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TB AND HIV/TB CO-INFECTION: ADHERENCE TO DRUG TREATMENT IN THREE SELECTED PROVINCES IN SOUTH AFRICA (SA)

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INTRODUCTION: Despite the downward trend in the “absolute number of TB cases” since 2006 and the fall in the incidence rates since 2001, the burden of TB disease remains a global health challenge.¹ TB is completely curable through the intake of a strict drug treatment regimen. The DOTS strategy introduced by the World Health Organization (WHO) and subsequently the Stop TB Strategy is an inexpensive strategy that could prevent millions of TB cases and deaths. TB is the leading cause of death among people who are HIV positive. In the African region, which accounted for 82% of the new TB cases that were also HIV positive, an estimated 900 000 (39%) of the 2.3 million people who developed TB were living with HIV.¹

Adherence to anti-TB treatment and to treatment for HIV/TB co-infection

Poor adherence to the treatment programmes is one of the factors associated with low cure rates for TB. In addition, inconsistent adherence to the anti-TB drug regimen may lead MDR-TB and XDR-TB. In individuals with TB/HIV dual infection receiving treatment, correct adherence to anti-TB drugs and ART are also essential for good treatment outcomes.

The categories of factors influencing adherence to drug treatments for most health-related conditions, include: practitioner’s negative assumptions about their patients; psychological attributes of the patient; environmental, social and cultural factors; treatment characteristics; and the doctor-patient relationship.² Many quantitative and qualitative studies conducted in SA have identified factors known to influence adherence to anti-TB treatment.

Given the fact that high levels of adherence are necessary for treatment success, the aim of this study is to investigate the factors that are associated with adherence to anti-TB drugs for those with active TB and to ART and anti-TB drugs taken by individuals who have dual infection.

METHOD: *Study design, sample and procedure:* This study is a cross-sectional survey conducted in 14 public primary health care clinics with the highest TB caseload in only one district in each of three provinces, namely, Northern Cape, Eastern Cape and Kwa-Zulu Natal.

All new TB and new retreatment patients were consecutively screened within one month of anti-TB treatment. Only TB patients who had been on TB treatment for at least three weeks were included (N=3107) and a sub-sample, where ART adherence information was available (N=757), was also included. The screening interview was conducted by trained research assistants for a period of 6 months in 2011. A health care provider who identified a new TB treatment or retreatment patient 18 years and above informed the patient about the study and referred the patient for participation if interested. A consenting procedure was adopted prior to start of the screening interview. Ethical approval was received from the Human Sciences Research Council Research Ethics Committee (Protocol REC No.1/16/02/11) and the Department of Health in SA.

Data Collection Tools: (1) Socio-demographic questionnaire; (2)^{3 4} The Kessler Psychological Distress Scale (K-10) was used to measure global psychological distress by recording symptoms over the preceding 30 days. The r coefficient for the K-10 in this study was $\alpha = 0.92$.; (3) The 10-item Alcohol Disorder Identification Test (AUDIT)⁵ which assesses alcohol consumption level, symptoms of alcohol dependence and problems associated with alcohol use. The AUDIT is reported to be less sensitive at identifying risk drinking in women⁶ so it was recommended that the cut-off points for binge drinking in women (4 units) were reduced by one unit as compared with men (5 units).⁷ Cronbach alpha for the AUDIT in this sample was 0.92; (4) Other Self-Report Measures included measures of tobacco use and adherence to anti-TB treatment and ART.

Data Analysis: Data were analyzed using Statistical Package for the Social Sciences (SPSS-version 19). Frequencies, means, standard deviations, were calculated to describe the sample. Associations of TB medication and ART non-adherence were identified using logistics regression analyses.

RESULTS: *Characteristics of the sample*

The sample included 671 (21.8%; N=3079) retreatment cases, 2408 (78.2%; N=3079) new TB cases and 55.9% HIV infected (N=2802). A little below half the sample was 35 years and older. Half the sample reported medium levels of poverty, and good to very good perceived health status. Other characteristics of significance include: 776 (25%) met the criteria for severe psychological distress; and 16.4% were at the medium risk category for alcohol misuse on the AUDIT. Finally, 26.1% were non-adherent to the anti-TB treatment.

A sub-sample of 757 participants was on anti-TB and ART. The characteristics of this group were: the majority of participants were between the ages of 25 and 44 years; half the sample reported medium levels of poverty; nearly 60% reported good to very good perceived health status; 15.9% were at the medium risk category for alcohol misuse on the AUDIT; 38.2% had a partner who was HIV positive; and 42.4% were non-adherent to ART. Of a total of 268 participants 83.8% were not adherent for both TB and ART medication ($r=0.71$).

Predictors of adherence to anti-TB medication only and combination treatment for TB/HIV co-infection: See Tables 1 & II

Table I: Predictors of TB medication non-adherence (N=3107)

| <i>Sociodemographics</i> | Crude OR (95% CI) | Adjusted OR (95% CI)^{a,b} |
|---|--------------------------|---|
| Age 18 -24 | 1.00 | 1.00 |
| Age 25 -34 | 0.76 (0.59-0.97)* | 0.93 (0.65-1.32) |
| Age 35 -44 | 0.77 (0.60-1.00) | 1.00 (0.68-1.45) |
| Age 45 and older | 0.80 (0.61-1.05) | 0.65 (0.43-1.00) |
| Female | 1.00 | 1.00 |
| Male | 1.26 (1.07-1.48)** | 1.09 (0.86-1.38) |
| Grade 7 or less | 1.00 | 1.00 |
| Grade 8-11 | 0.88 (0.72-1.06) | 1.07 (0.80-1.43) |
| Grade 12 or more | 0.68 (0.55-0.85)*** | 0.76 (0.54-1.07) |
| Poverty low | 1.00 | 1.00 |
| Poverty medium | 1.97 (1.62-2.41)*** | 1.73 (1.34-2.24)*** |
| Poverty high | 4.01 (3.12-5.10)*** | 1.65 (1.14-2.39)** |
| <i>Health variables</i> | | |
| <i>Perceived health status</i> | | |
| Very good/good | 1.00 | 1.00 |
| Good | 0.36 (0.29-0.45)*** | 0.50 (0.37-0.67)*** |
| Fair/Poor | 0.24 (0.20-0.30)*** | 0.44 (0.32-0.60)*** |
| TB retreatment patient | 1.00 | --- |
| New TB patient | 0.82 (0.67-1.00) | |
| HIV positive | 1.00 | 1.00 |
| HIV negative | 0.40 (0.34-0.48)*** | 0.44 (0.33-0.59)*** |
| <i>Chronic conditions</i> | | |
| Zero | 1.00 | 1.00 |
| One | 1.54 (1.23-1.93)*** | 1.86 (1.41-2.46)*** |
| Two | 1.84 (1.34-2.51)*** | 2.44 (1.68-3.56)*** |
| Three or more | 1.98 (1.34-2.92)*** | 2.37 (1.45-3.88)*** |
| Severe psychological distress (K \geq 30) | 1.31 (1.09-1.57)** | 0.94 (0.73-1.22) |
| Alcohol: low risk (AUDIT 0-7) | 1.00 | 1.00 |
| Medium (AUDIT 8-19) | 1.74 (1.42-2.19)*** | 1.65 (1.23-2.29)*** |

| | | |
|------------------------------|---------------------|---------------------|
| High (AUDIT 20-40) | 2.42 (1.76-3.32)*** | 3.06 (1.94-4.81)*** |
| Current tobacco use | 2.09 (1.76-2.49)*** | 1.35 (1.04-1.75)* |
| On ART | 0.70 (0.56-0.86)*** | 0.78 (0.60-1.03) |
| Partner HIV negative/unknown | 1.00 | 1.00 |
| Partner HIV positive | 1.41 (1.16-1.70)*** | 1.43 (1.10-1.84)** |

^a Using "enter" LR selection of variables

^b Hosmer and Lemeshow Chi-square 7.68, df8, 0.466; Cox and Snell R² 0.11; Nagelkerke R² 0.16

* P<0.05; ** P<0.01; *** P<0.001

Table II: Predictors of ART non-adherence (N=757)

| <i>Sociodemographics</i> | Crude OR (95% CI) | Adjusted OR (95% CI) ^{a,b} |
|--------------------------------------|----------------------|-------------------------------------|
| Age 18 -34 | 1.00 | 1.00 |
| Age 35 -44 | 0.68 (0.49-0.95)* | 0.63 (0.38-1.03) |
| Age 45 and older | 1.12 (0.76-1.64) | 0.90 (0.49-1.67) |
| Female | 1.00 | 1.00 |
| Male | 1.61 (1.20-2.16)*** | 1.49 (0.95-2.32) |
| Grade 7 or less | 1.00 | 1.00 |
| Grade 8-11 | 0.66 (0.47-0.93)* | 1.13 (0.67-1.93) |
| Grade 12 or more | 0.79 (0.53-1.17) | 1.19 (0.65-2.18) |
| Poverty low | 1.00 | 1.00 |
| Poverty medium | 3.14 (2.05-4.79)*** | 2.60 (1.46-4.65)*** |
| Poverty high | 7.13 (4.36-11.66)*** | 3.89 (1.87-8.12)*** |
| <i>Health variables</i> | | |
| <i>Perceived health status</i> | | |
| Very good/good | 1.00 | 1.00 |
| Good | 0.41 (0.28-0.59)*** | 0.69 (0.40-1.17) |
| Fair/Poor | 0.20 (0.14-0.29)*** | 0.28 (0.17-0.49)*** |
| TB retreatment patient | 1.00 | 1.00 |
| New TB patient | 0.51 (0.37-0.71)*** | 0.67 (0.42-1.07) |
| <i>Chronic conditions</i> | | |
| Zero | 1.00 | 1.00 |
| One | 1.39 (0.91-2.12) | 1.72 (1.01-2.94)* |
| Two | 1.50 (0.87-2.58) | 2.73 (1.31-5.65)** |
| Three or more | 2.45 (1.33-4.45)** | 5.33 (2.27-12.55)*** |
| Severe psychological distress (K≥30) | 1.00 (0.72-1.37) | --- |
| Alcohol: low risk (AUDIT 0-7) | 1.00 | 1.00 |
| Medium (AUDIT 8-19) | 1.65 (1.11-2.45)* | 1.08 (0.56-2.09) |
| High (AUDIT 20-40) | 2.76 (1.30-5.86)** | 13.09 (2.96-57.99) |
| Current tobacco use | 2.30 (1.65-3.19)*** | 1.44 (0.85-2.43) |
| Partner HIV negative/unknown | 1.00 | 1.00 |
| Partner HIV positive | 2.41 (1.75-3.32)*** | 3.12 (1.84-5.29)*** |
| Had sex in past 3 months | 1.44 (1.07-1.93)* | 1.48 (0.96-2.28) |
| Sex partner on ART | 0.51 (0.35-0.74)*** | 0.50 (0.25-0.97)* |

^a Using "enter" LR selection of variables

^b Hosmer and Lemeshow Chi-square 13.14df8, 0.107; Cox and Snell R² 0.24; Nagelkerke R² 0.33

* P<0.05; ** P<0.01; *** P<0.001

DISCUSSION/CONCLUSION: The TB/HIV co-infection rate of over 50% in this study is similar to the national average in the public health sector in SA. The sub-sample of HIV positive patients on ART in this study, shared a similar economic and alcohol misuse profile to the total sample of TB infected patients. In addition, nearly 40% of patients on ART reported having a partner who is HIV positive. Finally, the self-report of non-adherence to ART is high in this sub-sample (42.4%) but comparable to the figures reported in the literature.⁸ Non-adherence to both ART and anti-TB drugs was also of concern in this sub-group. However, given the fact that this sub-group has a dual infection requires that they take two sets of drugs, which could prove to be quite burdensome. The use of a multiple drug regimen may also lead to drug reactions causing unmanageable side-effects ultimately leading to treatment default.^{9 10} The complexity of the drug treatment regimen and the impact on the daily lives of these patients are also factors that are associated with poor adherence in these patients.

The three common predictive factors independently associated with non-adherence to anti-TB drugs and to ART were poverty, co-morbid disease conditions and having a HIV positive partner. This finding is consistent with the literature on the relationship between the social determinants of health and health outcome and/or the quality of life of individuals with one or more disease condition.¹³ In this study non-adherent behavior for both anti-TB drugs and ART was associated with a lack of economic resources (poverty) and negative personal circumstances (co-morbid conditions and a HIV positive partner). Clearly the lack of social, personal and economic resources is a barrier to adherence. Of concern, however, is the fact that HIV negative patients with a HIV positive partner who were non-adherent to anti-TB drugs, placed not only themselves but their partners at risk for poor health outcomes. Inconsistent adherence to anti-TB drugs may not only lead to MDR and XDR-TB but may increase the risk of transmission of TB to others. The HIV positive patients' not adhering to ART, in this study, placed themselves at risk for drug resistance which could in turn reduce their life-span. Two additional factors (alcohol mis-use and tobacco) were independently associated with non-adherence to TB treatment drugs. There are many studies that confirm the association between alcohol misuse and treatment default.^{14 15} It is plausible that those patients' mis-using alcohol have poor judgement and consequently make poor health decisions, such as not adhering to their anti-TB medication. Individuals who mis-use alcohol and smoke tobacco may be conceived of as having a personality with an "increased risk profile" which makes them prone to engaging in undesirable behaviours regardless of the consequences.

Despite the limitation of this study as a cross-sectional one, the results do provide insight into the factors that are associated with treatment default among TB patients and those co-infected with

HIV. The factors found to be associated with non-adherence indicate that a comprehensive patient-centred treatment programme is needed for TB patients in the public health care system.

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REFERENCES: Given on request