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Skeletal Deconditioning and HIV status in South African Tuberculosis Patients

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Degree to be awarded: MPH

Global Epidemiology

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Skeletal Deconditioning and HIV status in South African Tuberculosis Patients

By

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2025

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Abstract

Skeletal Deconditioning and HIV status in South African Tuberculosis Patients

By Anushua Bhattacharya

Background: Chronic diseases often lead to skeletal deconditioning with a loss of muscle mass which impairs mobility and quality of life. Our understanding of skeletal deconditioning in people with tuberculosis (TB) disease remains limited. This study explores the association between HIV coinfection and grip strength, a marker of skeletal deconditioning and frailty, in patients with TB.

Methods: In this cross-sectional study, we enrolled participants with and without HIV who were newly diagnosed with pulmonary TB in Johannesburg, South Africa. Data were collected through questionnaires and clinical assessments; grip strength was measured with a dynamometer. An independent sample t-test was used to compare grip strength by HIV status. Multiple linear regression models examined the association between HIV status and grip strength.

Results: Among 186 participants with pulmonary TB (median age 37, IQR 30-46), 25% were women and 36% had HIV coinfection. The mean right-hand grip strength was 32.24 kg (SD 9.19) and left-hand grip strength was 30.73 kg (SD 9.04)**.** Participants with HIV exhibited significantly lower grip strength in both hands compared to participants without HIV, with p-values of 0.03 and 0.01 in the right and left hands, respectively. In an unadjusted model, participants with HIV had significantly lower grip strength in both hands (left: $\beta = -3.72$, $p = 0.0097$**;** right**:** $\beta = -3.24$, $p = 0.027$**)**. In a model adjusted for age, sex, and BMI, the association between HIV status and grip strength was significant in both hands (left: $\beta = -2.74$, $p = 0.02$**;** right**:** $\beta = -2.44$, $p = 0.05$). In a third model adjusted for CXR severity in addition to age, sex, and BMI**,** grip strength was associated with HIV status in the left hand ($\beta = -2.74$, $p = 0.03$) but not for the right hand.

Conclusion: We found that among people with active pulmonary TB disease, those with HIV coinfection have lower grip strength than those without HIV, suggesting HIV may impact skeletal deconditioning. This difference persisted after adjusting for age, sex, and BMI, but weakened with further adjustment for extent of radiographic disease, suggesting that factors related to TB severity influences muscle strength.

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INTRODUCTION

Tuberculosis (TB) is a complex, multi-organ disease caused by the bacterium *Mycobacterium tuberculosis*. According to the World Health Organization (WHO), in 2023, approximately 10.8 million new cases of TB were reported, leading to nearly 1.25 million deaths.[1] Alarmingly, 97% of these cases occur in low- and middle-income countries, with regions such as India, sub-Saharan Africa, Micronesia, and the islands of Southeast Asia reporting the highest incidence rates—often exceeding 100 cases per 100,000 people each year.[1] High-burden countries including India, Pakistan, the Philippines, China, South Africa, Indonesia, and Nigeria bear the brunt of TB's devastating morbidity and mortality.[2]

There are several risk factors associated with both acquiring *Mycobacterium tuberculosis* infection and progressing to active TB disease. The risk for infection is driven by close contact to active TB, particularly in overcrowded living conditions, poor ventilation, and high TB-endemic residential areas.[3] In individuals infected with TB, the bacterium can exist without causing symptoms or becoming transmissible – a state known as latent TB infection. However, certain conditions can weaken the immune system and increase the likelihood of progression from latent TB to active disease. Risk factors for progression include immunosuppression, malnutrition, chronic lung disease, active use of tobacco products, and intravenous drug abuse.[4] Once active, TB presents with symptoms such as chronic cough, hemoptysis, fever, and night sweats. Certain immunosuppressive conditions impair the function of CD4+ and CD8+ T cells, which are crucial for mounting an effective immune response against the mycobacterium.[5]

Individuals with Human Immunodeficiency Virus (HIV) are especially vulnerable, experiencing a 20- to 30-fold higher risk of progressing to active TB compared to individuals without HIV.[6] HIV infection results in progressive immunodeficiency characterized by chronic inflammation, persistent immune activation, and a subsequent decline in overall physical function. Notably, TB is the leading cause of death among individuals living with HIV globally.[7] Recent research highlights a significant relationship between HIV and skeletal deconditioning—a condition marked by muscle wasting, reduced grip strength, and frailty.[8] Despite advancements in antiretroviral therapy (ART), individuals living with HIV continue to experience persistent systemic inflammation and immune activation, which contribute substantially to muscle wasting and frailty.[9] Multiple studies have established frailty as a prevalent condition among people living with HIV.[10] Frailty in people with HIV is associated with reduced physical function, impaired

quality of life, and higher mortality rates.[8] For example, a cross-sectional study demonstrated that individuals with HIV exhibited higher frailty scores compared to those without HIV, even after adjusting for age, ART usage, and immune status.[11] Furthermore, HIV-related frailty has been linked to persistently elevated levels of chronic inflammatory biomarkers such as interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor-alpha (TNF-α), reflecting a state of chronic immune activation.[12]

A recent finding has also suggested that TB infection alone may lead to bone demineralization, sarcopenia, and osteoporosis, conditions closely tied to skeletal muscle health and function. A notable study utilizing data from the Korea National Health and Nutrition Examination Survey found an increased risk of sarcopenia and osteoporosis among male TB survivors, highlighting a potential connection between chronic infection and significant musculoskeletal deterioration.[14] Similarly, research in chronic lung diseases such as COPD has demonstrated how inflammation originating in pulmonary tissues can enter systemic circulation, resulting in skeletal muscle impairment.[15] Given these observations, it is plausible that similar pathophysiological mechanisms exist in pulmonary TB, and those may be impacted by HIV co-infection, although this remains inadequately explored.

Despite clear evidence linking HIV and frailty[16-17], studies explicitly examining skeletal deconditioning in people co-infected with TB and HIV remain sparse. This study aims to bridge this gap by investigating the relationship between skeletal deconditioning and HIV coinfection among South African adults newly diagnosed with pulmonary TB. By examining this intersection, the study seeks to improve understanding of the combined impacts of TB and HIV on musculoskeletal health, thereby informing targeted interventions to mitigate frailty and enhance quality of life in affected populations.

METHODS

Study Population

This cross-sectional cohort study used data from the Inflammation and Fibrosis in Pulmonary TB (INFIN-TB) study, an ongoing longitudinal cohort study at the Tembisa Clinical Research Centre of the Aurum Institute of Johannesburg, South Africa. To ensure a study population reflective of the region, participants were recruited from across the public health system

in the Ekurhuleni District, City of Johannesburg, City of Tshwane, and surrounding areas. Participants were recruited by the TB Suspect Register, an electronic record that captures all diagnosed cases of TB. Research staff at Aurum Tembisa identified patients with newly diagnosed TB through continuous review of the register.

Participants were either male or female, at least 18 years or older, with a first known episode of pulmonary TB who were within 14 days of initiation of anti-TB treatment. A diagnosis of TB was confirmed either microbiologically via acid-fast bacilli (AFB) smear or through Xpert MTB/RIF assay, a rapid molecular diagnostic test that simultaneously detects *Mycobacterium tuberculosis* (MTB) DNA and identifies resistance to rifampicin (RIF) within a few hours. The full inclusion and exclusion criteria are listed in Table 1. All participants completed the informed consent process with a member of the study team, with consent forms available in English and local languages, including, but not limited to Sepedi, Xitsonga, and Zulu.

Study Procedures

After informed consent, participants completed a baseline study visit which included vital signs, physical exam, urine pregnancy test, chest x-ray (CXR) imaging, pulmonary function testing (PFT), HIV testing (for those without a prior diagnosis of HIV or recent testing during their TB diagnostic evaluation), TB symptom assessment, self-reported questionnaires, and grip strength. For those with HIV, anti-retroviral therapy (ART) status and duration on medication, as well as CD4 cell count and viral load were collected. Grip strength was measured with a dynamometer (JAMAR Model #5030Jl), which quantifies muscle strength in kilograms by assessing maximal voluntary handgrip force. Participants were tested on the right hand and the left hand three times with the dynamometer. The average of these three measurements for each hand was recorded for analysis. Each CXR was evaluated to assess the radiographic extent and severity of disease. Severity was graded as minimal, moderately advanced, or far advanced using the NTRD scoring system, with two independent reviewers scoring each image followed by reconciliation of discrepancies.[18]

Primary Exposure: HIV Status

TB remains the leading cause of death among people living with HIV. In this study, we used HIV status as the primary exposure to investigate whether immune dysfunction drives skeletal deconditioning. To ensure accurate classification, all participants who self-reported as HIV-negative underwent confirmatory HIV testing at the intake visit. While collected, ART status and

CD4 cell count and viral load were not included in this analysis when assessing participants with HIV.

Primary Outcome: Skeletal Deconditioning

Skeletal deconditioning was measured via grip strength using a dynamometer, as described above. Grip strength is commonly used as a metric for skeletal deconditioning because it is a simple, non-invasive marker of muscle strength in the upper extremities. It is also reasonably easy to use for clinical testing.[19] Therefore, grip strength is a meaningful indication of skeletal deconditioning due to chronic illness or systemic inflammation. Because grip strength was evaluated separately for the right and left hands, potential bias due to handedness was considered. We assessed whether handedness influenced grip strength measurements by comparing strength values between dominant and non-dominant hands using a chi-square analysis and found that there was no significant difference by handedness.

A Directed Acyclic Graph (DAG) was developed to illustrate the hypothesized relationships between HIV status and grip strength, as an indicator of skeletal deconditioning, and potential confounding variables**,** including age, sex, BMI, and CXR severity (Figure 1)**.** The DAG guided the selection of covariates for the unadjusted and adjusted linear regression models, ensuring appropriate control for confounding factors and clarifying the direct and indirect pathways between HIV status and grip strength.

Covariates

Covariates in this analysis included age, sex, body mass index (BMI), and CXR severity. Age was included as a covariate given its well-known association with muscle strength, which could confound the relationship between HIV status and grip strength. Similarly, sex was included due to biological differences in muscle mass between males and females. BMI was included because it is a key determinant of overall muscle mass and nutritional status, both of which influence grip strength**.** Finally, CXR severity was included as a marker of TB disease burden, as more severe pulmonary involvement may contribute to greater systemic inflammation and muscle wasting, thereby impacting grip strength**.**

Statistical Analysis

Univariable analyses were performed on the overall sample and stratified by HIV status to examine the distribution of demographic factors (age, gender, BMI, and ethnicity) as well as SGRQ scores and CXR classification. Comparisons between participants with HIV and without

HIV were conducted using paired t-tests for age, gender, and BMI, Wilcoxon rank-sum test for SGRQ scores, and chi-squared test for CXR classification. Multiple multivariable linear regression models were used to assess the association HIV status and skeletal deconditioning (grip strength). Adjusted multivariable linear regression model controlled for age, sex and BMI, as well as CXR classification. All statistical analyses were conducted using R studio Version 2024.

RESULTS

The demographic characteristics of the 186 enrolled participants are summarized in Table 2. The largest proportion of participants were between 19 and 35 years old (79, 42.5%), making this the most represented age group. The cohort included 44 (24.7%) females, with a higher proportion of women in those with HIV (23/67, 34.3%) compared to those without HIV (21/119, 17.6%), although this difference was not statistically significant ($p = 0.06$). Participants were predominantly of Black ethnicity (176, 98.3%), with minimal representation from other racial or ethnic groups. There were no significant differences between participants with HIV versus those without HIV in age, sex, or BMI.

The SGRQ score, which measures respiratory health symptoms, was similar between participants with HIV and without HIV, with mean scores of 27.61 (SD 20.73) and 25.77 (SD 17.86), respectively. The difference was not statistically significant (p=0.63), indicating comparable respiratory health impairment across both groups. In a healthy population, SGRQ scores are typically below 10 indicating minimal or no respiratory symptoms.[20] In contrast, there were significant differences in CXR score by HIV status, reflecting the severity of pulmonary TB disease. Participants with HIV had a higher proportion of minimally advanced disease (18.5%) compared to participants without HIV (1.8%), while far-advanced disease was more prevalent among participants without HIV (67%) compared to participants with HIV (53.8%) (p=0.0003).

The mean grip strength measurements for the overall cohort and by HIV status are in Table 3. Participants with HIV had significantly lower grip strength than those without HIV for both right and left hands. Specifically, right-hand grip strength was 30.23 kg (SD 9.69) for participants with HIV compared to 33.47 kg (SD 8.77) for participants without HIV (p=0.03). Similarly, left-hand grip strength was 28.37 kg (SD 9.43) for participants with HIV and 32.09 kg (SD 8.65) for participants without HIV (p=0.01) (Figure 2).

In an unadjusted linear regression model of the association between HIV status and grip strength, participants with HIV had 3.72 kgs lower grip strength in the left hand and 3.24 kgs lower grip strength in the right hand compared to participants without HIV, and this finding was significant (left grip strength: β = -3.72, p=0.0097; right grip strength: β = -3.24, p=0.027) (Table 4). After adjusting for age, sex, and BMI, the association remained statistically significant, although slightly reduced. Participants with HIV had 2.74 kgs lower grip strength in the left hand and 2.44 kgs lower grip strength in the right hand compared to participants without HIV (left grip strength: β = -2.74, p=0.02; right grip strength: β = -2.44, p=0.05). In the third and final adjusted model in this study which included age, sex, BMI, and CXR severity, the association persisted for left grip strength. Participants with HIV having 2.74 kgs lower grip strength than participants without HIV (β = -2.74, p=0.03), but the relationship with right grip strength weakened and was no longer significant with participants with HIV having 2.02 lower grip strength compared to participants without HIV(β = -2.02, p=0.1).

DISCUSSION

In this cross-sectional study conducted among patients with newly diagnosed pulmonary TB in Johannesburg, South Africa, we investigated whether HIV coinfection was associated with grip strength, a marker of skeletal deconditioning. We hypothesized that individuals with HIV would experience greater immune dysregulation, leading to more pronounced skeletal impairment. We found a significant association between HIV status and skeletal deconditioning, as evidenced by lower grip strength among participants with HIV, in both an unadjusted model and one adjusted for age, sex, and BMI. However, the association was attenuated with additional adjustment for CXR severity and was only significant for the left-hand grip strength, suggesting that the severity of the TB pulmonary disease may play influence skeletal deconditioning. These statistically significant differences highlight a notable reduction in muscle strength among participants with HIV, suggesting a potential impact of HIV infection on skeletal deconditioning in the presence of TB co-infection. The attenuation in the adjusted models highlights the potential additive or synergistic role of TB-related factors such as reduced physical activity, systemic inflammation, and hypoxia in exacerbating skeletal deconditioning alongside HIV-associated immune dysfunction.[21]

Our finding that the association between HIV status and grip strength was attenuated after adjusting for CXR severity suggests that pulmonary disease burden may partially mediate the relationship between HIV and skeletal deconditioning. While individuals with HIV in our study had less advanced radiographic disease—consistent with their reduced capacity to mount a strong inflammatory response—we adjusted for these differences in our model, suggesting that the observed relationship may be mediated by factors beyond radiographic disease burden alone. Therefore, the diminished association in the right hand—but its persistence in the left—may reflect asymmetry, measurement variability, or unmeasured factors influencing muscle strength beyond what was captured by radiographic TB severity. However, given that the negative association remained in both hands, albeit without statistical significance in the right, this pattern may also be due to limited sample size and reduced power, rather than a true biological difference. Taken together with the attenuated beta coefficients after adjustment, this suggests that radiographic severity may partially confound but not fully explain the relationship between HIV co-infection and reduced grip strength.

Altogether, these results emphasize the complex dynamics between TB severity, HIV, and skeletal deconditioning, and highlight the importance of integrating both pulmonary and physical functional assessments when researching and treating HIV and TB co-infected populations. The attenuation of the association between HIV and grip strength after adjusting for CXR severity suggests that lung health and musculoskeletal health, while interrelated, may reflect distinct dimensions of disease burden. This underscores the need for independent evaluation of both systems to fully capture the health status of individuals with TB and HIV. Future longitudinal studies should also explore how ART and TB treatment influence musculoskeletal health over time.

There are several strengths to this study. To our knowledge, it is the first of its kind to investigate skeletal deconditioning in individuals newly diagnosed with pulmonary TB. By studying a cohort in a high TB and HIV burden region, the findings provide valuable insights relevant to similar contexts, although differences in factors such as HIV prevalence, genetics, and nutritional status should be considered when extrapolating these results to other high-burden settings. The study utilized a validated measure of skeletal deconditioning via dynamometry which then enhances the reliability and comparability of the data. By using validated tools, this study used a consistent measurement that allows for the results of this study to be interpreted within the

context of other existing studies. A final strength of this study was including the CXR severity data. These measures provided insight into the participant's symptom burden and gave a comprehensive assessment of disease severity.

Despite these strengths of the study, there are several limitations to consider. This study was a cross-sectional study which limited its ability to establish causality as it only provides a snapshot relationship between HIV status, TB severity, and grip strength. Despite adjusting for key variables like age, sex, BMI and CXR severity, other factors were not accounted for and could potentially lead to residual confounding. These variables include, but are not limited to, comorbidities such as diabetes mellitus, duration of HIV infection, CD4 count and viral load, ART treatment and adherence, and inflammatory markers. The findings may not be generalizable to populations outside of high HIV/TB burden regions. Finally, the small sample size limits the precision and reliability of the findings. Future studies with larger cohorts are needed to validate these results and provide more accurate estimates of the relationship between immune status and skeletal deconditioning in TB-affected populations.

CONCLUSION

In conclusion, this study demonstrated that people with pulmonary TB and HIV coinfection have lower grip strength than those with pulmonary TB without HIV, suggesting HIV coinfection may impact skeletal deconditioning. While this association persisted even after adjusting for demographic and physiologic factors, it diminished when accounting for TB disease severity as measured by the extent of radiographic disease. This suggests that other unmeasured factors related to illness severity may play a role in influencing muscle strength outcomes.

Future studies should account for CD4 cell count, HIV viral load, and ART treatment and duration, as well as follow grip strength longitudinally from TB diagnosis and treatment into the post-treatment period. Such longitudinal assessments could provide valuable insights into the trajectory of skeletal recovery with TB treatment and further explore and guide future interventions. Overall, this study highlights the potential impact of HIV co-infection on skeletal deconditioning and suggests that TB severity may play a key role in muscle strength outcomes, underscoring a need for further research in skeletal deconditioning and targeted interventions in this population.

TABLES AND FIGURES

Table 1: Inclusion and Exclusion Criteria used to select participants for the study

Inclusion Criteria	Exclusion Criteria
- Age ≥ 18 years old - First known episode of pulmonary TB - Chest X-ray at the time of study screening with minimal, moderate, or severe radiographic involvement (i.e., any chest x-ray findings - Have the ability to provide written informed consent	- Previous history of active TB disease - Recent (within <30 days prior to enrollment) use of corticosteroids or other immunomodulatory medications (dose-equivalent to >5mg prednisone per day) - Currently pregnant (a negative hCG pregnancy test is required for females of child-bearing potential prior to participation); - Current diagnosis of central nervous system TB (i.e., TB meningitis); - Current or upcoming planned incarceration - Determined by the investigator(s) to be clinically unsuitable for the study (e.g. based on screening visit and/or during study procedures)

Figure 1: Directed Acyclic Graph (DAG) illustrating the relationship between HIV status, skeletal deconditioning (measured by grip strength), and potential confounding variables such as age, sex, BMI, and CXR severity.

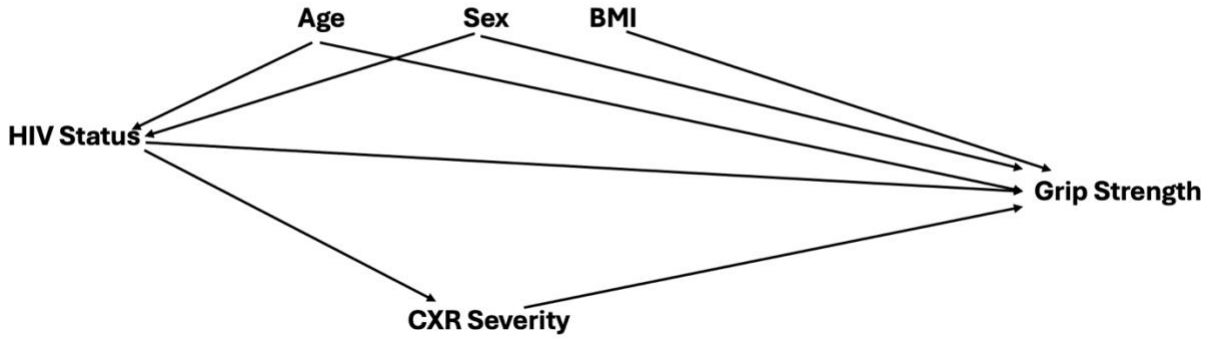

Table 2: Demographic and clinical characteristics of the study cohort overall and by HIV status. Paired t-tests*, Wilcoxon rank-sum test[+], and chi-squared test[#] were used to compare characteristics of those with and without HIV.

	All (n=186)	HIV Positive (n=67)	HIV Negative (n=119)	p-value

Age n(%) 19-35 36-50 51-74	 79 (42.47) 69 (37.09) 31 (16.67)	 21 (31.3) 30 (44.77) 13 (19.4)	 58 (48.7) 39 (32.77) 18 (15.12)	 0.39*
Female sex n(%)	44 (24.7)	21 (34.3)	23 (17.6)	0.06*
BMI mean (SD)	20.34 (4.32)	21.1 (5.29)	19.30 (3.67)	0.10*
Ethnicity n(%) White Black People of Color	 0 (0) 176 (98.3) 3 (1.67)	 0 (0) 67 (100) 0 (0)	 0(0) 112 (94.12) 7 (5.89)	
SGRQ Score mean (SD)	26.44 (18.85)	27.61 (20.73)	25.77 (17.86)	0.63[+]
CXR classification n(%) Minimally Mod. Advanced Far advanced	 14 (8) 53 (29) 115 (63)	 12 (18.5) 18 (27.7) 35 (53.8)	 2(1.8) 34 (29) 78 (67)	 0.0003[#]

Table 3: Grip Strength by HIV status. Paired t-tests* was used to compare the right and left hand in the whole study and in participants with and without HIV.

Grip Strength (kgs)	**All (n=186)**	**HIV Positive (n=67)**	**HIV Negative (n=119)**	**p-value**
Right	32.24 (9.19)	30.23 (9.69)	33.47 (8.77)	**0.03**
Left	30.73 (9.04)	28.37 (9.43)	32.09 (8.65)	**0.01**

Figure 2: Bar graph showing the distribution of grip strength between participants with and without HIV.

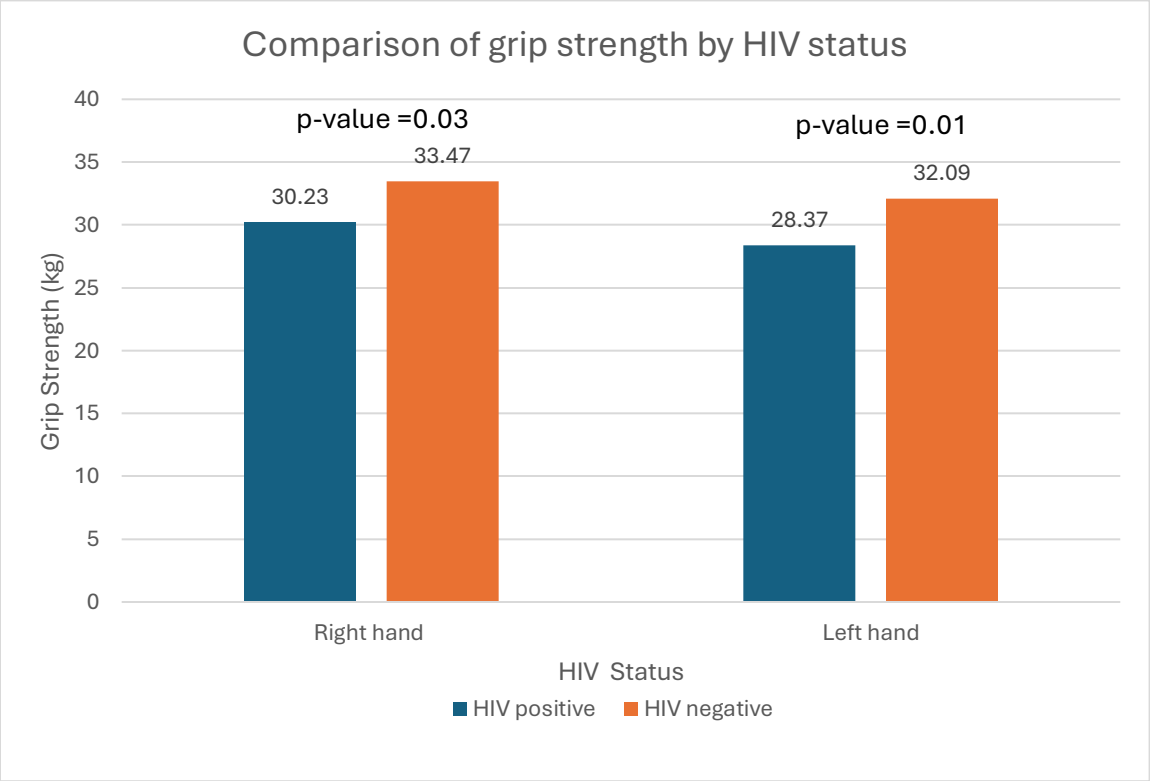

Table 4: Association between HIV status and Grip strength in unadjusted and adjusted multiple linear regression models

	Variable	Coefficient	p-value
Unadjusted model			
	L grip strength	**-3.72**	**0.0097**
	R grip strength	**-3.24**	**0.027**
Adjusted for age, sex, and BMI			
	L grip strength	**-2.82**	**0.02**
	R grip strength	**-2.44**	**0.05**
Adjusted for age, sex, BMI, and CXR severity			
	L grip strength	**-2.74**	**0.03**
	R grip strength	-2.02	0.1

CITATIONS

1. **World Health Organization.** (2023). *Tuberculosis fact sheet*. Retrieved from https://www.who.int/news-room/fact-sheets/detail/tuberculosis. Accessed February 12, 2025.
2. **International Organization for Migration.** (2022). *Global tuberculosis report 2022*. Retrieved from https://www.iom.int/sites/g/files/tmzbdl486/files/documents/2023-03/Global-TB-Report-2022.pdf Accessed February 12, 2025.
3. Lee, J. Y., Kwon, N., Goo, G. Y., & Cho, S. I. (2022). Inadequate housing and pulmonary tuberculosis: a systematic review. *BMC public health*, *22*(1), 622. https://doi.org/10.1186/s12889-022-12879-6
4. Narasimhan, P., Wood, J., MacIntyre, C. R., & Mathai, D. (2013). Risk factors for tuberculosis. *Pulmonary Medicine, 2013*, Article 828939. https://doi.org/10.1155/2013/828939
5. Behar, S. M., Divangahi, M., & Remold, H. G. (2014). Evasion of innate immunity by *Mycobacterium tuberculosis*. *Immunity, 40*(6), 845-859. https://doi.org/10.1016/j.immuni.2014.05.010
6. Bruchfeld, J., Correia-Neves, M., & Källenius, G. (2016). Tuberculosis and HIV coinfection. *Microbiology Spectrum, 4*(6). https://doi.org/10.1128/microbiolspec.TNMI7-0028-2016
7. World Health Organization. *Tuberculosis* fact sheet. Retrieved from https://www.who.int/news-room/fact-sheets/detail/tuberculosis. Accessed February 12, 2025.
8. Erlandson, K. M., Allshouse, A. A., Jankowski, C. M., Duong, S., Mawhinney, S., Kohrt, W. M., & Campbell, T. B. (2017). Risk factors for falls in HIV-infected persons. *Journal of Acquired Immune Deficiency Syndromes*, 76(3), e39–e44.
9. K. M., Allshouse, A. A., Jankowski, C. M., Duong, S., Mawhinney, S., Kohrt, W. M., & Campbell, T. B. (2017). Risk factors for falls in HIV-infected persons. *Journal of Acquired Immune Deficiency Syndromes*, 76(3), e39–e44.
10. Negin, J., Cumming, R. G., & de Lamballerie, M. R. (2016). A systematic review of prevalence and predictors of frailty in individuals with human immunodeficiency virus.

Journal of the American Geriatrics Society, 64(5), 1006-1014. https://doi.org/10.1111/jgs.14101

11. Levett, T. J., Cresswell, F. V., Malik, M. A., Fisher, M., & Wright, J. (2016). Systematic review of prevalence and predictors of frailty in individuals with human immunodeficiency virus. *Journal of the American Geriatrics Society, 64*(5), 1006-1014. https://doi.org/10.1111/jgs.14101
12. Desquilbet, L., Margolick, J. B., Fried, L. P., Phair, J. P., Jamieson, B. D., Holloway, M., & Jacobson, L. P. (2009). Relationship between a frailty-related phenotype and progressive deterioration of the immune system in HIV-infected men. *Aging Cell, 8*(3), 234-241. https://doi.org/10.1111/j.1474-9726.2009.00474.x
13. **Merck Manual Professional Version.** (n.d.). *Extrapulmonary tuberculosis (TB)*. Merck & Co., Inc. Retrieved from https://www.merckmanuals.com/professional/infectious-diseases/mycobacteria/extrapulmonary-tuberculosis-tb
14. Shin, H. J., Kim, C. H., Lee, J. H., Lee, J. J., Lee, J. H., & Lee, J. H. (2017). Risk of sarcopenia and osteoporosis in male tuberculosis survivors: Korea National Health and Nutrition Examination Survey. *Scientific Reports, 7*, 13127. https://doi.org/10.1038/s41598-017-12419-y
15. Byun, M. K., Cho, E. N., Chang, J., Ahn, C. M., & Kim, H. J. (2017). Sarcopenia correlates with systemic inflammation in COPD. *International Journal of Chronic Obstructive Pulmonary Disease, 12*, 669–675. https://doi.org/10.2147/COPD.S130790
16. Pathai, S., Gilbert, C., Weiss, H. A., Cook, C., Wood, R., & Lawn, S. D. (2013). **Frailty in HIV-infected adults in South Africa**. *Journal of Acquired Immune Deficiency Syndromes*, 62(1), 43–51. https://doi.org/10.1097/QAI.0b013e318276d110
17. **Greene, M., Covinsky, K. E., Astemborski, J., Del Bianco, K., Satterwhite, S., Young, M., Mehta, S. H., Kirk, G. D., & Gross, A. L.** (2020). Frailty transitions, inflammation, and mortality among people with HIV infection and injection drug use. *AIDS, 34*(10), 1425–1433. https://doi.org/10.1097/QAD.0000000000002552
18. National Tuberculosis and Respiratory Disease Association. (1969). *Diagnostic Standards and Classification of Tuberculosis*. New York: National Tuberculosis and Respiratory Disease Association.

19. Bohannon, R. W. (2011). Dynamometer-measured hand-grip strength predicts hospital discharge disposition after stroke. *Journal of Stroke and Cerebrovascular Diseases, 20*(2), 197–201. https://doi.org/10.1016/j.jstrokecerebrovasdis.2009.10.002
20. Shirley Ryan AbilityLab. (2012, July 25). *Saint George's Respiratory Questionnaire*. RehabMeasures Database. https://www.sralab.org/rehabilitation-measures/saint-georges-respiratory-questionnaire
21. Erlandson, K. M., Tian, F., Oursler, K. K., Araujo, S., Cook, R., Bartali, B., ... & Kalyani, R. R. (2020). Application of Selected Muscle Strength and Body Mass Cut Points for Sarcopenia and Sarcopenic Obesity in Men and Women With or At Risk for HIV Infection. *Journal of Acquired Immune Deficiency Syndromes*, *84*(2), 134–142. https://doi.org/10.1097/QAI.0000000000002327