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Room for Improvement: The HIV–Diabetes Care Continuum Over 15 Years in the Women’s Interagency HIV Study

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Background. Gains in life expectancy through optimal control of HIV infection with antiretroviral therapy (ART) may be threatened if other comorbidities, such as diabetes, are not optimally managed.

Methods. We analyzed cross-sectional data of the Women’s Interagency HIV Study (WIHS) from 2001, 2006, and 2015. We estimated the proportions of HIV-positive and HIV-negative women with diabetes who were engaged in care and achieved treatment goals (hemoglobin A1c [A1c] <7.0%, blood pressure [BP] <140/90 mmHg, low-density lipoprotein [LDL] cholesterol <100 mg/dL, not smoking) and viral suppression. Repeated-measures models were used to estimate the adjusted prevalence of achieving each diabetes treatment goal at each time point, by HIV status.

Results. We included 486 HIV-positive and 258 HIV-negative women with diabetes. In 2001, 91.8% visited a health care provider, 60.7% achieved the A1c target, 70.5% achieved the BP target, 38.5% achieved the LDL cholesterol target, 49.2% were nonsmokers, 23.3% achieved combined ABC targets (A1c, BP, and cholesterol), and 10.9% met combined ABC targets and did not smoke. There were no differences by HIV status, and patterns were similar in 2006 and 2015. Among HIV-positive women, viral suppression increased from 41% in 2001 to 87% in 2015 compared with 8% and 13% achieving the ABC goals and not smoking. Viral suppression was not associated with achievement of diabetes care goals.

Conclusions. Successful management of HIV is outpacing that of diabetes. Future studies are needed to identify factors associated with gaps in the HIV–diabetes care continuum and design interventions to better integrate effective diabetes management into HIV care.

Keywords. care continuum; diabetes; HIV; quality.
of diagnosis and treatment necessary to achieve and maintain viral suppression [8]. The continuum assesses the proportion of HIV-positive patients aware of their condition who are engaged in care, retained in care, and achieving viral suppression. It is now the standard for measuring the quality of HIV care and assessing overall progress in controlling the HIV epidemic [9]. The care continuum serves as a critical tool to understand where gaps in care exist and where to target both clinical and population-based interventions [10]. More recently, the care continuum was applied to DM in the United States, showing a decline in each step from diagnosis of diabetes to being engaged/retained in diabetes care to achieving important clinical benchmarks for diabetes control [11]. Both the HIV and DM care continua are characterized by suboptimal disease control and significant health disparities in age, gender, and race/ethnicity [11, 12].

Few studies have reported on the achievement of DM treatment goals among PLHIV [13, 14], and no study has yet comprehensively described the DM care continuum among PLHIV. Motivated by the impact of the HIV care continuum on informing HIV quality improvement interventions, we characterized and compared being at target for DM care goals among HIV-positive and matched HIV-negative women from the Women’s Interagency HIV Study (WIHS) over the past 15 years. Gaps identified along the HIV–DM care continuum can guide further research and programs to improve DM care among PLHIV.

METHODS

Participants

The WIHS was established in 1994 and is the largest multicenter prospective cohort study of comparable HIV-positive and HIV-negative women aimed to investigate the natural history of women with HIV and those at risk for HIV infection in the United States [15]. From 1994 to 2012, the WIHS was comprised of 6 sites (Bronx/Manhattan, NY; Brooklyn, NY; Chicago, IL; Washington, DC; San Francisco, CA; and Los Angeles, CA). Since 2012, the WIHS has been comprised of 5 of the 6 original sites (the Los Angeles, CA, site is no longer included), and 5 southern sites have been added (Miami, FL; Atlanta, GA; Jackson, MS; Birmingham, AL; and Chapel Hill, NC). We analyzed cross-sectional data from all WIHS sites at 3 time points: 2001 (6 sites), 2006 (6 sites), and 2015 (10 sites). The years were selected based on availability of A1c data in the cohort. A total of 4982 women (n = 3678 HIV-positive, n = 1304 HIV-negative) were enrolled in 4 waves, 1994–1995 (n = 2623), 2001–2002 (n = 1143), 2011–2012 (n = 371), and 2013–2015 (n = 845). The WIHS site and recruitment wave were considered for each participant.

In the current analysis, we included participants with confirmed diabetes, defined as having at least 1 of the following: (1) self-reported use of antidiabetic medication; (2) a fasting glucose (FG) ≥126 mg/dL, confirmed by A1c ≥6.5% or a subsequent FG ≥126 mg/dL; (3) a hemoglobin A1c ≥6.5%, confirmed by a FG ≥126 mg/dL; (4) a self-report of diabetes, confirmed by 2 FG ≥126 mg/dL; or (5) a hemoglobin A1c ≥6.5% concurrent with an FG ≥126 mg/dL [6]. Duration of DM represents the period in which a woman had DM while enrolled in the WIHS cohort.

Data Collection

WIHS participants completed semi-annual study visits consisting of a comprehensive physical exam, collection of serum and plasma for laboratory analyses, and an interviewer-administered survey collecting information such as demographics, social characteristics, disease characteristics, and medication-related information. Study design, survey instruments, and data collection methods were previously described [15].

Care Goal Measurements

Measures to define diabetes (A1c, blood pressure [BP], cholesterol, smoking status) and HIV care goals (viral load) were collected using standardized techniques that have been described in detail elsewhere [16]. All laboratory measures were conducted annually, whereas BP measurements and smoking behavior were measured every 6 months. Some clinical data were only collected on alternating visits, and those data were obtained from the next consecutive visit.

Covariate Definitions

HIV-positive and -negative participants were classified as having seen any health care provider if they provided a positive response to the question “Have you seen a health care provider (HCP) since your last WIHS visit?” This question was asked at every WIHS visit, or every 6 months across all years for both HIV-positive and -negative participants. This question was used as a surrogate for engagement in care. Other covariates included age, race/ethnicity, self-reported health insurance status (ie, present or absent), income, education level, and body mass index (BMI; kg/m²). Waist circumference was measured in centimeters. Medication use related to diabetes, hypertension, hyperlipidemia, and HIV was self-reported. The HIV viral load was measured using TaqMan HIV-1 RNA quantitative polymerase chain reaction.

Diabetes and Treatment Goal Definitions

We used an A1c goal <7.0% and BP goal of systolic blood pressure (SBP) <140 mmHg and diastolic blood pressure (DBP) <90 mmHg, based on the American Diabetes Association 2017 standards [17]. The cholesterol goal was low-density lipoprotein (LDL) <100 mg/dL, consistent with primary prevention in the American College of Cardiology/American Heart Association (ACC/AHA) 2013 guidelines and the older Adult Treatment Panel (ATP) III Guidelines [18]. Viral suppression was considered the last HIV-1 RNA being <200 copies/mL or undetectable. ABC control was defined as achieving control of A1c, BP, and cholesterol. ABC + nonsmoking was defined as achieving control of A1c, BP, cholesterol, and not smoking.
Statistical Analysis
Descriptive statistics (counts and percentages for categorical variables, means and SDs for continuous variables, and medians and interquartile ranges for continuous non–normally distributed variables) were assessed by study year (2001, 2006, 2015) and HIV status. Univariate analyses, including chi-square or Fisher exact tests for categorical variables and t tests or Wilcoxon rank-sum tests for continuous variables, were used to compare demographic and clinical characteristics by HIV status and by study year. Care continuums were developed for each study year and included A1c control, BP control, cholesterol control, smoking, engagement in care, viral suppression, ABC control, and ABC control + nonsmoking. For viral suppression, A1c, BP, and cholesterol control, we determined the proportion of participants treated with medication.

To account for repeated measures in longitudinally collected WIHS data, logistic generalized estimating equation (GEE) models with a compound symmetry covariance structure were used to estimate the prevalence of achieving the control outcome of interest in each of the 3 years (2001, 2006, 2015) and by HIV status. Covariates included insurance status, income, age, WIHS site and recruitment wave, race/ethnicity, education, BMI, waist circumference, and duration of DM. In addition to the aforementioned covariates, models were adjusted for other variables clinically relevant to the specific situations. The A1c control model included use of DM medication, the BP control model included use of BP medication, the LDL control model included use of cholesterol medication, and the ABC model included use of DM, BP, and cholesterol medications. The viral suppression model included any ART use and was restricted to HIV-positive women. As a sensitivity analysis, to evaluate the effect of repeated measures, all GEE models were re-analyzed assuming independent observations. Model fit was assessed using Hosmer-Lemeshow, diagnostic plots, and/or predictive ability.

RESULTS
Population Characteristics
Of 681 HIV-positive and HIV-negative women with DM during the study period, 605 were included in the current analysis. Supplementary Figure 1 shows the criteria for DM that each participant met. We excluded women with missing information about health care providers (n = 20), A1c (n = 46), BP (n = 1), and LDL (n = 9). Characteristics of the analytical subsample in 2001, 2006, and 2015 are reported in Table 1. The HIV-positive and HIV-negative women were similar in demographic characteristics, except for the proportion with a high school degree in 2006, insurance status in 2006 and 2015, and BMI and waist circumference in 2001 and 2006.

Care Continuum Outcomes Over Time
Figure 1 shows the HIV–DM care continuum by HIV status among women with DM in 2001 (A), 2006 (B), and 2015 (C). The values plotted in Figure 1 are reported in Supplementary Table 1. In 2001, 122 HIV-positive and -negative women had DM, 314 in 2006, and 412 in 2015. Most women had visited a health care provider since their last study visit across the 3 time points (91.8%, 91.4%, and 92.2%, respectively). The proportion of women achieving the A1c goal was 60.7% in 2001, 73.2% in 2006, and 58.0% in 2015. The proportion achieving the BP goal was similar across 2001, 2006, and 2015 (70.5%, 74.5%, and 72.8%, respectively). There was a small but steady increase in the proportion of women achieving the cholesterol goal: 38.5% in 2001, 47.5% in 2006, and 53.2% in 2015. The proportion of women not smoking also increased, from 49.2% in 2001 to 52.2% in 2006 and 59.6% in 2015. The proportion of women achieving combined ABC goals was low across the 3 time points (23.3% in 2001, 26.4% in 2006, and 22.3% in 2015), and even fewer women achieved combined ABC goals and did not smoke (10.9% in 2001, 12.5% in 2006, and 11.4% in 2015). We also explored DM care goals continuously (unadjusted) and report means for HIV-positive and HIV-negative women in Supplementary Table 2. The overall means during the 3 time points ranged as follows: mean A1c (range, 6.6–7.4); mean BP (SBP range, 127–128 mmHg; DBP range, 76–81 mmHg); and mean LDL (range, 100–113 mg/dL).

Care Continuum Outcomes by HIV Status
In 2001, there were no differences in achieving any of the DM care goals in HIV-positive compared with HIV-negative women (Figure 1). In 2006, more HIV-positive compared with HIV-negative women saw a health care provider (96.0% vs 80.4%, P < .0001), achieved BP control (79.3% vs 63.0%, P = .003), and were nonsmokers (57.7% vs 39.1%, P = .003). In 2015, more HIV-positive compared with HIV-negative women saw a health care provider (94.3% vs 87.7%, P = .02) and were nonsmokers (64.4% vs 49.2%, P = .004). Notably, there were no differences among HIV-positive and HIV-negative women in terms of achieving A1c goals, cholesterol goals, ABC, or the ABC + nonsmoking goals in any year.

Standard multivariable logistic regression models did not differ appreciably from the repeated-measures model (Table 2). HIV-negative women experienced improvement in glycemic control from 2001 to 2015 with prevalence estimates of 0.34 (95% confidence interval [CI], 0.16–0.59) in 2001, 0.56 (95% CI, 0.40–0.70) in 2006, and 0.66 (95% CI, 0.54–0.77) in 2015 (P = .033), whereas the HIV-positive women did not. There were no gains in BP, cholesterol, ABC control, or ABC + nonsmoking in either HIV-positive or -negative women (Table 2).

Viral Suppression
The unadjusted proportion of HIV-positive women with diabetes who achieved viral suppression steadily increased from 2001 (35/86, 40.7%) to 2006 (136/222, 61.5%) to 2015 (245/282, 86.9%). Of those who were virologically suppressed, 91.4%, 92.6%, and 97.6% self-reported being on antiretroviral therapy during the respective years. In the logistic regression models,
the viral suppression prevalence estimates were 0.50 (95% CI, 0.29–0.71), 0.60 (95% CI, 0.41–0.77), and 0.79 (95% CI, 0.65–0.89) in 2001, 2006, and 2015, respectively, demonstrating improvement from 2001 to 2015 ($P = .0022$) (Table 2). The proportion of HIV-positive women achieving any of the single or combined DM care goals did not differ between women achieving and not achieving viral suppression.

**DISCUSSION**

We aimed to comprehensively assess and compare the DM care process between HIV-positive and HIV-negative women from the WIHS over the past 15 years. We found no differences in the proportion of HIV-positive and HIV-negative women achieving glycemic control or optimal DM control (ie, ABC goals), nor did we find improvements in either group for optimal DM control from 2001 to 2015. Among HIV-positive women, we found that HIV control (ie, viral suppression) has improved over time, but DM control has not. HIV-negative women, however, did have significant improvement in glycemic control from 2001 to 2015. Overall, these findings reinforce the importance of considering HIV a chronic infectious disease, for which the aggressive management of comorbid cardio-renal risk factors, such as diabetes, will be important.

We observed increases in the prevalence of HIV-positive women who achieved viral suppression over 15 years (from 51% in 2001 to 81% in 2015), which aligns with findings from other cohort studies [19, 20]. These improvements in viral suppression reflect a combination of changing guidelines, making more patients eligible for antiretroviral therapy; increased tolerability, potency, and durability of ART; and a shift in clinical and public health programs, to focus more on care continuum metrics and medication adherence. Despite these positive gains in control of HIV, we found that DM control was not optimal (ie, ABC goals) and did not improve from 2001 to 2015. Among HIV-negative women, only glycemic control improved (from 34% in 2001 to 66% in 2015), whereas neither BP nor cholesterol control improved over time in either the HIV-positive or HIV-negative women. Overall, less than 15% of HIV-positive and -negative women achieved ABC goals and did not smoke, meaning most women did not achieve the targets to avoid cardio-renal complications of DM. However, despite

<table>
<thead>
<tr>
<th>2001</th>
<th>2006</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+</td>
<td>HIV-</td>
<td>HIV+</td>
</tr>
<tr>
<td>n = 86</td>
<td>n = 36</td>
<td>n = 222</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>45.7 (7.7)</td>
<td>43.5 (7.5)</td>
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<tr>
<td>Race, %</td>
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<td>5.6</td>
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<td>AA, NH</td>
<td>62.8</td>
<td>66.7</td>
</tr>
<tr>
<td>Hispanic</td>
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<tr>
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<tr>
<td>Education, %</td>
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</tr>
<tr>
<td>&lt;HS</td>
<td>31.4</td>
<td>41.7</td>
</tr>
<tr>
<td>HS</td>
<td>36.1</td>
<td>38.9</td>
</tr>
<tr>
<td>&gt;HS</td>
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<td>19.4</td>
</tr>
<tr>
<td>Income, %</td>
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<td></td>
</tr>
<tr>
<td>&lt;$12 000</td>
<td>72.1</td>
<td>63.9</td>
</tr>
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<td>WIHS site, %</td>
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<tr>
<td>BMI, mean (SD), kg/m²</td>
<td>32.0 (8.5)</td>
<td>36.4 (8.8)*</td>
</tr>
<tr>
<td>Waist circum., mean (SD), cm</td>
<td>98.7 (16.5)</td>
<td>109.5 (18.3)*</td>
</tr>
<tr>
<td>Duration diabetes, median (IQR), y</td>
<td>2.7 (0.5–6.1)</td>
<td>1.1 (0.2–5.3)</td>
</tr>
<tr>
<td>CD4 count, mean (SD), cells/µL</td>
<td>521 (354)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: AA, African American; BMI, body mass index; IQR, interquartile range; NH, non-Hispanic; WIHS, Women’s Interagency HIV Study.

*Statistically significant differences between the HIV-positive and -negative populations are indicated: $P < .05$.

"Duration of diabetes indicates the duration of diabetes while the participant was enrolled in WIHS."
disappointing numbers achieving these care goals, the mean levels of A1c, BP, and cholesterol were not far from goal.

A greater proportion of HIV-positive compared with HIV-negative women were nonsmokers, which is contrary to national estimates, where 83% of the general population and 66% of the HIV-positive population were nonsmoking [21]. The difference is mainly that the HIV-negative population in our cohort has much higher smoking rates than the general HIV-negative population for reasons that are not yet clear.

The trends in the HIV–DM care continuum presented here mirror those observed in the US diabetes care continuum for the general adult population, where only 25% achieved ABC control and 21% combined ABC control plus nonsmoking [11]. Achievement of DM care goals in this study using data from the WIHS was either similar to or better than that previously reported in retrospective cross-sectional studies, yet it was still suboptimal [13, 14]. As the WIHS cohort study was conducted in academic health care settings where guideline-concordant

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**Figure 1.** Care continuum for HIV-positive and HIV-negative adult women with diabetes, Women’s Interagency HIV Study (A, 2001; B, 2006; C, 2015). Data are presented as a percentage of the prevalent cases of diabetes in each cross-section. In columns with dark and light shading, the column represents those at goal. The lighter shading represents the proportion of patients not on medications, and the darker shading represents patients who self-report taking medications for that diagnosis. Seen HCP: defined by self-report of visiting a health care provider in the prior 12 months. Viral suppression: defined by last viral load of the year being <200 copies/mL. Glycemic control: defined by hemoglobin A1c target of <7.0%. BP control: defined by systolic BP <140 mmHg and diastolic BP <90 mmHg. Cholesterol control: defined by low-density lipoprotein (LDL) <100 mg/dL. Nonsmoker: defined by self-report of not smoking. ABC control: combined control of hemoglobin A1c level, blood pressure, LDL cholesterol level. ABC + nonsmoker: ABC control plus being nonsmoker. Abbreviations: ABC, A1c, BP, and cholesterol; BP, blood pressure; HCP, health care provider.
SMS tools have been shown to improve adherence to ART [25]. 1-on-1 adherence education, pill boxes, reminder alarms, and of care goals are available for both HIV and DM. In HIV care, once viral suppression is achieved, contributing to why viral suppression may not coincide with lifestyle changes in addition to taking pills [23]. Another factor contributing to why viral suppression may not coincide with DM control is that providers may not be comfortable optimizing diabetes treatment regimens [24]. Together, these factors contribute to the challenge of DM control among PLHIV, even once viral suppression is achieved.

Strategies to improve medication adherence and achievement of care goals are available for both HIV and DM. In HIV care, 1-on-1 adherence education, pill boxes, reminder alarms, and SMS tools have been shown to improve adherence to ART [25]. Similarly, meta-analyses have shown that quality improvement interventions in patients with DM can improve A1c by 0.37% and BP control by 3.13/1.88 mmHg [26]. Further, a recent pragmatic trial demonstrated the effectiveness of using care coordinators and electronic clinical decision support software to improve DM management in outpatient low- to middle-income country settings [27]. In settings where HIV is already being successfully managed as a chronic disease, overlaying proven DM care strategies with existing chronic care models should be feasible. In a setting where the vast majority of patients with HIV and DM achieve viral suppression, optimally managing both comorbidities and HIV infection is imperative. As such, future studies should focus on identifying barriers to quality DM care, testing strategies to close gaps identified in the HIV–DM care continuum, and determining, longitudinally, if achieving DM targets is associated with fewer complications of DM.

As with all research studies and analyses, the present study has some limitations. First, although the WIHS cohort includes major urban centers in the United States affected by the HIV epidemic, a broader geographic representation of the United States is lacking and our samples sizes are relatively small. Our reported DM control estimates may be underestimates as the southeastern sites were recruited at a later stage, and the southeastern United States is an area where there are more DM-related complications [28]. Second, the repeated cross-sectional nature of the analyses resulted in some women being included in more than one analysis per year.
than 1 of the cross-sectional time points. To account for this potential limitation, we used both logistic regression models (treating each encounter as 1) and generalized estimating equations (accounting for individuals with multiple visits), and the results were similar. Third, we were unable to determine true DM duration, as our baseline sample included existing DM cases. Fourth, we did not capture undiagnosed diabetes; therefore, our continuum begins with the presumption of diagnosed diabetes and excludes the step of diagnosis. Fifth, it was not possible to assess visit frequency for HIV or DM appointments (outside of study visits), a traditional measure of the HIV continuum, so a surrogate was used (eg, self-reported health care provider visits since the last WIHS study visit). Sixth, the type of health care provider was unknown. This makes it difficult to ascertain if poor outcomes may be due to lack of medical expertise/interest vs other systems-level or patient-level factors. PLHIV may receive HIV care in a primary care setting, subspecialty setting, or through a combined approach. Therefore, PLHIV may have their HIV managed by a provider who may or may not be simultaneously addressing DM or other chronic illness, where expertise affects quality indicators [29, 30]. A recent survey among infectious diseases physicians found that the majority of those providing HIV care also acted as the patient’s primary care provider, but primary care screening by this group was suboptimal [31]. Barriers, cited in the survey, to completing these screening tests included time constraints in the clinic and financial/insurance limitations, and the same barriers may also contribute to suboptimal management of comorbidities in HIV care settings [32]. Future studies should strive to create longitudinal measurements for care continua outcomes.

There are several strengths of our current analysis, which outweigh limitations. First, we were able to evaluate 15 years of data collected using a consistent measurement approach. Second, the HIV viral suppression variable was comparable with that observed in US national care continua. Third, measurement of glycemic control, cholesterol control, BP control, ABC, and ABC + nonsmoking was equivalent to the methods used in national estimates [11]. Finally, inclusion of HIV-positive and HIV-negative matched controls allows for valuable comparisons from both patient-level and systems-level perspectives.

CONCLUSIONS

This study is the first to apply the care continua approach for both HIV and DM and provides a comprehensive assessment of the diabetes care process (ie, engagement in health care, HIV viral suppression, and diabetes care goals) in people living with HIV. Though there were no differences in DM control between HIV-positive and HIV-negative women, DM control was poor among both groups. In contrast, HIV control (ie, viral suppression) did improve from 2001 to 2015 among HIV-positive women, though viral suppression was not associated with better DM control. These findings reinforce the importance of considering HIV a chronic infectious disease for which management of comorbid cardio-renal risk factors, such as diabetes, is important. Identifying the barriers and possible innovations for how to optimize management of these comorbidities is a priority across all aspects of the health care and research continuum.

Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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