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Self-reported low physical function is associated with diabetes mellitus and insulin resistance in HIV-positive and HIV-negative men

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Abstract

Aim—To investigate the association between self-reported physical function (as a surrogate for physical activity) and diabetes mellitus (DM) and insulin resistance (IR) among HIV-positive and -negative men.

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Method—A total of 384 HIV-negative and 274 HIV-positive men from the Pitt Men's Study contributed data. DM was defined by fasting serum glucose levels. IR was calculated using the homeostasis model assessment. The Physical Functioning 10 Scale from the Short Form-36 Health Survey measured physical function. Multivariate logistic regression assessed the independent association between physical function and DM and IR.

Results—Physical function, older age and Black race were associated with DM in multivariate analyses. Physical function/HIV interaction, older age, higher body mass index, HIV infection and Black race were associated with IR in multivariate analyses.

Conclusion—Self-reported low physical function is associated with DM and IR in HIV-negative and -positive men.

Keywords

diabetes mellitus; HIV-positive; insulin resistance; physical function

The widespread use of HAART presents unforeseen clinical challenges in the dynamic HIV epidemic. As the paradigm of HIV treatment shifted from palliative care to chronic disease management, new metabolic complications surfaced, including insulin resistance (IR) and diabetes mellitus (DM) [1,2]. A full understanding of these complications remains elusive, but may involve a combination of antiretroviral therapy and duration of HIV infection as well as lifestyle, BMI, age, sex and genetic predisposition [3,4]. Prospective studies in HIV-negative individuals suggest that participation in physical activity plays a significant role in the prevention of Type 2 DM and IR [5,6]. However, the role of physical inactivity as a contributing factor to the development of DM has been overlooked in most studies of HIV-positive populations. The few studies that have assessed physical inactivity as a risk factor for DM yielded conflicting results [7,8]. Physical inactivity was found to be associated with previously diagnosed diabetes among HIV-positive women; however, despite similar methods and sample sizes, this observation was not replicated in HIV-positive men [7,8]. These studies by Howard *et al.* used a high-risk cohort of mostly older Black and Hispanic individuals without a standardized assessment of physical activity. Therefore, results may not generalize to other ethnic populations [7,8].

Although related, physical activity and physical function have differences. Physical activity is defined as any voluntary movement produced by the skeletal muscles that results in increased energy expenditure [9], whereas physical function is defined as one's ability to carry out various activities that require physical capability, ranging from self-care (activities of daily living) to more vigorous activities that require increasing degrees of mobility, strength or endurance [10]. Despite these differences, numerous studies in HIV-negative populations have established that physical activity levels are correlated with physical function performance. Both cross-sectional and prospective studies suggest that low physical activity levels are an independent predictor of low physical function [10–15]. Among HIV-positive populations, resistance training has been shown to improve self reported physical function in patients with HIV wasting [16]. Therefore, the use of physical function as a surrogate for physical activity is justified.

Recent studies document a substantial prevalence and incidence of DM in HIV-positive men. Data from the Multicenter AIDS Cohort Study (MACS) reported a 14% prevalence of DM among HIV-positive men compared with 5% among HIV-negative men and an incidence rate of 4.7 cases per 100 person-years compared with an incidence rate of 1.4 cases per 100 person-years among HIV-negative men [17]. There is also a greater reported prevalence of IR in HIV-positive patients with lipodystrophy (35%) compared with matched

controls without HIV (5%) [18]. This trend is also noted in HIV-positive patients without lipodystrophy (5.6% IR prevalence) as compared with controls (3.3% IR prevalence) [18].

Given the strong association between low physical activity and DM among HIV-negative individuals as well as the known risk for DM and IR development in HIV-positive men, the role of low physical activity in the HIV-positive population warrants further investigation. Therefore, the objective of this study was to investigate the role of self-reported low physical function as a surrogate for low physical activity as a potential contributor to DM and IR among HIV-positive and -negative men.

Methods

Study participants

All study participants were from the Pitt Men's Study in Pittsburgh (PA, USA), one of four clinical centers that contribute data to the MACS. The MACS is an ongoing multicenter, prospective cohort study of HIV infection in homosexual and bisexual men. Briefly, the MACS follows a 6-month visit schedule and involves detailed data collection regarding medical history, physical examination and collection of biological specimens. Institutional review boards at each site approved the MACS protocol, and each participant provided informed consent. Further detail can be found in Kaslow *et al.* [19]. The MACS is currently in the 47th consecutive 6-month follow-up period of the original cohort.

The current study includes data taken after implementation of the MACS Metabolic Study in April 1999 (visit 31), at which time fasting (8 h) serum samples were added to measure glucose and insulin levels and for use in diagnosing diabetes. A total of 772 men from the Pitt Men's Study were eligible for inclusion in this study. Of these, 658 participants (384 HIV-negative and 274 HIV-positive) had a fasting serum sample from which insulin and glucose concentrations were obtained.

Outcome ascertainment: DM & IR

For the purpose of this study, a diabetes outcome was defined by fasting serum glucose levels drawn at each bi-annual visit from 1 April 1999 to 31 March 2006. The first visit at which a participant underwent a fasting serum determination was defined as the baseline visit. Participants with a fasting glucose level of less than 100 mg/dl for all visits were classified as 'normoglycemic'; participants with at least one fasting glucose level between 100 and 126 mg/dl were classified as 'prediabetic', and participants with at least one fasting glucose level of 126 mg/dl and above were classified as having diabetes. This diabetes definition was chosen based upon a similar definition used by recently published literature in HIV-positive cohorts [17,20]. Using this definition, 86 men were classified as diabetic. Of these 86, 38 had confirmed glucose levels of more than or equal to 126 mg/dl at their next visit; an additional eight were placed on diabetes medications and nine had a second nonconsecutive visit with a glucose measurement of more than or equal to 126 mg/dl. Participants with glucose levels consistent with diabetes (≥ 126 mg/dl) at baseline were not excluded from analysis ($n = 10$).

Insulin concentrations were also obtained from the fasting serum samples with normal insulin defined as less than or equal to 15 μ U/ml and high insulin defined as more than 15 μ U/ml based on the published normal range for the insulin assay used. IR was calculated using the homeostasis model assessment (HOMA): (fasting insulin [μ U/ml] $\times$ fasting glucose [mmol/l])/22.5 [21]. HOMA-IR levels were further classified into a dichotomous variable for use in logistic regression based on the median level of 3 μ U/ml $\times$ mmol/l. Glucose levels were converted to mmol/l by dividing mg/dl by 18.

Exposure: self-reported physical function

The Physical Functioning (PF) 10 scale from the Medical Outcomes Study Short Form (SF)-36 Health Survey served as a surrogate for a measure of physical activity [22]. The SF-36 is one of the most widely used Health Related Quality of Life Instruments and consistently demonstrates high levels of both reliability (>0.70) and validity [23]. Specifically, for the PF-10, Jenkinson *et al.* report a Cronbach's α of 0.93 [24], while relative validity has been reported at 1.00 [25].

This study includes data from PF-10 questionnaires administered at each bi-annual visit from 1 April 1999 to 31 March 2006 (except visit 43: 1 April 2005 to 30 September 2005). During the administration of the PF-10, participants were asked the following question regarding physical activities that might be done in a typical day: 'Does your health now limit you in these activities? If so, how much?' Participants chose between 'Yes, limited a lot', 'Yes, limited a little' or 'No, not limited at all' for vigorous activities (running and lifting heavy objects), moderate activities (vacuuming and golf), lifting or carrying groceries, climbing several flights of stairs, climbing one flight of stairs, bending, kneeling or stooping, walking more than a mile, walking several blocks, walking one block, bathing or dressing (Box 1). Each item was scored on a 0–100 range as follows: 100 = not limited at all; 50 = limited a little; and 0 = limited a lot, based on the RAND scoring method [26]. A mean of the ten activities was then calculated to determine an overall score for the PF-10 ranging from 0 to 100, with a score of 100 indicating that a participant's health did not limit his ability to complete physical activity. Thus, a lower score indicates lower physical function. The first visit at which a participant has a PF score was defined as the baseline visit. Given the strong correlation between an individual's baseline physical function score and his overall mean physical function score ($r = 0.82$; $p < 0.0001$), the baseline score was used in the analysis.

Covariates

Covariates of interest included age, race, HIV status, AIDS status, BMI and CD4 count, and were obtained for all individuals from the baseline visit, defined as the visit at which a participant had an initial recording of the covariate during visits 31–44. These covariates were chosen because of their association with physical function and/or diabetes development [27,28].

Statistical methods

SAS Version 9.1 was used for all statistical analysis. The Fisher Exact, Wilcoxon and Kruskal–Wallis nonparametric tests, as appropriate, were used to test for differences in proportions and distributions for both HIV serostatus and diabetes status groups. Differences in physical function scores between glycemic groups (normal, pre-diabetes and diabetes) were assessed using the Kruskal–Wallis test. These differences were also tested after stratification by HIV status as well as AIDS status. Chi-square and Wilcoxon Rank Sum tests were used to assess associations between physical function scores for insulin levels and HOMA scores stratified by HIV serostatus. Statistical significance was determined using two-tailed tests with an p -value of 0.05. Univariate logistic regression analysis was performed to assess unadjusted associations between predictors and the binary outcome of interest; diabetes status. We compared individuals with diabetes to those with normoglycemia; individuals with pre-diabetes were excluded from the regression analysis, thus reducing the sample size to 289 for this analysis only. Multivariate logistic regression using a forward stepwise methodology for the addition of significant variables was used to assess the association between DM and baseline physical function score, as well as to assess the association between IR and baseline physical function using a p -value cut-off of less than 0.05 for inclusion in the model. Predictors that were not significant in the multivariate

analysis were not retained in the model, regardless of statistical significance in univariate analysis. Regression analysis was also completed separately for HIV-negative and -positive men to determine whether or not risk factors for elevated glucose and IR differed by HIV status.

Results

The baseline characteristics of the 658 men stratified by glucose level and HIV serostatus are displayed in Table 1. A total of 75% of men were White. Overall, HIV-negative men were older than HIV-positive men. BMIs were significantly lower among HIV-positive men with pre-diabetes and diabetes and among HIV-positive men with normoglycemia, although the difference was not significant. CD4 counts, as expected, were significantly lower in HIV-positive men independent of diabetes status. Fasting insulin levels and HOMA scores were higher among the HIV-positive men across all glucose levels, although the differences were not statistically significant.

Men with DM were older and had higher BMIs than men with normoglycemia and pre-diabetes. A higher proportion of Black men as well as HIV-positive men with AIDS had fasting glucose levels consistent with diabetes. In both HIV-positive and -negative men, IR and hyperinsulinemia increased progressively from those with normoglycemia to pre-diabetes and diabetes.

Table 2 shows the individual mean self-reported physical function scores by diabetes status for 13 6-month periods commencing 1 April 1999. Men with diabetes consistently had the lowest physical function scores, while men with normoglycemia and pre-diabetes had relatively similar scores. Significant differences between the three glucose levels occurred in later visits, likely owing to larger sample sizes (accounting for a second MACS recruitment).

In both HIV-negative and -positive men, baseline physical function scores were lower for men with hyperinsulinemia. In addition, physical function scores were lower in HIV-positive men compared with HIV-negative men for both insulin levels. Similarly, baseline physical function scores were lower in men with HOMA levels of more than three, in both HIV-negative and -positive men. HIV-positive men had lower physical function scores than HIV-negative men, regardless of HOMA level (Table 3A & B).

The relationship between DM status and baseline physical function by HIV serostatus and men with AIDS is illustrated in Figure 1. Overall, the best physical function scores were observed among HIV-negative men with normoglycemia. HIV-negative males had better physical function scores compared with HIV-positive males in each of glucose levels. Among HIV-negative males, mean physical function scores decreased as glucose levels increased ($p < 0.0001$). The men with normoglycemia had the highest physical function scores, while the men with diabetes had the lowest scores in HIV-negative men, HIV-positive men and men with AIDS; however, significant differences were only observed in the HIV-negative group, likely due to the small number of men with HIV-infection and AIDS. In addition, the mean physical function scores for men with AIDS were lower than both the HIV-negative men and HIV-positive men in all three of the glucose levels. Men with both diabetes and AIDS had the lowest mean physical function score among all groups.

In the univariate analysis (Table 4), lower physical function score (odds ratio [OR]: 1.9 per 25-unit decrease; $p < 0.0001$), higher BMI (OR: 1.6 per 5 units; $p = 0.0012$) and older age (OR: 1.5 per 5 years; $p < 0.0001$) were found to be independently associated with diabetes. Baseline CD4 counts, AIDS status, HIV status and race were not significantly associated with diabetes in the univariate analysis. However, in the multivariate analysis, lower physical function score (OR: 1.5 per 25-unit decrease; $p = 0.02$), older age (OR: 1.5 per 5

years; $p < 0.0001$) and Black race (OR = 2.8; $p = 0.002$) were found to be significantly associated with diabetes. BMI and AIDS were not found to be significant at $p = 0.05$, and thus were not included in the final model. However, given the known relationship between BMI and DM in HIV-negative populations [29,102], a sensitivity analysis was completed to determine if results changed with BMI forced into the model [LONGENBERGER A, LIM JY, KINGSLEY LA, UNPUBLISHED DATA]. All three variables: physical function, age and race, remained significant with BMI in the model, suggesting that BMI did not influence DM in this study; therefore, BMI was removed from the model for parsimony. Given the observation that physical function scores were slightly lower among HIV-positive men compared with HIV-negative men, an interaction between HIV serostatus and mean physical function scores was tested in both univariate and multivariate analysis. This interaction was not statistically significant ($p = 0.9$) [LONGENBERGER A, LIM JY, KINGSLEY LA, UNPUBLISHED DATA]. After Stratification by HIV infection, age and race remained significantly associated with DM status, regardless of HIV status; however, BMI was associated with diabetes in HIV-negative men. Physical function was not associated with diabetes in either HIV group after stratification.

Table 4 also shows univariate and multivariate associations with IR. In the univariate analysis, physical function score (OR: 2.4 per 25-unit decrease; $p < 0.0001$), older age (OR: 1.3 per 5 years; $p < 0.0001$), higher BMI (OR: 2.6 per 5 units; $p < 0.0001$), HIV infection (OR: 1.5; $p = 0.01$) and Black race (OR: 2.0; $p = 0.006$) were associated with IR. However in the multivariate analysis, the HIV-physical function interaction became significant (OR: 2.1; $p = 0.0003$), while older age (OR: 1.3 per 5 years; $p < 0.0001$), higher BMI (OR: 2.8 per 5 units; $p < 0.0001$), HIV infection (OR: 11.3; $p = 0.0002$) and Black race (OR: 2.0; $p = 0.002$) remained associated with IR. Neither CD4 count nor AIDS status were associated with IR in either univariate or multivariate analyses. After stratification by HIV infection, BMI, age and race were associated with IR in HIV-negative men, while age, BMI and physical function were associated with IR in HIV-positive men.

Discussion

Our data suggest that self-reported low physical function as a surrogate for low physical activity is associated with DM, independent of HIV status. After adjustment for age and race, physical function remained significantly associated with DM such that for every 25-unit decrease in physical function score, the odds of having DM increased by 50% ($p < 0.05$). This result is strengthened by our observation that insulin levels and IR were also associated with lower physical function scores, especially among HIV-positive men (Table 3A & B). While the main effect of physical function score was not associated with IR in multivariate analysis, the significance of the physical function-HIV status interaction deserves attention. This indicates that the effect of low physical function on IR depends upon HIV status such that the odds of having IR were greater for men with both low physical function scores and HIV infection (OR: 2.1; $p = 0.0003$). Alternatively, the association between HIV infection and IR, but not DM, may simply indicate that IR precedes DM, and we had greater statistical power to detect this. While this association needs to be replicated in other cohort studies, it is important to encourage physical activity among individuals with HIV. Using previously published studies that support the use of physical function as a surrogate for physical activity [10–15], it is plausible to suggest that low physical activity levels may be associated with the onset of IR and DM in HIV-positive men.

In addition, our finding that physical function scores were lowest among persons with AIDS provides important information regarding DM in our population, despite the lack of statistical significance. As shown in Figure 1, persons with AIDS contributed strongly to lower physical function scores among those with diabetes. This association is highly plausible, as persons with late-stage HIV infection and AIDS have likely experienced

multiple events that contributed to lower physical function over a long history of HIV infection. It is possible that the lack of statistical significance was due to the limited sample of persons with AIDS ($n = 28$). Studies with larger samples of individuals with AIDS should be completed to further clarify the contribution of AIDS to the complex relationship between physical function and DM in the HIV-positive population.

BMI was not found to be associated with DM in the multivariate analysis in this study. While higher BMI is a known risk factor for DM, BMIs among HIV-positive individuals tend to be lower with subsequent loss of subcutaneous adipose tissue (without increases in visceral adipose tissue) compared with the HIV-negative population [30–32]. This was true in our study, in which 40.3% of HIV-negative men were overweight compared with 36.5% in the HIV-positive group. The HIV-negative men also had higher frequencies of obesity compared with the HIV-positive men. Therefore, the lack of association between BMI and DM after adjustment for HIV status and the other covariates is not surprising. Our result was strengthened by the observation that BMI was associated with DM in HIV-negative men but not in HIV-positive men. This seemingly contradictory finding highlights the difficulty in assessing the role of BMI as a risk factor for most metabolic disturbances common to those with HIV infection. We were unable to measure visceral fat as a component of BMI in this study, and therefore our inferences are limited to BMI.

Our findings using physical function as a surrogate for physical activity support a previous observation by Howard *et al.* that physical activity may be independently associated with DM in HIV-positive women [7]. However, this result was not replicated in their similarly designed study in a sample of HIV-positive men [8]. Likewise, Danoff *et al.* failed to find an association with physical activity and diabetes among HIV-positive women [20]. The current study differs from these three previous studies as it is composed primarily of Caucasian men (75%) rather than the African-American and Hispanic cohorts. Compared with the Howard men's study [8], the HIV-positive men in our cohort have a younger median age (42 years) but similar BMI compositions (45% with normal BMI). The differing demographics between studies may partially explain the discrepancy between our findings and those in the Howard study. Because both older age and African-American race are known risk factors for DM [27], our cohort of younger Caucasian men may allow for an increased association of low physical function and DM compared with the older African-American cohort in the Howard study. However, comparisons between our study and the Howard studies are difficult, given our use of physical function data as a surrogate for physical activity level.

The present study had several limitations. First, given the design of this study, a temporal relationship between impaired physical function and diabetes development was not determined. Therefore, it is possible that the lower physical function scores are a result of the diabetes, rather than a precursor to its onset. Recent literature suggests that the presence of diabetes may independently contribute to impaired exercise capacity [33]. Left ventricular dysfunction [33], aging, female sex, poor diabetes control, reduced heart-rate recovery, obesity [34,35], race [35], impaired femoral-arterial blood flow [36] and impaired exercise stroke volumes [37], as well as microvascular diabetic complications including neuropathy and retinopathy [38], may be associated with impaired exercise capacity in Type 2 diabetes. Regensteiner *et al.*, also observed a reduced rate of increase in oxygen consumption during treadmill testing of healthy patients with noninsulin-dependent diabetes, indicating that oxygen-delivery limitations may lead to impaired exercise performance [39]. However, given the noted correlation between the baseline and overall mean physical function scores in our study, it is reasonable to suggest that physical function scores did not drastically decrease following the onset of diabetes. It is also important to note that other factors such as ongoing substance abuse, depression and chronic physical and mental health issues may

also affect physical function. Future research using larger cohort studies to establish incident diabetes cases are necessary to establish a temporal association and to verify the results of this analysis while simultaneously assessing the contribution of additional factors to low physical activity. Secondly, the physical function measure used in this study does not objectively measure physical activity but rather serves as a surrogate by assessing how a person's health status limits his ability to complete physical function tasks. As previously discussed, numerous studies in HIV-negative populations established that physical activity levels are correlated with physical function performance. Brach *et al.* observed a correlation between pedometer readings as a measure of physical activity with the Functional Status Questionnaire ($r = 0.34$), the Physical Performance Test ($r = 0.41$) and gait speed ($r = 0.52$) [10]. Both cross-sectional and prospective studies suggest that low physical activity levels are an independent predictor of both measured and self-reported low physical function [10–15]. A recent study in 8702 American and 1507 British middle-aged adults (aged 50–69 years), found that physical activity was protective against impaired incident physical function (self-reported and measured), independent of BMI [40]. Participants who reported more than or equal to 3 days of activity per week had a lower incidence of physical impairment than individuals who reported less activity in each BMI category (recommended weight, overweight and obese). Hillsdon *et al.* also show that regular physical activity (defined as 2.5 h per week of moderate physical activity or more than or equal to 1 h of vigorous activity per week) is associated with high self-reported physical function (OR: 1.6; 95% confidence interval: 1.3–1.98 adjusted for age, gender, chronic illness, baseline physical function, BMI, smoking and socio-economic status) in a cohort of 6398 middle-aged men and women (aged 39–63 years) [13]. Despite the lack of objectively measured physical activity, these studies are important because they extend the protective effect of physical activity to slightly younger populations. While similar studies have not yet been conducted in HIV-positive cohorts, Roubenoff and Wilson reported an increase in physical function status in patients with HIV wasting who completed a resistance-training program [16]. Therefore, the use of physical function as a surrogate for physical activity, although not ideal, was justified. Studies that objectively measure physical activity levels will need to be completed to verify and strengthen our results. Finally, this study was unable to assess the impact of antiretroviral therapy on DM, as over 90% of the HIV-positive men utilized HAART at some point during the study period and there was little variation in the duration of HAART usage. However, this inability to assess the association of HAART and DM does not detract from our inference that impaired physical function is associated with DM, given that physical function scores were significantly lower in both HIV-negative and HIV-positive men with diabetes.

Conclusion

Despite evidence that physical inactivity may play a role in the development of DM among HIV-negative individuals [5,6,41], the majority of studies of DM and IR in HIV-positive populations have not accounted for physical activity, potentially overestimating the role of antiretroviral therapy as a cause of diabetes in this population [42–44]. This study found that self-reported low physical function as a surrogate for physical activity was associated with DM and IR in both HIV-positive and -negative men. Given these results, future research using objective physical activity measures is warranted to further understand the contribution of low physical activity to DM and IR among HIV-positive populations. Ongoing HIV cohort studies addressing the issues of glucose metabolism in HIV-infected populations should address the role of physical activity.

Future perspective

Over the next decade, clinical trials among HIV-positive populations similar to those completed in HIV-negative populations would be required in order to establish a casual association between low physical activity and the onset of DM and IR. This will take time. At present, researchers and clinicians alike are encouraged to consider the potential for a similar benefit to HIV-positive individuals as demonstrated in the general population. As this relationship becomes more clearly recognized, increased physical activity will become an integral part of diabetes prevention and management in HIV-positive individuals.

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**Box 1. Physical Function 10 questions from the Medical Outcomes Study
36-Item Short Form Health Survey**

'The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much'

<i>Yes, limited a lot</i>	<i>Yes, limited a little</i>	<i>No, not limited at all</i>
<ul style="list-style-type: none"> ■ Vigorous activities, such as running, lifting heavy objects and participating in strenuous sports ■ Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf ■ Lifting or carrying groceries ■ Climbing several flights of stairs ■ Climbing one flight of stairs ■ Bending, kneeling or stooping ■ Walking more than a mile ■ Walking several blocks ■ Walking one block ■ Bathing or dressing yourself 		

Taken from [22].

Executive summary

- HIV-positive men had lower physical-function scores than HIV-negative men, regardless of insulin level and homeostasis model assessment (HOMA) score.
- Men with diabetes had consistently lower mean physical-function scores than both the pre-diabetic and normoglycemic men.
- Baseline physical function scores were lower for men with hyperinsulinemia and men with HOMA levels more than three among HIV-negative and -positive participants.
- Men with both diabetes and AIDS had the lowest mean physical-function score among all men.
- In multivariate analysis, lower physical function score (odds ratio [OR]:1.5 per 25-unit decrease; $p = 0.02$), older age (OR: 1.5 per 5 years; $p < 0.0001$) and Black race (OR: 2.8; $p = 0.002$) were found to be significantly associated with diabetes.
- In a multivariate analysis, older age (OR: 1.3 per 5 years; $p < 0.0001$), higher BMI (OR: 2.8 per 5 units; $p < 0.0001$), HIV infection (OR: 11.3; $p = 0.01$), Black race (OR: 2.0; $p = 0.004$) and the interaction between HIV and physical function (OR: 2.1; $p = 0.0003$) were associated with insulin resistance (IR).
- This study concluded that low-physical function (as a surrogate for physical activity) was associated with diabetes mellitus (DM) and IR in both HIV-positive and -negative men.
- Future research using objective physical activity measures is warranted to further understand the contribution of low physical activity to DM and IR among HIV-infected populations.

Figure 1. Mean baseline physical function scores by diabetes status for HIV-negative men, HIV-positive men and men with AIDS (mean + 1 standard deviation)

Table 1

Baseline demographics by HIV serostatus and glucose levels.

Baseline characteristic	Normal (n = 203)		Pre-diabetes (n = 369)		Diabetes (n = 86)		Overall p-value [¶]
	HIV-negative (n = 125)	HIV-positive (n = 78)	HIV-negative (n = 209)	HIV-positive (n = 160)	HIV-negative (n = 50)	HIV-positive (n = 36)	
Age							<0.0001
• Median	41.5	39.0	45.5	42.6	52.9	48.0 [§]	
• Range	18.7–76.9	22.7–57.2	18.6–70.9	21.8–64.2	30.7–79.1	24.0–68.4	
Race n (%)							0.05
• White	95 (76.6)	65 (83.3)	176 (84.2)	133 (83.1)	34 (69.4)	26 (72.2)	
• Black	27 (21.8)	13 (16.7)	30 (14.4)	24 (15.0)	15 (30.6)	8 (22.2)	
• Other	2 (1.6)	0 (0)	3 (1.4)	3 (1.9)	0 (0)	2 (5.6)	
BMI (median)	25.3	23.8	26.3	25.4 [‡]	28.2	25.2 [§]	0.0008
AIDS n (%)	N/A	10 (4.9)	N/A	11 (3)	N/A	8 (9.30)	
CD4 (median)	851.0	548.0 [*]	942.0	496.0 [‡]	927.5	471.5 [§]	0.7
Insulin n (%)							<0.0001
• 15 µU/ml	92 (73.6)	50 (64.1)	91 (43.5)	57 (35.6)	8 (16)	1 (2.78)	
• >15 µU/ml	33 (26.4)	28 (35.9)	118 (56.5)	103 (64.4)	42 (84)	35 (97.2)	
HOMA-IR, median µU/ml × mmol/l	2.2	2.4	3.0	3.3	6.5	6.7	<0.0001

Wilcoxon Rank Sum was used for continuous variables and Fisher's Exact was used for categorical variables for serostatus comparisons.

Kruskal-Wallis was used for continuous variables or Fisher's Exact was used for categorical variables for overall glucose comparisons.

^{*} p < 0.05 between HIV-negative and -positive men with normoglycemic[‡] p < 0.05 between HIV-negative and -positive with pre-diabetes.[§] p < 0.05 between HIV-negative and -positive with diabetes.[¶] Exact p-value for comparisons between the three glucose groups with HIV-negative and -positive combined.

HOMA-IR: Homeostasis model assessment insulin resistance; N/A: Not available.

Table 2

Mean cross-sectional Physical Function 10 scores from Short Form-36 by diabetes status at each visit date (HIV-negative and -positive men).

Visit date	Normoglycemic	Pre-diabetes	Diabetes	p-value
4/1/1999–9/30/1999 (n = 27)	90.7	97.3	89.0	0.89
10/1/1999–3/31/2000 (n = 114)	85.5	89.1	86.1	0.96
4/1/2000–9/30/2000 (n = 106)	96.9	88.9	78.8	0.23
10/1/2000–3/31/2001 (n = 119)	89.0	92.4	84.4	0.42
4/1/2001–9/30/2001 (n = 101)	90.0	91.3	86.3	0.79
10/1/2001–3/31/2002 (n = 190)	86.9	91.4	89.5	0.35
4/1/2002–9/30/2002 (n = 202)	89.6	90.6	82.8	0.01 *
10/1/2002–3/31/2003 (n = 245)	93.5	91.1	87.6	0.09
4/1/2003–9/30/2003 (n = 340)	91.4	90.7	77.9	<0.0001 *
10/1/2003–3/31/2004 (n = 337)	93.6	89.4	79.0	0.008 *
4/1/2004–9/30/2004 (n = 370)	90.7	90.8	80.8	0.009 *
10/1/2004–3/31/2005 (n = 375)	91.5	88.6	78.2	0.003 *
10/1/2005–3/31/2006 (n = 388)	92.2	88.1	77.5	<0.0001 *

Kruskal–Wallis Test for all comparisons.

* Indicates significant at $p < 0.05$

Table 3

A. Baseline characteristics of study population by HIV serostatus and insulin levels.						
HIV-negative(n = 366)			HIV-positive (n = 239)			
Insulin 15 µU/ml	Insulin >15 µU/ml	p-value	Insulin 15 µU/ml	Insulin >15 µU/ml	p-value	
Physical function score (mean)	93.4	87.1	0.0008	90.9	82.1	0.05
Age (median)	42.4	50.4	<0.0001	41.2	42.7	0.05
BMI (median)	25.5	27.5	<0.0001	25.4	24.3	0.13
Race n (%)			0.02			0.15
• White	221 (59.6)	77 (20.8)		136(54)	61 (27)	
• Black	39(10.5)	29(7.8)		22 (8.7)	20(8.3)	

B. Baseline physical function score by HIV serostatus and HOMA score.						
HOMA-IR 3 µU/ml<mmol/l	HOMA-IR >3 µU/ml<mmol/l	p-value	HOMA-IR 3 µU/ml<mmol/l	HOMA-IR >3 µU/ml<mmol/l	p-value	
Physical function score (mean)	93.4	86.5	<0.0001	91.4	80.8	0.008

Wilcoxon Rank Sum for continuous variables and Chi-square test for categorical variables.
HOMA-IR: Homeostasis model assessment homeostasis model assessment insulin resistance

Multivariate logistic regression analysis of baseline factors associated with diabetes and insulin resistance among HIV-positive and -negative men.

Table 4

Risk factor	Diabetes (n = 262)			Insulin resistance (HOMA-IR) (n = 239)		
	Unadjusted OR	p-value	Adjusted OR	Unadjusted OR	p-value	Adjusted OR
Physical function score (per 25-unit decrease)	1.9	<0.0001	1.5	2.4 [§]	<0.0001	1.2
Age (per 5-year increase)	1.5	<0.0001	1.5	1.3	<0.0001	1.3
BMI (per 5-unit increase)	1.6*	0.0012		2.6	<0.0001	2.8
AIDS status [¶]	2.0*	0.2		1.5 [‡]	0.3	
HIV status [#]	1.2*	0.6		1.5	0.01	11.3
Race ^{**}	1.6	0.1	2.8	2.0	0.006	2.0
CD4	1.0*	0.9		1.0 [‡]	0.4	
Physical function/HIV interaction						2.1
						0.0003

* Variable did not remain in the final diabetes multivariate model.

[‡] Variable did not remain in the final insulin resistance multivariate model.

[§] Physical function score remained in model due to significant interaction with HIV status.

[¶] Reference: no AIDS.

[#] Reference: HIV-negative.

^{**} Reference: White.

HOMA-IR: Homeostasis model assessment insulin resistance; OR: Odds ratio.

'The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much'		
<i>Yes, limited a lot</i>	<i>Yes, limited a little</i>	<i>No, not limited at all</i>
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Taken from [22].