Med J.* 1996;89:112–114.
24. Goulet JL, Fultz SL, McGinnis KA, et al. Relative prevalence of comorbidities and treatment contraindications in HIV-mono-infected and HIV/HCV-co-infected veterans. *AIDS*. 2005;19(suppl 3):S99–S105.
25. Marengoni A, Rizzuto D, Wang HX, et al. Patterns of chronic multimorbidity in the elderly population. *J Am Geriatr Soc.* 2009;57: 225–230.