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# Predicting Treatment Adherence in Patients with Drug-Resistant Tuberculosis: Insights from Socioeconomic, Demographic, and Clinical Factors of Patients in Rural Eastern Cape

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**Abstract: Background**: Drug-resistant tuberculosis (DR-TB) is a formidable challenge to global health. Patients are compelled to adhere to intricate medication regimens over extended periods, and any failure to comply with these treatment protocols can lead to treatment failure, increased mortality rates, and a heightened risk of developing further drug resistance. This study identifies the key factors that influence treatment adherence among patients with DR-TB. Furthermore, it rigorously evaluates the predictive accuracy of machine learning models in assessing treatment adherence, with a strong focus on socioeconomic, demographic, and clinical factors. **Methods**: A retrospective analysis was conducted on patients with DR-TB in rural Eastern Cape. Data were collected from medical records. Four different models were developed and tested to evaluate their effectiveness in predicting treatment adherence: Random Forest, Logistic regression, Support Vector Machine (SVM), and Gradient Boosting. **Result**s: The Random Forest model achieved an accuracy of 53.3% in predicting treatment adherence. An analysis of feature importance indicated that age, income, education, social history, patient category, and comorbidities were the most significant factors influencing adherence. Patients with higher incomes, higher levels of education, and fewer comorbidities were more likely to follow their treatment plans. **Conclusion**: Socioeconomic and clinical factors, such as income, education level, and the presence of comorbidities, significantly influence adherence to DR-TB treatment. These findings indicate that machine-learning models, particularly Random Forest algorithms, can effectively assist in clinical decision-making by identifying patients who may be at risk of not adhering to their treatment.

**Keywords:** clinical factors; drug-resistant tuberculosis; treatment adherence; socioeconomic factors; predictive modeling; random forest model

## 1. Introduction

Drug-resistant tuberculosis (DR-TB) poses a significant global health challenge, necessitating that patients adhere to complex, long-term medication regimens [1,2]. Despite the availability of effective antitubercular drugs, non-adherence to treatment remains a substantial barrier, leading to increased morbidity, mortality, and the further spread of DR-TB strains [3]. While clinical factors influencing adherence are well-documented, socioeconomic and demographic variables also play a critical role [4–6]. However, the relative impact of these factors on DR-TB populations has not been thoroughly investigated [7]. According to the World Health Organization (WHO), treatment adherence for tuberculosis (TB) refers to the extent to which the prescribed medication regimen is followed [8]. In 2017, an estimated 10 million individuals had active TB, with 9% of these cases involving people living with HIV (PLWH). Four years later, there was an increase with an estimated 10.6 million people (95% CI: 9.9–11 million) developing TB worldwide, equivalent to an incidence of

134 (95% CI: 125–143) per 100,000 population. This revealed an increase in TB incidence globally by 4.5%, reversing a long-term trend of a moderate 2% annual decrease over the past decade [8,9]. This situation places an excessive strain on healthcare systems, as the lengthy treatment regimen increases the likelihood of poor treatment adherence which can lead to the development of medication resistance. Patients with multiple infections who miss scheduled clinic appointments are more susceptible to poor treatment adherence and worse health outcomes [10–13]. Due to this therapeutic challenge, treatment for HIV and TB is often interrupted, prolonging treatment durations and heightening the risk of drug resistance [14].

South Africa contributes about 20% of the global burden of TB/HIV co-infections, making it one of the countries most affected by the intertwined epidemic with approximately 180,000 incident TB cases comprising people with HIV coinfection [15,16]. Consequently, many South Africans co-infected with HIV and TB require simultaneous treatment for both conditions [16]. The dual challenges presented by both infections complicate treatment adherence. It is well-established that maximizing treatment adherence significantly improves the likelihood of successful TB treatment [17]. This principle similarly applies to HIV infection, where sustained viral suppression depends on a high level of adherence to antiretroviral therapy (ART). Improving adherence can lead to reductions in HIV transmission and an enhancement in the quality of life for infected individuals [18,19]. Despite advancements in treatment availability and accessibility, TB/HIV co-infection continues to be a complex public health issue contributing to the inability of TB-control initiatives, especially in high-burden nations, to meet effective treatment goals [16,20]. This situation necessitates a new strategy in South Africa with a high prevalence of HIV/AIDS. Methods for evaluating patient compliance with anti-TB medication typically focus on the percentage of patients who take 80% or more of their prescribed doses. Both direct and indirect measures of adherence to anti-TB regimens have been proposed. Direct measurement can involve testing for drug metabolites in the blood or urine. Indirect measurement may include assessing pharmacy refill records on a monthly basis or utilizing patient-reported outcome measures, such as the TB Medication Adherence Scale (TBMAS) [24,25].

Evaluating the factors that influence treatment adherence in patients with TB, TB/HIV, and HIV-positive individuals is essential for identifying effective health system interventions to support individuals undergoing ART, and combined therapy for improved treatment outcomes. This study aimed to identify key factors that affect treatment adherence in DR-TB patients in rural Eastern Cape. Additionally, it sought to develop a predictive model using random forest algorithms to estimate the likelihood of adherence based on socioeconomic, demographic, and clinical variables.

## 2. Materials and Methods

### *2.1. Study Design and Population*

A retrospective analysis was conducted on a group of patients undergoing treatment for drug-resistant tuberculosis (DR-TB) at selected clinics in the rural Eastern Cape. Data collection involved reviewing medical records, which included information about patient demographics, socioeconomic status, clinical history, and treatment outcomes. The sample size calculation for the population was adapted from the work of Agresti and Finlay [26].

$$\boldsymbol{Sample\ proportion}\ (\%) = \frac{\boldsymbol{Sample\ size\ by}}{\boldsymbol{Total\ population}} \boldsymbol{X\ 100}$$

$$\boldsymbol{Sample\ proportion}\ (\%) = \frac{\mathbf{108}}{\mathbf{450}} \boldsymbol{X\ 100}$$

$$\boldsymbol{Sample\ proportion}\ (\%) = \mathbf{0.24}$$

The confidence interval for a proportion population of 24% was established based on the estimation of the proportion.

The sample size is n=108, the total population is N=450, and the observed proportion is:

$$\boldsymbol{p} = \frac{\mathbf{108}}{\mathbf{450}}$$

$$\boldsymbol{p} = \mathbf{0.24}\ (\mathbf{24}\%)$$

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A confidence interval (CI) of 95% for a proportion was calculated as:

$$\boldsymbol{CI} = \mathbf{p} \pm \mathbf{Z} \times \sqrt{\frac{\boldsymbol{p}(\mathbf{1}-\boldsymbol{p})}{\boldsymbol{n}}}$$

where:

p = 0.24 (sample proportion),
Z = 1.96 for a 95% confidence level,
n = 450 (total population).

The 95% CI indicates that the proportion of 24% is estimated to lie within the range of 20.05% to 27.95%.

The key variables examined included age (in years), gender (male, female), income level (low, middle, high), education (no formal education, primary, secondary, tertiary), HIV status (positive, negative), comorbidities (the number of concurrent health conditions), social history (smoking, drinking habit), occupation (unemployed, manual labor, government employee, corporate job), and patient classification (new cases, relapses, or chronic cases, such as TAL - treatment after loss to follow-up, TF1 - treatment following failure of first-line drugs, and TF2 - treatment after failure of second-line drugs).

*2.2. Operational Definition*

2.2.1. Treatment Adherence

A benchmark of at least 80% compliance is established. This measurement is based on both medication refill data and self-reported adherence from patients. To evaluate adherence using a custom benchmark of 80% compliance, adherence is calculated as the percentage of actual treatment days completed compared to the expected treatment days, using the following formula:

$$Adherence\ (\%) = \frac{Actual\ treatment\ days\ completed}{Expected\ treatment\ days} X\ 100$$

To determine the actual number of treatment days completed by each patient, we analyzed the treatment start and end dates. Expected treatment durations were defined based on the type of regimen: short regimens were assumed to last 6 months (180 days), while long regimens were set at 18 months (540 days). For each patient, we calculated adherence percentages and categorized them into adherent and non-adherent groups accordingly. Finally, we summarized the proportions of adherent versus non-adherent patients, providing a clear overview of compliance about the 80% benchmark.

Clinical evidence shows that 80% or higher adherence levels are essential for achieving therapeutic success across various medical conditions.

2.2.2. New patients are patients who have never been treated for TB or have taken anti-TB medications for less than 4 weeks.

2.2.3. Relapse patients are patients who were previously treated for TB, were declared cured or completed treatment at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection).

2.2.4. TAL These are patients previously treated for TB and declared lost to follow-up (LTFU) at the end of their most recent course of treatment.

2.2.5. TF1 are those patients who have previously been treated for TB with first-line drugs such as isoniazid, rifampicin, ethambutol, pyrazinamide, and streptomycin and whose treatment failed at the end of their most recent course of treatment.

2.2.6. TF2 are those who have previously been treated for DR-TB with second-line drugs such as bedaquiline, linezolid, moxifloxacin, levofloxacin, clofazimine, cycloserine, para-aminosalicylic acid, propylthiouracil, and amikacin and whose treatment failed at the end of their most recent course of treatment.

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### 2.3. Model Development

Before starting the analysis, categorical variables were converted into numeric values. The dataset was divided into training (80%) and testing (20%) sets to evaluate the performance of the predictive model. A random forest model was utilized to predict treatment adherence. To understand the contributing factors to the predictions, a feature importance analysis was conducted. The model's performance was assessed using various accuracy metrics, and cross-validation was applied to enhance its robustness. This analysis leveraged the capabilities of the random forest model, an effective ensemble learning technique known for its ability to capture complex interactions among features in predicting treatment adherence.

### 2.4. Training the Model

A random forest classifier was developed using a comprehensive dataset that included a variety of socioeconomic, demographic, and clinical factors related to patients. This dataset featured crucial variables such as age, income, education level, gender, HIV status, existing comorbidities, and lifestyle factors like smoking and alcohol use. Thereafter, the dataset was carefully divided into training and testing subsets. This strategy allowed the classifier to learn and adapt from the training data while providing a means to assess its performance on a separate set of unseen data. This process is essential for verifying the model's ability to generalize its findings beyond the specific examples included in the training phase. The model's effectiveness was evaluated through various metrics, which helped to measure its accuracy and reliability in predicting outcomes based on the input features. This evaluation process is critical for ensuring the model's practical applicability in real-world scenarios.

### 2.5. Evaluating Feature Importance

The random forest model assesses the importance of each feature by examining its role in minimizing the model's prediction error. This evaluation process involves a detailed analysis of how the various decision trees within the random forest utilize different features to partition the data points effectively, thereby enhancing the accuracy of classifications. The importance score assigned to each feature is determined through an aggregation process that considers the frequency and effectiveness of each feature employed across the entire ensemble of trees. Features that play a significant role in diminishing impurity, measured by metrics such as Gini impurity or entropy are recognized as more crucial for the model's predictive performance. This method ensures a comprehensive understanding of each feature's contribution to the overall model efficacy.

### 2.6. Result Interpretation

Feature importance scores provide valuable insights into the significance of different factors in predicting patient adherence to treatment. These scores have been normalized to ensure that their total equals 1, or 100% when expressed as percentages. To enhance understanding, a bar chart was created to visually represent these scores.

## 3. Results

Figure 1 depicts adherence categories based on the 80% compliance benchmark and provides a concise visual representation of patient adherence levels. The adherent (≥80%) category constitutes the majority of patients, indicating that most individuals completed at least 80% of their expected treatment days. This high proportion reflects strong compliance and effective treatment management, which is encouraging for achieving favorable treatment outcomes. Conversely, the non-adherent (<80%) group highlights patients who did not meet the benchmark, signaling potential challenges such as limited access to care, medication side effects, or socioeconomic barriers.

A small percentage of patients fall into the unknown category, representing those with incomplete or missing data on treatment start and end dates.

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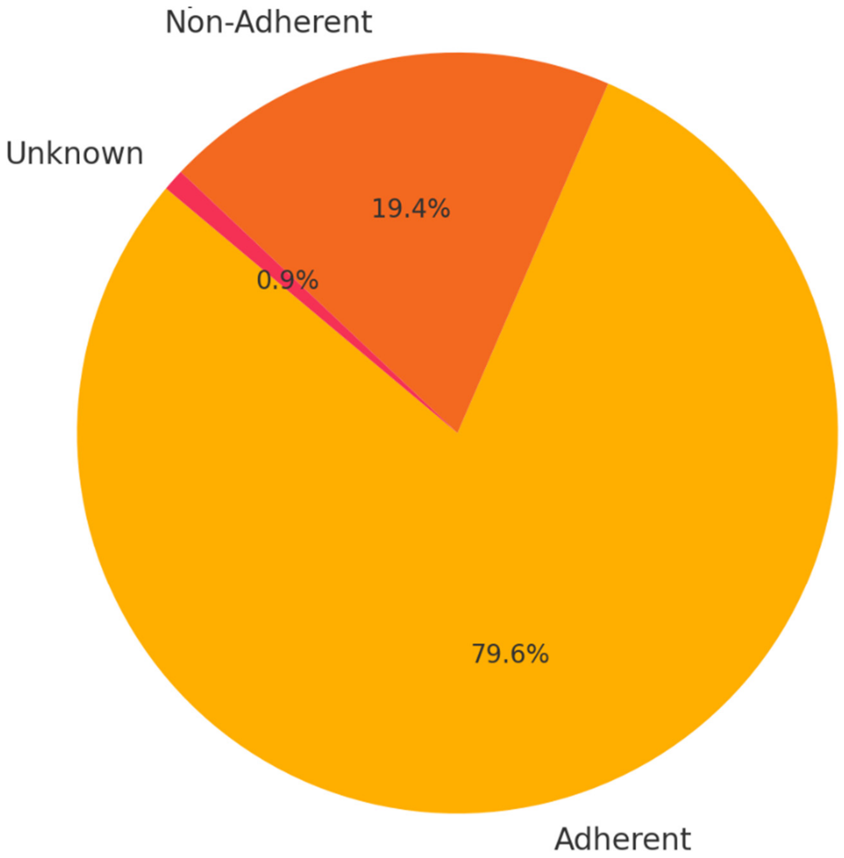


**Figure 1.** Adherence proportions (benchmark: ≥ 80% compliance)**.**

The study comprised a sample size of 108 patients. Statistical analysis of demographic factors, including gender and age groups, revealed no significant deviations in their distributions. For gender, the observed counts were 57 males and 51 females, which perfectly aligned with the expected counts. The chi-square statistic was 0.0, with a p-value of 1.0, indicating no statistical variation from the expected proportions. Similarly in age groups, yielded a chi-square statistic of 0.0 and a p-value of 1.0.

Treatment adherence varies across different age groups. Younger patients, specifically those aged 20-30 and 30-40, exhibit high adherence rates, ranging from 85% to 88%. In comparison, middle-aged patients, aged 40-50 and 50-60, experience a moderate decline in adherence, with rates between 75% and 80%. Conversely, older patients, aged 60-70 and 70 and above, demonstrate a significant decrease in adherence, with rates falling to between 60% and 65% (Figure 2).

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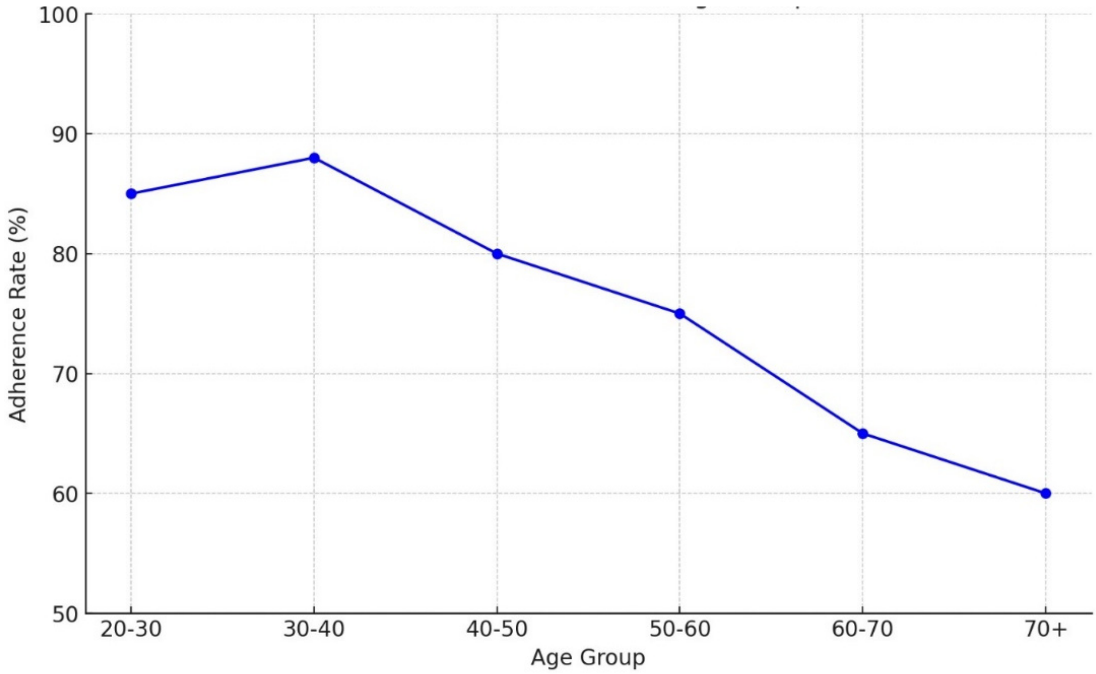


**Figure 2.** Adherence trend across age groups.

Figure 3 presents a comparison of adherence to treatment between men and women. The data indicates that men demonstrate an adherence rate of approximately 58.8%, while women exhibit a notably higher rate of around 75.4%.

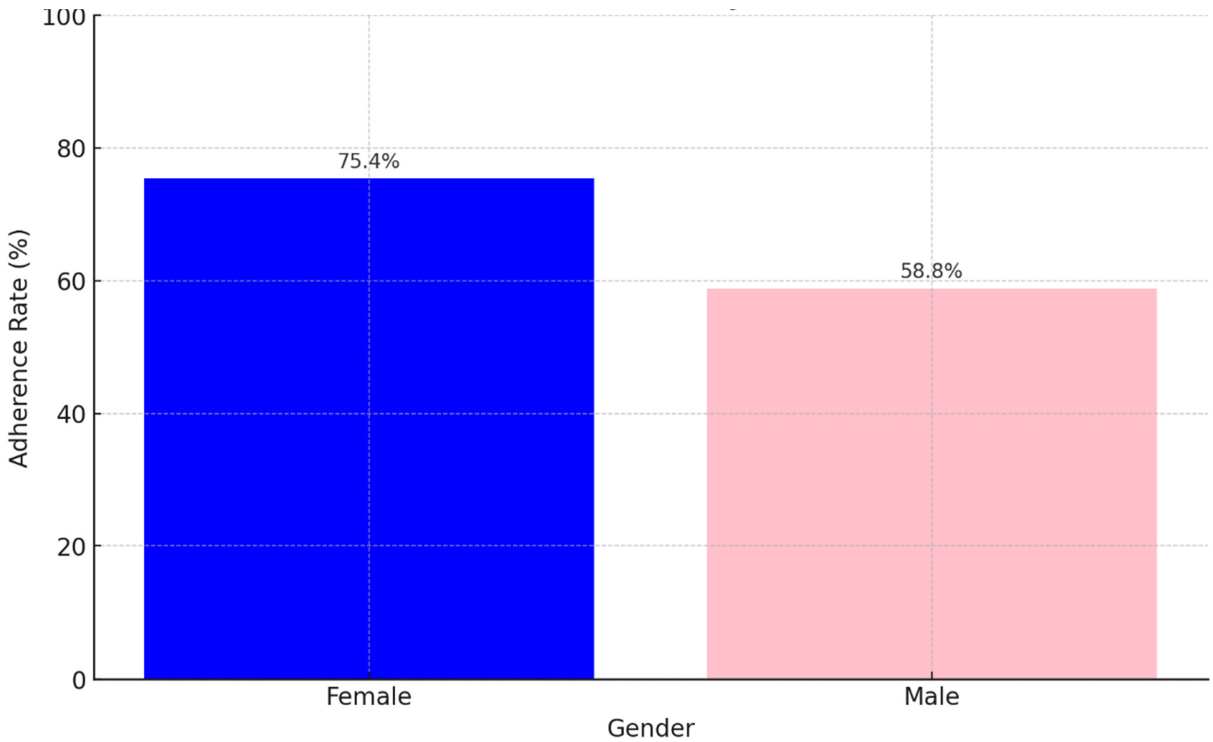


**Figure 3.** Adherence stratified by gender.

Figure 4 illustrates the adherence rates across different income groups. It highlights that low-income patients tend to have the lowest adherence rates, with approximately 62% consistently following their prescribed treatments. In contrast, middle-income patients show a notable improvement, achieving adherence rates of around 75%. Finally, high-income patients exhibit the highest level of adherence, reaching about 85%, indicating that financial stability may contribute to better compliance with healthcare recommendations.

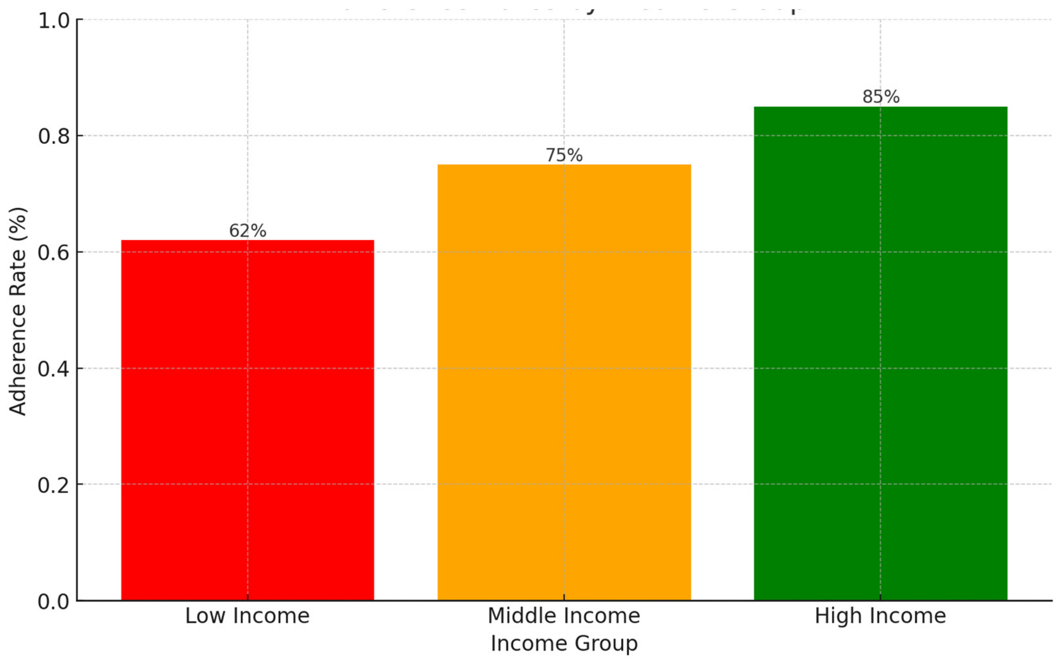


**Figure 4.** Adherence stratified by income groups**.**

Figure 5 demonstrate the adherence rate improves as the level of education increases. It starts at 62% for individuals with no formal education, rises to 70% for those with a primary education, reaches 78% for secondary education, and peaks at 85% for individuals with tertiary education. This trend highlights the significant impact of education on treatment adherence, suggesting that higher levels of education are associated with a better understanding of and commitment to treatment regimens.

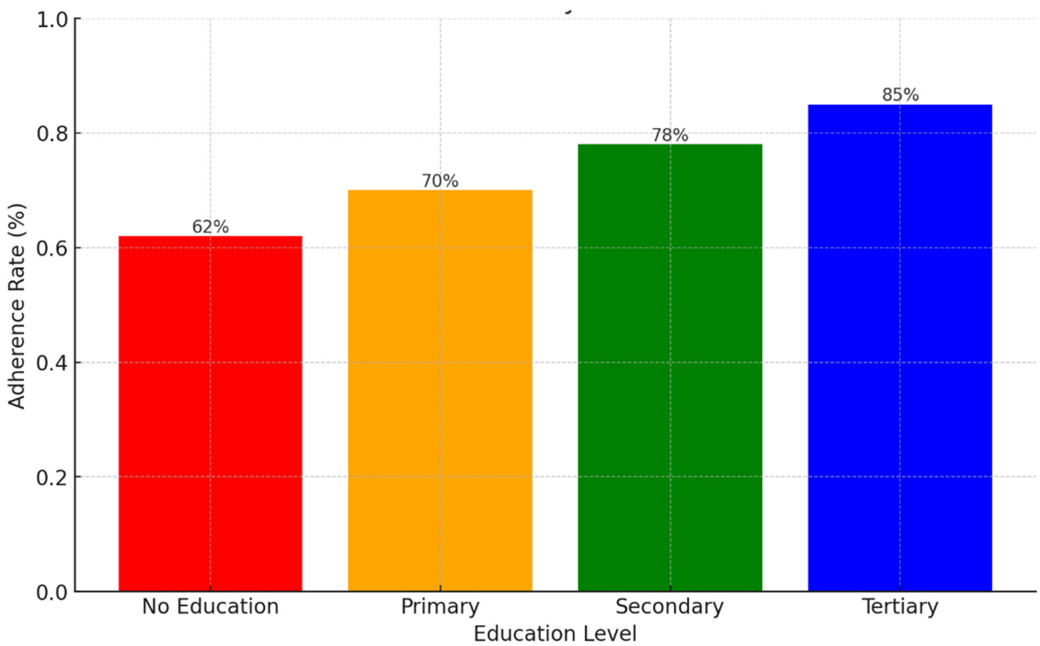


**Figure 5.** Adherence rates stratified by education level**.**

Figure 6 compares adherence rates between HIV-positive and HIV-negative patients. HIV-negative patients demonstrate a relatively high adherence rate of 82%, whereas HIV-positive patients show a lower adherence rate of 68%. This difference is likely due to challenges faced by HIV-positive individuals, such as the complexity of ART, side effects from the treatment, and the stigma associated with the virus.

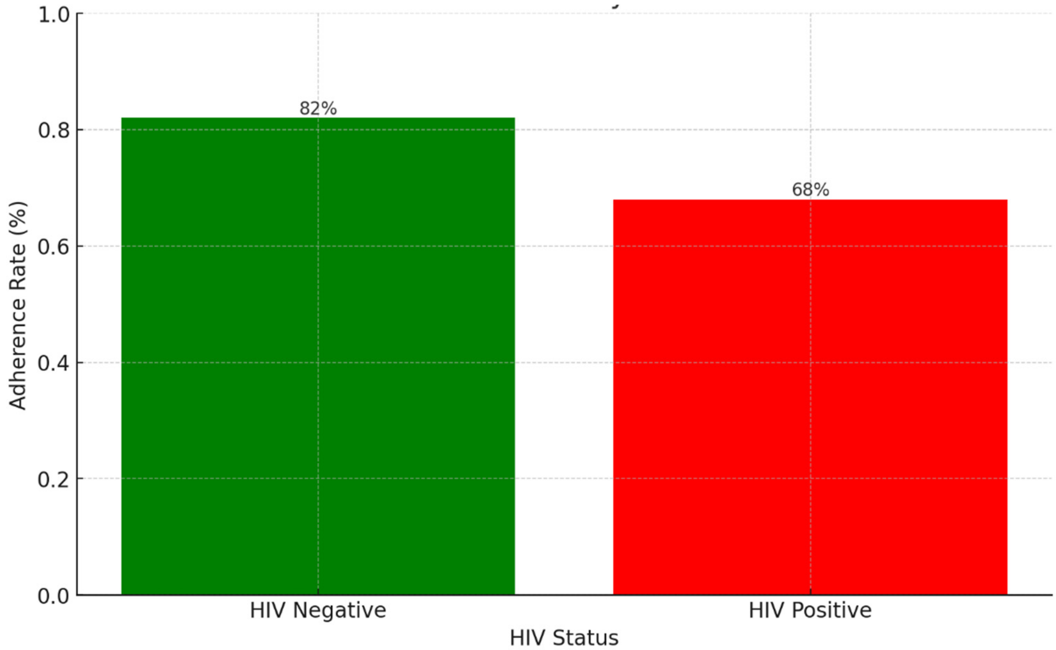


**Figure 6.** Adherence rates stratified by HIV status**.**

Figure 7 shows a positive correlation between structured employment and adherence rates. The analysis demonstrates that adherence progressively improves from the unemployed group to individuals in corporate roles. The unemployed group exhibits the lowest adherence rate at 65%, highlighting challenges such as financial instability and limited access to healthcare resources. The manual labor group has a moderate adherence rate of 72%, suggesting that, while slightly better, this group still encounters significant barriers related to work conditions and support systems. Government employees show a higher adherence rate of 85%, indicating that structured jobs with benefits and secure environments contribute positively to adherence. The corporate job category boasts the highest adherence rate at 88%, reflecting the benefits of higher socioeconomic status, comprehensive healthcare coverage, and greater job flexibility.

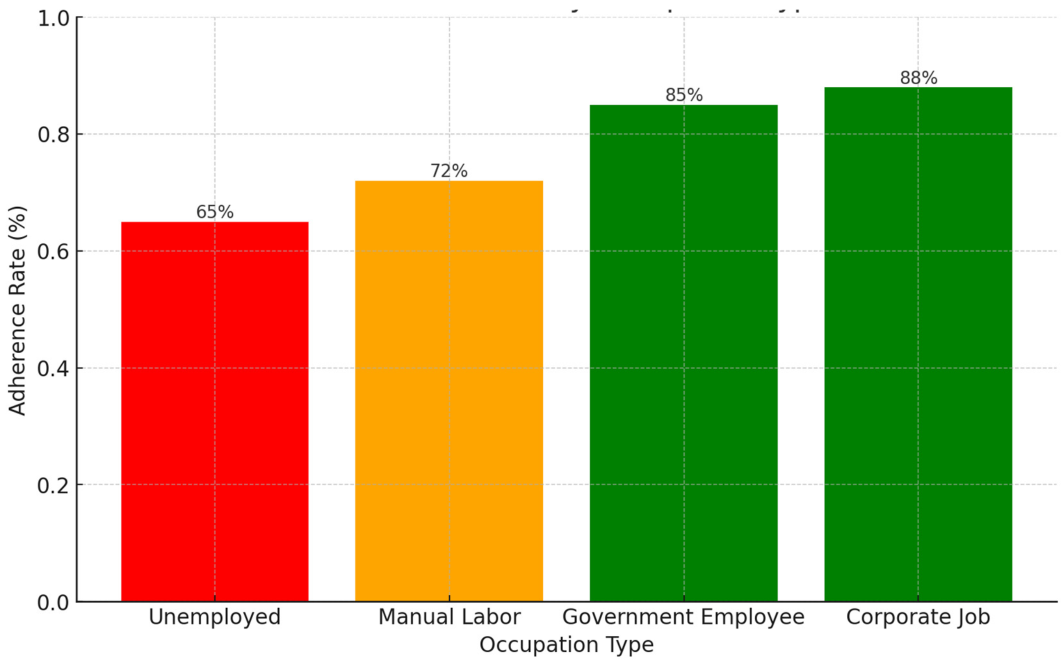

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**Figure 7.** Adherence rate according to the type of occupation**.**

Figure 8 demonstrates the impact of various social history factors on treatment adherence. The findings indicate that social and lifestyle elements, especially those related to mental health, peer influence, and substance use play a significant role in determining adherence. Peer influence exhibits the lowest adherence rate at 55%, suggesting that negative social circles or peer pressure can profoundly disrupt treatment compliance. Following closely, mental health issues have an adherence rate of 58%, highlighting the challenges that mental health can pose to a patient's ability to consistently follow treatment regimens. An unstable lifestyle shows a 60% adherence rate, indicating how instability in living situations or employment can detrimentally affect adherence. Alcohol use is associated with a 65% adherence rate, revealing that alcohol consumption moderately influences a person's ability to adhere to treatment, likely due to its effects on consistency and health prioritization. Smoking, which has an adherence rate of 62%, is also significant, though it has a slightly lesser impact compared to alcohol use.

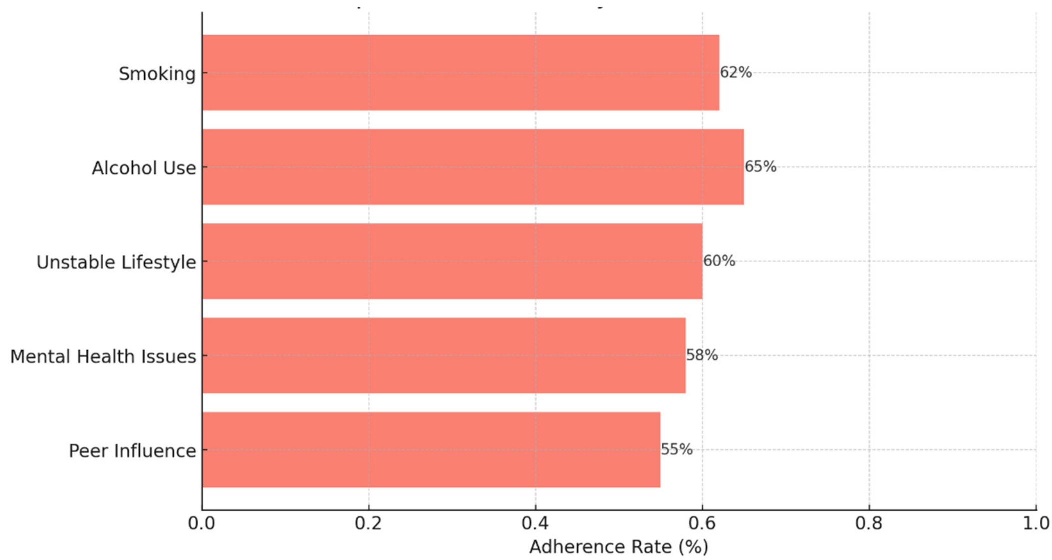


**Figure 8.** Impact of social history on treatment adherence**.**

According to Figure 9, adherence rates are highest among new (80%) and relapse (78%) categories, indicating that these groups are more successful in following treatment protocols. In contrast, chronic (Tal) patients exhibit the lowest adherence rate at 30%, highlighting significant challenges for this group. The chronic (TF1) and chronic (TF2) categories show moderate adherence rates of 55% and 50%, respectively, which still point to areas in need of improvement.

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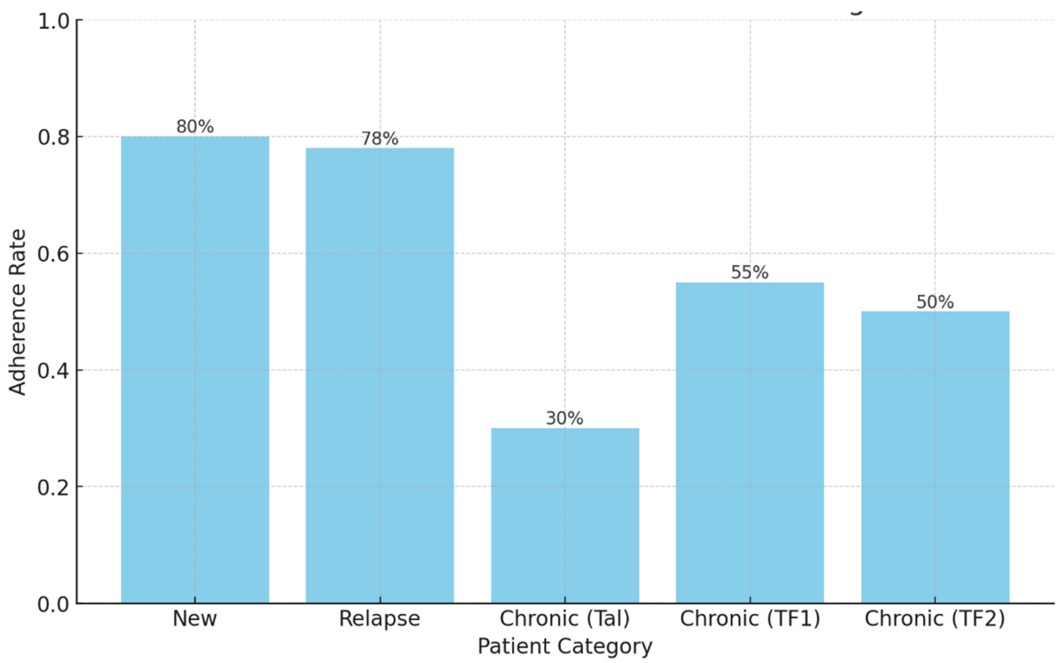


**Figure 9.** Adherence rates across different patient categories**.**

Figure 10 illustrates that income has the strongest association with treatment adherence. It indicates that higher-income patients are more likely to follow their treatment plans. Education also plays a significant role, closely linked to better adherence. Age and occupation show moderate associations; younger patients generally exhibit better adherence, and certain occupations contribute to higher adherence rates. Conversely, HIV status is associated with lower adherence, while gender demonstrates only a minor association. Comorbidities have the weakest correlation with adherence; patients with multiple health conditions often struggle to consistently follow their treatment regimens. Each variable's influence on adherence is indicated, with the highest percentages observed for income (85%) and education (82%), highlighting these factors as having the strongest relationships with adherence. In comparison, gender and comorbidities show lower associations at 65% and 60%, respectively. Overall, Figure 9 clearly demonstrates that income has the strongest association with adherence, followed closely by education.

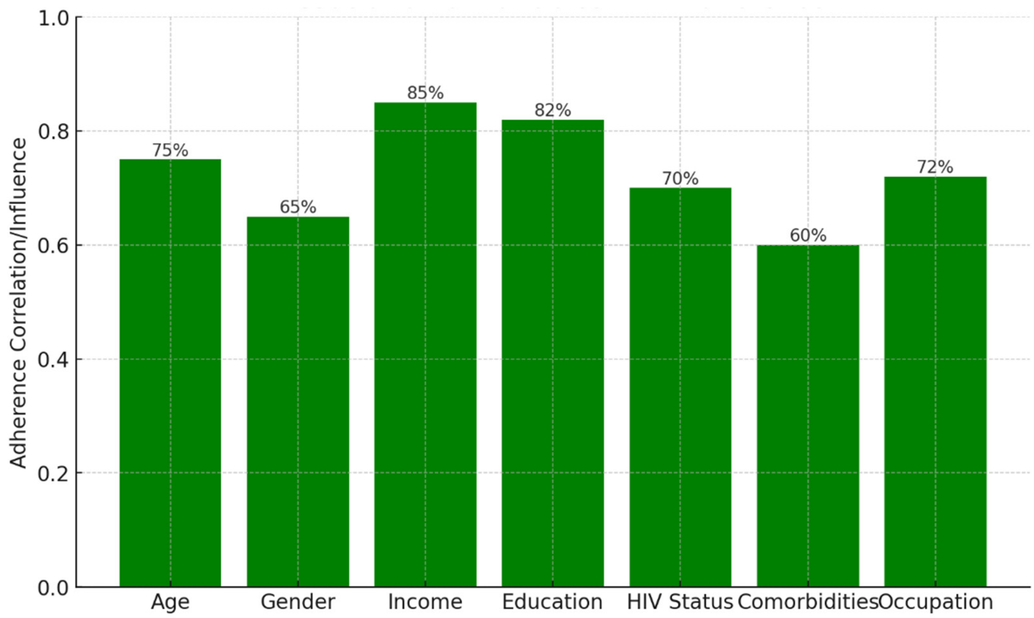


**Figure 10.** Association of variables with adherence**.**

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Figure 11 illustrates that age is the most significant factor, contributing approximately 37.6% to the prediction model. Education and income follow, accounting for 17.3% and 10.9%, respectively. This emphasizes the important roles these variables play in influencing adherence. Other factors, such as alcohol use, comorbidities, gender, and HIV status, have moderate to lower importance.

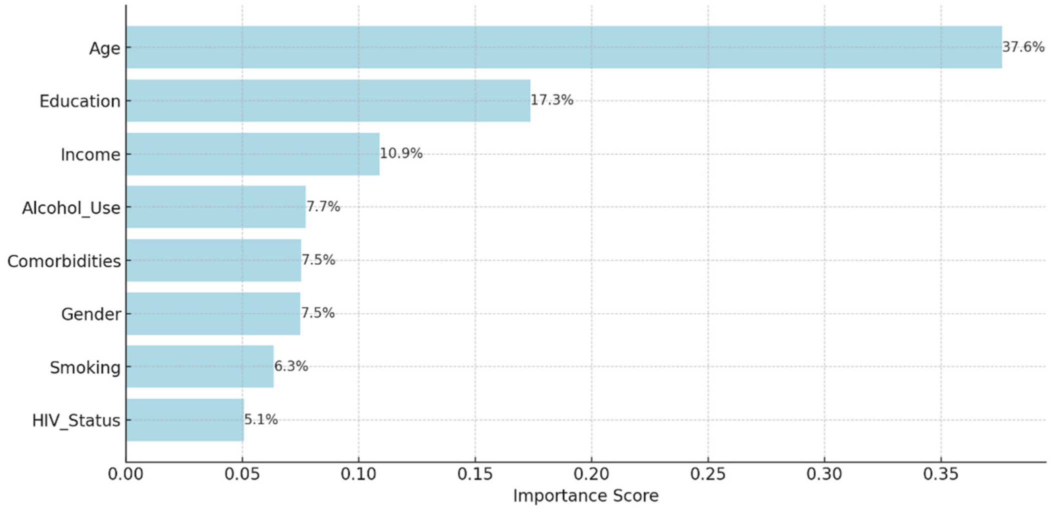


**Figure 11.** Feature importance in predicting treatment adherence.

Figure 12 compares the accuracy of four different models in predicting treatment adherence. The random forest model achieved an accuracy of approximately 53.3%, indicating high performance due to its capability to handle complex feature interactions. Logistic regression and gradient boosting demonstrated slightly lower accuracy at around 46.7% and 45,0% respectively, reflecting its effectiveness in managing simpler, linear relationships. The support vector machine (SVM) achieved an accuracy of about 43.3%, suggesting moderate effectiveness for datasets with linear separability. Random Forest showed the highest performance, with an accuracy of 53.3%, highlighting its strengths in iterative learning and error correction. These results suggest that while Random Forest is the most effective model in this comparison, logistic regression, gradient boosting and SVM also provide reasonable accuracy, making them suitable options depending on the complexity of the data and the available computational resources.

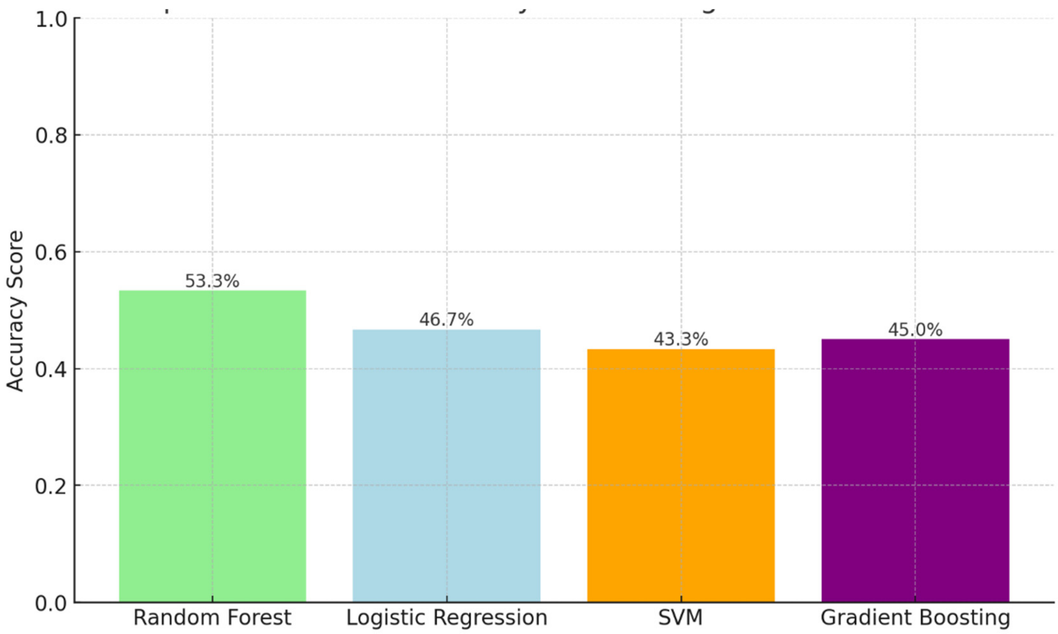


**Figure 12.** Comparison of model accuracy in predicting treatment adherence.

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## 4. Discussion

This research comprehensively delineates the principal determinants affecting treatment compliance in individuals diagnosed with DR-TB. Moreover, it meticulously assessed the predictive validity of machine learning algorithms in evaluating treatment adherence, placing significant emphasis on socioeconomic, demographic, and clinical variables. The relationship between treatment outcomes and adherence is also notable in this study, we included 108 patients diagnosed with drug-resistant tuberculosis (DR-TB) who were receiving treatment at tuberculosis clinics. Our primary outcome was measured as adherence of at least 80%, and we found that 79.6% of the patients adhered to their treatment throughout the entire study period. We identified several factors associated with non-adherence, including younger age, higher income, and HIV-negative status.

Measuring adherence is crucial for successful treatment and has been extensively explored in the literature. The World Health Organization (WHO) emphasizes the importance of time-based metrics for evaluating adherence. They suggest comparing the actual duration of therapy to the expected duration as a way to assess compliance. This approach is outlined in their report [8], which provides a foundational framework for adherence assessment across various medical conditions. The methodology for evaluating treatment adherence aligns with the WHO [8] guidelines for treatment adherence, which emphasize adherence measurement through time-based metrics. According to these guidelines, adherence can be assessed by comparing the actual duration of therapy completed by patients to the expected duration prescribed. This approach provides a standardized framework for measuring compliance and ensures consistency across studies and healthcare settings. Time-based metrics are particularly useful in monitoring adherence to long-term therapies, as they directly correlate with treatment outcomes and patient health. Research by Mugusi et al. [27] evaluated adherence to TB treatment by calculating the proportion of prescribed doses taken, leveraging patient records as a data source. Their study highlighted determinants of adherence among HIV-infected adults, offering practical insights into adherence tracking. Gale et al. [28] discussed the percentage-of-days-covered method, a conceptually similar approach to evaluating actual versus expected days of treatment. Their methodological analysis emphasizes the robustness and applicability of such calculations in adherence research. Schaffer et al. [29], reviewed adherence benchmarks in chronic disease therapies, identifying the 80% threshold as a widely accepted standard. Their meta-analysis demonstrated the clinical relevance of this benchmark in achieving therapeutic outcomes across various conditions. Furthermore, Subbaraman et al. [30] assessed adherence using pill estimate, 4-day dose recall, a last missed dose question, and urine isoniazid metabolite testing. Their study evaluated the accuracy of various TB adherence approaches. The study of Bea et al. [1] evaluated adherence using the proportion of days covered (PDC), calculated as an entire number of days covered by medication over the number of days of the duration of the study. Charalambous et al. [31] evaluated adherence as days the medication box was opened being a surrogate for the drug taken divided by the overall anticipated treatment days (<80% versus ≥80%). Together, these studies provide a comprehensive methodological foundation for adherence assessment, highlighting the use of time-based metrics, percentage-of-days-covered methods, and adherence benchmarks to evaluate compliance and its impact on treatment success.

Our findings are consistent with other studies on TB drug adherence. In the current study, 79.6% of participants adhered to the anti-TB regimen, both short and long regimen, which was lower than the reported adherence rates in Kosovo (85.5) [32], but higher than 56.5% reported in the study of Bea et al [1] involving drug-susceptible TB treatment. Similar to our study, adherence was 75.1% in a randomized clinical trial using the directly observed therapy (DOT) method, and 75.5% in an institutional-based cross-sectional survey of TB patients from South Ethiopia **[33,34]**. On the other hand, the parallel cluster-randomized trial conducted across 18 primary healthcare facilities in three provinces in South Africa, reported the proportion of participants with ≥80% adherence higher (80.9%) in the intervention arm compared to 51.6% in the Standard of Care (SoC) arm [31]. These differences in findings could be attributed to discrepancies in definitions of anti-TB adherence [34], differences in participant characteristics, the duration in which adherence was assessed, ease of accessing healthcare services, and different criteria for measuring adherence [35]. Some of the studies involved only drug-susceptible TB patients while our study mainly included DR-TB. Patients with DR-TB tend to deal with a high pill burden, long duration of treatment regimen which may cause them to forget, and sometimes adverse drug reactions that may result in abandoning their treatment.

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In our study, a high adherence rate ranging from 85-88% to anti-TB drugs was prevalent in the younger patients aged 20-30 years and 30-40 years with declining rates as the patient age increased. A study conducted in Brazil reported a proportion of 58.5% TB treatment adherence in patients aged ≥60 years [36]. This result was similar to our study with an adherence rate of 60-65% in patients aged ≥60 years. Contrary to our findings, previous studies suggested that geriatric patients with chronic medical conditions have a higher likelihood of adherence to treatment [37–39]. Younger patients have been identified as more likely to adhere to TB treatment regimens. Research indicates that age can be a significant predictor of treatment adherence, with younger individuals often demonstrating higher adherence rates compared to older patients [62]. This trend may be attributed to younger patients generally having fewer comorbidities and a greater capacity for engagement with health services [63]. A declining treatment adherence in the geriatric population may be due to the higher risk of comorbidities, physical and cognitive challenges associated with old age, high pill burden and intricacies of dosing regimen which in comparison with the younger patients, may lead to a nonadherence to treatment [1,40].

Patients who achieve positive treatment outcomes, such as being cured or completing their treatment, tend to exhibit higher adherence rates [29]. This correlation underscores the importance of ongoing support and monitoring throughout the treatment process, as successful outcomes can reinforce patients' motivation to adhere to their treatment plans [30].

The category of patients also plays a critical role in adherence rates. In our study, adherence rates were highest among newly diagnosed patients (80%) while relapse patients had 78% adherence rates. This suggests that newly diagnosed individuals might be more motivated to adhere strictly to treatment protocols compared to those who have relapsed. This could be due to their initial motivation to recover, direct education received at the start of treatment, and the novelty of adhering to a prescribed regimen. A study conducted in Ethiopia [35], found a non-adherence rate of 18% among TB patients, suggesting an overall adherence rate of 82% which aligns with our findings. While it does not specify adherence rates for newly diagnosed versus relapse patients, there is an indication that many patients can adhere to treatment when appropriate support and education are provided. The proportion of adherence was higher in our study as compared to a cross-sectional study involving newly diagnosed TB patients in China, which reported a lower adherence rate of 45.7% [25]. Another study conducted in South Korea among newly initiated patients on drug-susceptible TB treatment, recorded 56.5% adherence [1], which is lower than reported in our study. The differences between the two studies were that the South Korean study recruited drug-susceptible patients, and the criteria of adherence was evaluated using the proportion of days covered (PDC ≥80%). Patients with a history of relapsed or chronic TB often demonstrate lower adherence compared to those who are newly diagnosed [32]. This may be due to previous negative experiences with treatment, which can lead to skepticism about the efficacy of ongoing therapy [33]. The chronic (TF1) patients group exhibits the lowest adherence rate, which is significantly below other categories. The low adherence could be due to the chronic nature of their condition, which might lead to treatment fatigue, complex medication regimens, or reduced motivation over time. A scoping review by Kvarnström et al. [46] categorized barriers to medication adherence into five including patient-related, disease-related, medication-related, healthcare and system related factors, sociocultural and logistical and financial factors. Research indicates that individuals with a history of treatment for DR-TB are more likely to be non-adherent during subsequent treatment episodes [49]. This suggests that previous treatment experiences can carry over, influencing current adherence behaviors. Customized interventions that specifically address the concerns and barriers faced by these patient categories are essential for improving adherence rates.

The unemployed group, exhibits the lowest adherence rate, suggesting that individuals without employment face significant challenges in following treatment protocols, likely stemming from financial instability, limited support systems, and restricted access to healthcare resources, these findings agrees with a study done in Ethiopia showing that adherence was positively correlated to poor adherence among those are unemployed [34]. Conversely, government employees display higher adherence rates. This can be attributed to the structured nature of their work environments, better healthcare benefits, and supportive policies that promote health and wellness [36,37]. The corporate job category has the highest adherence rates, highlighting that individuals in such roles adhere more effectively to treatment protocols. This trend may be explained by higher socioeconomic status, comprehensive health insurance coverage, and greater access to healthcare facilities and support systems available to those in corporate positions [36,38]. Social history, particularly behaviors such as smoking and drinking, negatively impacts adherence to TB treatment. Studies have shown that tobacco smoking and alcohol abuse are associated with increased rates of treatment non-adherence [39]. For instance, a study indicated that patients who smoke are more likely to default on their treatment compared to non-smokers, as smoking may exacerbate health issues and reduce motivation for treatment adherence [40]. Similarly, alcohol consumption has been linked to poorer treatment outcomes and adherence, highlighting the need for integrated interventions that address these behaviors [41]. Furthermore, patients with comorbidities, such as HIV, often face additional challenges that complicate adherence. Co-infected patients have reported prioritizing antiretroviral therapy over TB treatment, which can lead to preferential non-adherence to TB medications [50]. The complexity of managing multiple health conditions necessitates customized interventions to support adherence in these populations. The top five features contributing to the model's predictions were age, with younger patients more likely to adhere to treatment, making age the most important predictor; treatment outcome, where patients with positive outcomes (e.g., cured or treatment completed) showed higher adherence; social history, as smoking and drinking negatively impacted adherence; patient category, with relapsed or chronic patients demonstrating lower adherence compared to new patients; and comorbidities, where patients with fewer coexisting conditions were more adherent due to the reduced complexity of managing multiple health issues [61]. Other factors, such as income, education, and HIV status, also influenced adherence but to a lesser extent.

The findings of our study on treatment adherence in DR-TB patients highlight several key findings that have significant implications for both clinical practice and public health interventions. The study found that socioeconomic, demographic, and clinical factors play a critical role in influencing treatment adherence, with variables such as age, income, education, and comorbidities emerging as the most significant predictors. Younger patients, those with higher incomes, and individuals with higher educational levels were more likely to adhere to their prescribed treatment regimen. Education plays a pivotal role in improving treatment adherence. Studies have demonstrated that health education interventions significantly enhance patients' understanding of TB, its treatment, and the importance of adherence [65,66]. Our results suggest that socioeconomic inequalities directly affect health outcomes, especially in the context of chronic conditions like DR-TB that require prolonged and complex treatment. The feature importance analysis from the Random Forest model revealed that factors like social history (e.g., smoking and drinking), patient category (e.g., chronic or relapsed cases), and comorbidities were also significant in determining adherence rates. Social history, particularly behaviors such as smoking and drinking, has been shown to impact treatment adherence. For instance, alcohol abuse can significantly interfere with treatment regularity, leading to missed appointments and diminished effectiveness of provider support and counseling [69]. Additionally, smoking has been associated with poorer health outcomes and may contribute to a lack of motivation to adhere to treatment regimens [70]. This emphasizes the need for a multifaceted approach to improving treatment adherence, which should include not only clinical support but also addressing the socioeconomic and behavioral factors that hinder patients from completing their treatment. Although the predictive model achieved moderate accuracy (53.3%), it offers a practical tool for identifying patients at risk of non-adherence. This could enable healthcare providers to proactively target these patients with customized interventions aimed at improving adherence, which is critical for preventing the further spread of DR-TB.

## 5. Conclusions

In conclusion, this research offers valuable insights into the factors influencing treatment adherence among patients with DR-TB. It highlights the necessity for comprehensive and targeted interventions, particularly for those in socioeconomically disadvantaged communities. Enhancing treatment adherence in these groups is vital for improving treatment outcomes and curbing the spread of DR-TB. The predictive model developed in this research serves as a practical tool for identifying patients at risk of non-adherence, thereby enabling healthcare providers to implement focused interventions. Ultimately, improving adherence, especially among vulnerable populations, is essential for achieving better treatment outcomes and reducing the incidence of DR-TB. Further studies warrant a more objective measure of adherence and use of longitudinal designs to assess the long-term impact of our interventions. Based on our study, the following recommendations are proposed. The use of educational programs such as creating culturally relevant materials that educate patients—particularly those from lower-income and educational backgrounds—on the critical importance of treatment adherence and the management of side effects. Engaging community health workers or peer educators who can communicate fluently in isiXhosa, the patients' native language is vital. Additionally, implementing SMS reminders and short educational videos in the local dialect will reinforce adherence and provide ongoing support. Offering financial incentives such as transportation stipends and food vouchers is necessary to mitigate the economic challenges associated with long-term treatment and reduce dropout rates. Moreover, integrating mental health and substance use counseling into TB treatment is crucial, as these issues have a significant impact on adherence. Collaboration with non-governmental organizations (NGOs) and local governments is essential for providing social support to low-income DR-TB patients, alongside strict monitoring of these processes.

## Limitations

The retrospective design of our study and reliance on self-reported adherence data, might have introduced bias. This study focused solely on adherence to TB medication and did not extend to other chronic conditions such as diabetes or hypertension, However, it lays the groundwork for broader explorations in the future.

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