ASSOCIATION BETWEEN TREATMENT ADHERENCE AND PERSONALITY TRAITS, ANXIETY, AND DEPRESSION AMONG ADULT PATIENTS WITH HIV IN NORTHWEST PENINSULAR MALAYSIA

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Dissertation Submitted in Partial Fulfilment of The Requirement for The Degree of Master of Medicine (Psychiatry)

UNIVERSITI SAINS MALAYSIA

2021

Acknowledgement

I want to thank all those who had given me tremendous help and support in completing this research project. I truly appreciate my supervisor, Assoc. Prof. Dr Mohd Azhar Bin Mohd Yasin and my co-supervisor Dr Alwi Bin Muhd Besari, for allowing me to undertake this project in the first place. I also want to thanks my colleague Dr Karniza bt Khalid and Dr Amalina bt Anuar for their guidance and assistance throughout completing this project. I would not have been finishing my dissertation on time if without their help and guidance.

My deepest thanks to all my colleagues, who helped me to be more 'computer-literate', and to those who had volunteered for the study as well.

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List of Abbreviations and Symbols

AACTG: Adult AIDS Clinical Trials Group

AIDS: Acquired Immunodeficiency Syndrome

ART: Antiretroviral Therapy

BDI: Beck Depression Inventory

CDQ: Clinical Diagnostic Questionnaire

CES-D: Center for Epidemiologic Studies Depression Scale

CHIP: Coping in Health and Illness Project

CIDI-SF: Composite International Diagnostic Interview- Short Form

DASS-21: Depression, Anxiety, and Stress Scale 21

FFM: Five-factor model

GAD: General Anxiety Disorder

GAM: Global AIDS Monitoring

GHPP: General Hospital Pulau Pinang

HADS: Hospital Anxiety and Depression Scale

HIV: Human Immunodeficiency Virus

HSB: Hospital Sultanah Bahiyah

HTF: Hospital Tuanku Fauziah

INSIGHT: International Network for Strategic Initiatives in Global HIV trial

JEPeM: Jawatankuasa Etika Penyelidikan (Manusia)

MINI: MINI International Neuropsychiatric Interview

MMAS-8: Morisky Medication Adherence Scale-8

MREC: Medical Research and Ethic Committee's

MSM: Men Sex Men

NEO-PI-R: Revised NEO Personality Inventory

NSPEA: National Strategic Plan for Ending AIDS

OPD: Outpatient Department.

PHQ: Patient Health Questionnaire

PLHIV: People Living with Human Immunodeficiency Virus

SCID-I: Structured Clinical Interview for DSM-IV Axis I

SPSS: Statistical Package of Social Science

START: Strategic Timing of Antiretroviral Treatment

TLFB: Timeline follow back

UMMC: University Malaya Medical Centre

WHO: World Health Organization

ZKPQ-M-40-CC: Zuckerman-Kuhlman Personality Questionnaires 40 items Malay Version.

Abstrak

Tajuk Kalian : **Hubungan di antara Kepatuhan Rawatan dengan Ciri-ciri Personaliti, Tahap Kebimbangan dan Kemurungan dalam kalangan pesakit dewasa HIV di Negeri-negeri Utara Semenanjung Malaysia**.

Pengenalan: Terapi antiretroviral adalah rawatan untuk menyelamatkan nyawa individu yang hidup dengan "Human Immunodeficiency Virus". Namun untuk menurunkan paras virus di dalam tubuh badan dengan sepenuhnya, mereka perlu mematuhi rawatan setiap hari. Faktor-faktor yang mempengaruhi kepatuhan terhadap "Antiretroviral Therapy" (ART) telah dikaji oleh penyelidik-penyelidik di negara Barat dan Asia seperti Malaysia. Namun, sehingga kini masih kekurangan kajian khususnya, fokus pada pemahaman hubungan antara kepatuhan rawatan dan kebimbangan, kemurungan dan ciri-ciri personaliti di kalangan pesakit dewasa yang menghidap penyakit HIV yang menerima "Antiretroviral Therapy" di Malaysia. **Objektif**: Kajian ini adalah bertujuan untuk memahami hubungan antara kepatuhan rawatan dan kebimbangan, kemurungan dan ciri-ciri personaliti di kalangan pesakit dewasa yang menerima rawatan terapi antiretroviral di Hospital Perlis dan Kedah. **Kaedah**: Kajian berbentuk "cross-sectional" dijalankan bermula pada Julai 1, 2018 sehingga April 31, 2020 di kalangan 229 pesakit dewasa di bawah rawatan susulan klinik "Human Immunodeficiency Virus Outpatient Department" (HIV OPD). Peserta yang memenuhi kriteria telah dipilih melalui kaedah "purposive sampling". Data-data peserta dikumpulkan melalui borang-borang kajian soal selidik dan maklumat dari rekod perubatan yang dikepilkan bersama-sama borang maklumat penyelidikan ini. Kebimbangan dan kemurungan peserta dinilai melalui skala "Hospital Anxiety and Depression Scale" (HADS). Ujian ciri-ciri personaliti

peserta dinilai melalui “Ujian Personaliti Zuckerman-Kuhlman” (ZKPQ-M-40-CC). Manakala kepatuhan rawatan antiretroviral dijalankan melalui sesi bancian kepatuhan ubat mengikut “Timeline follow –back” (TLFB). Sosio-demografi, ciri-ciri klinikal, psikososial dan keperibadian telah dikumpulkan. Seramai 229 peserta melengkapkan HADS, ZKPQ-M-40-CC, dan TLFB. **Keputusan:** Terdapat 220(96.1%) peserta daripada 229 peserta yang mematuhi rawatan. Individu yang lebih tua 167(97.7%) lebih mematuhi rawatan berbanding dengan individu yang lebih muda 53(91.4%); (*p*-value=0.033). Individu yang telah berkahwin 91 (98.9%) lebih mematuhi rawatan berbanding dengan individu yang bujang 107 (95.5%) atau bercerai 25 (88.0%); (*p*-value = 0.044). Hanya 2(3.2%) daripada 62 peserta yang mengalami gangguan kebimbangan yang tidak mematuhi rawatan; (*p*-value = 0.542). Hanya 5(5.0%) daripada 100 peserta yang mengalami gangguan kemurungan tidak mematuhi rawatan; (*p*-value=0.509). Individu yang mempunyai ‘Active’ personaliti lebih mematuhi rawatan 30(±5.8); (*p*-value=0.014) berbanding dengan individu yang mempunyai ‘Sociability’ personaliti 24(±5.0); (*p*-value=0.320), ‘Agressiveness-Hostility’ personaliti 18 (±6.3); (*p*-value=0.650), ‘Impulsive-Sensation-Seeking’ personaliti 18(±6.3); (*p*-value=0.688), dan ‘Neuroticism-Anxiety’ personaliti 18(±6.3); (*p*-value=0.623). Selain daripada itu “multiple logistic regressions” telah dilaksanakan dan telah mendapati bahawa domain personaliti yang Aktif adalah satu-satunya faktor yang ada hubungan secara langsung dengan kepatuhan rawatan “Antiretroviral therapy” setelah “control” usia, tahap pendidikan, dan viral load. Peningkatan dalam satu skor domain personaliti yang Aktif meramalkan 1.14 (95% CI: 1.02, 1.28) lebih patuh kepada rawatan. **Kesimpulan**: Hasil kajian menunjukkan bahawa ada hubungan secara langsung antara ciri-ciri personaliti ‘Active’ dengan

kepatuhan rawatan di mana skor yang lebih tinggi dalam domain personaliti yang Aktif meramalkan kepatuhan yang lebih tinggi terhadap rawatan. Manakala, tiada hubungan secara langsung antara kebimbangan dan kemurungan dengan kepatuhan rawatan. Justeru itu, ujian ciri-ciri personaliti dapat membantu dalam mengenalpasti pesakit HIV yang berisiko kurang mematuhi rawatan terutamanya untuk beliau yang skor rendah dalam domain personaliti yang Aktif. Oleh itu, dengan melaksanakan "behavioural modification" terapi terhadap pesakit yang berisiko dapat membantu menperbaiki dan meningkatkan kepatuhan terhadap rawatan.

Kata kunci*:* Kepatuhan rawatan, Kebimbangan dan Kemurungan, Ciri-ciri personaliti, Pesakit dewasa HIV, Negeri-negeri Utara Semenanjung Malaysia.

Abstract

Research title: Association between Treatment Adherence and Personality traits, Anxiety, and Depression among Patients with HIV in Northwest Peninsular Malaysia

Background: Antiretroviral therapy is a life-saving treatment for HIV-positive individuals. However, to achieve complete viral suppression, they must maintain adherence to treatment every day. Factors affecting adherence to Antiretroviral therapy has been studied by many researchers in Western and Asian countries like Malaysia. However, up until now, there is still a lack of studies focusing on understanding the association between treatment adherence and anxiety, depression, and personality traits among adult HIV patients receiving ART in Malaysia. **Objective**: To study treatment adherence in adult HIV patients receiving ART and its association with personality traits, anxiety, and depression at Hospital Perlis and Kedah. **Method:** A hospital-based cross-sectional study was conducted from July 1, 2018, to April 31, 2020, among 229 adult patients under outpatient department HIV clinic follow-up. Participants that fulfilled the criteria were selected via a purposive sampling method. Data were collected through an interviewer-guided questionnaire set. The anxiety and depression were evaluated through the Hospital Anxiety and Depression Scale (HADS), while the personality traits were examined through the Zuckerman-Kuhlman personality test (ZKPQ-M-40-CC). Adherence to ART was assessed through an interviewer-guided Timeline follow-back (TLFB). Sociodemographic, clinical characteristics, mood symptoms, and personality variables were collected. A total of 229 respondents completed HADS, ZKPQ-M-40-CC, and TLFB. **Result**: There were 220 (96.1%) out of 229 participants who adhered to therapy.

Older individuals 167(97.7%) more adhered to treatment as compared with younger individuals 53(91.4%); (*p*-value=0.033). Those who were married 91(98.9%) were more likely to adhere to treatment than those who were single 107(95.5%) or divorced 25(88.0%); (*p*-value=0.044). Only 2 (3.2 %) of the 62 participants who had an anxiety disorder did not adhere to therapy; (*p*-value=0.542). Only 5 (5.0%) of the 100 participants with a depressive disorder did not adhere to therapy; (*p*-value=0.509). An individual with an Activity type of personality trait more adhered to treatment 30 (±5.8); (*p*-value=0.014) as compared to an individual with Sociability 24(±5.0); (*p*-value=0.320), Aggression-Hostile 18(±6.3); (*p*-value=0.650), Impulsive-Sense-Seeking 18(±6.3); (*p*-value=0.688), and Neurotic-Anxious 18(±6.3); (*p*-value=0.623) type of personality traits. Multiple logistic regression found that the activity domain of the personality trait was the only factor significantly associated with ART treatment adherence after controlling for age, education level, and viral load. An increase in one score of the activity domain of the personality trait has a 1.14 (95% CI: 1.02, 1.28) higher odds of being adherent to therapy. **Conclusion:** The results of this study revealed that there was a direct relationship between Activity personality trait with treatment adherence where higher scores in the Active personality domain predicted higher adherence to treatment. Conversely, anxiety and depression are not associated with adherence to treatment. Personality trait assessment can help in the identification of HIV patients who are at risk for poor adherence especially for those who score low in the activity domain of personality trait. As such by conducting behavioural modification therapy for the vulnerable individual can help to improve and increase their treatment adherence.

Keywords: Adherence, Anxiety and Depression, Personality traits, Adult HIV patients, Northwest Peninsular Malaysia.

CHAPTER 1
Introduction

1.1. Overview

Based on WHO, the Definition of adherence can be broadly defined as "*the extent to which the patient follows medical instructions*" or "*the extent to which a person's behaviour-taking medication, following a diet, and or executing lifestyle changes, corresponds with agreed recommendations from a health care provider*." (Haynes et al., 1980)

Since complete cure from HIV is still not possible, the importance of treatment adherence has been repeatedly emphasized. This is because it has been long recognized that adherence to treatment regimens is essential to suppress virus load in the body and prevent drug resistance.

In Malaysia, the mode of transmission of HIV has changed over the last two decades. The country has seen gradual changes in the HIV epidemic landscape from the first wave to the third wave. The first wave of transmission through heterosexual intercourse with a partner originates mainly from Thailand, followed by a second wave of transmission through needle sharing between male drug users. The third wave of transmission through sexual intercourse between men and men (Barmania, 2013). According to the recent Malaysia Global AIDS reporting 2020, the proportion of sexual transmission increased to more than 90% in 2019.

Globally, there has been good progress across HIV testing and treatment cascade. However, as the United Nations General Assembly's Political

Declaration on Ending AIDS with the mission to achieve the 90-90-90 targets by 2020, most of the committed countries are off-track. Malaysia gained 89-56-85 in 2019, 89% of PLHIV know their status, 56% of them were receiving treatment, and 85% were virally suppressed. The effort to reach the second 90 is the biggest challenge. This is mainly associated with spreading the awareness and link the key population to care and retaining them in ART treatment. The key population here consist of the female sex workers, transgender, and men sex men (MSM) groups of people. Another big effort to reach the third 90, mainly due to poor retention in the care and several psychosocial factors affecting treatment adherence (Ahmed et al., 2019).

Most research investigating the psychosocial factors affecting ART adherence among PLHIV in Malaysia are social stigma and discrimination, lack of social support, anxiety, and depression. These psychosocial factors are the root cause that deterred PLHIV from seeking treatment. It is also among the stumbling block that hindered effective treatment and prevention of new HIV cases from increasing until today (Shrestha et al., 2017).

1.2. Research Background

The human immunodeficiency virus (HIV) attacks the human immune system by destroying the T-helper cell (commonly known as the CD4 cells) by invading the white blood cell and replicates inside these cells. HIV progressively weakens the immune system. Eventually, by the 10th year of the infection period, the body will be too weak to fight against infection, thus developing a set of symptoms called (AIDS) acquired immune deficiency syndrome. Both

HIV-1 and HIV-2 will cause AIDS. Malaysian's Ministry of Health reported the first HIV case in Malaysia in 1986. Over the years, HIV-infected cases increased tremendously, with the cumulative reported cases by the Ministry of Health's statistic in 2014 were 105,189 cases Ministry of Health Malaysia (2015). It demonstrates an increasing trend of 3,517 cases in 2014 from 3,393 in 2013. New cases were mostly among homo/bisexual and heterosexual communities. Infected adults were mostly in their early 20s and 30s, with those aged between 20-29 years old comprised of about 31% of cases and those aged 30-39 years old comprised of about 35% of cases in 2013.

Although transmission continues and cannot be eliminated, new HIV/AIDS infections and new HIV/AIDS-related deaths have significantly decreased with the onset of antiretroviral therapy. As Malaysia has increased the accessibility and availability of ART to government hospitals and public health facilities across the country, new HIV/AIDS infections and related deaths between 2000 and 2015 have been significantly reduced, as indicated in the Global AIDS Response Progress Report 2016.

As opportunities to enrol on life-saving ART are open to all Malaysian for free, the adherence rate became a growing concern for policymakers. United Nations use the cut-off period of 12 months adherence as an indicator of effectiveness in response to ART (UNAIDS, 2011b) and early warning for ART resistance (WHO, 2012). Per WHO (2005), minimum adherence levels of 95% needed for treatment success. Recent evidence suggests that with 95% adherence to ART, the viral suppression approaches 78%, whereas, with 80% adherence to ART,

the viral suppression reduced to 20% (Yu et al., 2018; Bezabhe et al., 2016; Knobel et al., 2009).

Poor treatment adherence will lead to treatment failure subsequently causes treatment-resistant follow by disease progression and death WHO (2007). Low viral suppression not only endangers individual health but also increase disease transmission to others.

The rate of treatment adherence to ART in Ethiopia is 88.2%, in China is 85.5%, in Myanmar is 84.0%, in Northern Tanzania is 71.0% and in Ghana is 62.2% (Abadiga et al., 2020). In Malaysia, the rate of adherence to ART is 80% among HIV patients in Hospital Sungai Buloh (Surajudeen Abiola et al., 2015). Treatment adherence is a complicated behaviour that is influenced by various factors, such as disease-related, personal-related, health-related, cognitive and psychosocial factors (Audrey et al., 2020). A considerable amount of local literature has examined associated factors related to treatment adherence. There were sociodemographic factors, clinical characteristic, socioeconomic factors associated with treatment adherence as the study done by Ibrahim et al.(2014) or adverse effect of ART associated with treatment adherence done by Murphy, Wilson, Durako, Muenz, & Belzer. (2001); Yagoub et al.(2012) but there is still a lack of study focus on the psychological factors especially in personality traits, depression and anxiety among adult patients with HIV in particular in the local context.

1.3. Problem Statement

Since ART was made available and accessible in Malaysia's public health setting, the issue of adherence has received considerable critical attention.

An RCT conducted by Surajudeen Abiola et al.(2015) found that the mean baseline adherence for a cohort of 242 Malaysian patients was 80.1 ± 19.6 for the intervention group and 85.1 ± 15.8 for control groups. The mean baseline CD4 count for the same study was 222.97 ± 143.7 cells/mm^3, while the mean viral load was 255237.85 ± 470618.9. The data showed there is still suboptimal adherence among HIV patients in Malaysia enrolled in ART. Among the most common barriers and challenges that existed among HIV patients enrolled in ART are anxiety, depression, and personality traits.

Although adherence to ART has long been recognized as a serious concern for global public health, there is still a lack of research to date a focus on understanding the association between treatment adherence and personality traits, anxiety, and adult HIV patients in Malaysia suffering from depression.

1.4. The Rationale and Significance of the Study

Up to 2015, there were already 90,603 people living with HIV (PLHIV), nevertheless only 25,700 PLHIV received ART. Malaysia's national strategic plan for 2016-2030 includes having more than, or equal to 95% of PLHIV are diagnosed, 95% will receive ART, and 95% have adequate viral suppression by the year 2030. Personality, anxiety, and depression are known factors that may contribute to poor adherence to ART treatment. Hence, if PLHIV poorly adheres to treatment due to their personality, or anxiety and/or depression, then

despite the 95% of people with access to ART, there is a probability of not achieving the 95% target of adequate viral suppression.

The findings of the study may therefore serve as the basis for future studies, further assist clinicians in initiating intervention programs and policy changes to allocate resources to improve adherence to treatment and reduce the number of patients who fail to respond to ART, thereby avoiding unintended costs for treatment and therapeutic options (Furtado dos Santos et al., 2020).

1.5. Scope of the Study

The scope of the study is limited to the area of the hospital. The aim of this research is to be performed in outpatient HIV clinics in the Northwest Peninsula of Malaysia for persons 18 years and older who have worked in the ART program for at least 12 months. Indirectly, the emphasis is on the individual who has gone through the adjustment period. The United Nations use the cut-off period of 12 months adherence as an indicator of effectiveness in response to ART (UNAIDS, 2011b) and early warning for ART resistance (WHO, 2012).

1.6. Research Questions

1. Are adult HIV patients adhere to ART?
2. What is the prevalence of anxiety, depression, and multiple personalities in adult ART patients?
3. Is there any association between treatment adherence and sociodemographic characteristic among adult HIV patients receivingART?
4. Is there any association between anxiety, depression, and treatment adherence among adult HIV patients receiving ART?

5. Is there any association between the different dimensions of personality traits and treatment adherence among adult HIV patients receiving ART?

1.7. Research Objective

1.7.1. General Objectives

To study treatment adherence in adult HIV patients receiving ART at outpatient HIV clinics in the Northwest Peninsula of Malaysia and its association with personality traits, anxiety, and depression.

1.7.2. Specific objectives

1. To determine the proportion of treatment adherence among HIV patients receiving ART in hospital HTF and HSB.

2. To determine the sociodemographic characteristic, personality traits, prevalence of anxiety and depression among HIV patients receiving ART in hospital HTF and HSB.

3. To examine the association between treatment adherence and anxiety, depression and personality traits among HIV patients receiving ART.

4. To determine the associated factors to poor adherence among adult patients with HIV via logistic regression analysis.

1.8. Research Hypothesis

1. There is an association between adherence to treatment and sociodemographic characteristic among adult HIV patients receiving ART.
2. Anxiety and depression are associated with poor adherence to treatment in adult HIV patients who receive ART.
3. There is an association between different dimensions of personality traits and adherence to ART in adult HIV patients.

1.9. Operational Definition

Table 1.1: Operational Definition

No	Variables	Operational Definition
1	Adherence	**Timeline follow back** They are based on day-to-day recall via the visual calendar to measure the quality of adherence in the latest past 14 days before the scheduled appointment date. According to Schensul et al. (2017), adherence is characterised as following the prescribed 14-day doses 100 % of the time, whereas non-adherence is defined as not following the prescribed doses 100 % of the time.
		Viral load count Adherence is characterised as viral suppression below 20 copies/mL in the last six months, and non-adherence is defined as viral suppression above 20 copies/mL.
		However, achieving an undetectable viral load not synonymous with adherence, nor does failure to accomplish this goal are attributable to non-adherence. Many other factors mediate this relationship (Basu & Garg, 2017). Thus, the rate of therapy adherence in this study is largely determined by the results of the Timeline follow back the self-rated questionnaire.
2	Anxiety	A validated Malay version of the HADS-A questionnaire was used to measure symptoms of anxiety. (Fariza, Y. & Zahiruddin, O, 2015; Zigmond & Snaith,1983) **A score of 11 or more denotes anxiety**.
3	Depression	A validated Malay version of the HADS-D questionnaire was used to measure symptoms of depression. (Fariza, Y. & Zahiruddin, O, 2015; Zigmond & Snaith, 1983) **A score of 11 or more denotes depression**.

4	Personality traits	Scored based on the Zuckerman-Kuhlman personality test (validated Malay version). The five domains of personality are described as • Active personality trait • Social personality trait • Aggressive-Hostile trait • Impulsive-Sense-Seeking trait • Neurotic-Anxious trait Scoring based on the score in the respective domain. The highest score will determine that an individual have dominant in that particular personality traits (Zuckerman et al., 2002)

CHAPTER 2
Literature Review

2.1. Introduction.

This chapter showed an outline of literature related to the definition, the theoretical framework of the association between treatment adherence and personality, anxiety, and depression among patients with HIV in Northwest Peninsular Malaysia. They were followed by reviewing the relationship between the variables of interest and their relationship with treatment adherence.

In the literature review, the definition of their relationship with anxiety, depression and personality is also clarified. Besides, this chapter also discusses the measuring method used for this analysis.

2.2. Search Term and Database.

The databases used to search for literature were PubMed.*gov*, EThOS, Science Direct, Research Gate, BioMed Central, Google Scholar, and PubMed Central. The search included articles up to the year 2019. The search terms were a combination of terms "antiretroviral," "adherence," "adherence and anxiety and depression," "adherence and personality traits," "temperament," and "Malaysia."

2.3. Antiretroviral Therapy in HIV

The International Network conducted the first large randomized clinical trial by Strategic Timing of Antiretroviral Treatment (START), (Health, 2015) for Strategic Initiatives in Global HIV trial (INSIGHT) over 215 sites in 25 countries. There were 4685 HIV-infected men and women identified. The participants' ages were 18 and above with the median age of 36 years old.

The participants were randomized into a first treatment group and a deferred treatment group. The time-lapse of CD4 count decline to 350cells/mm3 was observed. Both groups were followed up for three years. The results demonstrated that those in the early treatment group had shown a 53% reduced risk of developing severe illness or death compared to those in the deferred group. The early treatment group also showed pronounced risk-reduction of AIDS-related events. The findings were impeccably consistent across the different regions. Besides reducing the viral load, ART also reduced the risk of HIV transmission to an uninfected sexual partner.

The advent of antiretroviral therapy (ART), followed by the free supply of antiretroviral drugs by the Malaysian Ministry of Health since 1996, has undoubtedly brought more hope to the patients in need (Nuesch, 2009). The drug has prolonged their lifespan and improved their quality of life, allowing them to live a normal life and continuously contribute to their family and nation. However, the government faced another challenge as the subsidised drug costs a hefty amount of RM800 per month. Overall, the drug costs about RM3mil to treat 1,500 HIV/AIDS patients per year. Even though ART cannot offer a cure, without it, the HIV-infected patients would not have lived over 5 to 6 years from the time of diagnosis due to progression to AIDS. In the final stage, there was a high risk of mortality due to opportunistic infections. In ART, morbidity and mortality from HIV infection in developing countries like Malaysia have drastically reduced.

In this era, all HIV patients are given equal opportunities to receive ART. This study aims to ensure that all patients adhere to ART treatment. Even though ART has a significantly prolonged HIV-patients' lifespan, it does not necessarily improve their quality of life. Adherence to ART is another challenge for the patients to abide by due to the specific medication timing, fear of being labelled, fear of rejection, experiencing resistance or side effects of the drugs taken, and the fear of the burden and dependent to the caregiver as referred to Perez *et al.*,(2005). Undesirably, early ART treatment might predispose a physically healthy person to develop undesirable and intolerable side effects of the drugs. The patient's lifespan may be prolonged, but the patients will also subject to possible adverse drug reactions.

2.3.1. Malaysia policy

Malaysia has made substantial progress in increasing its antiretroviral availability and accessibility after it became an integral part of the diagnosis, treatment and prevention continuum in 1990. (HIV/STI SECTION Disease Control Division Ministry of Health Malaysia, 2016).

According to the national surveillance system, the incidence of new HIV infection has declined by 50% between 2000 and 2015. About 92,895 people living with HIV (PLHIV) at the end of 2015, 90,603 (97.5%) have been notified. Out of 90,603 PLHIV, 3300 people are newly infected with HIV, and 25,700 people were on life-saving antiretroviral therapy (ART).

The latest Malaysia Global AIDS reporting 2020 by Suleiman (2019) showed about 87,000 people living with HIV, 78,000 were notified. About 3564 people who are newly infected were notified in 2019. The result is somewhat counterintuitive, 56% of estimated new HIV infection in 2019, showing a rising of disease in the past two years. About 50% of the new HIV cases in Malaysia mainly accumulated in Selangor, Kuala Lumpur, and Johor's urbanized cities.

2.3.2. The National Strategic Plan for Ending AIDS (NSPEA)

The first phase of fast-tracking of NSPEA during 2016-2020 was planned to achieve the 90-90-90 goals, which represent 90% of the most significant HIV-tested populations and their knowledge of outcomes, 90% of those infected with HIV with ART, 90% of whom follow the therapy with viral suppression. The rapid monitoring process also aimed to hit 80% of main prevention populations.

In the second fast-tracking process of NSPEA, Malaysia has committed to "Ending AIDS" by 2030, meeting the 95-95-95 target, which is 95% of main HIV-tested populations, 95% of those HIV-infected receiving ART, and 95% of those adhering to ART achieving suppressed viral burden. The undertaking protects up to 90% of main communities with successful prevention.

However, until 2019, Malaysia only gained 89-56-85 where it represents 89% of PLHIV know their status, 56% of them were receiving treatment, and 85% who were virally suppressed are clearly off-track.

No doubts our Harm Reduction Program had successfully reduced the number of new HIV infections since 2002. Several states such as Kelantan, Terengganu, and Pahang have revealed a tremendous reduction in new infections from 2010 to 2019.

Surprisingly, most urbanized states like Selangor, Kuala Lumpur, and Penang showed a rise in the number of new infections from 2010 to 2019.

2.3.3. Local statistic of HIV in Malaysia (2018)

According to Country Progress Report 2019 by states (2018), Selangor accounted for the highest PLHIV at 28%, followed by Wilayah Persekutuan Kuala Lumpur at 13%, Johor 9%, Sarawak 8%, Pulau Pinang 7%, Sabah 6%, Kedah 6%, Perak 5%, Pahang 4%, Negeri Sembilan 4%, Kelantan 3%, Terengganu 3%, Melaka 2% and finally Perlis at mere 1%. Out of 14 states, three (3) states – Johor, Selangor and Wilayah Persekutuan Kuala Lumpur accounted for half (50%) of all PLHIV in Malaysia.

2.3.4. Lack of local studies on factors associate with ART treatment adherence.

So far, the available local studies associate ART treatment adherence with socioeconomic status, family support, gender, employment, a side effect of treatment, etc.

For instance, Abdulrahman *et al.* (2017) reported that PLHIV from the high-income family background and good family support is comparably more adherent to ARTs than those from low socioeconomic backgrounds low-income family support about Ibrahim *et al.*, (2014).

Apart from that, other factors that have been theorized to predispose to poor treatment adherence are depression as referred to Murphy et al. (2001), female gender, younger people, unemployed, more severe symptoms, poor perception

of health status, lack of family support in reference to Ibrahim et al., (2014) and the side effect due to treatment. On top of that, there were no local studies that associate personality traits with treatment adherence among PLHIV.

WHO (2005) is striving for effectiveness in care with a minimum degree of adherence of 95 percent to inhibit viral replication and protect the immune system. However, medication adherence is always below the target standard of clinical practice. The findings from a cohort of 242 patients receiving ART, according to Yagoub et al (2012), were still suboptimal baseline adherence, low CD4 counts and a higher viral load, of approximately 20% of patients who required adherence procedures from the beginning.

In Perlis and Kedah's clinical practices, the physician will follow-up clinically stable patients every four months with regular CD4 count monitoring. Regular monitoring schedules and strict medication adherence may subject the patients to a wide range of psychological and emotional disturbance, contributing to treatment non-adherence.

2.4. Treatment Adherence

2.4.1. Definition, theoretical framework, and measurement tools

Definition of treatment adherence

The most widely quoted definition of adherence is Haynes' "the extent to which a person's behaviour (in terms of taking medications, following diets, or executing lifestyle changes) coincides with medical or health advice" (Trostle, 1997).

Background concept of treatment adherence

Adherence is a continuous variable. The majority of non-adherence is partial, not total. The effect of non-adherence is associated with different clinical outcomes in HIV(Paterson et al., 2000). Yet, various reasons resulted in absolute adherence untenable within HIV. To date, the exact amount of each ART required to achieve ideal viral suppression still cannot precisely be identified. Sometimes, the drug's efficacy does not achieve because its absorption, metabolism, and excretion from the body differ in various people (Rainsford, 1999).

World Health Organization WHO (2005) suggests a minimum adherence level of 95% being required to suppress viral replication. However, adherence here necessitates accurate doses at a fixed timing, special dietary, and refrigeration of medications. It is not only the consumption of the requisite number of pills.

How treatment adherence is measured and reported in the studies

Measuring enforcement is often a methodological problem. Every approach had issues. Problems. During the previous visit, patients must carry their pill bottles to pill counting appointments.

The total number of pills dispensed is the inverse of the total number of pills. The lack of this approach is that it does not take account of the proper use of the pills (Basu & Garg, 2017). Patients often do not recall taking all drug bottles. If non-adherent patients know that they have their pills counted, they may have a pill dumping phenomenon, so they can dispose of additional pills before appointments. This approach may overrepresent the product of adherence (Ickovics & Meisler, 1997). To address this issue, some researchers (Fredericksen et al., 2014) adopt unannounced pill counts. Some used computer microchips incorporating the pill bottles' lid to record the date and time the bottle is opened. However, these methods measure medication dispense rather than measure medication use (Stip et al., 2013). The Medication Event Monitoring System (MEMS) can address accurate details about whether a patient takes medication or not and when medication is taken. However, the challenge here is patients might empty pills needed for the day and make this method a setback to measure dosage times. Another setback to pills counts and electronic adherence measurement systems is that it is costly, lacks consistent or standardized data interpretation guidelines, and impacts doctor-patient relationships. Sensitive patients might perceive it as a threat or feel not being trusted.

Several studies take viral suppression, as suggested by WHO, as the "gold standard" to measure adherence as well as its relationship with clinical outcome (Chendi et al., 2019). However, achieving an undetectable viral load not synonymous with adherence, nor does failure to accomplish this goal are attributable to non-adherence. Many other factors mediate this relationship (Basu & Garg, 2017).

Self-reported (percentage) adherence or self-reported adherence through a validated questionnaire like Aids Clinical Trial Group. The former conduct by asking the patient to report the number of days in which there were missed medication episodes during a specified period. The latter method conduct via a self-administered questionnaire. However, the patient's self-desirability bias and recall bias when specific duration extended also tend to overestimate the treatment adherence rate (Basu & Garg, 2017).

2.5. Variables of Interest and their Relationship with Treatment Adherence

2.5.1. Anxiety

ART has increased PLHIV's life expectancies, but another challenge has arisen. Numerous literature has studied the rate of anxiety disorders among HIV patients in developed and developing countries. Factors thought to be contributing to anxiety symptoms are related to increased physical limitations, either indirectly related to the ART's side effect or directly due to the illness progression where reduced immune system requiring frequent hospitalization due to acquired opportunistic infections(Brandt et al., 2017). An extended period of hospitalization is another stressor to the patient and caretaker.

Other stressful life events were witnessing spouse, partner, or friends, died after a complicated treatment regime and eventually died due to HIV complications. Parenting stress, social stigma, and discrimination, fatigue, substance abuse as a way to cope with stress, lack of disclosure to family members, poor social and financial support were among the most common factors that make them missed pills and missed medical appointments at follow-up (Brandt et al., 2017; Campos et al., 2010c; Fonsah et al., 2017; Reif et al., 2012; Sewell et al., 2000).

A longitudinal study by Campos et al. (2010c) discovered the anxiety symptoms before ART initiation was 12.6% among HIV-infected people in Brazil. In another prospective cohort study by Orlando et al.(2002) that encompassed 2864 participants receiving ART, approximately 15.8% of participants met GAD's criteria, and 10.5% met the panic disorder criteria.

In respect to measurement tools, the most commonly used measurement tools were Structured Clinical Interview for DSM-IV Axis I (SCID-I), Composite International Diagnostic Interview- Short Form (CIDI-SF), Clinical Diagnostic Questionnaire (CDQ), Hospital Anxiety and Depression Scale (HADS), and MINI International Neuropsychiatric Interview (MINI) (Brandt et al., 2017).

Data from the local study conducted by Radzniwan et al. (2016) assessed using a self-administered Depression, Anxiety, and Stress Scale 21 (DASS-21) showed the prevalence of anxiety among HIV patients in Northern Peninsular Malaysia was 45.1%. In another recent study conducted by Yousuf et al. (2020) among 357 HIV-positive women in two public hospitals in Ethiopia revealed the prevalence of anxiety was 28.9%. The study was conducted via a self-administered structured screening tool, the Hospital Anxiety and Depression Scale (HADS).

2.5.2. Depression

Data from several sources have identified one of the barriers to adherence is associated with moderate to severe degree of depression, where the depressed individual stopped ART on his own due to extreme subjective feelings of hopelessness, helplessness, and diminished health-related quality of life (Betancur et al., 2017).

Furthermore, numerous studies in the past found relationships between the immune system's status, infection status, disease progression rate, the period of survival or living with the illness, and depression (Cook et al., 2004).

Hence, these data supported the presence of either direct or indirect relationships between depression, the well-being or life expectancy of HIV seropositive individuals, and treatment adherence.

In respect to objective assessment tools that were frequently used were the Beck Depression Inventory (BDI), Patient Health Questionnaire (PHQ scores), Hospital Anxiety and Depression Score (HADS), Center for Epidemiologic Studies Depression Scale (CES-D), and Depression, Anxiety and Stress Scale (DASS).

The most recent research in the local setting by Radzniwan et al.(2016) used a self-administered Depression, Anxiety and Stress Scale 21 (DASS-21). The results revealed the prevalence of depression among HIV patients in Northern Peninsular Malaysia was 36.9%.

A study investigating the moderated mediation model among incarcerated Malaysian Men with HIV and opioid dependence in Kajang prison Malaysia also noted that depression mediates the effect of HIV related stigma and negatively associated with health-related quality of life (Shrestha et al., 2017). The measurement tool used to assess depression was the Center for Epidemiological Studies Depression Scale (CES-D). It is a self-report screening measure that has been extensively used in studies of HIV patients. In another study, Guan (2009) found that 32 % of depression scores from PHQ9 and 19% of depression scores from HADS among the HIV infected patients attending infectious disease clinic in University Malaya Medical Centre (UMMC).

2.5.3. Anxiety, depression, and treatment adherence

The presence of anxiety or depression is strongly related to reduced treatment adherence (Been et al., 2019; Campos et al., 2010c; Gonzalez et al., 2011; Murphy et al., 2001; Uthman et al., 2014). Severe anxiety at the beginning of ART initiation was associated with strong predictors of treatment non-adherence (Campos et al., 2010c).

Anxiety and depression have a severe impact on the immune system. In a stressful situation, cortisol level is raised, interferon-γ is reduced, and the interleukin-10 is increased, cumulatively inhibiting the anti-HIV response of the many immune system cells in the body, hence worsening the already weakened immune system. More evidence also showed that compared to individuals without lost a close friend to AIDS, individuals with the loss had a lower number of CD4+ cells (Batten & Upchurch, 2010; Ngum et al., 2017).

The most recent study conducted by Yousuf et al. (2020) among 357 HIV-positive women in two public hospitals in Ethiopia revealed the prevalence of anxiety was 28.9%. Another recent study by Ngum et al. (2017) in the Southwest Region of Cameroon revealed that depression prevalence was 26.7% (95% CI 20.6-33.7%) among those on ART. They contributed 75.0% among those with poor adherence to ART compared to those without depression, 37.3% (p<0.001).

A meta-analysis by Jane (2008) reviewed longitudinal studies from all English language articles from 1990 to July 2007. Both before and after the advent of antiretroviral therapy (ART) found evidence of chronic depression, trauma, and

stressful events, causing a decrease in CD4 T lymphocytes, causing clinical deterioration, and further increasing viral load mortality.

Upon the initial diagnosis of positive HIV, patients commonly relate their feeling as dreadful, comparing it to a death sentence. In a similar study by Sherman (2010), death anxiety among AIDS patients was higher than their caregivers. Overall, the quality of life of AIDS patients is lower, especially in the psychological domain**.** In a study conducted by Sherman (2010), death anxiety was higher in AIDS patients than cancer patients. The younger AIDS patients can partly explain this as compared to cancer patients. Older adults are less apprehensive of death as compared to their younger counterparts. Hence, the long-term illness and uncertainty of the remaining life with a super-imposed feeling of loneliness, rejection, and a sense of dependency have significantly impaired their quality of life.

There were earlier studies on the stress of the bereavement process in HIV-infected persons among homosexual communities who is either had a partner or had a close friend died due to AIDS about Jane, (2008). All 85 HIV-infected homosexual men who either had a close friend or a partner died of AIDS displayed a more rapid decline in the CD4+ count during a 3-4-year follow-up. However, the study did not adjust the findings based on the different antiretroviral medication used and their health habits. Another cohort study on 96 homosexual men by CHIP (Coping in Health and Illness Project) investigators explored the effect of stressful life events (i.e., change in job career, relationships, deaths, finance, and health) disease progression. They have

consistently reported adverse immunological and health effects affected by stressful life events and predicted a faster progression to AIDS during the nine-year follow-up (Leserman, 2008).

2.5.4. Personality traits

Personality traits are being defined as "Enduring patterns of perceiving, relating to, and thinking about oneself and the environment that is exhibited in a wide range of social and personal contexts" (American Psychiatric Association, 1994, p. 630).

According to Folkman & Lazarus (1985), individuals use various coping strategies in different circumstances.

Costa & Mccrae, (2012) points out that personality traits are patterns of thoughts and behaviour where it will determine how one individual behave throughout their life. There are varieties of personality models established to measure personality traits. By far, the most well-known used model used to describe personality is the five-factor model (FFM). According to the Revised NEO Personality Inventory (NEO-PI-R), Neuroticism describes the degree of emotional maturity, the degree of interpersonal contact estimates extraversion, the willingness to consider novel ideas, consent tests the quality of interpersonal orientation and conscientiousness describes the motivation of target-oriented conduct.