FACTORS PREDICTING NUTRITIONAL SCORES IN HIV-INFECTED ELDER RECEIVING ANTIRETROVIRAL THERAPY IN THAILAND

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ปัจจัยทำนายคะแนนโภชนาการในผู้สูงอายุที่ติดเชื้อเอชไอวีและได้รับการบำบัดด้วยยาต้านไวรัสในประเทศไทย

น.ส.เดเลีย เท็ต

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต
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By	Miss Daylia Thet
Field of Study	Pharmaceutical Care
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เดเลีย เท็ต : ปัจจัยทำนายคะแนนโภชนาการในผู้สูงอายุที่ติดเชื้อเอชไอวีและได้รับการบำบัดด้วยยาต้านไวรัสในประเทศไทย. (FACTORS PREDICTING NUTRITIONAL SCORES IN HIV-INFECTED ELDER RECEIVING ANTIRETROVIRAL THERAPY IN THAILAND) อ.ที่ปรึกษาหลัก : ผศ. ภญ. ดร. ทิพวรรณ ศิริเทียรทอง, อ.ที่ปรึกษาร่วม : พญ. ดร.อัญชลี อวิหิงสานนท์

วัตถุประสงค์การวิจัย: (1) เพื่อเปรียบเทียบค่าเฉลี่ยคะแนนประเมินภาวะโภชนาการและคะแนนประเมินภาวะซึมเศร้าของผู้สูงอายุที่ติดเชื้อเอชไอวีและได้รับยาต้านไวรัส ระหว่างปีพ.ศ. 2559 และพ.ศ. 2563 (2) เพื่อศึกษาความสัมพันธ์ระหว่างคะแนนประเมินภาวะโภชนาการและคะแนนประเมินภาวะซึมเศร้า (3) เพื่อสร้างแบบจำลองทำนายคะแนนประเมินภาวะโภชนาการ ระเบียบวิธีวิจัย: งานวิจัยนี้เป็นงานวิจัยเชิงสำรวจแบบย้อนหลังระยะยาวในประชากรผู้สูงอายุชาวไทยที่มีอายุตั้งแต่ 50 ปีบริบูรณ์ขึ้นไป ซึ่งติดเชื้อเอชไอวีและได้รับการรักษาด้วยยาต้านไวรัส รวมถึงเคยเข้าร่วมการวิจัย ณ ศูนย์ประสานความร่วมมือระหว่างไทย ออสเตรเลีย เนเธอร์แลนด์ เพื่อการศึกษาวิจัยทางคลินิกด้านโรคเอดส์ (HIV-NAT center), กรุงเทพฯ, ประเทศไทย ในระหว่างเดือนมีนาคม พ.ศ. 2559 ถึงเมษายน พ.ศ. 2560 มาก่อน ขนาดตัวอย่างสำหรับการวิเคราะห์การถดถอยเชิงพหุคูณคำนวณจาก 1 ตัวแปรอิสระควรได้ข้อมูลจากผู้ป่วยจำนวน 15 คน การวิจัยนี้มีตัวแปรอิสระ 16 ตัวแปรจึงต้องการข้อมูลจากผู้ป่วยอย่างน้อย 240 คน โดยใช้วิธีการสุ่มตัวอย่างแบบเจาะจง ผลการวิจัย: จากผู้เข้าร่วมการวิจัยทั้งหมด 250 (100%) คน ส่วนใหญ่เป็นผู้ชาย (60.8%) อายุเฉลี่ยเท่ากับ 59.78 ± 5.6 ปี มีค่าเฉลี่ยคะแนนประเมินภาวะโภชนาการในปี พ.ศ. 2563 ลดลงเมื่อเทียบกับคะแนนในปีพ.ศ. 2559 (24.85 vs 25.78, $p < 0.001$). ค่าเฉลี่ยของคะแนนประเมินภาวะซึมเศร้าก็ลดลงเช่นกัน (3.14 vs 3.83, $p = 0.001$) ผู้เข้าร่วมการวิจัยที่มีภาวะซึมเศร้ามีแนวโน้มที่ภาวะโภชนาการจะแย่ลงเมื่อเวลาผ่านไปมากกว่าผู้ที่ไม่มีภาวะซึมเศร้า แบบจำลองการทำนายคะแนนทางโภชนาการที่ยืนยันโดยการวิเคราะห์การถดถอยเชิงพหุคูณแบบลำดับขั้นคือ คะแนนภาวะโภชนาการ = -0.470 คะแนนประเมินภาวะซึมเศร้า** – 0.301 จำนวนยาที่ได้รับ** – 0.193 ระดับไขมันเอชดีแอล (HDL-C)** + 0.126 ระดับไตรกลีเซอไรด์* + 0.105 ระดับ CD4* สรุป: คะแนนประเมินภาวะซึมเศร้า, จำนวนยาที่ได้รับ, ระดับไขมันเอชดีแอล, ระดับไตรกลีเซอไรด์และระดับ CD4 เป็นตัวทำนายที่สำคัญของคะแนนภาวะโภชนาการ

สาขาวิชา การบริบาลทางเภสัชกรรม ลายมือชื่อนิสิต .....

ปีการศึกษา 2563 ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

ลายมือชื่อ อ.ที่ปรึกษาร่วม .....

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KEYWORD: HIV, Elder, ART, Nutritional status, Depression, Factors

Daylia Thet : FACTORS PREDICTING NUTRITIONAL SCORES IN HIV-INFECTED ELDER RECEIVING ANTIRETROVIRAL THERAPY IN THAILAND. Advisor: Asst. Prof. TIPPAWAN SIRITIENTONG, Ph.D. Co-advisor: Anchalee Avihingsanon, Ph.D.

Objectives: (1) To compare means of nutritional scores and means of depression scores from 2016 and 2020 (2) To investigate relationship between nutritional scores and depression scores (3) To establish nutritional score prediction model. Methodology: A longitudinal retrospective survey study was performed. Population were human immunodeficiency virus (HIV)-infected Thai elderly patients aged 50 years and above who were receiving HIV care and had previously participated in the aging cohort study conducted from March 2016 to April 2017 at the HIV-NAT Center, Bangkok, Thailand. Sample size for multiple regression analysis is calculated as 15 cases per 1 independent variable. This study contained 16 variables; then, 240 participants should be included. Purposive sampling method was executed. Results: A total of 250 (100%) participants were included in this study. Most of them were male (60.8%). The mean age was 59.78 ± 5.6 years. The means of nutritional scores declined in 2020 compared to 2016 (24.85 vs 25.78, $p < 0.001$). The mean depression scores declined in 2020 compared to 2016 (3.14 vs 3.83, $p = 0.001$). The participants with depression were more likely to be deteriorated in nutritional status over time than those without depression. Nutritional score prediction model confirmed by hierarchical stepwise multiple regression analysis was Nutritional scores =– 0.470 Depression scores** – 0.301 Number of medications** – 0.193 high-density lipoprotein cholesterol (HDL-C) ** + 0.126 triglyceride* + 0.105 CD4* Conclusion: Depression scores, number of medications, HDL-C, triglyceride and CD4 were significant predictors of nutritional scores.

Field of Study:	Pharmaceutical Care	Student's Signature .....
Academic Year:	2020	Advisor's Signature .....
		Co-advisor's Signature .....

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LIST OF ABBREVIATIONS

AIDS	=	Acquired immunodeficiency syndrome
ANOVA	=	Analysis of variance
ART	=	Antiretroviral therapy
BMI	=	Body mass index
CC	=	Calf circumference
CD4	=	Cluster of differentiation 4
GDS	=	Geriatric depression scale
HBV	=	Hepatitis B virus
HC	=	Hip circumference
HCV	=	Hepatitis C virus
HDL-C	=	High-density lipoprotein cholesterol
HIV	=	Human immunodeficiency virus
HIV-NAT	=	HIV-Netherlands-Australia-Thailand
hs-CRP	=	High-sensitivity C-reactive protein
IOC	=	Item objective congruence
IRB	=	Institutional review board
LDL-C	=	Low-density lipoprotein cholesterol
MAC	=	Mid-arm circumference
MNA	=	Mini nutritional assessment

MNA-SF	=	Mini nutritional assessment-short form
PLHIV	=	People living with human immunodeficiency virus
TDS	=	Thai depression scale
TG	=	Triglyceride
TGDS	=	Thai geriatric depression scale
VAS	=	Visual analogue scale
WC	=	Waist circumference
WHR	=	Waist-hip-ratio

CHAPTER I INTRODUCTION

1.1 Background and rationale

Human immunodeficiency virus (HIV) infection and nutritional issues have a complex relationship. Malnutrition in HIV-infected population is a common public health threat[1]. In the treatment of HIV infection, effective combination of antiretroviral therapy (ART) has been developed to prolong the longevity of people living with HIV (PLHIV)[2]. The number of PLHIV aged 50 years and above has increased globally[3]. Although the life expectancy rates of PLHIV have increased, various geriatric complications including nutritional problems and depressive disorders are accompanied following treatments.

With the advance in age, elderly people may experience changes in physical and physiological functions. Age related changes in metabolism such as anorexia due to loss of sensation, hormonal imbalances and functional disability may result in malnutrition[4]. In elderly PLHIV, diarrhea, lipid abnormalities, muscle wasting, peripheral neuropathy and depression due to ART side effects or HIV are interrelated to one another and may predispose the nutritional issues[1, 5]. The occurrence of malnutrition in elderly PLHIV is usually higher than that in uninfected elderly population. A previous cross-sectional study showed the high prevalence of malnutrition in the HIV-infected Thai elderly[6]. The study included participants aged 50 years and above due to the detrimental effects of the diseases following the increase in age. According to the Mini Nutritional Assessment (MNA) scores, the HIV-infected elderly had higher risk of malnutrition than uninfected elderly people (18.1% and 6.8% respectively, $p = 0.005$).

Together with social and environmental effects, HIV per se affects central nervous system of PLHIV which leads to psychological problems mainly depression, bipolar disorders and cognitive impairment[7]. In addition to aging effect, socially isolated elderly PLHIV due to HIV-related stigma may have depressive disorders. The unrecognized nature of depression also increases the severity of depressive symptoms in PLHIV. Therapeutic failure is inevitably occurred in depressive patients.

As a result, depression becomes a vital problem to be solved in HIV population. In Thailand, the prevalence of depression was higher in PLHIV than non-infected population according to the recent study[8]. The HIV-infected aging population had higher risk of depression compared to the HIV-negative group showing the prevalence of 24.71% vs 13.73%, respectively (p = 0.019).

Malnutrition in HIV-infected patients can be improved by adopting effective nutritional screening and assessment. Therefore, signs and symptoms of malnutrition can be regulated timely prior to serious adverse events occur. Similarly, screening and assessment of depressive symptoms should be carried out to optimize treatment outcomes in HIV-infected patients. Following the increased longevity, the high prevalence of malnutrition and depression supports the implementation of assessments of both conditions in the HIV-infected elderly. The improvement or severity of nutritional issues and depressive symptoms are needed to clarify because they have impacts on health care plans and outcomes of the patients. The longitudinal studies assessing changes in nutritional scores and depression scores over time especially in the HIV-infected elderly have not been much explored yet. Moreover, to the best of our knowledge, the relevant factors of malnutrition are still in discrepancies between previous studies. The purpose of this study was to investigate the changes in nutritional scores and depression scores over 4 years period in Thai HIV-infected elderly patients who have previously participated in the aging study at the HIV-Netherlands-Australia-Thailand Research Collaboration (HIV-NAT) Center, Bangkok, Thailand. The nutritional scores prediction model was established by depression, medication adherence and demographic data.

1.2 Objectives of the study

1. To compare means of nutritional scores from 2016 and 2020
2. To compare means of depression scores from 2016 and 2020
3. To investigate relationship between nutritional scores and depression scores
4. To establish nutritional scores prediction model by depression, medication adherence and demographic data

1.3 Scope of the study

This study mainly focused on the nutritional assessment by Mini Nutritional Assessment (MNA) and depression assessment by Thai Depression Scale (TDS) in the HIV-infected elderly. These patients had previously participated in the aging study conducted from March 2016 to April 2017 at the HIV-NAT Center, Bangkok, Thailand. The potential factors related to changes in nutritional status and depression were also investigated.

1.4 Benefits of the study and applications

This study showed the changes in nutritional and depression scores over a period of four years assessing whether the conditions become improved or worsen in the HIV-infected elderly. The relationship between malnutrition and depression, and the possible predicting factors of changes in nutritional scores namely, (1) medication adherence, (2) demographic factors such as age, gender, drinking and smoking, (3) clinical factors such as duration of HIV, duration of ART, number of medications and comorbidities, and (4) laboratory parameters such as CD4, serum insulin, albumin, hs-CRP, hemoglobin and lipid profiles will also be analyzed. The findings of the study may be applied in the managements of malnutrition and depression-induced complications in the HIV-infected elderly receiving antiretroviral therapy.

1.5 Operational variables

Nutritional status

Nutritional status is the condition of the body health which is influenced by the nutrient levels in a person's diet and the ability of these nutrients to maintain normal metabolic functions[9].

Malnutrition

Malnutrition is characterized by the imbalance of nutrients required for normal body mechanisms which leads to substantial adverse effects on body composition and functional ability[4].

Depression

Depression is a kind of mental disorder commonly characterized by sadness, lack of interest or pleasure, sleep disturbances, poor concentration and loss of appetite. The state may be influenced by complex interactions between social, psychological and biological factors[10].

Medication adherence

Medication adherence is the degree to which a person' s behavior corresponds with the agreed recommendations from a health care provider and taking 95% or more of the prescribed doses on time and in correct way[11].

CHAPTER II LITERATURE REVIEWS

2.1 Aging and malnutrition in HIV infection

HIV infection is a major global health problem which gives rise to Acquired Immunodeficiency Syndrome (AIDS) followed by serious complications. By 2030, it has been expected to end the AIDS epidemic in Thailand[12]. The strategies to achieve the treatment targets include prevention of disease transmission, control of viral progression and upgrading health care programs for infected population. In current situation, treatment of HIV infection in every age population is carried out effectively to reduce mortality and morbidity rates. With high accessibility of combination ART regimens, the disease progression and viral resistance problems become diminished giving PLHIV sense of wellbeing and their longevity will be increased[2].

However, mostly with the increase in age, there are high risks of geriatric complications in the HIV-infected elderly. Common geriatric complications include falls, frailty, functional decline, sarcopenia, malnutrition, depression, and cognitive dysfunction[13]. Physiological functions usually decline after the age of 50 years and immunological responses have become poor at this age[14]. By the study of the World Health Organization in African aging population, 50 years of age and older persons have been defined as the elderly[15]. The previous cross-sectional aging studies in HIV population also used cut-off age at 50 years and above[13, 14]. A Netherlands aging cohort study predicted that the proportion of PLHIV aged 50 years or older will be increased from 28% in 2010 to 73% in 2030 [16].

Nutrient requirement in HIV-infected patients is considerably higher than that in general population because of immune dysfunction and secondary infections[5]. HIV clinical symptoms and viral suppression are optimized by adopting ART which controls viral load levels and lengthens survival rates of patients. However, despite the benefits of ART, many patients encounter long-term complications mostly bone loss, fat redistribution syndrome, hyperglycemia, and hyperlipidemia[5]. Moreover, impaired glucose metabolism, insulin resistance, oral candidiasis, mouth and

gastrointestinal ulcers, anorexia and swallowing problems can affect the nutritional status giving rise to malnutrition in PLHIV[1]. Most of these side effects are inevitable and increase energy expenditure in older HIV patients. In the presence of opportunistic infections, HIV-infected patients have about 20-30% higher resting metabolism which leads to muscle wasting and weight loss compared to uninfected people[1].

A systematic review performed by Todowede et al.[17] observed that the HIV-positive patients receiving ART were found to have two times higher prevalence of metabolic syndrome compared to the negative people (21.5% and 12.0%, respectively). Hypertension, diabetes, hypertriglyceridemia, visceral obesity were major components of metabolic syndrome irrespective of CD4 and viral loads.

Gebremichael et al.[18] conducted the institution-based cross-sectional study in HIV population about the nutritional status and associated factors of malnutrition. It was found that the malnutrition rate of HIV/AIDS adult patients was 23.6% (95% CI: 19.7-27.4) based on body mass index (BMI). According to Naidoo et al.[19] the prevalence of malnutrition risk in South Africans elderly assessed by the Mini Nutritional Assessment (MNA) was 43.4%.

Malnutrition in the HIV-infected elderly should be regularly screened before it becomes serious. There are many methods for the evaluation of nutritional status which are recommended to perform routinely[5]. MNA has been widely applied in the nutritional assessment of elderly population. The MNA scores range from 0-30 in which higher scores refer to normal nutritional status and lower scores refer to malnutrition. It is a well-validated tool which had 96% sensitivity, 98% specificity and 97% positive predictive value according to the study by Guigoz et al.[20]. In Thailand, the validity of Thai version MNA has been found in the elderly outpatients and inpatients by Techakriengkrai et al.[21]. There were 50% sensitivity, 94.9% specificity, 53.3% positive predictive value and 94.2% negative predictive value in Thai-MNA.

2.2 Depression in HIV infection and its association with malnutrition

Depression is an age-related psychiatric problem. It includes poor concentration, social avoidance, loss of appetite, lack of sleep, fatigue, and sadness

contributing to disability and health complications[10]. The HIV-infected elderly may suffer from depressive disorders as consequences of physical dependency or as a part of geriatric syndrome, stigma and neurotoxicity side effects of ART[10, 13]. Some HIV-related opportunistic infections such as meningitis and brain tumor may exacerbate depressive disorders. A cross-sectional study about geriatric syndromes in HIV-infected older adults aged 50 years and above has shown the prevalence of depression as 40% which supported the findings of high prevalence of depression in HIV-infected elderly patients in the previous literature[13]. The prevalence of depression among HIV-infected patients varies among studies because of the different study design. In a recent systematic review, it has been demonstrated that the prevalence of moderate to severe depression was 24.4% (95% CI: 12.5–42.1) in PLHIV in low- and middle- income countries[22].

The co-occurrence of depression as a non-communicable disease following HIV infection has been postulated (24.4%, 95% CI: 12.5-42.1)[22]. Thus, most malnourished HIV-infected elderly patients may have high susceptibility to suffer from depressive disorders which induce suicidal thoughts and severe cognitive dysfunctions. One of the geriatric complications, frailty was found to be associated with the nutritional status and depression in the HIV-infected elderly aged 55 years and above[23]. A recent cohort study stated that frailty had positive correlations with the nutritional status ($r = 0.347$, $p = 0.02$) and depression ($r = 0.473$, $p = 0.001$)[23].

According to Weldehaweria et al.[24], depression represented as an independently associated factor of malnutrition in PLHIV receiving ART in 2017. This matched case-control study used BMI for the evaluation of nutritional status and Patient Health Questionnaire-9 for depression screening. The findings showed that depressed patients had higher risk of malnutrition than non-depressed patients (AOR = 2.8, 95% CI: 1.3-6.1).

Depression was a significant determinant of malnutrition in a Polish study by Wojszel et al.[25] in 2006. The study focused on the assessment of nutritional status in 109 nursing home elderly population which used MNA for the assessment of nutritional status and Geriatric Depression Scale (GDS) for the depression screening. The multivariate regression analysis of independent variables associated with total

MNA scores showed that higher GDS scores were significantly associated with lower MNA scores ($p < 0.0001$).

A South African survey study in 984 community-dwelling older adults also showed that depressed elderly people had about 2.8 times higher risk of malnutrition than those who were not depressed ($p < 0.001$). The study used the short form MNA (MNA-SF) for the screening of nutritional status and the Centre for Epidemiologic Studies Depression Scale for the screening of depression[19].

Depressive disorders should be routinely screened in elderly population, and many methods have been developed. Thai version Geriatric Depression Scale which is called TDS or TGDS was found to be sensitive in the previous study[26]. The TDS scores range from 0-15 in which higher scores refer to high risk of depression and lower scores refer to little or no risk of depression. In Thailand, the sensitivity and reliability of TDS were tested by Wongpakaran et al.[26] in 2013. A sensitivity of 92% and a specificity of 87% were found in the screening of geriatric outpatients while the positive predictive value was 83.3%.

Although elderly PLHIV have depressive disorders, they may be unrecognized because some depressive symptoms such as appetite disturbances and sleep abnormalities are generally similar to common HIV related symptoms[22]. The severity and changes in depressive symptoms over a period of time in elderly PLHIV were rarely studied. The follow-up evaluations of nutritional status are also currently not much well-known among aging HIV-infected population. Therefore, depression screenings and nutritional assessments should be regularly performed in elderly PLHIV to set up appropriate health care plan over malnutrition and depressive symptoms.

2.3 Association of malnutrition with poor medication adherence

One of the important factors in achieving therapeutic outcome in HIV treatment is adherence to medication. Poor adherence to ART (<95% dose taken by patients) such as missing or skipping doses may be related to poor nutrition in HIV-infected patients. A matched case-control study about psychosocial factors correlated to the nutritional status among PLHIV stated that the non-adherent

patients on ART had significantly higher risk of malnutrition compared to the adherent patients (AOR=6.8, 95% CI: 2.0-23.0)[24]. The failure of treatment to suppress viral replication strongly resulted in poor nutritional status.

According to study by Mulu et al.[27], the malnutrition rates were high in the hospitalized HIV-infected patients. Their cross-sectional study demonstrated that the overall malnutrition prevalence was 46.8% and 44.1% according to BMI and mid upper arm circumference, respectively. Their findings reported that poor medication adherence was one of the independent variables significantly associated with poor nutritional status ($p < 0.05$).

Similar result was found in a study by Jerome et al.[28] in which medication adherence was a dependent variable. Based on BMI, the non-adherent patients had higher rates of malnutrition than the adherent patients (38% Vs 28%, $p = 0.01$) referring < 18 kg/m^2 of BMI as malnutrition.

2.4 Predicting factors of nutritional status

Malnutrition is a multifactorial condition, and it can be affected by several independent variables including demographic factors, clinical factors and biological factors.

(1) Demographic factors

Demographic factors included the following variables.

Age

Aging may affect nutritional status in several ways because of the impaired immune function and dysregulation of physiological mechanism. Many studies showed the effect of age on the nutritional status. The nutrient requirement in elderly population is considerably higher than other age population. With the increase in age, functional decline and metabolic complications become common accompanied by nutritional issues. Higher age was found to be a significant risk factor of malnutrition in the community Greek elderly population ($p < 0.001$)[29].

In HIV-infected population, the elderly aged 50 years and above were found to have higher risk of malnutrition. Apornpong et al.[6] conducted a cross-sectional

study about the prevalence of malnutrition in the HIV-infected elderly aged above 50 years in Thailand. In this study, aging was found to be a significant risk factor associated with malnutrition (AOR = 1.06, 95% CI: 1.01-1.12, p = 0.03).

Gender

Several studies showed the significant relationship of gender status and nutritional status[19, 25, 29-31]. They reported the differences in malnutrition risks based on gender in general and HIV population. A previous study by Wojszel et al.[25] showed that in nursing home elderly population, lower MNA scores were independently associated with female gender ($p < 0.05$). Similarly, in HIV population, female patients had high risks of malnutrition in a recent study by Odwee et al.[30].

However, contrarily, a recent aging study showed that the elderly females have decreased risk of malnutrition compared to males in community-dwelling older adults[29]. In HIV-infected adult patients, males had higher prevalence of malnutrition than females (43% Vs 14%), ($p = 0.002$)[31]. Naidoo et al.[19] also confirmed that men were more likely to have higher risk of malnutrition than women ($p = 0.008$).

Drinking

Alcohol consumption was one of the independently associated factors of malnutrition in HIV population in a study of Weldehaweria et al.[24]. In that case-control study, about 48% of malnourished patients had history of drinking alcohol and 18.8% malnourished patients were consuming alcohol currently. HIV-infected patients on ART who consumed alcohol after starting ART had higher risk of malnutrition than their counterparts (AOR = 4.7, 95% CI: 1.8-12.3).

Smoking

Smoking cigarettes or tobacco use was one of the significant risk factors of malnutrition in a previous HIV-infected population study[24]. The study showed that patients who had history of ever using cigarettes were 7.6 times more likely to be malnourished compared to matched counterparts (AOR =7.6, 95% CI: 2.3-25.5).

(2) Clinical factors

Clinical factors included the following variables.

Duration of HIV

According to Mulu et al[27], the longer duration of HIV more than 2 years since diagnosis was significantly associated with malnutrition in hospitalized HIV-infected patients in Ethiopia.

Duration of ART

The longer period of ART treatment may improve clinical outcomes and immune system of patients resulting in better physiological status and nutritional status. Duration of ART was an independent factor significantly associated with nutritional status according to the study by Gebremichael et al.[18]. Lower prevalence of malnutrition was found in patients who had been on ART for a longer period (AOR = 1.8, 95% CI: 1.2-2.9)[18].

Number of medications

The high number of medications may increase risk of malnutrition. High number of drugs were significantly associated with lower MNA scores in Polish elderly people living in nursing home ($p < 0.05$)[25]. Similar results had been found in the Nepalese elderly in the community setting (OR=3.01, 95%CI: 1.53-5.92)[32].

Comorbidities

In addition to HIV infection, elderly PLHIV may have other health concerns due to immune deficiency or metabolic abnormalities. A recent cross-sectional study in Thai HIV-infected elderly aged above 50 years found that diabetes was a significant risk factor of malnutrition (AOR = 2.21, 95% CI: 1.003-4.87, $p = 0.049$)[6]. In the U.S adults, the prevalence of low muscle mass was significantly higher in those who had chronic hepatitis C virus (HCV) infection ($p < 0.001$). Mid upper arm circumference and triceps skinfold thickness were significantly lower in HCV-infected patients ($p = 0.006$ and $p < 0.001$, respectively). Moreover, the prevalence of HIV infection was higher in HCV population[33].

(3) Laboratory factors

Laboratory factors included the following variables.

CD4

Previous studies reported a significant association between CD4 counts and malnutrition risk. In Tanzania, Kabalimu et al.[31] stated that HIV-infected adults with

CD4 counts less than 100 cells/mm^3 were more likely to be malnourished compared to other patients with higher CD4 counts. Moreover, in 2011, another cross-sectional study in Brazil showed that HIV-infected patients with CD4 level lower than 200 cells/mm^3 had higher risk of malnutrition ($p = 0.01$)[34]. In this study, the statistically significant differences in CD4 count, weight loss and low albumin were found ($p < 0.01$). The findings of the cross-sectional study in hospitalized HIV-infected adults in Ethiopia showed that low CD4 level was an independent predictor of malnutrition in this population[27].

Lipid profiles

In HIV infection, one of metabolic complications due to ART is dyslipidemia [increased triglycerides (TG), increased low-density lipoprotein cholesterol (LDL-C) and decreased high-density lipoprotein cholesterol (HDL-C)] which is related to cardiovascular risk. Plasma lipid concentrations were recommended to assess annually in HIV population[5]. The study of malnutrition in HIV-infected and uninfected drug user males showed that HIV-infected men had higher TG ($p = 0.03$), lower LDL-C ($p < 0.001$) and lower HDL-C ($p < 0.001$) than their counterparts although both groups had poor nutritional status[35].

Serum insulin

Insulin resistance is a known risk factor of cardiovascular disease and diabetes mellitus in HIV population. Besides, there is a growing recognition that hyperinsulinemia may lead to coronary artery disease[5].

Serum albumin

Serum albumin is a predictor of mortality in HIV-infected patients[5]. Moreover, it was associated with poor nutritional status in previous studies. According to Santos et al.[34], albumin was a significant biochemical predictor of malnutrition showing hypoalbuminemia was associated with weight loss ($p = 0.01$) in hospitalized HIV-infected patients. Similarly, a cross-sectional study of the hospitalized HIV/AIDS patients by Mulu et al.[27] found that lower serum albumin (< 3.5 g/dL) was associated with malnutrition in HIV-infected patients.

Serum high sensitivity C-reactive protein (hs-CRP)

Malnourished patients have high risk of cardiovascular diseases and inflammation which can be predicted by serum hs-CRP level[5]. Higher serum hs-CRP levels were associated with cardiovascular complications ($p < 0.0001$)[36].

Hemoglobin

Anemia seems to be a contributing factor of poor nutritional status. Santos et al.[34] showed that 84% of HIV-infected adult patients had hemoglobin level lower than 12 mg/dL, and that was associated with malnutrition. Furthermore, the anemic condition was associated with lower CD4 count and lower albumin levels in these populations. The association of hemoglobin level with nutritional status was supported by another study of hospitalized HIV-infected adults[27]. Serum hemoglobin less than 7 mg/dL was significantly associated with malnutrition.

From the literature reviews, the predicting factors of malnutrition in the HIV-infected elderly were varied individually due to several factors such as disease conditions, medication adherence problem, mental status etc. To explore more about the predictive effect of these factors on nutritional changes in the HIV-infected elderly population, different designs of further studies are required.

CHAPTER III RESEARCH METHODOLOGY

3.1 Study design

A longitudinal retrospective survey study was performed between 2016 and 2020.

3.2 Population and samples

The population of this study were HIV-infected Thai elderly patients aged 50 years and above who were receiving HIV care and had previously participated in the aging cohort study conducted from March 2016 to April 2017 at the HIV-NAT Center, Bangkok, Thailand (the previous IRB approval number 442/58). The IRB approval number for the current study was 507/63.

3.2.1 Inclusion and exclusion criteria

The HIV-infected patients aged 50 years and above treated with antiretroviral therapy who had been previously assessed by Mini Nutritional Assessment (MNA), Thai Depression Scale (TDS) and agreed to participate in the study were included in this study. However, hospitalized debilitated patients, unconscious patients, and the loss of follow-up patients were excluded.

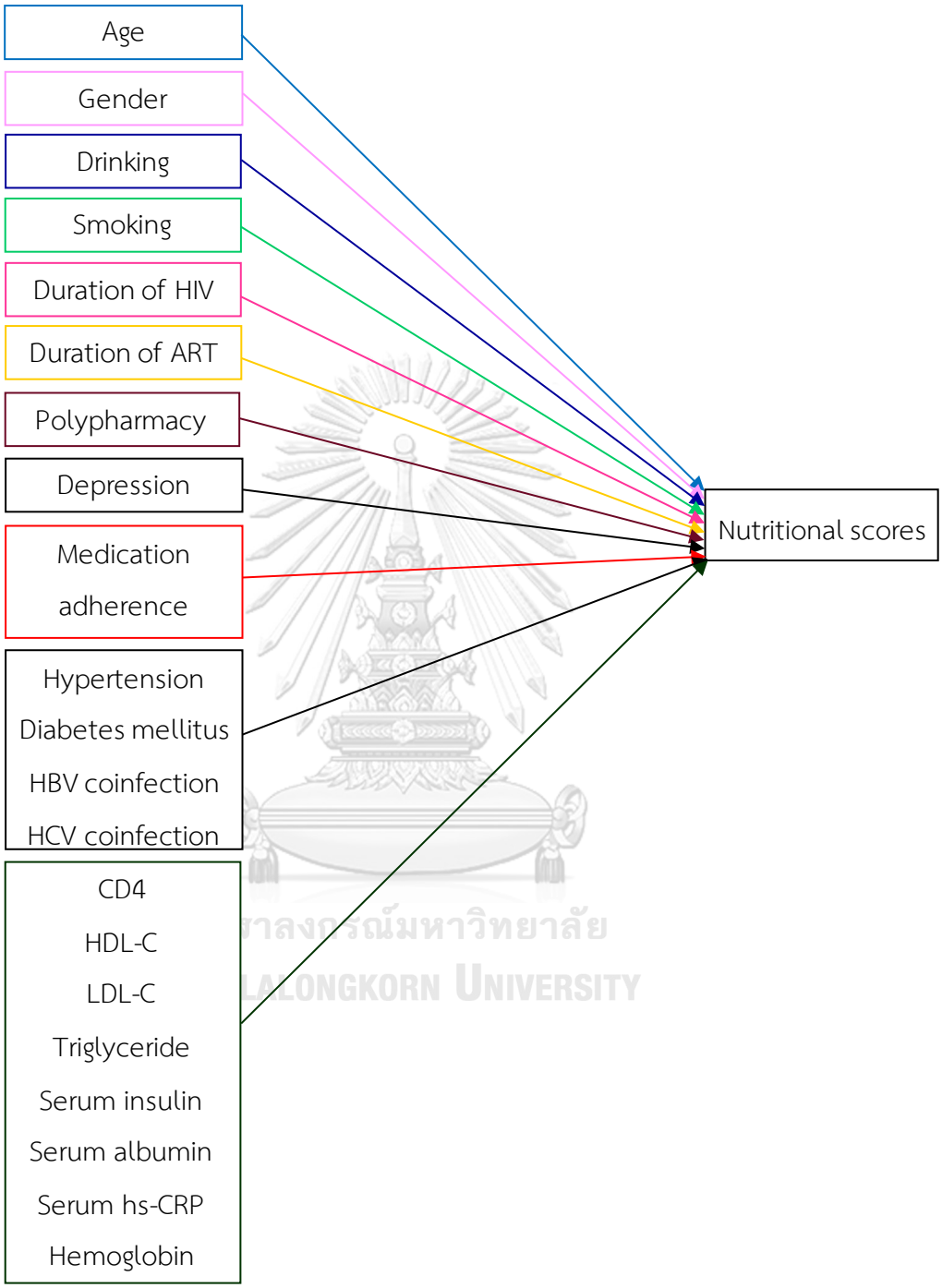
3.2.2 Sample size calculation

According to Hair et al.[37], sample size (n) for multiple regression analysis is 15 cases per 1 independent variable. There were 16 independent variables in this study, therefore sample size of 15 x 16= 240 participants were included.

3.2.3 Sampling method

The purposive sampling method was applied by gathering the data of the HIV-infected Thai elderly who had done MNA and TDS questionnaire previously[38].

3.3 Conceptual framework



3.4 Instruments

A case record form consisted of MNA, TDS, Visual Analogue Scale (VAS) and demographic data.

Demographic, clinical and laboratory data were recorded using a case record form to obtain information of participants including age, gender, marital status, occupation, smoking, drinking, duration of HIV, duration of ART, number of current medications, comorbidities, CD4, viral loads, lipid profiles, serum insulin, albumin, creatinine, hs-CRP and hemoglobin.

3.4.1 Mini nutritional assessment

Nutritional scores were measured by the validated MNA-Thai version. It is divided into 2 sections: screening and assessment. It included participant-administered items and researcher-administered physical assessment items. The questionnaire consisted of 4 main constructs (18 variables) namely: (1) dietary habits (**table 1**); (2) anthropometric measurements (**table 2**); (3) general characters (**table 3**); and (4) subjective assessment (**table 4**). Malnourished condition was defined as scores less than 17 points, risk of malnutrition was defined as 17-23.5 points, and normal nutritional status was defined as 24-30 points. The higher the scores, the better the nutritional status. The detail scoring is as following:

Table 1 Dietary assessment

Questions	Scores
Question A Severe decrease Moderate decrease No decrease	0, 1, 2
Question J 1 meal 2 meals 3 meals	0, 1, 2
Question K 0 or 1 yes	0.0, 0.5, 1.0

2 yes 3 yes	
Question L No Yes	0, 1
Question M < 3 cups 3-5 cups > 5 cups	0.0, 0.5, 1.0
Question N Unable to eat without assistance Self-fed with some difficulties Self-fed without any problem	0, 1, 2

A. The score in this part came from the question "Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?". Score 0 refers to "severe decrease", score 1 refers to "moderate decrease" and score 2 refers to "no decrease".

J. The score in this part came from the question "How many full meals does the patient eat daily?". Score 0 refers to "1 meal", score 1 refers to "2 meals" and score 2 refers to "3 meals".

K. The score in this part came from the question "Selected consumption markers for protein intake (1) At least one serving of dairy products (milk, cheese, yoghurt) per day, (2) Two or more servings of legumes or eggs per week and (3) Meat, fish or poultry everyday". If the participants choose "Yes" in only one of these 3 parts or "No" in all these 3 parts, the score is 0.0. If the participants choose "two yes", score is 0.5. If the participants choose "Yes" in all parts, score is 1.0.

L. The score in this part came from the question "Consumes two or more servings of fruit or vegetables per day?". Score 0 refers to "No" and score 1 refers to "Yes".

M. The score in this part came from the question "How much fluid (water, juice, coffee, tea, milk...) is consumed per day?". Score 0.0 refers to "less than 3 cups", score 0.5 refers to "3-5 cups" and score 1.0 refers to "more than 5 cups".

N. The score in this part came from the question "Mode of feeding". Score 0 refers to "unable to eat without assistance", score 1 refers to "self-fed with some difficulties" and score 2 refers to "self-fed without any problem".

Table 2 Anthropometric assessment

Questions	Scores
Question B Weight loss > 3kg Does not know Weight loss 1-3 kg No weight loss	0, 1, 2, 3
Question F BMI <19 kg/m^2 BMI 19- <21 kg/m^2 BMI 21- <23 kg/m^2 BMI ≥ 23 kg/m^2	0, 1, 2, 3
Question Q MAC <21 cm MAC 21-22 cm MAC >22 cm	0.0, 0.5, 1.0
Question R CC <31 cm CC ≥ 31 cm	0, 1

B. The score in this part came from the question "Weight loss during the last 3 months". Score 0 refers to "weight loss > 3kg", score 1 refers to "does not know", score 2 refers to "weight loss 1-3 kg" and score 3 refers to "no weight loss".

F. The score in this part came from the calculation of BMI by the researcher. If the participants have "BMI less than 19 kg/m^2", score is 0; if "BMI 19 to less than 21 kg/m^2", score is 1; if "BMI 21 to less than 23 kg/m^2", score is 2; and if "BMI 23 kg/m^2 or greater", score is 3.

Q. The score in this part came from the measurement of mid-arm circumference (MAC) by the researcher. Score 0.0 refers to "MAC less than 21 cm", score 0.5 refers to "MAC 21 to 22 cm" and score 1.0 refers to "MAC greater than 22 cm".

R. The score in this part came from the measurement of calf circumference (CC) by the researcher. Score 0 refers to "CC less than 31 cm" and score 1 refers to "CC 31 cm or greater".

Table 3 General assessment

Questions	Scores
Question C Bed or chair bound Able to get out of bed/chair but does not go out Goes out	0, 1, 2
Question D Yes No	0, 2
Question E Severe dementia or depression Mild dementia No psychological problems	0, 1, 2
Question G Yes No	0, 1
Question H Yes No	0, 1
Question I	0, 1

Yes No	

C. The score in this part came from the question "Mobility". Score 0 refers to "bed or chair bound, score 1 refers to "able to get out of bed/chair but does not go out" and score 2 refers to "goes out".

D. The score in this part came from the question "Has suffered psychological stress or acute disease in the past 3 months?". Score 0 refers to "Yes" and score 2 refers to "No".

E. The score in this part came from the question "Neuropsychological problems". Score 0 refers to "severe dementia or depression", score 1 refers to "mild dementia" and score 2 refers to "no psychological problems".

G. The score in this part came from the question "Lives independently (not in nursing home or hospital)". Score 1 refers to "Yes" and score 0 refers to "No".

H. The score in this part came from the question "Takes more than 3 prescription drugs per day". Score 0 refers to "Yes" and score 1 refers to "No".

I. The score in this part came from the question "Pressure sores or skin ulcers". Score 0 refers to "Yes" and score 1 refers to "No".

Table 4 Subjective assessment

Questions	Scores
Question O Views self as being malnourished Is uncertain of nutritional state Views self as having no nutritional problem	0, 1, 2
Question P Not as good Does not know As good Better	0.0, 0.5, 1.0, 2.0

O. The score in this part came from the question "Self-view of nutritional status". Score 0 refers to "views self as being malnourished", score 1 refers to "is uncertain of nutritional state" and score 2 refers to "views self as having no nutritional problem".

P. The score in this part came from the question "In comparison with other people of the same age, how does the patient consider his/ her health status?". Score 0.0 refers to "not as good", score 0.5 refers to "does not know", score 1.0 refers to "as good" and score 2.0 refers to "better".

3.4.2 Thai depression scale

Depression was assessed by the participant-administered Thai Depression Scale (TDS). It consisted of 15 measurement variables measuring 3 constructs namely: sadness, interest, and self-view of patients. They were divided into 15 variables namely:

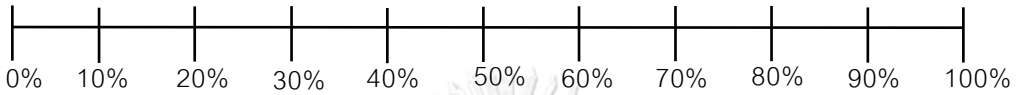
1. I felt mentally dull. (almost all day)
2. I felt unhappy and want to cry.
3. I felt despair.
4. I felt a little interest or pleasure in doing things.
5. I felt disappointed in myself.
6. I felt loss of self-confidence.
7. I felt to be alone and deflected.
8. I felt I was not worth much as person.
9. I cannot think of it right now.
10. Forgetfulness.
11. Thinking slowly.
12. I dawdle and do slowly that other people notice.
13. I felt tiredness or weakness.
14. I felt appetite and eating less.
15. Trouble going to sleep/ Sleepless.

TDS gave score between 0-15 in ratio scale. In each question, "Yes" gave 1 score and "No" gave 0 score. Then the depression scores were categorized into 3

groups. Score 0-5 was normal, score 6-9 was likely to have depression and score 10-15 was at high risk of depression. In scoring TDS, the higher the score, the greater the risk of depression.

3.4.3 Medication adherence

Medication adherence was assessed by the VAS. The percentage of medication doses that the participant had taken as prescribed (0-100%) was analyzed.



3.4.4 Scale validity and reliability

1. Validity

Validity refers to how well a test measures what it is supposed to measure[39]. Face and content validity of the questionnaire were evaluated by the experienced and qualified three judges from Chulalongkorn University. The item objective congruence (IOC) score of more than 0.5 was considered to indicate good content validity. Experts were also invited to comment on the wording of items and response format, and to suggest other items to be added to the scale.

2. Pilot test

Pilot test was conducted to confirm the appropriateness of the items and the suitability of written language and response options. In this step, a face validity was also conducted to see how they interpret or understand the meaning of items and their response options, and whether or not these items can reflect the construct of interest based on their perceptions. Then, an adjustment of items was performed to achieve the final version of the questionnaire[40].

3.4.5 Dependent variable

Nutritional scores were measured by MNA in ratio scale (0-30).

3.4.6 Independent variables

1. Depression scores were measured by TDS in ratio scale (0-15).
2. Medication adherence scores were measured by VAS in ratio scale (0-100%).

3. Demographic data consisted of 4 variables of socio-economic factors which were age, gender, drinking and smoking.
4. Clinical data consisted of 4 variables: duration of HIV infection, duration of ART, polypharmacy, and comorbidities.
5. Laboratory data consisted of 6 variables: CD4, lipid profiles (TG, LDL-C, HDL-C), serum insulin, albumin, hs-CRP, and hemoglobin.

3.5 Data collection

The study was conducted at the HIV-Netherlands-Australia-Thailand Research Collaboration (HIV-NAT) Center, Thai Red Cross Society, Bangkok, Thailand. The case record form was developed for data collection which was mentioned in the **appendix**. Participant interviews were carried out with the help of nurses/staff. The information about the study was thoroughly explained to the participants. After the participants willingly signed the informed consent, the researcher collected demographic, clinical and laboratory data of participants from electronic health records. The self-administered questionnaire was distributed to participants who were receiving follow-up treatment and HIV care at the HIV-NAT Center. All the physical measurements (measurements of weight, height, mid-arm circumference, and calf circumference) were done by the researcher. The overall assessment time for each participant was about 15-20 minutes. The previous MNA and TDS scores which were assessed four years ago were also recorded from the electronic health record.

3.6 Data analysis and interpretation

Classification of objectives, research questions and hypotheses of the study

Objective 1: To compare means of nutritional scores from 2016 and 2020

Research question 1: Do nutritional scores decrease over four years?

Hypothesis 1: $\mu_{\text{nutritional scores in 2016}} = \mu_{\text{nutritional scores in 2020}}$

Ha 1: $\mu_{\text{nutritional scores in 2016}} > \mu_{\text{nutritional scores in 2020}}$

Paired t-test was used to compare means of pretest-posttest of nutritional ratio score variables.

Objective 2: To compare means of depression scores from 2016 and 2020

Research question 2: Do depression scores increase over four years?

Hypothesis 2: $\mu_{\text{depression scores in 2016}} = \mu_{\text{depression scores in 2020}}$

Ha 2: $\mu_{\text{depression scores in 2016}} < \mu_{\text{depression scores in 2020}}$

Paired t-test was used to compare means of pretest-posttest of depression ratio score variables.

Objective 3: To investigate relationship between nutritional scores and depression scores

Research question 3: Can depression scores predict nutritional scores?

Hypothesis 3: $r_{\text{nutritional status and depression status}} = 0$

Ha 3: $r_{\text{nutritional status and depression status}} \neq 0$

Pearson's correlation was used to investigate the strength of linear relationship between nutritional scores (ratio scale) and depression scores (ratio scale).

Objective 4: To establish nutritional score prediction model by depression, medication adherence and demographic data

Research question 4: Which factors are significant predictors of nutritional scores?

Hypothesis 4: Nutritional score=β_1 depression score+ β_2 medication adherence score+ β_3 age+ β_4 gender+ β_5 drinking+ β_6 smoking+ β_7 duration of HIV+ β_8 duration of ART+ β_9 medications+ β_{10} comorbidities+ β_{11} CD4+ β_{12} serum albumin+ β_{13} hemoglobin+ β_{14} serum hs-CRP+ β_{15} serum insulin+ β_{16} lipid profiles

Hierarchical stepwise multiple regression analysis was used to investigate the relationship between nutritional scores (ratio scale) and those predictors (ratio and nominal scales).

3.7 Statistical procedures

Descriptive statistics

All data were reported in the aggregate to avoid inadvertent identification of an individual. Data were described as frequencies, percentage and crosstab table for non-metric data and means with standard deviations (SD) for metric data. All analyses were performed using SPSS version 22.0. A $p < 0.05$ was set as the level of statistical significance.

Inferential statistics

1. Paired t-test was used to compare means of nutritional scores and depression scores from 2016 and 2020.
2. Pearson's chi-squared test was employed to find the association of non-metric measurement variables between malnutrition stage (ordinal scale) and depression stage (ordinal scale).
3. Pearson's product moment correlation was employed to confirm the relationship of metric measurement variables between nutritional scores (ratio scale) and depression scores (ratio scale).
4. Hierarchical stepwise multiple regression analysis was employed to establish nutritional score prediction equation.

The plan of analysis for each variable with hypotheses and the statistics methods were summarized in **table 5**.

Table 5 Plan of analysis

Hypothesis	Variables	Statistics	Scale	Attributes
Means of nutritional scores at baseline were greater than means of nutritional scores at follow-up.	Nutritional score	Paired-t test	Ratio	0-30
Means of depression scores at baseline were greater than means of depression scores at follow-up.	Depression score	Paired-t test	Ratio	0-15
Patients with higher depression scores had lower nutritional scores.	Depression score	Pearson's correlation test	Ratio	0-15
Patients with poor medication adherence were more likely to be malnourished.	Medication adherence	Pearson's Chi-squared test	Ratio	0-100%
The risk of malnutrition was higher with the increase in age.	Age (years)	Pearson's correlation test	Ratio	50-100
Females had higher risk of malnutrition than males.	Gender	Pearson's Chi-squared test	Nominal	0 Male, 1 Female
Patients who drank alcohol had high risk of malnutrition than those who did not drink.	Drinking	Pearson's Chi-squared test	Ratio	0-800
Patients who were used cigarettes were more likely to be malnourished than those who did not use.	Smoking	Pearson's Chi-squared test	Ratio	0-30
Longer duration of HIV infection was associated with malnutrition.	Duration of HIV infection (years)	Pearson's correlation test	Ratio	3-40
Patients with longer ART duration had lower prevalence of malnutrition than those with shorter ART duration.	Duration of ART (years)	Pearson's correlation test	Ratio	3-30
The higher number of medications were associated with lower nutritional scores.	Number of medications	Pearson's correlation test	Ratio	1-20
Diabetes mellitus was a risk factor of malnutrition.	Diabetes mellitus	Pearson's Chi-squared test	Nominal	1 Yes, 0 No
Hypertension was a risk factor of malnutrition.	Hypertension	Pearson's Chi-squared test	Nominal	1 Yes, 0 No
HBV coinfection was a risk factor of malnutrition.	HBV coinfection	Pearson's Chi-	Nominal	1 Yes, 0 No

		squared test		
HCV coinfection was a risk factor of malnutrition.	HCV coinfection	Pearson's Chi-squared test	Nominal	1 Yes, 0 No
Patients with high levels of CD4 counts had higher nutritional scores.	CD4 (cells/mm^3)	Pearson's correlation test	Ratio	0-2000
Patients with high triglycerides had higher nutritional scores.	Triglycerides (mg/dL)	Pearson's correlation test	Ratio	0-800
Patients with high HDL-C levels had lower nutritional scores.	HDL-C (mg/dL)	Pearson's correlation test	Ratio	0-300
Patients with high LDL-C levels had lower nutritional scores.	LDL-C (mg/dL)	Pearson's correlation test	Ratio	0-300
High insulin levels were associated with low nutritional scores.	Serum insulin (μU/mL)	Pearson's correlation test	Ratio	0-70
High albumin levels were associated with low nutritional scores.	Serum albumin (g/dL)	Pearson's correlation test	Ratio	0-10
High hs-CRP levels were associated with low nutritional scores.	Serum hs-CRP (mg/dL)	Pearson's correlation test	Ratio	0-10
High hemoglobin levels were associated with high nutritional scores.	Hemoglobin (g/dL)	Pearson's correlation test	Ratio	0-20
Nutritional scores could be predicted by depression, medication adherence, age, gender, drinking, smoking, duration HIV infection, duration of ART, number of medications, hypertension, diabetes mellitus, HBV coinfection, HCV coinfection, CD4, triglycerides, HDL-C, LDL-C, serum insulin, serum albumin, serum hs-CRP and hemoglobin.		Hierarchical stepwise multiple regression analysis		

HIV, human immunodeficiency virus; ART, antiretroviral therapy; HBV, hepatitis B virus; HCV, hepatitis C virus; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein

3.8 Ethical considerations

The ethics in human was approved by the Institutional Review Board, Faculty of Medicine, Chulalongkorn University on 29 July 2020 (IRB approval number-507/63). The ethical approval was granted before the study commenced. Investigator concerned about the rights of patients to be or not to be participated in the study according to their willingness. The study was conducted based on ethical principles: (1) respect for person, (2) beneficence and (3) justice. All the oral and written information about the study were given thoroughly to all patients to make their own judgements before recruitments. All the study procedures were under a careful inspection in order to make patients harmless and to maximize the benefits. The participants were selected in well-prepared procedures to ensure fair distribution of benefits and risks. Investigator did not expose any data of the patients to keep their confidentiality, and all the information were locked in a private place. The study used weight, height and circumference measurements, assessment forms, and some questionnaires to investigate the nutritional status, depression, and related factors of the patients. All study data were kept confidential and presented only the overall results. The study has been approved by the Institutional Review Board before conducting the research.

CHAPTER IV RESULTS

4.1 Demographic and clinical characteristics of participants

A total of 250 PLHIV were included in this study. The characteristics of the participants at baseline and follow-up were described in **table 6**. The mean duration of follow-up was 49.93 ± 3.6 months. Most of the participants were male (60.8%). The mean age was 59.8 ± 5.6 years. The mean BMI was 23.2 ± 3.6 kg/m^2. According to the Asian BMI classification, 7.6% were underweight, 64.0% were normal weight and 28.4% were overweight[41]. In addition, there were 69.1% of males and 87.8% of females with abdominal obesity in follow-up period where the abdominal obesity was defined by waist-hip ratio (WHR) (> 0.9 in males and > 0.8 in females)[42]. More than half of the participants were receiving NNRTI-based regimen. Abacavir/lamivudine plus rilpivirine (18%), dolutegravir/ emtricitabine/tenofovir alafenamide (15.6%), and tenofovir disoproxil fumarate/emtricitabine plus rilpivirine (14.8%) were commonly used. The participants in this study had good medication adherence with a mean VAS score of 95.2 ± 7.8. In this elderly population, the mean number of comorbidities was four. Hypertension was found in 42.0% of the participants. The mean number of current medications were four in which about two ART regimens and two non-ART drugs were prescribed. It was of note that 169 (67.6%) participants took more than 3 prescription pills. The comparisons of the categorical results of both nutritional status and depression between baseline (2016) and follow-up (2020) were shown in **figure 1** and **figure 2**.

Table 6 Characteristics of the participants and prevalence of malnutrition and depression at baseline and follow-up periods

Characteristics	Baseline (N = 250)		Follow-up (N = 250)	
	N	%	N	%
Age (years), mean ± SD	56.11 ± 5.4		59.78 ± 5.6	
Gender				
▪ Male	152	60.8	152	60.8
▪ Female	98	39.2	98	39.2
Occupation				
▪ Employed	198	79.2	197	78.8
▪ Unemployed	52	20.8	53	21.2
Drinking				
▪ Yes	25	10.0	53	21.2
▪ No	125	90.0	197	78.8
Smoking				
▪ Yes	37	14.8	28	11.2
▪ No	213	85.2	222	88.8
Comorbidities				
▪ Hypertension	96	38.4	105	42.0
▪ Diabetes mellitus	37	14.8	43	17.2
▪ HBV coinfection	24	9.6	17	6.8
▪ HCV coinfection	27	10.8	1	0.4
Anthropometric measurements				
▪ BMI (kg/m^2), mean ± SD	23.05 ± 3.4		23.23 ± 3.6	
• Underweight (BMI <18.5kg/m^2)	19	7.6	19	7.6
• Normal (BMI 18.5-<25kg/m^2)	169	67.6	160	64.0
• Overweight (BMI ≥25kg/m^2)	62	24.8	71	28.4
▪ Mid-arm circumference (<21cm)	12	4.8	2	0.8
▪ Mid-arm circumference (21-22cm)	17	6.8	18	7.2
▪ Mid-arm circumference (>22cm)	221	88.4	230	92.0
▪ Calf circumference (<31cm)	34	13.6	40	16.0

▪ Calf circumference (≥31cm)	216	86.4	210	84.0
▪ Waist circumference (cm), mean ± SD	83.89 ± 9.5		85.98 ± 9.6	
▪ Hip circumference (cm), mean ± SD	91.00 ± 6.6		93.94 ± 7.4	
▪ Waist-hip ratio, mean ± SD	0.92 ± 0.07		0.91 ± 0.07	
Disease parameters				
▪ CD4 counts (cells/mm^3), mean ± SD	656.65 ± 252.8		641.15 ± 241.8	
▪ Viral load (<50 copies/mL)	244	97.6	246	98.4
▪ Duration of HIV infection (years), mean ± SD	17.72 ± 4.9		21.60 ± 4.8	
▪ Duration of ART (years), mean ± SD	15.41 ± 4.4		19.15 ± 4.4	
Biochemical parameters				
▪ Albumin (g/dL), mean ± SD	4.23 ± 0.5		4.26 ± 0.5	
▪ Hemoglobin (g/dL), mean ± SD	14.02 ± 1.6		14.00 ± 1.6	
▪ Creatinine (mg/dL), mean ± SD	0.90 ± 0.2		0.98 ± 0.6	
▪ hs-CRP (mg/L), mean ± SD	0.31 ± 0.8		0.29 ± 0.7	
▪ Insulin (μU/mL), mean ± SD	9.28 ± 9.2		9.28 ± 9.2	
▪ Triglycerides (mg/dL), mean ± SD	174.78 ± 104.1		154.41 ± 112.6	
▪ LDL-C (mg/dL), mean ± SD	123.27 ± 38.9		126.60 ± 39.2	
▪ HDL-C (mg/dL), mean ± SD	49.41 ± 14.5		50.45 ± 13.9	
ART regimen				
▪ NNRTI-based regimen	137	54.8	155	62.0
▪ PI-based regimen	79	31.6	45	18.0
▪ INSTI-based regimen	12	4.8	44	17.6
Nutritional status				
▪ MNA scores, mean ± SD	25.78 ± 2.6		24.85 ± 3.1	
▪ Normal	210	84.0	177	70.8
▪ At risk of malnutrition	37	14.8	67	26.8
▪ Malnourished	3	1.2	6	2.4
Depression status				
▪ TDS scores, mean ± SD	3.83 ± 3.6		3.14 ± 3.1	
▪ Normal	186	74.4	201	80.4
▪ At risk of depression	48	19.2	44	17.6
▪ High risk of depression	16	6.4	5	2.0

HBV, hepatitis B virus; HCV, hepatitis C virus; BMI, body mass index; HIV, human immunodeficiency virus; ART, antiretroviral therapy; hs-CRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor; MNA, Mini Nutritional Assessment; TDS, Thai Depression Scale

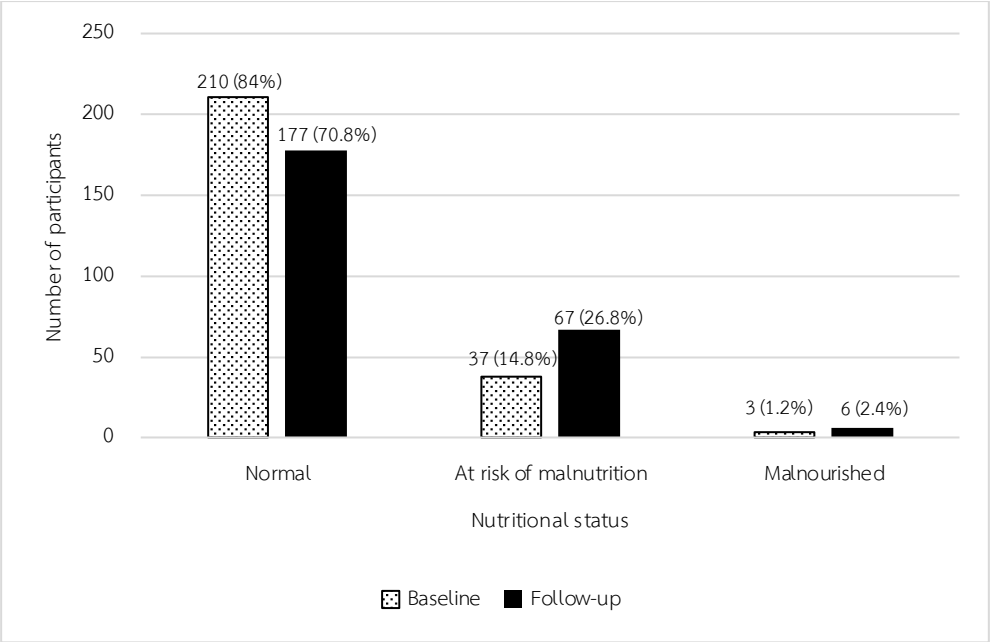


Figure 1 Nutritional status of participants at baseline and follow-up

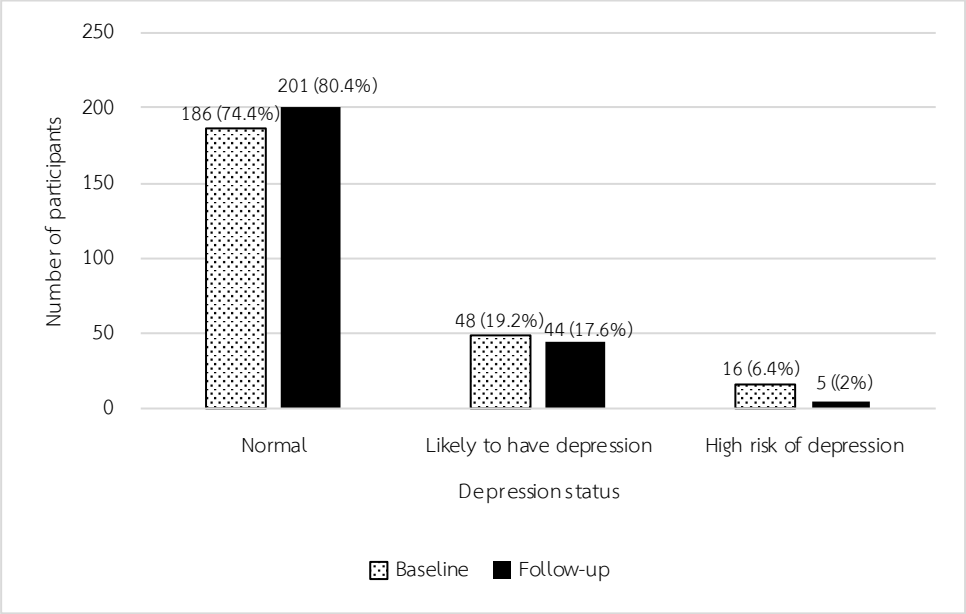


Figure 2 Depression status of participants at baseline and follow-up

4.2 Changes in nutritional scores and depression scores

The participants with the MNA scores of 24-30 were considered to have normal nutritional status, those with scores of 17-23.5 were classified as at risk of malnutrition, and those with less than 17 points were considered malnourished. The responses to each question of the MNA were described in **table 7** where at risk of malnutrition and malnourished were combined as the abnormal nutritional status category. In addition, the participants who were likely to have depression or had high risk of depression responded with the lower scores to each question of the MNA than those without depression. The responses were mentioned in detail in the **appendix**.

Table 7 Responses to each question of the Mini Nutritional Assessment by nutritional status at the follow-up study

		Normal nutritional status N = 177		Abnormal nutritional status N = 73		Total N = 250	
		N	%	N	%	N	%
A	Has food intake declined over the past 3 months due to loss of appetite, digestive problem, chewing, or swallowing difficulties?						
	0 = severe decrease in food intake	1	0.6	7	9.6	8	3.2
	1 = moderate decrease in food intake	24	13.5	33	45.2	57	22.8
	2 = no decrease in food intake	152	85.9	33	45.2	185	74.0
B	Weight loss during the last 3 months						
	0 = weight loss greater than 3 kg (6.6lbs)	2	1.1	12	16.5	14	5.6
	1 = does not know	4	2.3	6	8.2	10	4.0
	2= weight loss between 1 and 3 kg (2.2 and 6.6lbs)	45	25.4	32	43.8	77	30.8
	3= no weight loss	126	71.2	23	31.5	149	59.6
C	Mobility						
	0 = bed or chair bound	0	0.0	3	4.1	3	1.2
	1 = able to get out of bed/chair but does not go out	0	0.0	3	4.1	3	1.2
	2 = goes out	177	100.0	67	91.8	244	97.6
D	Has suffered psychological stress or acute disease in the past 3 months?						
	0 = yes	6	3.4	17	23.3	23	9.2
	2 = no	171	96.6	56	76.7	227	90.8
E	Neuropsychological problems						

	0 = severe dementia or depression	0	0.0	1	1.4	1	0.4
	1 = mild dementia	17	9.6	29	39.7	46	18.4
	2 = no psychological problems	160	90.4	43	58.9	203	81.2
F	Body mass index (BMI) = weight in kg/ (height in m)^2						
	0 = BMI less than 19	6	3.4	20	27.4	26	10.4
	1 = BMI 19 to less than 21	23	13.0	23	31.5	46	18.4
	2 = BMI 21 to less than 23	36	20.3	14	19.2	50	20.0
	3 = BMI 23 or greater	112	63.3	16	21.9	128	51.2
G	Lives independently (not in nursing home or hospital)						
	1 = yes	172	97.2	73	100.0	245	98.0
	0 = no	5	2.8	0	0.0	5	2.0
H	Takes more than 3 prescription drugs per day						
	0 = yes	113	63.8	56	76.7	169	67.6
	1 = no	64	36.2	17	23.3	81	32.4
I	Pressure sores or skin ulcers						
	0 = yes	8	4.5	6	8.2	14	5.6
	1 = no	169	95.5	67	91.8	236	94.4
J	How many full meals does the patient eat daily?						
	0 = 1 meal	0	0.0	1	1.3	1	0.4
	1 = 2 meals	26	14.7	31	42.5	57	22.8
	2 = 3 meals	151	85.3	41	56.2	192	76.8
K	Selected consumption markers for protein intake						
	At least one serving of dairy products (milk, cheese, yoghurt) per day	95	53.7	31	42.5	126	50.4
	Two or more servings of legumes or eggs per week	164	92.7	66	90.4	230	92.0
	Meat, fish or poultry everyday	153	86.4	57	78.1	210	84.0
	0.0 = if 0 or 1 yes	23	13.0	12	16.4	35	14.0
	0.5 = if 2 yes	70	39.5	41	56.2	111	44.4
	1.0 = if 3 yes	84	47.5	20	27.4	104	41.6
L	Consumes two or more servings of fruits or vegetables per day?						
	0 = no	19	10.7	19	26.0	38	15.2
	1 = yes	158	89.3	54	74.0	212	84.8
M	How much fluid (water, juice, coffee, tea, milk...) is consumed per day?						
	0.0 = less than 3 cups	39	22.0	31	42.5	70	28.0
	0.5 = 3 to 5 cups	32	18.1	13	17.8	45	18.0
	1.0 = more than 5 cups	106	59.9	29	39.7	135	54.0
N	Mode of feeding						
	0 = unable to eat without assistance	0	0.0	0	0.0	0	0.0
	1 = self-fed with some difficulty	0	0.0	0	0.0	0	0.0
	2 = self-fed without any problem	177	100.0	73	100.0	250	100.0

O	Self-view of nutritional status						
	0 = views self as being malnourished	1	0.5	5	6.8	6	2.4
	1 = is uncertain of nutritional state	27	15.3	28	38.4	55	22.0
	2 = views self as having no nutritional problem	149	84.2	40	54.8	189	75.6
P	In comparison with other people of the same age, how does the patient consider his/her health status?						
	0.0 = not as good	2	1.1	9	12.3	11	4.4
	0.5 = does not know	8	4.5	15	20.5	23	9.2
	1.0 = as good	72	40.7	37	50.7	109	43.6
	2.0 = better	95	53.7	12	16.4	107	42.8
Q	Mid-arm circumference (MAC) in cm						
	0.0 = MAC less than 21	0	0.0	2	2.7	2	0.8
	0.5 = MAC 21 to 22	5	2.8	13	17.8	18	7.2
	1.0 = MAC greater than 22	172	97.2	58	79.5	230	92.0
R	Calf circumference (CC) in cm						
	0 = CC less than 31	11	6.2	29	39.7	40	16.0
	1 = CC 31 or greater	166	93.8	44	60.3	210	84.0

As mentioned in **table 6**, the participants with normal nutritional status in the follow-up study were 70.8% whereas 84.0% found in the baseline study showing lower MNA scores (24.8 vs 25.8). The significant difference in mean nutritional scores between baseline and follow-up were described in **table 8** (p = <0.001).

Table 8 Nutritional and depression score differences between baseline and follow-up

	Paired differences		95% confidence interval of the difference		Paired sample t-test	
	Mean	SD	Lower	Upper	t	p-value
MNA scores (Baseline-Follow-up)	0.932	2.903	0.570	1.2936	5.076	<0.001
TDS scores (Baseline-Follow-up)	0.680	3.101	0.294	1.067	3.467	0.001

Paired t-test

MNA, mini nutritional assessment; TDS, Thai depression scale

Figure 3 showed the number of patients whose nutritional status were (1) remained normal, (2) remained abnormal, (3) better, and (4) worsen in the follow-up study compared to the baseline. There were the deteriorations or improvements in the nutritional status of 250 participants after 4-year duration. As described in **table 9**, there were 51 patients with deteriorated nutritional status, 16 patients with improved nutritional status, 161 patients with maintained normal nutritional status, and 22 patients with maintained abnormal nutritional status. Among the participants with normal nutritional status at baseline, about 23% of the patients turned to have abnormal nutritional status at follow-up period. Pearson's chi-squared results showed the significant differences in nutritional status between baseline and follow-up ($p < 0.001$).

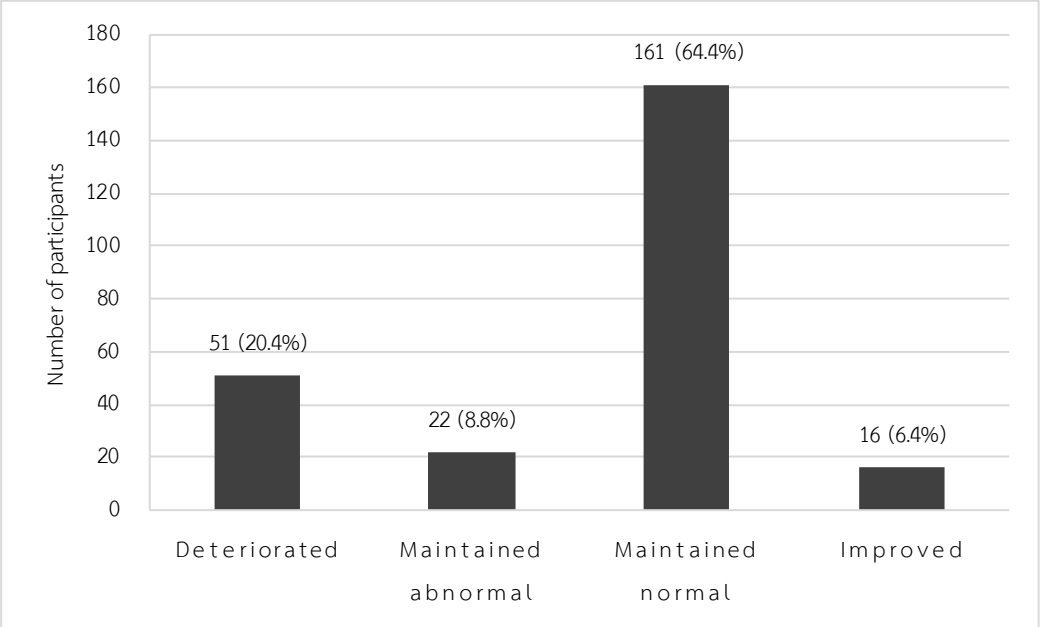


Figure 3 Changes in nutritional status of participants over four years

Table 9 Changes in nutritional status and depression from baseline to follow-up

MNA	Follow-up			
	Normal nutritional status	At risk of malnutrition	Malnourished	N
Baseline				
Normal nutritional status, n (%)	161 (76.7)	47 (22.3)	2 (1.0)	210
At risk of malnutrition, n (%)	16 (43.2)	19 (51.4)	2 (5.4)	37
Malnourished, n (%)	0 (0.0)	1 (33.3)	2 (66.7)	3
N	177	67	6	250
p-value*				< 0.001
TDS	Follow-up			
	Normal	At risk of depression	High risk of depression	N
Baseline				
Normal, n (%)	167 (89.8)	18 (9.7)	1 (0.5)	186
Likely to have depression, n (%)	30 (62.5)	17 (35.4)	1 (2.1)	48
High risk of depression, n (%)	4 (25.0)	9 (56.3)	3 (18.7)	16
N	201	44	5	250
p-value*				< 0.001

*Pearson's chi squared test

The mean depression scores were lower in this study compared to the baseline (3.1 vs 3.6). The lower the score of TDS, the better the condition. The mean differences were described in **table 8** (p = 0.001). The changes in depression status from baseline to follow-up showed that there were 20 deteriorations, 34 improvements, 167 participants maintained without depression and 29 maintained with depression (**table 9**). Pearson's chi-squared results showed the significant differences in depression status between baseline and follow-up (p <0.001). Twenty-five percent of patients with high risk of depression and 62.5% of patients who were likely to have depression at the baseline became normal at the follow-up. The proportion of the patients with at risk of malnutrition or malnutrition who chose "yes" to the TDS questions was higher than that of the normal patients. The responses indicated that the malnourished patients seemed more likely to have depression. The responses to each question of TDS by nutritional status and depression status were described in **appendix**.

Figure 4 showed the changes in nutritional status in patients with and without depression. The changes were categorized into (1) deteriorated nutritional status, (2) remained abnormal nutritional status, (3) remained normal nutritional status, and (4) improved nutritional status from baseline to the follow-up study. Among the patients with depression, 34.7% had deteriorated nutritional status whereas only 2% had improvement in nutritional status. Although there was no depressive condition, 16.9% of the participants became deteriorated in nutritional status over time.

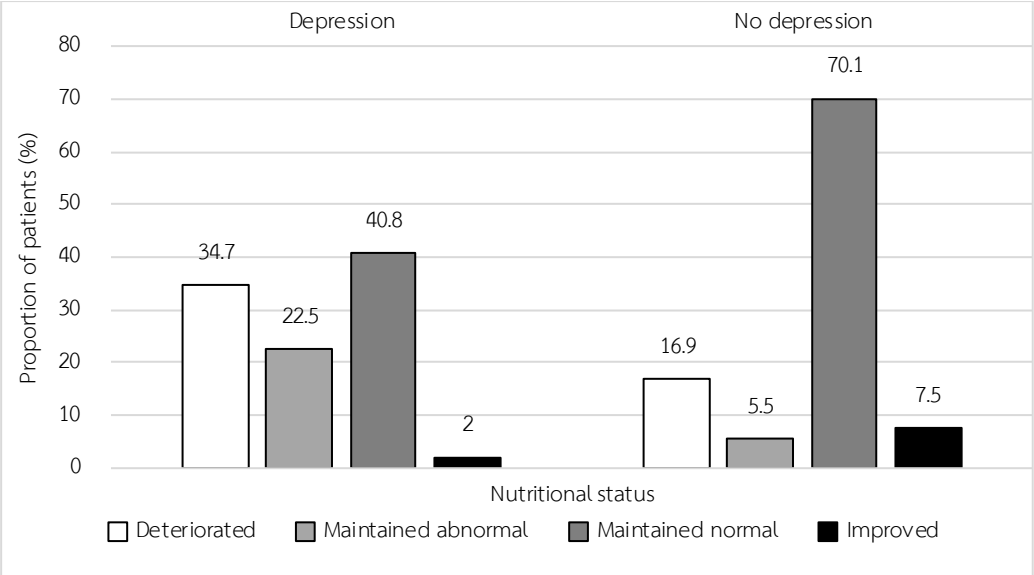


Figure 4 Rates of changes in nutritional status of patients with and without depression

4.3 Associated factors of the nutritional status

After the categorical variables were analyzed by Pearson's Chi-square test, there were some factors which had significant association with the nutritional status. It was categorized into normal and abnormal (at risk and malnourished) nutritional status. Gender, BMI, and depression status were significantly associated with the nutritional status. The results were described in **table 10**.

Table 10 Association of categorical variables and nutritional status

N = 250	Normal nutritional status N = 177		Abnormal nutritional status N = 73		p-value*
	N	%	N	%	
Gender					
■ Male	115	75.7	37	24.3	**0.035**
■ Female	62	63.3	36	36.7	
Drinking					
■ Yes	41	77.4	12	22.6	0.237
■ No	136	69.0	61	31.0	
Smoking					
■ Yes	18	64.3	10	35.7	0.421
■ No	159	71.6	63	28.4	
Marital status					
■ Single	39	68.4	18	31.6	0.575
■ Married	58	75.3	19	24.7	
■ Others	80	69.0	36	31.0	
Occupation					
■ Employed	141	71.6	56	28.4	0.604
■ Unemployed	36	67.9	17	32.1	
BMI					
■ Underweight (BMI <18.5kg/m^2)	6	31.6	13	68.4	**<0.001**
■ Normal (BMI 18.5-<25kg/m^2)	108	67.5	52	32.5	
■ Overweight (BMI ≥25kg/m^2)	63	88.7	8	11.3	
Hypertension					0.510

▪ Yes	72	68.6	33	31.4	
▪ No	105	72.4	40	27.6	
Diabetes mellitus					
▪ Yes	29	67.4	14	32.6	0.595
▪ No	148	71.5	59	28.5	
HBV coinfection					
▪ Yes	14	82.4	3	17.6	0.409**
▪ No	163	70.0	70	30.0	
HCV coinfection					
▪ Yes	0	0.0	1	100.0	0.292**
▪ No	177	71.1	72	28.9	
Depression					
▪ Yes	21	42.9	28	57.1	**<0.001**
▪ No	156	77.6	45	22.4	

*Pearson Chi-square test; **Fisher's exact test

BMI, body mass index; HBV, hepatitis B virus; HCV, hepatitis C virus

There were some factors which had significant association with nutritional scores after the continuous variables were analyzed. Age, depression scores, the number of medications, the number of comorbidities, and laboratory parameters including albumin and HDL-C were negatively associated with the nutritional scores. However, body weight, BMI, mid-arm circumference, waist circumference, hip circumference, waist-hip ratio, calf-circumference and hemoglobin were positively associated with the nutritional scores which showed significant p-values (**table 11**). Some results met the study hypothesis described in **table 5**. The older age was associated with lower nutritional scores. The correlation matrix showing the correlation coefficients between variables was described in **table 12**.

Table 11 Coefficients of association of continuous variables and nutritional scores

N = 250	Coefficient	p-value*
Age (years)	-0.151	**0.017**
Body weight (kg)	0.458	**<0.001**
BMI (kg/m^2)	0.514	**<0.001**
Mid-arm circumference (cm)	0.452	**<0.001**
Waist circumference (cm)	0.425	**<0.001**
Hip circumference (cm)	0.447	**<0.001**
Waist-hip ratio	0.165	**0.009**
Calf-circumference (cm)	0.414	**<0.001**
Depression (TDS) scores	-0.465	**<0.001**
Number of medications	-0.305	**<0.001**
Medication adherence/ VAS scores	0.103	0.105
Number of comorbidities	-0.191	**0.002**
Duration of HIV infection (years)	-0.118	0.061
Duration of ART (years)	-0.107	0.092
CD4 (cells/mm^3)	0.078	0.218
Albumin (g/dL)	-0.156	**0.014**
Creatinine (mg/dL)	-0.024	0.711
hs-CRP (mg/L)	0.018	0.780
Triglyceride (mg/dL)	0.069	0.277
LDL-C (mg/dL)	0.120	0.064
HDL-C (mg/dL)	-0.163	**0.010**
Hemoglobin (g/dL)	0.185	**0.003**
Insulin (μU/mL)	-0.035	0.582

*Pearson correlation

BMI, body mass index; TDS, Thai depression scale; ART, antiretroviral therapy; VAS, visual analogue scale; HIV, human immunodeficiency virus; hs-CRP, high sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol

Table 12 Correlation matrix table

Variables	Statistics	MNA scores	TDS scores	VAS scores	Age	HIV duration	ART duration	No. of medications	No. of comorbidities	CD4	Alb	hs-CRP	LDL-C	HDL-C	TG	Hb	Insulin
MNA scores	R	—															
	p-value	—															
TDS scores	R	-0.465	—														
	p-value	<0.001	—														
VAS scores	R	0.103	-0.161	—													
	p-value	0.105	0.011	—													
Age	R	-0.151	0.147	0.112	—												
	p-value	0.017	0.020	0.076	—												
HIV duration	R	-0.118	0.115	0.022	0.066	—											
	p-value	0.061	0.070	0.726	0.295	—											
ART duration	R	-0.107	0.078	0.039	0.120	0.767	—										
	p-value	0.092	0.221	0.542	0.058	<0.001	—										
No. of medications	R	-0.305	0.131	0.028	0.179	0.048	0.014	—									
	p-value	<0.001	0.039	0.656	0.005	0.453	0.825	—									
No. of comorbidities	R	-0.191	0.154	0.038	0.315	0.229	0.299	0.338	—								
	p-value	0.002	0.015	0.547	<0.001	<0.001	<0.001	<0.001	—								
CD4	R	0.078	0.078	-0.013	-0.001	0.068	0.091	0.062	0.108	—							
	p-value	0.218	0.218	0.836	0.986	0.283	0.151	0.328	0.087	—							
Albumin	R	-0.156	0.041	-0.055	0.055	0.062	0.011	0.093	0.107	0.088	—						
	p-value	0.014	0.517	0.390	0.388	0.333	0.862	0.143	0.094	0.166	—						
hs-CRP	R	0.018	-0.096	0.011	0.041	-0.025	0.010	-0.036	0.044	-0.064	-0.006	—					
	p-value	0.780	0.132	0.864	0.516	0.689	0.878	0.567	0.488	0.310	0.927	—					
LDL-C	R	0.120	-0.043	0.026	-0.143	-0.098	-0.035	-0.204	-0.176	-0.033	-0.096	0.012	—				
	p-value	0.064	0.512	0.690	0.027	0.131	0.588	0.002	0.006	0.606	0.141	0.859	—				
HDL-C	R	-0.163	-0.073	-0.070	0.030	-0.017	-0.064	-0.148	-0.154	-0.052	0.157	-0.056	0.086	—			
	p-value	0.010	0.253	0.269	0.637	0.785	0.311	0.019	0.015	0.409	0.013	0.381	0.187	—			
TG	R	0.069	0.177	-0.025	-0.033	0.033	0.006	0.181	0.126	0.147	-0.006	0.007	0.028	-0.338	—		
	p-value	0.277	0.005	0.690	0.607	0.606	0.919	0.004	0.047	0.020	0.920	0.912	0.664	<0.001	—		
Hemoglobin	R	0.185	-0.150	0.061	-0.124	-0.137	-0.157	-0.160	-0.146	-0.029	0.016	-0.122	0.042	-0.066	0.119	—	
	p-value	0.003	0.018	0.334	0.018	0.030	0.013	0.011	0.021	0.650	0.801	0.054	0.517	0.298	0.061	—	
Insulin	R	-0.035	0.118	0.030	-0.045	0.047	0.011	0.161	0.193	0.059	-0.024	0.023	-0.140	-0.315	0.163	0.085	—
	p-value	0.582	0.062	0.632	0.477	0.457	0.863	0.011	0.002	0.353	0.703	0.718	0.030	<0.001	0.010	0.181	—

MNA, mini nutritional assessment; TDS, Thai depression scale; VAS, visual analogue scale; ART, antiretroviral therapy; hs-CRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride

4.4 Factors predicting nutritional scores

Hierarchical stepwise multiple regression analysis generated some predictive factors for the nutritional scores in the final model (**table 12**). The depression scores, the number of medications and HDL-C were independently predictive of lower nutritional scores. Triglycerides and CD4 counts were predictive factors for the increase in nutritional scores. The analysis including all the models was mentioned in **appendix**.

Table 13 Final model showing predicting factors of nutritional scores at follow-up by hierarchical stepwise multiple regression analysis

Predictors	Unstandardized coefficients		Standardized coefficients	t	R^2	p-value	95% confidence interval for B	
	B	Std. Error	Beta				Lower bound	Upper bound
(Constant)	29.267	0.950		30.808	0.359	<0.001	27.396	31.139
TDS scores	-0.473	0.054	-0.470	-8.763		<0.001	-0.580	-0.367
Number of medications	-0.469	0.084	-0.301	-5.594		<0.001	-0.634	-0.304
HDL-C	-0.043	0.013	-0.193	-3.457		0.001	-0.068	-0.019
TG	0.003	0.002	0.126	2.193		0.029	0.000	0.007
CD4	0.001	0.001	0.105	1.976		0.049	0.000	0.003

TDS, Thai depression scale; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride

R^2 value of 0.359 could be interpreted that 35.9% of the nutritional scores could be predicted by TDS scores, number of medications, HDL-C, triglyceride and CD4 in the regression model while 64.1% of nutritional scores could be predicted by the other excluded variables.

The nutritional score prediction equation could be generated as the following:

Nutritional scores =– 0.470 TDS scores** – 0.301 Number of medications** – 0.193 HDL-C** + 0.126 triglyceride* + 0.105 CD4*

- The model predicted that if the TDS scores increased in one unit while other independent variables were constant, the nutritional scores would decrease by 0.470 unit.
- The model predicted that if the number of medications increased in one unit while other independent variables were constant, the nutritional scores would decrease by 0.301 unit.
- The model predicted that if the level of HDL-C increased in one unit while other independent variables were constant, the nutritional scores would decrease by 0.193 unit.
- The model predicted that when the level of triglyceride increased in one unit while other independent variables were constant, the nutritional scores would increase by 0.126 unit.
- The model predicted that if the CD4 count increased in one unit while other independent variables were constant, the nutritional scores would increase by 0.105 unit.

CHAPTER V DISCUSSION

The deterioration in nutritional status of the elderly PLHIV seemed to be underestimated. The limited studies explored the changes in the nutritional scores over a period of time. In the elderly PLHIV, there were satisfactory CD4 cell levels, and the viral loads were successfully controlled in this study. The good compliance of the participants resulted in better outcomes. In addition to hypertension, diabetes mellitus, HBV and HCV coinfections, some comorbidities such as lipodystrophy (48.4%), fatty liver (14.8%), dyslipidemia (10%), osteoporosis (4%), hypertriglyceridemia (2.8%) were found in the elderly PLHIV. The findings suggested that the high number of comorbidities was associated with the lower nutritional scores. We observed that body weight, mid-arm circumference, waist circumference, hip circumference, calf circumference, and waist-hip ratio were associated with the nutritional scores in the follow-up study.

There were some improvements in nutritional status at the follow-up period. The nutritional scores of the participants with at risk of malnutrition at baseline was changed into normal nutritional status over time. However, the proportion of participants who became deteriorated in nutritional status outweighed those who became improved in nutritional status. Moreover, the nutritional scores became lower in the follow-up period compared to the baselines. This result was in line with the study of a one-year follow-up changes in nutritional status of HIV-uninfected care-dependent elderly with dementia by Meyer et al.[43]. By contrast, the study by Conzade et al.[44] observed the increased nutritional scores in the community-dwelling elderly without HIV infection over 6 months follow-up in which the prevalence of malnutrition or at risk of malnutrition declined from 29% to 15%. We also found that the prevalence of underweight in this study was higher than that of community dwelling Thai people aged 60 years or above (7.6% vs 6.9%), respectively[45].

The prevalence of malnutrition and at risk of malnutrition in this study were lower than the previous general elderly outpatient study in Thailand (6.0% vs 8.3%

malnourished and 26.8% vs 35.5% at risk of malnutrition)[46]. Unlike nutritional status, there were improvements in depression status in this follow-up study compared to baseline study. Most of the previously depressed participants became improved to normal condition in this study. Therefore, the results proved that the good management in previously depressed patients had achieved to get the better outcomes. In this study, the depression scores, the number of medications, HDL-C, TG and CD4 were independently predictive of nutritional scores. The result of this study was complied with the study of the nursing home elderly which the lower MNA scores were independently associated with the higher depression scores[25]. Moreover, the finding was consistent with the study of community-living Japanese elderly in which higher depression score was predictive of lower nutritional scores[47]. Likewise, the result was in line with the study of the geriatric outpatients in Thailand that depression was significantly associated with malnutrition[46]. It can be hypothesized that depression may lead to appetite and weight changes, resulting in malnutrition. Additionally, this can be clarified by loss of motivation to personal care in depressed patients. Given higher depression among malnutrition and it could be a reversible cause of malnutrition in geriatric population, it is important to evaluate both conditions in HIV treatment and care.

There has been a high prevalence of polypharmacy in the HIV population in the ART era. In this population, 67.6% of participants were receiving more than 3 medications in which 14.6% were on more than 6 medications. In the Spanish elderly PLHIV, 71.6% were receiving more than 6 medications which was considerably higher than that was found in this study[48]. The increased use of medications was significantly associated with the lower nutritional scores in this study. This study finding was consistent with the previous literatures that the relationship between polypharmacy and malnutrition has been observed in the general elderly people[25, 32, 49]. Depression could affect appetite and weight changes. Polypharmacy can lead to depressive symptoms in geriatric population; therefore, healthcare providers need being aware of the risk of depression that comes with all common prescription drugs, both ART (such as efavirenz, dolutegravir) and other medications which many of them are available over the counter. There was evidence that polypharmacy and

malnutrition have synergistic negative effect on outcomes of older population [50]. Importantly, several drugs that are commonly used among older PLHIV, including common antihypertensive medications, proton pump inhibitors, statins, and metformin have drug-nutrient interaction, resulting in malnutrition. Many of which cause appetite loss or taste changes and the drug-induced physiological changes result in poor nutrition including weight loss[51]. This study also showed that there were high levels of HDL-C in the patients with malnutrition or at risk of malnutrition which can be comparable with the previous literature[52].

The strength of this study was the use of well-validated MNA and TDS questionnaires. The study explored the predictive factors and the longitudinal assessments over the changes in nutritional scores. Most of the study participants were well-educated and had good compliance to HIV care. Aside from the disease, other factors affecting the nutritional status can be revealed. However, there were also some limitations in this study. This study did not have control group as HIV-negative participants to compare the data. There were confounding factors such as patient lifestyle, calorie intake or dietary pattern. Moreover, elderly patients may face with recall bias during the questionnaire responses.

To the best of our knowledge, this was the first study which examines the long-term changes of the nutritional scores in the elderly PLHIV in Thailand. The results showing the predictive factors of nutritional scores recommended the nutritional support team in which the consultants or dieticians can closely monitor the malnourished patients.

CHAPTER VI CONCLUSION

This study explored the changes in nutritional scores over time, and the predictive factors of the nutritional scores in the elderly PLHIV. Over one-fourth of the participants had at risk of malnutrition or malnutrition. During 4-year longitudinal follow-up, 20% of the participants has deterioration of nutritional status. High TDS scores, polypharmacy, and high HDL-C levels were significant predictive factors of lower nutritional scores. The findings of this study confirmed that the risk of malnutrition or malnutrition is an important health issue in the elderly PLHIV. Further studies of the nutritional status in the elderly PLHIV using various combined nutritional assessment methods, nutritional interventions, and control groups are highly warranted.

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APPENDICES

APPENDIX A Supplementary table 1

Responses to each question of Mini Nutritional Assessment questionnaire by depression status

		Normal N = 201		At risk/ Depressed N = 49		Total N = 250	
		N	%	N	%	N	%
A	Has food intake declined over the past 3 months due to loss of appetite, digestive problem, chewing, or swallowing difficulties?						
	0 = severe decrease in food intake	3	1.5	5	10.2	8	3.2
	1 = moderate decrease in food intake	37	18.4	20	40.8	57	22.8
	2 = no decrease in food intake	161	80.1	24	49.0	185	74.0
B	Weight loss during the last 3 months						
	0 = weight loss greater than 3 kg (6.6lbs)	9	4.4	5	10.2	14	5.6
	1 = does not know	6	3.0	4	8.2	10	4.0
	2= weight loss between 1 and 3 kg (2.2 and 6.6lbs)	59	29.4	18	36.7	77	30.8
	3= no weight loss	127	63.2	22	44.9	149	59.6
C	Mobility						
	0 = bed or chair bound	0	0.0	3	6.1	3	1.2
	1 = able to get out of bed/chair but does not go out	0	0.0	3	6.1	3	1.2
	2 = goes out	201	100.0	43	87.8	244	97.6
D	Has suffered psychological stress or acute disease in the past 3 months?						
	0 = yes	8	4.0	15	30.6	23	9.2
	2 = no	193	96.0	34	69.4	227	90.8
E	Neuropsychological problems						
	0 = severe dementia or depression	0	0.0	1	2.0	1	0.4
	1 = mild dementia	25	12.4	21	42.9	46	18.4
	2 = no psychological problems	176	87.6	27	55.1	203	81.2
F	Body mass index (BMI) = weight in kg/ (height in m)^2						
	0 = BMI less than 19	21	10.4	5	10.2	26	10.4
	1 = BMI 19 to less than 21	35	17.4	11	22.4	46	18.4
	2 = BMI 21 to less than 23	39	19.4	11	22.4	50	20.0
	3 = BMI 23 or greater	106	52.7	22	44.9	128	51.2
G	Lives independently (not in nursing home or hospital)						
	1 = yes	199	99.0	46	93.9	245	98.0

	0 = no	2	1.0	3	6.1	5	2.0
H	Takes more than 3 prescription drugs per day						
	0 = yes	134	66.7	35	71.4	169	67.6
	1 = no	67	33.3	14	28.6	81	32.4
I	Pressure sores or skin ulcers						
	0 = yes	12	6.0	2	4.1	14	5.6
	1 = no	189	94.0	47	95.9	236	94.4
J	How many full meals does the patient eat daily?						
	0 = 1 meal	0	0.0	1	2.0	1	0.4
	1 = 2 meals	40	19.9	17	34.7	57	22.8
	2 = 3 meals	161	80.1	31	63.3	192	76.8
K	Selected consumption markers for protein intake						
	At least one serving of dairy products (milk, cheese, yoghurt) per day	103	51.2	23	46.9	126	50.4
	Two or more servings of legumes or eggs per week	186	92.5	44	89.8	230	92.0
	Meat, fish or poultry everyday	169	8.1	41	83.7	210	84.0
	0.0 = if 0 or 1 yes	28	13.9	7	14.3	35	14.0
	0.5 = if 2 yes	86	42.8	25	51.0	111	44.4
	1.0 = if 3 yes	87	43.3	17	34.7	104	41.6
L	Consumes two or more servings of fruits or vegetables per day?						
	0 = no	30	14.9	8	16.3	38	15.2
	1 = yes	171	85.1	41	83.7	212	84.8
M	How much fluid (water, juice, coffee, tea, milk...) is consumed per day?						
	0.0 = less than 3 cups	52	25.9	18	36.7	70	28.0
	0.5 = 3 to 5 cups	35	17.4	10	20.4	45	18.0
	1.0 = more than 5 cups	114	56.7	21	42.9	135	54.0
N	Mode of feeding						
	0 = unable to eat without assistance	0	0.0	0	0.0	0	0.0
	1 = self-fed with some difficulty	0	0.0	0	0.0	0	0.0
	2 = self-fed without any problem	201	100.0	49	100.0	250	100.0
O	Self-view of nutritional status						
	0 = views self as being malnourished	3	1.5	3	6.1	6	2.4
	1 = is uncertain of nutritional state	37	18.4	18	36.7	55	22.0
	2 = views self as having no nutritional problem	161	80.1	28	57.1	189	75.6
P	In comparison with other people of the same age, how does the patient consider his/her health status?						
	0.0 = not as good	4	2.0	7	14.3	11	4.4
	0.5 = does not know	13	6.5	10	20.4	23	9.2
	1.0 = as good	89	44.3	20	40.8	109	43.6
	2.0 = better	95	47.2	12	24.5	107	42.8
Q	Mid-arm circumference (MAC) in cm						

	0.0 = MAC less than 21	1	0.5	1	2.0	2	0.8
	0.5 = MAC 21 to 22	15	7.5	3	6.1	18	7.2
	1.0 = MAC greater than 22	185	92.0	45	91.8	230	92.0
R	Calf circumference (CC) in cm						
	0 = CC less than 31	33	16.4	7	14.3	40	16.0
	1 = CC 31 or greater	168	83.6	42	85.7	210	84.0

APPENDIX A Supplementary table 2

Responses to each question of Thai Depression Scale questionnaire by depression status

No		Normal N = 201		At risk/ depressed N = 49		Total N = 250	
		N	%	N	%	N	%
1	รู้สึกจิตใจหม่นหมองหรือไม่ (เกือบตลอดทั้งวัน) I felt mentally dull. (Almost all day)						
	Yes	3	1.5	19	38.8	22	8.8
	No	198	98.5	30	61.2	228	91.2
2	รู้สึกเป็นทุกข์จนอยากร้องไห้ I felt unhappy and want to cry.						
	Yes	4	2.0	11	22.4	15	6.0
	No	197	98.0	38	77.6	235	94.0
3	รู้สึกหมดอาลัยตายอยาก I felt despair.						
	Yes	1	0.5	9	18.4	10	4.0
	No	200	99.5	40	81.6	240	96.0
4	รู้สึกไม่มีความสุข หมดสนุก กับสิ่งที่เคยชอบและเคยทำ I felt a little interest or pleasure in doing things						
	Yes	12	6.0	23	46.9	35	14.0
	No	189	94.0	26	53.1	215	86.0
5	รู้สึกผิดหวังในตนเอง และโทษตนเองในสิ่งที่เกิดขึ้น I felt disappointed in myself.						
	Yes	10	5.0	20	40.8	30	12.0

	No	191	95.0	29	59.2	220	88.0
6	รู้สึกสูญเสียความเชื่อมั่นในตนเอง I felt loss of self-confidence.						
	Yes	9	4.5	24	49.0	33	13.2
	No	192	95.5	25	51.0	217	86.8
7	รู้สึกอยากอยู่คนเดียวไม่อยากสุงสิงกับใคร I felt to be alone and deflected.						
	Yes	18	9.0	24	49.0	42	16.8
	No	183	91.0	25	51.0	208	83.2
8	รู้สึกว่าตนเองไม่มีคุณค่า I felt I wasn't worth much as a person						
	Yes	7	3.5	14	28.6	21	8.4
	No	194	96.5	35	71.4	229	91.6
9	คิดอะไรไม่ออก I can't think of it right now.						
	Yes	23	11.4	33	67.3	56	22.4
	No	178	88.6	16	32.7	194	77.6
10	หลงลืมง่าย Forgetfulness						
	Yes	75	37.3	41	83.7	116	46.4
	No	126	62.7	8	16.3	134	53.6
11	คิดอะไรได้ช้ากว่าปกติ Thinking slowly						
	Yes	61	30.3	43	87.8	104	41.6
	No	140	69.7	6	12.2	146	58.4
12	ทำอะไรอืดอาด เชื่องช้ากว่าปกติ I dawdle and do slowly that other people notice.						
	Yes	37	18.4	41	83.7	78	31.2
	No	164	81.6	8	16.3	172	68.8
13	รู้สึกอ่อนเพลียง่ายเหมือนไม่มีแรง I felt tiredness or weakness.						
	Yes	31	15.4	34	69.4	65	26.0
	No	170	84.6	15	30.6	185	74.0

14	รู้สึกเบื่ออาหาร กินได้น้อยกว่าเดิม I felt appetite and eating less.						
	Yes	18	9.0	25	51.0	43	17.2
	No	183	91.0	24	49.0	207	82.8
15	นอนหลับๆตื่นๆ หลับไม่สนิท Trouble going to sleep/ Sleepless						
	Yes	78	38.8	39	79.6	117	46.8
	No	123	61.2	10	20.4	133	53.2

APPENDIX A Supplementary table 3

Responses to each question of Thai Depression Scale questionnaire by nutritional status

No		Normal nutritional status N = 177		At risk/ Malnutrition N = 73		Total N = 250	
		N	%	N	%	N	%
1	รู้สึกจิตใจหม่นหมองหรือไม่ (เกือบตลอดทั้งวัน) I felt mentally dull. (Almost all day)						
	Yes	6	3.4	16	21.9	22	8.8
	No	171	96.6	57	78.1	228	91.2
2	รู้สึกเป็นทุกข์จนอยากร้องไห้ I felt unhappy and want to cry.						
	Yes	4	2.3	11	15.1	15	6.0
	No	173	97.7	62	84.9	235	94.0
3	รู้สึกหมดอาลัยตายอยาก I felt despair.						
	Yes	3	1.7	7	9.6	10	4.0
	No	174	98.3	66	90.4	240	96.0
4	รู้สึกไม่มีความสุข หมดสนุก กับสิ่งที่เคยชอบและเคยทำ I felt a little interest or pleasure in doing things						
	Yes	17	9.6	18	24.7	35	14.0
	No	160	90.4	55	75.3	215	86.0

5	รู้สึกผิดหวังในตนเอง และโทษตนเองในสิ่งที่เกิดขึ้น I felt disappointed in myself.						
	Yes	15	8.5	15	20.5	30	12.0
	No	162	91.5	58	79.5	220	88.0
6	รู้สึกสูญเสียความเชื่อมั่นในตนเอง I felt loss of self-confidence.						
	Yes	17	9.6	16	21.9	33	13.2
	No	160	90.4	57	78.1	217	86.8
7	รู้สึกอยากอยู่คนเดียวไม่อยากสุงสิงกับใคร I felt to be alone and deflected.						
	Yes	21	11.9	21	28.8	42	16.8
	No	156	88.1	52	71.2	208	83.2
8	รู้สึกว่าตนเองไม่มีคุณค่า I felt I wasn't worth much as a person						
	Yes	8	4.5	13	17.8	21	8.4
	No	169	95.5	60	82.2	229	91.6
9	คิดอะไรไม่ออก I can't think of it right now.						
	Yes	34	19.2	22	30.1	56	22.4
	No	143	80.8	51	69.9	194	77.6
10	หลงลืมง่าย Forgetfulness						
	Yes	71	40.1	45	61.6	116	46.4
	No	106	59.9	28	38.4	134	53.6
11	คิดอะไรได้ช้ากว่าปกติ Thinking slowly						
	Yes	59	33.3	45	61.6	104	41.6
	No	118	66.7	28	38.4	146	58.4
12	ทำอะไรอืดอาด เชื่องช้ากว่าปกติ I dawdle and do slowly that other people notice.						
	Yes	45	25.4	33	45.2	78	31.2
	No	132	74.6	40	54.8	172	68.8
13	รู้สึกอ่อนเพลียง่ายเหมือนไม่มีแรง						

	I felt tiredness or weakness.						
	Yes	36	20.3	29	39.7	65	26.0
	No	141	79.7	44	60.3	185	74.0
14	รู้สึกเบื่ออาหาร กินได้น้อยกว่าเดิม I felt appetite and eating less.						
	Yes	18	10.2	25	34.2	43	17.2
	No	159	89.8	48	65.8	207	82.8
15	นอนหลับๆตื่นๆ หลับไม่สนิท Trouble going to sleep/ Sleepless						
	Yes	72	40.7	45	61.6	117	46.8
	No	105	59.3	28	38.4	133	53.2

APPENDIX A Supplementary table 4

Full models by hierarchical stepwise multiple regression analysis

Model		Unstandardized coefficients		Standardized coefficients	t	R^2	R^2 change	p-value	95% confidence interval for B	
		B	Std. Error	Beta					Lower bound	Upper bound
1	(Constant)	26.328	0.255		103.270	0.216	0.216	<0.001	25.826	26.830
	TDS scores	-0.468	0.058	-0.465	-8.087				-0.582	-0.354
2	(Constant)	27.991	0.447		62.593	0.277	0.061	<0.001	27.110	28.872
	TDS scores	-0.436	0.056	-0.433	-7.747			<0.001	-0.546	-0.325
	Number of medications	-0.386	0.087	-0.248	-4.448			<0.001	-0.557	-0.215
3	(Constant)	30.938	0.798		38.751	0.332	0.055	<0.001	29.365	32.510
	TDS scores	-0.448	0.054	-0.445	-8.267			<0.001	-0.555	-0.342
	Number of medications	-0.438	0.085	-0.282	-5.186			<0.001	-0.605	-0.272
	HDL-C	-0.058	0.012	-0.237	-4.384			<0.001	-0.077	-0.029
4	(Constant)	30.031	0.873		34.397	0.348	0.017	<0.001	28.311	31.752
	TDS scores	-0.468	0.054	-0.465	-8.621			<0.001	-0.575	-0.361
	Number of medications	-0.464	0.084	-0.298	-5.501			<0.001	-0.630	-0.298

	HDL-C	-0.043	0.013	-0.193	-3.434			0.001	-0.068	-0.018
	TG	0.004	0.002	0.140	2.439			0.015	0.001	0.007
5	(Constant)	29.267	0.950		30.808	0.359	0.011	<0.001	27.396	31.139
	TDS scores	-0.473	0.054	-0.470	-8.763			<0.001	-0.580	-0.367
	Number of medications	-0.469	0.084	-0.301	-5.594			<0.001	-0.634	-0.304
	HDL-C	-0.043	0.013	-0.193	-3.457			0.001	-0.068	-0.019
	TG	0.003	0.002	0.126	2.193			0.029	0.000	0.007
	CD4	0.001	0.001	0.105	1.976			0.049	0.000	0.003

APPENDIX B Ethical approvement of the study

COA No. 928/2020

IRB No. 507/63

INSTITUTIONAL REVIEW BOARD

Faculty of Medicine, Chulalongkorn University

1873 Rama 4 Road, Patumwan, Bangkok 10330, Thailand, Tel 662-256-4493

Certificate of Approval

The Institutional Review Board of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, has approved the following study which is to be carried out in compliance with the International guidelines for human research protection as Declaration of Helsinki, The Belmont Report, CIOMS Guideline and International Conference on Harmonization in Good Clinical Practice (ICH-GCP)

Study Title : FACTORS PREDICTING NUTRITIONAL SCORES IN HIV-INFECTED ELDER RECEIVING ANTIRETROVIRAL THERAPY IN THAILAND

Study Code : -

Principal Investigator : Miss Daylia Thet

Affiliation of PI : Faculty of Pharmaceutical Sciences, Chulalongkorn University.

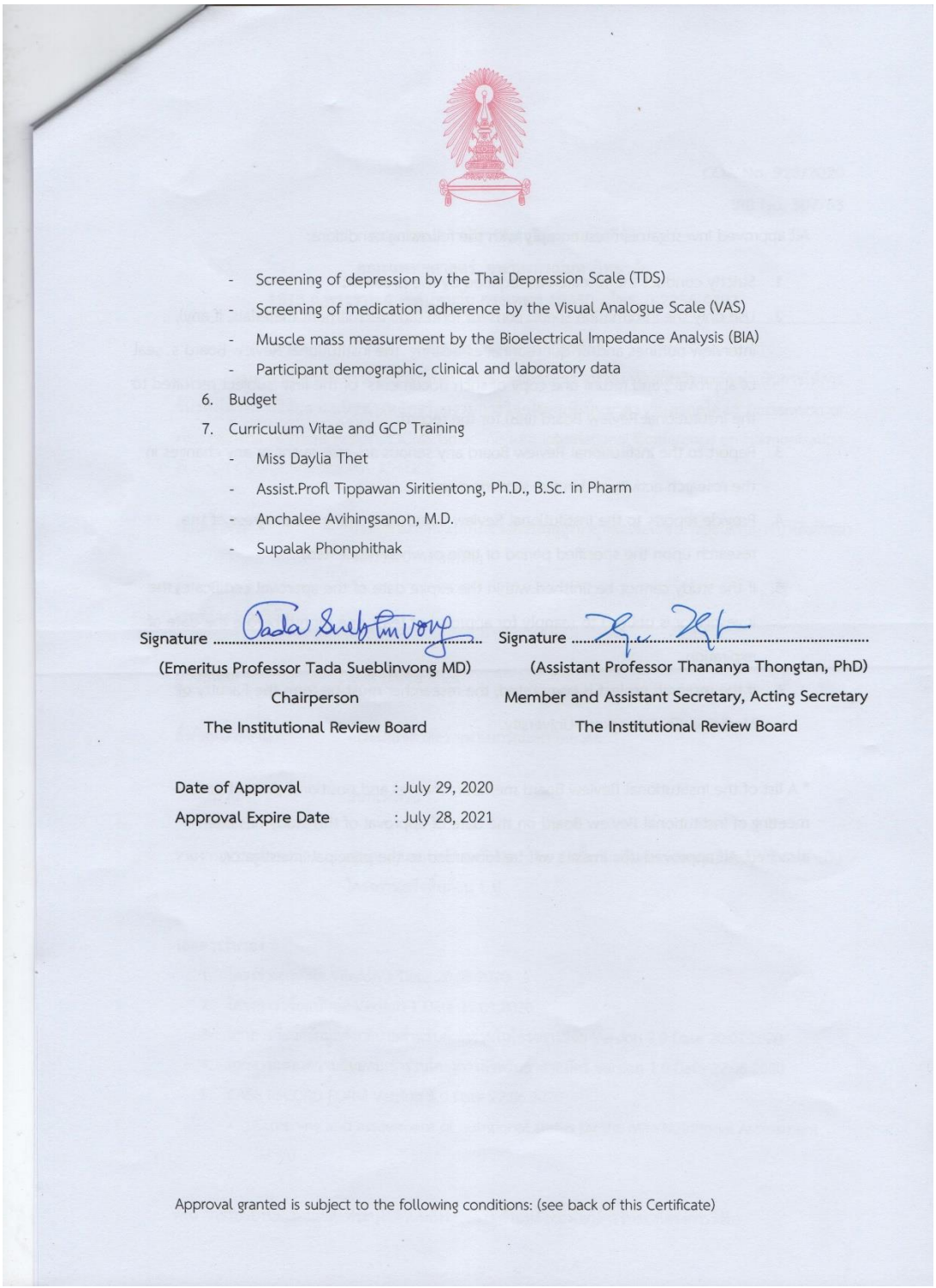
Review Method : Expedited

Continuing Report : At least once annually or submit the final report if finished.

Document Reviewed :

1. Research Proposal Version 1 Date 20.06.2020
2. Protocol Synopsis Version 1 Date 17.01.2020
3. Information sheet for research participant Version 2.0 Date 20.07.2020
4. Informed Consent Form Version 1.0 Date 22.06.2020
5. CASE RECORD FORM Version 1.0 Date 22.06.2020
   - Screening and assessment of nutritional status by the Mini Nutritional Assessment (MNA)

Approval granted is subject to the following conditions: (see back of this Certificate)



- Screening of depression by the Thai Depression Scale (TDS)
- Screening of medication adherence by the Visual Analogue Scale (VAS)
- Muscle mass measurement by the Bioelectrical Impedance Analysis (BIA)
- Participant demographic, clinical and laboratory data

6. Budget
7. Curriculum Vitae and GCP Training
   - Miss Daylia Thet
   - Assist.Profl Tippawan Siritientong, Ph.D., B.Sc. in Pharm
   - Anchalee Avihingsanon, M.D.
   - Supalak Phonphithak

Signature ..... Signature .....

(Emeritus Professor Tada Sueblinvong MD) (Assistant Professor Thananya Thongtan, PhD)

Chairperson Member and Assistant Secretary, Acting Secretary

The Institutional Review Board The Institutional Review Board

Date of Approval : July 29, 2020

Approval Expire Date : July 28, 2021

Approval granted is subject to the following conditions: (see back of this Certificate)

APPENDIX C CASE RECORD FORM

The included items belong to the study about "**FACTORS PREDICTING NUTRITIONAL SCORES IN HIV-INFECTED ELDER RECEIVING ANTIRETROVIRAL**

THERAPY IN THAILAND". All the data of every participant will be confidential and will not have an impact on treatment and HIV care.

This case record form includes mainly 4 parts:

1. Screening and assessment of nutritional status by the Mini Nutritional Assessment (MNA)
2. Screening of depression by the Thai Depression Scale (TDS)
3. Screening of medication adherence by the Visual Analogue Scale (VAS),
4. Participant demographic, clinical and laboratory data

The questionnaires are participant-administered and researcher-filled items. Participants can fill the right check box next to each question.

Date of informed consent (dd/mmm/yyyy): |__|__|-|__|__|__|-|__|__|__|__|

Data	
Assessment date (dd/mmm/yyyy): |__|__|-|__|__|__|-|__|__|__|__|	
แบบประเมินภาวะโภชนาการ (the Mini Nutritional Assessment (MNA); Thai version) **ขอให้ท่านทำเครื่องหมาย ☑ หน้าข้อที่ตรงกับท่านมากที่สุด**	
การคัดกรอง	**คะแนน**
A. ในช่วง 3เดือนที่ผ่านมารับประทานอาหารได้น้อยลง เนื่องจากความอยากอาหารลดลง มีปัญหาการย่อย การเคี้ยว หรือปัญหาการกลืนหรือไม่ ☐ 0= รับประทานอาหารน้อยลงอย่างมาก ☐ 1= รับประทานอาหารน้อยลงปานกลาง ☐ 2= การรับประทานอาหารไม่เปลี่ยนแปลง	
B. ในช่วง 3เดือนที่ผ่านมา น้ำหนักลดลงหรือไม่ ☐ 0= น้ำหนักลดมากกว่า 3กิโลกรัม ☐ 1= ไม่ทราบ ☐ 2= น้ำหนักลดระหว่าง 3- 1กิโลกรัม ☐ 3= น้ำหนักไม่ลดลง	
C. สามารถเคลื่อนไหวได้เองหรือไม่	

☐ 0= นอนบนเตียง หรือ ต้องอาศัยรถเข็นตลอดเวลา ☐ 1= ลุกจากเตียงหรือรถเข็นได้บ้าง แต่ไม่สามารถไปข้างนอกได้เอง ☐ 2= เดินและเคลื่อนไหวได้ตามปกติ	
D. ใน 3เดือนที่ผ่านมา ท่านมีความเครียดรุนแรงหรือป่วยเฉียบพลันหรือไม่ ☐ 0= มี ☐ 2= ไม่มี	
E. มีปัญหาทางจิตประสาท หรือไม่ ☐ 0= ความจำเสื่อม หรือ ซึมเศร้า อย่างรุนแรง ☐ 1= ความจำเสื่อมเล็กน้อย ☐ 2= ไม่มีปัญหาทางประสาท	
F. ดัชนีมวลกาย (BMI)= น้ำหนัก (กก.) / [ส่วนสูง (ม.)]^2 หมายเหตุ ข้อนี้ผู้วิจัยเป็นผู้กรอก ☐ 0= BMI น้อยกว่า 19 ☐ 1= BMI ตั้งแต่ 19 แต่น้อยกว่า 21 ☐ 2= BMI ตั้งแต่ 21 แต่น้อยกว่า 23 ☐ 3= BMI ตั้งแต่ 23 ขึ้นไป	
G. ช่วยเหลือตัวเองในชีวิตประจำวันได้ ☐ 1= ใช่ ☐ 0= ไม่ใช่	
H. รับประทานยามากกว่า 3 ชนิด ต่อวัน ☐ 0= ใช่ ☐ 1= ไม่ใช่	
I. มีแผลกดทับหรือแผลที่ผิวหนังหรือไม่ ☐ 0= ใช่ ☐ 1= ไม่ใช่	
J. ท่านรับประทานอาหารเต็มมื้อ ได้กี่มื้อต่อวัน ☐ 0= 1 มื้อ ☐ 1= 2 มื้อ ☐ 2= 3 มื้อ	
K. ท่านรับประทานอาหารจำพวกโปรตีนเหล่านี้บ้างหรือไม่	

•นมหรือผลิตภัณฑ์จากนม (เช่น ชีส โยเกิร์ต) อย่างน้อย 1แก้วหรือกล่อง/วัน ใช่☐ ไม่ใช่☐ •ถั่วหรือไข่ อย่างน้อย 2หน่วยบริโภค/สัปดาห์ ใช่☐ ไม่ใช่☐ •เนื้อสัตว์ ปลา หรือสัตว์ปีก ทุกวัน ใช่☐ ไม่ใช่☐ 0= ถ้าตอบไม่ใช่ทุกข้อ หรือใช่เพียง 1 ข้อ 0.5= ถ้าตอบใช่ 2 ข้อ 1.0= ถ้าตอบใช่ 3 ข้อ	
L. ท่านรับประทานผักหรือผลไม้อย่างน้อย 2หน่วยบริโภคต่อวัน ☐ 0= ไม่ใช่ ☐ 1= ใช่	
M. ดื่มเครื่องดื่ม (น้ำ น้ำผลไม้ กาแฟ ชา นม หรืออื่น ๆ) ปริมาณเท่าไหร่ต่อวัน ☐ 0.0= น้อยกว่า 3ถ้วย ☐ 0.5= 3- 5ถ้วย ☐ 1.0= มากกว่า 5ถ้วย	
N. การรับประทานอาหารของท่าน ☐ 0= ต้องการผู้ช่วยเหลือขณะรับประทานอาหาร ☐ 1= รับประทานได้เองแต่ค่อนข้างลำบาก ☐ 2= รับประทานอาหารได้เอง/ ไม่มีปัญหา	
O. ท่านคิดว่าตนเองมีภาวะโภชนาการเป็นอย่างไร ☐ 0= ขาดสารอาหาร ☐ 1= ไม่แน่ใจว่ามีภาวะโภชนาการเป็นอย่างไร ☐ 2= ไม่ขาดสารอาหาร	
P. เมื่อเทียบกับคนในวัยเดียวกัน ท่านคิดว่าสุขภาพของตนเป็นอย่างไร ☐ 0.0= ด้อยกว่า ☐ 0.5= ไม่ทราบ ☐ 1.0= พอกัน ☐ 2.0= ดีกว่า	
หมายเหตุ ข้อนี้ผู้วิจัยเป็นผู้กรอก Q. เส้นรอบวงแขน (Mid-arm circumference; MAC) ☐ 0.0= MAC น้อยกว่า 21 ซม. ☐ 0.5= MAC 21 ถึง 22 ซม. ☐ 1.0= MAC ตั้งแต่ 22 ซม. ขึ้นไป	

หมายเหตุ ข้อนี้ผู้วิจัยเป็นผู้กรอก R. เส้นรอบวงน่อง (Calf circumference; CC) ☐ 0= CC น้อยกว่า 31 ซม. ☐ 1= CC ตั้งแต่ 31 ซม. ขึ้นไป	
คะแนนรวมการประเมินทั้งหมด	
การแปลผล 24 - 30 คะแนน ☐ มีภาวะโภชนาการปกติ 17 - 23.5 คะแนน ☐ มีความเสี่ยงต่อภาวะขาดสารอาหาร น้อยกว่า 17 คะแนน ☐ ควรปรึกษาแพทย์	

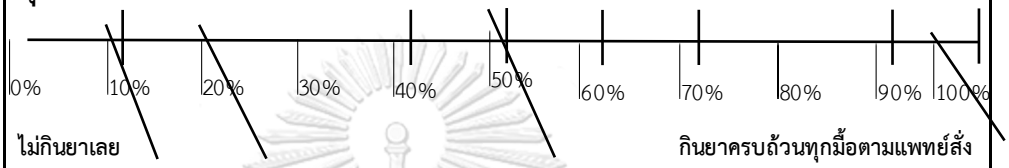
แบบคัดกรองภาวะซึมเศร้า [Thai Depression Scale (TDS)]

ขอให้ท่านเลือกคำตอบที่สอดคล้องกับความรู้สึกของท่านในช่วง 1 สัปดาห์ที่ผ่านมา	มี	ไม่มี
1. รู้สึกจิตใจหม่นหมองหรือไม่ (เกือบตลอดทั้งวัน)		
2. รู้สึกเป็นทุกข์จนอยากร้องไห้		
3. รู้สึกหมดอาลัยตายอยาก		
4. รู้สึกไม่มีความสุข หมดสนุก กับสิ่งที่เคยชอบและเคยทำ		
5. รู้สึกผิดหวังในตนเอง และโทษตนเองในสิ่งที่เกิดขึ้น		
6. รู้สึกสูญเสียความเชื่อมั่นในตนเอง		
7. รู้สึกอยากอยู่คนเดียวไม่อยากสุงสิงกับใคร		
8. รู้สึกว่าตนเองไม่มีคุณค่า		
9. คิดอะไรไม่ออก		
10. หลงลืมง่าย		
11. คิดอะไรได้ช้ากว่าปกติ		
12. ทำอะไรอืดอาด เชื่องช้ากว่าปกติ		
13. รู้สึกอ่อนเพลียง่ายเหมือนไม่มีแรง		
14. รู้สึกเบื่ออาหาร กินได้น้อยกว่าเดิม		
15. นอนหลับๆตื่นๆ หลับไม่สนิท		

การแปลผลคะแนน 0 ☐ ไม่มีภาวะซึมเศร้า >5 ☐ เสี่ยงซึมเศร้าน้อย >10 ☐ ควรปรึกษาแพทย์			

การประเมินความร่วมมือในการใช้ยา [the Visual Analogue Scale (VA$)]

กรุณาทำเครื่องหมายกากบาท X บนเส้นที่สอดคล้องกับร้อยละการทานยาของคุณในช่วงเดือนที่ผ่านมา



ดื่มสุราหรือเครื่องดื่มแอลกอฮอล์อื่นๆ (Drinking):

☐ มี ☐ ไม่มี

☐ เหล้าขาว (Traditional alcohol) จำนวนแก้วต่อวัน (No. of cups per day): _____

☐ เบียร์ (Beer) จำนวนแก้วต่อวัน (No. of cups per day): _____

☐ ไวน์ (Wine) จำนวนแก้วต่อวัน (No. of cups per day): _____

☐ แชมเปญ (Champagne) จำนวนแก้วต่อวัน (No. of cups per day): _____

☐ วิสกี้ (Whiskey) จำนวนแก้วต่อวัน (No. of cups per day): _____

สูบบุหรี่ (Smoking):

☐ มี ☐ ไม่มี

จำนวนมวนต่อวัน (No. of cigarettes per day): _____

Waist circumference (cm): _____

Hip-circumference (cm): _____

Waist-hip ratio: _____

Investigator Signature: _____

Investigator Name: _____

Date of Signature (dd/mmm/yyyy): |__|__|-|__|__|__|-|__|__|__|__|

Data extracted from the Electronic health record database of HIV-NAT

Age: _____ Years

Gender: ☐ Male ☐ Female

Marital status: ☐ Single ☐ Married ☐ Other

Occupation: ☐ Employed ☐ Unemployed

Duration of HIV (dd/mmm/yyyy)

(Year of diagnosis): |__|__|-|__|__|__|-|__|__|__|__|

Duration of ART (dd/mmm/yyyy)

(Year of treatment): |__|__|-|__|__|__|-|__|__|__|__|

Current ART regimens:

ART Dose per day

Current other medications:

Comorbidities:

Hypertension ☐ Yes ☐ No

Diabetes ☐ Yes ☐ No

HBV ☐ Yes ☐ No

HCV ☐ Yes ☐ No

Others.....

Laboratory data (within 12 months)

Test	Result	Unit
CD4	|__|__|__|__|	cells/mm^3

HIV1-RNA	<☐ =☐ >☐ |__|__|__|__|__|__|__|	copies/mL
Albumin	|__|__|.|__|__|	g/dL
Creatinine	|__|__|.|__|__|	mg/dL
Hs-CRP (if any)	|__|__|.|__|__|	mg/L |__| Not done
Triglyceride	|__|__|__|	mg/dL
LDL-C	|__|__|	mg/dL
HDL-C	|__|__|	mg/dL
Insulin	|__|__|.|__|__|	μU/mL
Hemoglobin	|__|__|.|__|__|	g/dL

Previous depression scores assessed by TDS

Scores	Assessment date (dd/mmm/yyyy)
☐ ≤ 5 points ☐ > 5 points หรือระบุคะแนนที่ประเมินได้	|__|__|-|__|__|__|-|__|__|__|__|

Previous nutritional scores assessed by MNA

Scores	Assessment date (dd/mmm/yyyy)
☐ <24 points ☐ ≥24 points หรือระบุคะแนนที่ประเมินได้	|__|__|-|__|__|__|-|__|__|__|__|

VITA

NAME	Miss Daylia Thet
DATE OF BIRTH	22 January 1994
PLACE OF BIRTH	Myothit, Magway Division, Myanmar
INSTITUTIONS ATTENDED	University of Pharmacy, Mandalay, Myanmar (2011) University of Pharmacy, Yangon, Myanmar (2012-2014)
HOME ADDRESS	No.201, 5D, Joe Phyu Street, Innwa Housing, South Dagon Township, Yangon, Myanmar
PUBLICATION	Antiretroviral therapy-associated metabolic complications: Review of the recent studies