EFFECT OF DIETARY ADVICE ON THE COMPONENTS OF METABOLIC SYNDROME IN HIV/AIDS PATIENTS WITH METABOLIC SYNDROME

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A Thesis Submitted in Partial Fulfillment of the Requirements
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ผลของการให้คำแนะนำเกี่ยวกับอาหารต่อองค์ประกอบของกลุ่มอาการเมแทบอลิกในผู้ป่วยติดเชื้อเอชไอวีหรือผู้ป่วยเอดส์ที่มีกลุ่มอาการเมแทบอลิก

น.ส.พัชรี เกตุเฉลียว

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต
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พัชรี เกตุเฉลียว : ผลของการให้คำแนะนำเกี่ยวกับอาหารต่อองค์ประกอบของกลุ่มอาการเมแทบอลิกในผู้ป่วยติดเชื้อเอชไอวีหรือผู้ป่วยเอดส์ที่มีกลุ่มอาการเมแทบอลิก. (EFFECT OF DIETARY ADVICE ON THE COMPONENTS OF METABOLIC SYNDROME IN HIV/AIDS PATIENTS WITH METABOLIC SYNDROME) อ.ที่ปรึกษาหลัก : รศ. ภญ. ดร.กุลวรา เมฆสวรรค์

กลุ่มอาการเมแทบอลิกเป็นภาวะแทรกซ้อนที่พบได้ในผู้ป่วยติดเชื้อเอชไอวีหรือผู้ป่วยเอดส์ ทำให้ผู้ป่วยมีความเสี่ยงในการเกิดโรคหัวใจและหลอดเลือดมากขึ้น การได้รับคำแนะนำเกี่ยวกับการรับประทานอาหารที่เหมาะสมอาจช่วยลดปัญหาดังกล่าวได้ การศึกษานี้มีวัตถุประสงค์เพื่อ ศึกษาผลของการให้คำแนะนำเกี่ยวกับอาหารต่อองค์ประกอบของกลุ่มอาการเมแทบอลิก ได้แก่ สัดส่วนของร่างกาย ระดับไขมันและระดับน้ำตาลในเลือด และความดันโลหิต ในผู้ติดเชื้อเอชไอวีหรือผู้ป่วยเอดส์ที่มีกลุ่มอาการเมแทบอลิก และได้รับการรักษาด้วยยาต้านไวรัสชนิดที่มีประสิทธิภาพสูง การศึกษานี้เป็นการศึกษาแบบสุ่มและมีกลุ่มควบคุม มีผู้เข้าร่วมการศึกษาทั้งสิ้น 60 คน แบ่งเป็น กลุ่มทดลอง 30 คน และกลุ่มควบคุม 30 คน ผู้เข้าร่วมการศึกษาทุกคนได้รับคำแนะนำพร้อมกับคู่มือในการรับประทานอาหารที่ดีต่อสุขภาพตามธงโภชนาการ มีเพียงกลุ่มทดลองเท่านั้น ที่ได้รับคำแนะนำและคู่มือเกี่ยวกับการรับประทานอาหารที่ดัดแปลงมาจากคำแนะนำของ National Cholesterol Education Program Adult Treatment Panel III, European Aids Clinical Society Guidelines และ Mediterranean diet เพื่อให้เหมาะสมกับผู้ติดเชื้อเอชไอวีหรือผู้ป่วยเอดส์ที่มีกลุ่มอาการเมแทบอลิกชาวไทย (the modified NEM diet) เพิ่มเติม จากนั้นติดตามผู้เข้าร่วมการศึกษาเป็นเวลา 24 สัปดาห์ ผลการศึกษาพบว่า กลุ่มทดลองมีน้ำหนักลดลงที่สัปดาห์ที่ 12 และ 24 เมื่อเทียบกับช่วงเริ่มต้นการศึกษา และมีค่าดัชนีมวลกายและเส้นรอบเอว ลดลงอย่างมีนัยสำคัญทางสถิติ ที่สัปดาห์ที่ 24 มีระดับไตรกลีเซอไรด์และน้ำตาลในเลือดหลังอดอาหารลดลงอย่างมีนัยสำคัญทางสถิติ เมื่อเทียบกับช่วงเริ่มต้นการศึกษา ($p = 0.008$ และ $p < 0.001$ ตามลำดับ) และมีระดับไตรกลีเซอไรด์ต่ำกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติเมื่อสิ้นสุดการศึกษา ($p = 0.014$) นอกจากนี้ผู้เข้าร่วมการศึกษาในกลุ่มทดลองยังมีความดันซิสโทลิกลดลงอย่างมีนัยสำคัญทางสถิติ ($p < 0.001$) เทียบกับเมื่อเริ่มต้นการศึกษา และเมื่อสิ้นสุดการศึกษา ทั้งความดันซิสโทลิกและความดันไดแอสโทลิกในกลุ่มทดลอง มีค่าต่ำกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ ($p < 0.001$ และ $p = 0.024$ ตามลำดับ) ในขณะที่ทุกองค์ประกอบของกลุ่มอาการเมแทบอลิกของผู้เข้าร่วมการศึกษาในกลุ่มควบคุม ไม่มีการเปลี่ยนแปลง พบว่าเมื่อสิ้นสุดการศึกษา ผู้เข้าร่วมการศึกษาในกลุ่มทดลองได้รับพลังงานรวมจากการรับประทานอาหารลดลง ได้รับคาร์โบไฮเดรต ไขมัน ไขมันอิ่มตัว และน้ำตาลลดลง มีการรับประทานโปรตีนและใยอาหารเพิ่มขึ้น และ ผู้เข้าร่วมการศึกษาที่มีภาวะกลุ่มอาการเมแทบอลิกมีจำนวนลดลง หลังจากได้รับคำแนะนำการรับประทานอาหาร การศึกษานี้แสดงให้เห็นว่า การให้คำแนะนำการรับประทานอาหารตามแบบ modified NEM diet ช่วยให้ผู้ป่วยติดเชื้อเอชไอวีหรือผู้ป่วยเอดส์ที่มีกลุ่มอาการเมแทบอลิก มีองค์ประกอบของกลุ่มอาการทางเมแทบอลิกดีขึ้น ดังนั้นจึงสามารถนำมาประยุกต์ใช้เป็นแนวทางในการจัดการกลุ่มอาการเมแทบอลิกในผู้ป่วยเหล่านี้ต่อไป

สาขาวิชา	อาหารเคมีและโภชนศาสตร์ทางการแพทย์	ลายมือชื่อนิสิต .....
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5976112433 : MAJOR FOOD CHEMISTRY AND MEDICAL NUTRITION
KEYWORD: metabolic syndrome, HIV-infected patient, AIDs, dietary advice
Patcharee Ketchaleaw : EFFECT OF DIETARY ADVICE ON THE COMPONENTS OF METABOLIC SYNDROME IN HIV/AIDS PATIENTS WITH METABOLIC SYNDROME. Advisor: Assoc. Prof. KULWARA MEKSAWAN, Ph.D.

Metabolic syndrome is a complication found in HIV/AIDs patients. The patients with metabolic syndrome had increased risk of cardiovascular disease. An appropriate dietary advice may help ameliorate this problem. This study aimed to investigate the effect of dietary advice on components of metabolic syndrome including anthropometric parameters, lipid profiles, fasting blood sugar, and blood pressure in the HIV/AIDs with metabolic syndrome who were on highly active antiretroviral therapy. This study was a randomized controlled trial. Sixty participants were randomly assigned into an intervention group (n = 30) and a control group (n = 30). All patients received the advice with the booklet about healthy diet for Thai people according to Thai nutrition flag, and only the intervention group additionally received the advice with the booklet providing the information about modified NEM diet which was derived from the dietary recommendations of National Cholesterol Education Program Adult Treatment Panel III, European Aids Clinical Society Guidelines and Mediterranean diet and was appropriately modified for Thai HIV/AIDs patients. The participants were followed for 24 weeks. The results showed that the participants in the intervention group had significantly decreased weight at week 12 and week 24 when compared with baseline while BMI and WC were significantly decreased at week 24 when compared with baseline. They had significantly lower TG and FBS levels when compared with baseline (p = 0.008 and $p < 0.001$, respectively) and had significantly lower TG level than those in the control group at week 24 (p = 0.014). In addition, blood pressure, both systolic and diastolic, of the participants in the intervention group was significantly lower than those in the control group ($p < 0.001$ and p = 0.024, respectively). There were no changes in any parameters in the control group throughout the study. At the end of the study, the participants in the intervention group had decreased consumption of total calories, carbohydrate, fat, saturated fat, and sugar but had increased protein and dietary fiber intakes. Moreover, the number of participants with metabolic syndrome decreased after receiving dietary advice. This study indicated that such dietary advice could improve metabolic components in HIV/AIDs patients with metabolic syndrome. Therefore, it can be included in guidelines for management of metabolic syndrome in these patients.

Field of Study:	Food Chemistry and Medical Nutrition	Student's Signature .....
Academic Year:	2020	Advisor's Signature .....

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Patcharee Ketchaleaw

TABLE OF CONTENTS

LIST OF TABLES

Page

LIST OF FIGURES

Page

LIST OF ABBREVIATIONS

AIDS	acquired immune deficiency syndrome
ART	antiretroviral therapy
ASCVD	atherosclerotic cardiovascular disease
AZT	zidovudine
BMI	body mass index
CD	Cluster of differentiation
DASH	Dietary Approaches to Stop Hypertension
DBP	diastolic blood pressure
EACS	European AIDS Clinical Society
EFV	Efavirenz
FA	fat accumulation
FBS	fasting blood sugar
FFQ	food frequency questionnaire
FR	fat redistribution
FW	fat wasting
HAART	highly active antiretroviral therapy
HDL-C	high density lipoprotein cholesterol
HIV	human immunodeficiency virus
IDF	International Diabetes Federation
LDL-C	low density lipoprotein cholesterol
LPV/r	Lopinavir/ritonavir
NCEP ATP III	National Cholesterol Education Program Adult Treatment Panel III
NVP	Nevirapine
SBP	systolic blood pressure
TC	total cholesterol
TG	triglyceride
WC	waist circumference
WHO	World Health Organization
WHR	waist to hip ratio

CHAPTER I
INTRODUCTION

1.1 Background and Rationale

Human immunodeficiency virus (HIV) infection alters the function of immune system, especially T-cells. The patients had increased risk for opportunistic infections. In 2007, approximately 36.9 million people worldwide were living with HIV/acquired immunodeficiency syndrome (AIDs) (World Health Organization, 2017). In Thailand, 1,526,028 HIV/AIDS people were reported in 2015 (Family Health International and Bureau of AIDS, 2015). The goals of HIV treatment include maximally and durably suppressing plasma viral load, restoring and preserving immunological function, preventing HIV transmission, reducing HIV-associated morbidity, prolonging survival, and improving quality of life. The use of highly active antiretroviral therapy (HAART) has shown to suppress the HIV replication and improve the clinical outcomes. Most of the HIV-infected patients on HAART have increased life expectancy (Lucas, 2012).

HAART consists of a combination of at least three antiretroviral drugs from at least two different antiretroviral classes. Although HAART has become the standard of care, the medications have been associated with the development of short-term and long-term adverse events. Short-term adverse events often occur within 6 months after taking antiretroviral drugs such as drug allergy, nausea, vomiting, dizziness, insomnia, diarrhea, and hepatotoxicity, while long-term adverse events usually occur at least 6 months after taking them. Long-term adverse events include bone toxicity, renal toxicity, dyslipidemia, neuropathy, lactic acidosis, gynecomastia, and metabolic syndrome (Montessori et al., 2004).

Metabolic syndrome is a group of cardiovascular risk factors which include diabetes and raised fasting plasma glucose, abdominal obesity, high cholesterol, and

high blood pressure (The International Diabetes Federation, 2006). Several organizations such as the International Diabetes Federation (IDF), World Health Organization (WHO) and the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) define criteria for diagnosing metabolic syndrome. The first definition was developed by WHO in 1998. An absolute requirement of WHO definition is evidence of insulin resistance including impaired glucose tolerance, impaired fasting glucose, type 2 diabetes, or other evidence of insulin resistance plus two of the criteria including obesity, hypertension, dyslipidemia, and microalbuminuria. According to NCEP ATP III definition, metabolic syndrome is presented if three or more following five criteria are met: blood pressure moreover 130/85 mmHg, waist circumference (WC) over 35 or 40 inches in women and men, respectively, fasting triglyceride (TG) level over 150 mg/dL, fasting blood sugar moreover 100 mg/dL, and high-density lipoprotein cholesterol (HDL-C) level less than 50 or 40 mg/dL in women and men, respectively. IDF published new criteria in 2005, and the absolute requirement is central obesity plus two of four criteria: fasting glucose equal to or greater than 100 mg/dL, TG more than or equal to 150 mg/dL, HDL-C level less than 50 or 40 mg/dL in women and men, respectively, and blood pressure more than 130/85 mmHg. Although the selected criteria differ, the components of metabolic syndrome including central obesity, raised TG, reduced HDL-C, high blood pressure, and impaired glucose tolerance were similar among the organizations.

The prevalence of metabolic syndrome worldwide in 2006 was 25 % (The International Diabetes Federation, 2006). The prevalence of 4 - 45 % was found in HIV-infected patients worldwide (Alencastro et al., 2011). The prevalence of metabolic syndrome in Thai-HIV infected patients was 15.9 - 24.9 % (Jureeporn et al., 2014). The risk factors of metabolic syndrome in HIV-infected patients included increasing age, body mass index (BMI) more than or equal to 25 kg/m^2, white race, HAART use, physical

inactivity, and improper diet (Kagaruki et al., 2015; Malangu, 2014). However, HIV infection and antiretroviral drugs may be the major cause of metabolic syndrome in these patients (Pao, Lee, and Grunfeld, 2008). It was found that HIV infection affects blood lipid levels. The patients initially have decreased HDL-C followed by decreased low-density lipoprotein cholesterol (LDL-C) levels in advanced stages. TG and very low-density lipoproteins levels were increased. The long-term inflammation initiates higher white blood cells count, which acts as a metabolic risk factor in pathogenesis of HIV. Complications associated with HAART depend on the antiretroviral use. Zidovudine, efavirenz and indinavir induce toxicity through induction of cardiomyocyte and endothelial cell apoptosis leading to vascular damage and endothelial dysfunction (Fiala et al., 2004). In addition, the imbalance in glucose metabolism occurs while using some nucleoside reverse transcriptase inhibitors such as stavudine, zidovudine, lamivudine, and didanosine as well as some protease inhibitors or non-nucleoside reverse transcriptase inhibitors including indinavir, lopinavir/ritonavir and efavirenze (Paula, Falcao, and Pacheco, 2013).

At present, there is no specific guideline for management of metabolic syndrome in HIV-infected patients. The main objective of guidelines for general patients with metabolic syndrome from pharmacotherapy self-assessment program is to reduce the risk of atherosclerotic cardiovascular disease (ASCVD) (Aquilante and Griend, 2008). The therapeutic lifestyle changes (TLC) have been suggested to be the first-line therapy against metabolic syndrome. All patients should be encouraged to reduce weight, increase physical activity and choose appropriate diet. They also should receive physical examination for assessing comorbidity including diabetes mellitus and ASCVD such as acute coronary syndrome, unstable angina, chronic stable angina, stroke, and peripheral arterial disease. When they have such diseases, the treatment should be started. The patients who do not have existing diseases were assessed 10-

year risk for coronary heart disease by the Framingham risk assessment tool and treated individual component. Although no specific guideline for management of metabolic syndrome in HIV-infected patients was established, European AIDS clinical society (EACS) recommended cessation of smoking, increasing physical activity and consumption of healthy diet in part of lifestyle intervention. Dietary counseling includes limited intake of saturated fat and cholesterol (less than 300 mg/day), reduced total fat intake to less than 30 % of total calories per day, emphasized intake of fruit, grain products with fiber, vegetables, lean meat, fish and low fat dietary intake, and maintenance in caloric intake balanced with energy expenditure (Lundgren, 2008).

There are many suggestions about consumption of traditional foods for metabolic syndrome treatment (Keane et al., 2013; Suliga et al., 2017). One of the suggested diets is the Mediterranean diet. This type of diet showed the benefit for metabolic syndrome patients (Babio, 2014; Tsiodras et al., 2009). The Mediterranean diet is the traditional healthy diet of people in the Mediterranean region. The diet is mostly plant-based with high consumption of fresh vegetables, fruits, whole grain, nuts, herbs, and spices in every meal. Fish and sea foods which are rich in omega-3 fatty acids should be consumed at least twice a week. The people are suggested to consume red meat less often, eat the sweets when having celebration events, and choose healthy fat such as olive oil. Babio et al. (2014) investigated the roles of the Mediterranean diet compared with low-fat diet in the patients who had high risk of cardiovascular disease for 4.8 years. The results showed significant decreases in both central obesity and high fasting blood glucose, which are the components of metabolic syndrome in patients who followed the Mediterranean diet. Tsiodras et al. (2009) investigated the association between adherence of the Mediterranean diet and metabolic syndrome components in HIV-infected patients who had antiretroviral treatment at least 6 months. According to the fat redistribution (FR) adjudication

committee, the participants were categorized into 4 groups including non-FR group, fat accumulation (FA) group, fat wasting (FW) group and mixed FR group. After adjusting confounding factors which were age, sex, CD4+ cell levels, time length of antiretroviral use, and HIV-infection, the results showed inversed relationship between MedDietScore, which indicated adherence to the Mediterranean diet and HOMA-IR index in mixed FR group and positive relationship between MedDietScore and HDL-C in total FR group.

In Thailand, the ingredients of traditional foods are different from those of the Western and Mediterranean diets. There were few studies about dietary advice based on NCEP ATP III guideline modified for Thai people (Chotivichien et al., 2016; Ketchaleaw, Pongthananikorn, and Meksawan, 2016). Chotivichen et al. (2016) evaluated the effect of dietary advice on lipid profiles in HIV-infected patients who had abnormal LDL-C for 24 weeks. The dietary intervention followed NCEP ATP III with the energy from fat less than 25 % of total calories per day. At the end of the study, only the patients in the intervention group had significant decreased total cholesterol (TC) and LDL-C levels. Similar results were found in the study by Ketchaleaw et al. (2016) in HIV-infected patients with dyslipidemia. In this 24-week study, the patients in the intervention group received dietary advice based on NCEP ATP III guidelines modified for Thais while those in the control group received dietary advice according to Thai nutrition flag. The results showed that TC and LDL-C levels were significantly decreased in the intervention group.

The results of the previous studies indicated that the healthy diet could reduce metabolic complications in HIV-infected patients. However, there was no study about the effect of dietary advice on components of metabolic syndrome in Thai HIV/AIDS patients with metabolic syndrome.

1.2 Objectives of study

To investigate the effect of dietary advice on components of metabolic syndrome in HIV/AIDS patients including anthropometric parameters, lipid profiles, fasting blood sugar, and blood pressure.

1.3 Benefits of the study

This study provides the dietary intervention booklet for HIV/AIDS patients with metabolic syndrome and the results on the effect of dietary advice according to the booklet in these patients. The information obtained from this study will be beneficial for HIV/AIDS patients with metabolic syndrome in using the booklet as a guide for management of such complication.

1.4 Scope of the Study

The study was conducted in HIV-infected patients with metabolic syndrome at Banbung Hospital, Chonburi Province.

1.5 Definition of term

Metabolic syndrome: a group of conditions following the International Diabetes Federation definition.

HIV infection: infection of HIV diagnosed based on positive HIV antibody testing either using rapid or laboratory-based enzyme immunoassay and confirmed with a second test using a different assay on the same specimen.

AIDS: the advanced stage of HIV infection when the patients present the number of CD4+ cells below 200 cells per cubic millimeter or one or more opportunistic infections regardless of the CD4 count.

CHAPTER II
LITERATURE REVIEW

2.1 Human immunodeficiency virus/Acquired immunodeficiency syndrome

HIV is virus in Retroviridae family. It is classified into type I (HIV-I) and type 2 (HIV-2). HIV-1 was originally transmitted from chimpanzee, while HIV-2 was from sooty mangabey monkeys (Maartens, Celum, and Lewin, 2014). HIV-1 is subdivided into four groups including group M, N, O, and P. Group N, O and P are restricted to West Africa whereas group M is the cause of the global HIV pandemic. Blood, semen, rectal fluid, vaginal fluid, and breast milk are five body fluids that can contain enough HIV for infection. Two main ways that HIV can pass from one HIV-infected person to another are unprotected sex or sharing needles. The genes of retroviruses are composed of ribonucleic acid (RNA) molecules whereas the genes of humans are made of deoxyribonucleic acid (DNA). After HIV passes to inside of the cell, it uses enzyme reverse transcriptase to convert its RNA into human DNA. The first step of viral replication is the viral attach particle to the CD4+ cell receptor and the chemokine coreceptors (CCR5 and CXCR4) of the host cell, after that the newly made HIV DNA moves to the nucleus of the cell. HIV integrase enzyme helps the viral DNA into the human's DNA and makes viral proteins. In the translation process, the messenger RNA (mRNA) transcribed from DNA and transported from the nucleus to the cytoplasm. Then, the proteins of HIV virus will be made by using the HIV mRNA as a template. The proteins are translated into the RNA, comprising core and the envelope. The gene products were spliced to smaller units by HIV protease, and then the virus can pinch off the cells and buds. A single cell can make many infectious particles of HIV.

After infection, there are three stages of disease including acute HIV infection, clinical latency (HIV inactivity or dormancy) and AIDs. During acute HIV infection stage,

the patients may have flu-like illness after two to four weeks of infection. Following the initial phase of HIV infection, the immune function is gradually deteriorated. HIV can infect CD4+ lymphocytes and the other cells such as thymocytes and monocytes. CD4+ cell plays a central role in the immune function. Although HIV is still active, it reproduces at very low levels in the clinical latency period. As the infection a progress, a viral load increases whereas the CD4+ cell count decreases. When CD4+ cell is less than 200 cells/mm^3, the infected people have high risk for serious opportunistic infection such as *Pneumocystis carinii* pneumonia, toxoplasmosis, and cytomegalovirus infection. When they have opportunistic infection or have CD4+ less than 200 cells/mm^3, they are considered having AIDs (Selik et al., 2014).

2.1.1 Prevalence of HIV/AIDS

Approximately 36.9 million people were living with HIV/AIDs worldwide (World Health Organization, 2017). In Thailand, 1,526,028 HIV/AIDS people were reported in 2015 (Family Health International and Bureau of AIDS, 2015). The prevalence of HIV-infected patients were decreased from 2.62 % in 2016 to 2.38 % in 2017 in men who came to check sexually transmitted disease, and the prevalence of HIV infection in blood donor group and the women who came to antenatal care were 0.15 % and 0.54 %, respectively (National AIDS Management Center Bureau of AIDS TB and STIs, 2017). The independent risk factors for HIV infection were a history of sex with a prostitute, male-to-male sex, Hepatitis C virus infection (Rangsin et al., 2015), injection drug abuse (Maan, Hussain, and Jamil, 2014), and multiple sexual partners (Arora, Nagelkerke, and Jha, 2012).

2.1.2 Treatment

Antiretroviral therapy (ART) is recommended for all people with HIV, regardless of CD4 cell count. Early use of ART is useful to prevent HIV transmission and decrease

the morbidity and mortality associated with HIV infection. Before starting ART, the patients will be educated the benefits and considerations of ART, addressing barriers to adherence and recommending strategies to optimize adherence. Antiretroviral regimen for treatment of HIV patient normally consists of two nucleoside reverse transcriptase inhibitors (NRTIs) combined with one of three drug classes including non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitor (PI) or integrase strand transfer inhibitor (INSTI). The recommended initial regimens for most HIV infection patients include bictegravir/ tenofovir /alafenamide /emtricitabine, dolutegravir/ abacavir/ lamivudine (only for patients who are HLA-B*5701 negative), dolutegravir plus tenofovir/emtricitabine, and raltegravir plus tenofovir/emtricitabine (A working Group of the Office of AIDS Research Advisory Council (OARAC), 2018).

In Thailand, the first regimens are tenofovir/emtricitabine or tenofovir/lamivudine in combination with efavirenze. These regimens are recommended because of high efficacy, less adverse events and improved compliance due to once daily administration (Masho, Wang, and Nixon, 2007). The use of ART can significantly increase CD4 levels and decrease viral load compared with before using ART (Attah et al., 2018).

2.1.3 Complications of HAART

Use of the HAART has shown to reduce the opportunistic infections and mortality and improve quality of life in HIV-infected patients (Lucas, 2012). However, the virus is still not eliminated from the body. Therefore, the patients need lifelong antiretroviral therapy. The use of antiretroviral therapy can cause many adverse events. The less severe but common adverse effects including nausea, bloating, diarrhea, headache, and fatigue are found with zidovudine use. Nightmare is also reported as an adverse effect of efavirenze. The use of NRTIs is associated with hypersensitivity reaction, neutropenia and anemia, while NNRTIs are associated with hepatotoxicity,

and PIs are associated with metabolic abnormalities. Metabolic syndrome is one of long-term complications that can be found in the HIV-infected patients on HAART (Carr and Cooper, 2000; Khan et al., 2014).

2.2 Metabolic syndrome

Metabolic syndrome is a group of risk factors for cardiovascular disease including diabetes and hyperglycemia, abdominal obesity, dyslipidemia, and hypertension. The patients with metabolic syndrome have three times higher risk of heart attack or stroke and are two times more likely to die from these complications than those without metabolic syndrome (The International Diabetes Federation, 2006). Several organizations have proposed the diagnostic criteria for metabolic syndrome including IDF, WHO and NCEP ATP III. Definitions of metabolic syndrome by these organizations are shown in Table 1. The components of metabolic syndrome in the criteria established by these organizations are mostly similar such as abdominal obesity, raised TG level, decreased HDL-C, increased blood pressure, and impaired glucose tolerance or previously diagnosed type 2 diabetes. According to the IDF definition, the patients to be diagnosed as having metabolic syndrome must have central obesity plus any two of other risk factors (Alberti et al., 2005). WHO focuses on impaired glucose tolerance and any two of other components (Alberti and Zimmet, 1998; Grundy, Cleeman, and Daniels, 2005), while NCEP ATP III does not set priority to any factors, but the patients must have at least three of five of the risk factors for metabolic syndrome (Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults, 2001).

2.2.1 Prevalence of metabolic syndrome and risk factors

Prevalence of metabolic syndrome in worldwide ranges from less than 10 % to 84 % depending on the region, urban or rural, race, age, sex, ethnicity of

population's study, and the definition of metabolic syndrome used in each study (Kolovou et al., 2007). Insulin resistance and central obesity are the underlying causes of metabolic syndrome (The International Diabetes Federation, 2006). Other risk factors include older age, physical inactivity and hormonal imbalance (Armstrong et al., 2006). In the United State, the prevalence of metabolic syndrome was 34.5 % and 39 % according to the criteria of NCEP ATP III and IDF, respectively (Ford, 2005), and the risk factors were increasing age, race and ethnicity. The prevalence of metabolic syndrome for each age group (20-39, 40 - 59 and $\geq$ 60 years) was as followed: 20 %, 41 % and 52 % in men and 16 %, 37 % and 54 % in women (Ervin, 2009). Based on the NCEP ATP III criteria, the prevalence of metabolic syndrome in Brazilian was 22.7 %, and the risk factors were increasing age, higher BMI, inactive or minimal active, low HDL-C, high blood pressure, and high WC (Moreira et al., 2014). In India, the prevalence of metabolic syndrome was 20 %, and low HDL-C and raised TG were the risk factors (Bajaj, Tyagi, and Bhargava, 2013). In Thailand, the prevalence of metabolic syndrome was 36.49 %, and the risk factors were BMI, age and lack of exercise (Yuenyongchaiwat, Pipatsitipong, and Sangprasert, 2017).

Table 1 The diagnostic criteria for metabolic syndrome

	IDF[1] (Must plus any two of other risk factors)	WHO[2] (Must plus any two of other risk factors)	NCEP ATP III[3] (Any three of five risk factors)
Central obesity (WC according to South Asians: M ≥ 90 cm; F ≥ 80 cm)	Must	✓	✓
Raised TG (≥ 150 mg/dL or specific treatment for dyslipidemia)	✓	✓	✓
Reduced HDL-C (M < 40 mg/dL; F < 50 mg/dL or drug treatment for reduced HDL-C)	✓	✓	✓
Raised blood pressure (SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or drug treatment for hypertension)	✓	(SBP ≥ 140 mmHg or DBP ≥ 90 mmHg)	✓
Impaired glucose tolerance (FPG ≤ 100 mg/dL or previously diagnosed type 2 diabetes)	✓	Must	≥ 110 mg/dL
Insulin resistance	-	✓	-
Microalbuminuria	-	✓	-

[1]Metabolic syndrome definition based on the International Diabetes Federation (IDF) (Alberti et al., 2005)

[2]Metabolic syndrome definition based on World Health Organization (WHO) (Alberti and Zimmet, 1998; Grundy et al., 2005)

[3]Metabolic syndrome definition based on National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) (Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults, 2001)

M = Male; F = Female; WC = Waist circumference; TG = Triglyceride; HDL-C = high-density lipoprotein cholesterol; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; FPG = fasting plasma glucose

2.2.2 Management of metabolic syndrome

The major goal of metabolic syndrome management is to reduce the risk of type 2 diabetes and atherosclerotic cardiovascular disease (ASCVD) (Aquilante and Griend, 2008). Lifestyle intervention has been suggested to decrease complications including abdominal obesity. The goal of weight reduction is to achieve BMI less than 25 kg/m^2 and WC less than 88 centimeters and 102 centimeters in women and men, respectively. The patients are advised to reduce 7 - 10 % total body weight within 6 - 12 months by reducing calories intake 500-1000 calories per day and increasing moderate intensity exercise for 30 - 60 minutes per day at least 5 days per week. The metabolic syndrome patients without type 2 diabetes and/or ASCVD were predicted a 10-years risk of coronary heart disease (CHD) by the Framingham risk assessment tool. This tool was used to estimate the probability that patients will develop cardiovascular disease within 10 years. Individuals with low risk have less than 10 % or less CHD risk at 10 years. The goal of blood pressure for them is less than 140/90 mmHg. However, for the patients with intermediate or high CHD risk, the goal of blood pressure was lower 130/80 mmHg.

2.3 HIV/AIDs and metabolic syndrome

2.3.1 Prevalence of metabolic syndrome in HIV/AIDS patients and risk factors

The global prevalence of metabolic syndrome in HIV-infected patients was estimated from 4 - 45 % (Alencastro et al., 2012), and the prevalence ranged from 15.9 - 24.9 % in Thai HIV-infected individuals according to the National Heart Lung and Blood Institute and American Heart Association (NHLBI and AHA) (Jureeporn et al., 2014). In HIV-infected patients who use antiretroviral therapy for 6 months and more, the prevalence of metabolic syndrome according to NCEP ATP III was found to be 52.8 % (Teekawong et al., 2017). When diagnosed by NCEP ATP III with modified WC cut

point for Asians, the prevalence of metabolic syndrome in HIV-infected patients who received HARRT for at least 12 months was 18.5 % (Pongthananikorn et al., 2018). Increasing age is one of the risk factors of metabolic syndrome in HIV-infected patients. The patients aged above 41 years old are more likely to have metabolic syndrome (two times more than younger age). The other risk factors are white race, BMI greater than or equal to 25 kg/m^2. The patients who have BMI more than or equal to 25 kg/m^2 have 16 times higher risk for metabolic syndrome than those who have lowered BMI. The duration of HAART therapy more than five years had increasing risk three times than those who had HAART therapy less than five years (Malangu, 2014). The prevalence of metabolic syndrome was higher among patients who came from urban than rural areas. The risk of metabolic syndrome in these study was never participated on vigorous intensity activity or participated on vigorous intensity activity less than 150 minute per week and consumed vegetables/fruits less than five days/week (Kagaruki et al., 2015).

2.3.2 Managements

All HIV-infected patients should be regularly assessed for metabolic abnormalities including diabetes mellitus, dyslipidemia, hypertension, and alteration of body composition. Lifestyle modification is the first recommendation for prevention and treatment of metabolic abnormalities. It is effective for metabolic syndrome patients both with and without HIV infection. It usually includes diet modification, smoking cessation and exercise promotion. In HIV-infected patients, if such modification is not effective, a change of antiviral drugs and using drugs for treatment of each metabolic condition should be considered (Lundgren, 2008).

Diet modification is the first recommendation for improve metabolic syndrome. Different types of diet have been used for metabolic syndrome treatment such as Dietary Approaches to Stop Hypertension (DASH) diet, Mediterranean diet and Nordic

diet. The characteristic of DASH diet is reduced sodium intake, moderate alcohol intake, increased intake of vegetables, fruit, low-fat dairy products, and decreased intake of total fats saturated fat and cholesterol. The use of this type of diet resulted in the reduction of both systolic and diastolic blood pressure, insulin levels, fasting blood glucose, weight, and triglyceride in both the patients with and without metabolic syndrome (Azadbakht et al., 2005; Hikmat and Appel, 2014). For patients with hypertension, following DASH dietary pattern in combination with weight loss and increased physical activity resulted in increased insulin sensitivity in 6 months (Ard et al., 2004).

Besides DASH dietary pattern, the Mediterranean diet was also examined for efficacy in metabolic syndrome patients. Mediterranean diet is a traditional diet of people from countries bordering the Mediterranean Sea. It is characterized as high consumption of vegetables, fruits, nuts, legumes, cereals, and whole grains, moderate consumption of fish, poultry, red wine, and low consumption of red meat. Consumption of the Mediterranean diet combined with aerobic exercise showed beneficial effects in decreasing abdominal circumference, systolic and diastolic blood pressure and increasing HDL-C level (Gomz-Huelgas et al., 2015).

Nordic diet is the type of diet that high in consumption of whole-grain and high-fiber products. Others characteristic was abundant intake of vegetables and fruits, especially berries. This type of diet restricts consumption of dairy products, red meat and processed meat. High quality meat such as fish and shellfish should be often consumed. In addition, refined sugar is restricted to less than 10 % of total calories per day. Previous study showed that the metabolic syndrome participants who received the healthy Nordic diet for 12 weeks had reduced diastolic blood pressure (Brader et al., 2014).

Different fatty acid contents appear to have an impact on metabolic syndrome. Monfort-Pires and Ferreira (2017) investigated the effects of two types of breakfast containing different fatty acid contents in overweight patients with presence of metabolic syndrome. The patients received two isocaloric breakfast interventions, Brazilian breakfast high in saturated fatty acids and modified breakfast high in unsaturated fatty acids, for 4 weeks with 2-week washout period. The results showed a significant reduction in the number of participants with metabolic syndrome in the modified breakfast group but increased in Brazilian breakfast group. Mean values of WC and diastolic blood pressure were decreased in the modified breakfast group. In addition, HDL-C level of the patients in modified breakfast group was higher at the end of the study, compared to those in the Brazilian breakfast group. This study showed that the diet rich in unsaturated fatty acid improved cardiometabolic risk profile while saturated fatty acid worsened the metabolic profile.

Early dietary counseling in the children showed reduced risk of metabolic syndrome. A previous study investigated the relationship between an infancy-onset dietary advice and risk of having metabolic syndrome in young adults aged between 15 and 20 years old (Nupponen et al., 2015). The counseling was given to the parents when the children were 6 months old and directly to the children when they were 7 years old at least twice a year until they were 20 years old. The target of counseling in this study was the replacement of saturated fat with unsaturated fat in the child's diet while the control group received only the basic health education. The results showed that consumption of whole-grain products led to increased fiber intake and introduced the appropriate quality carbohydrate. The long-term relative risk of metabolic syndrome was significantly lower in the intervention group when compared with the control group. In addition, the risk of high blood pressure decreased in the

intervention group. Based on the previous studies, it is revealed that the dietary modification is one of effective approaches to manage metabolic syndrome.

2.4 Dietary intervention in HIV/AIDs patients with metabolic syndrome

A multidisciplinary lifestyle intervention, a dietary program, a plan to quit smoking and an exercise recommendation, have shown to be effective in decreasing LDL-C levels at month 24 in HIV-infected patients with Framingham score more than 10 % (Saumoy et al., 2016). However, the most effective dietary pattern or nutrition supplement for metabolic syndrome and its component has not been established. Some dietary patterns have been studied in HIV/AIDs patients with metabolic syndrome and showed the beneficial outcome. The association between the adherence of the Mediterranean diet pattern and metabolic components in HIV-infected patient with different types of fat redistributions was studied. (Tsiodras et al., 2009) found inverse relationship between the Mediterranean Diet Score (MedDietScore) and Homeostatic Model Assessment of insulin resistance (HOMA-IR) index and positive relationship between MedDietScore and HDL-C in these patients. Policarpo et al. (2017) found that higher adherence of the Mediterranean diet had improved cardiovascular risk in HIV infected patients suggesting the benefit of the diet in HIV-infected patients with metabolic syndrome.

Richard et al. (2011) examined the efficacy of Mediterranean diet with and without weight loss on body compositions and metabolic components in male patients with metabolic syndrome. The first phase is controlled feeding condition (10-week weight-maintaining condition). All participants received isocaloric North American diet (control diet) for 5 weeks followed by the Mediterranean diet for 5 weeks. The second phase was 20-week weight loss period under free living conditions. This period recommended 500 kcal deficits in their daily energy intake. The Mediterranean diet

with weight maintaining phase was then followed again as the third phase of the study for 5 weeks. The Mediterranean diet plus weight loss program showed the significant decrease in SBP, DBP, insulin, fasting glucose, apolipoprotein B, and TG while the Mediterranean diet without weight loss showed the reduction of TC, LDL-C and TC/HDL-C ratio, compared with the control diet.

In Thailand, the characteristics of traditional foods were different from the Mediterranean diet. Few studies about specific dietary advice for HIV-infected patients have been performed, and some showed the benefit of dietary advice in Thai HIV-infected patients with dyslipidemia. Chotivichien et al. (2016) investigated the effect of nutritional counseling according to NCEP ATP III for 24 weeks in HIV-infected patients. The dietary advice including limiting the consumption of fat to less than 25 % total caloric intake and less than 7 % of total calories from saturated fat, cholesterol to less than 200 mg/day, while maintaining consumption of polyunsaturated fat for up to 10 % of total calories and total fiber to 20 - 30 g per day. It was found that the levels of TC and LDL-C of the patients in the intervention group were reduced when compared with those at baseline. Similarly, Ketchaleaw et al. (2016) investigated the effects of 24-week nutritional counseling on lipid profiles in HIV-infected patients with dyslipidemia. All participants received general advice about healthy diet based on Thai Nutrition Flag, and only the intervention group received nutritional counseling according to NCEP ATP III modified for Thai people. The results showed that TC and LDL-C levels were significantly decreased from baseline in the intervention group after 6 months of the counseling. These previous studies showed that TLC diet program improved blood lipid profiles, BMI and the percentage of body weight from fat was decreased after 12 weeks in HIV-infected patients who used ART at least 6 months. TLC dietary advice consists of dietary intervention among NCEP ATP III, low sodium

intake, promote exercise 30 to 60 minutes per day at least 4 days per week (Singhato, Buranasuksakul, and Rueangsri, 2018).

Besides the dietary counseling on types and characteristics of foods, the effects of dietary supplements in HIV-infected with metabolic syndrome were also investigated. Supplementation with omega-3 fatty acids for 24 weeks was found to decrease TG and VLDL-C levels in HIV-infected Brazilian patients. This study investigated the effect of fish oil (3 g per day) versus soy oil (3 g per day) supplementation for 24 weeks on metabolic outcomes including lipid profiles, insulin resistance and body fat distribution in 121 HIV-infected patients. The results showed no statistically significant differences in TC, LDL-C, HDL-C, TG, insulin resistance, and body fat distribution between group at the end of the study. No change in TG level may be due to low baseline TG level of the patients in this study (Oliveira et al., 2014).

Chromium is an essential micronutrient for the action of insulin and glucose metabolism. With this function, the effects of chromium supplementation were investigated in HIV-infected patient with insulin resistance (Aghdassi et al., 2010). This study was examined the effect of chromium nicotinate supplementation in the dose of 400 mg per day for 16 weeks on lipid profiles and insulin resistance in 46 HIV-infected patients. It was found that the patients had decreased TG level, insulin resistance and increased lean body mass after supplementation when compared to baseline.

Supplementation of soluble fiber showed beneficial effect on blood lipid profile of HIV-infected patients. The effects of passion fruit peel flour, a good source of soluble fiber, on lipid profile in HIV-patients with lipodystrophy were investigated (Marques, 2016). The patients were randomly assigned into the intervention group and the control group. The intervention group received 30 g of passion fruit peel flour per

day with diet counseling for 90 days, and the control group received only diet counseling. The results showed that the patients in the intervention group had significant lower TC and TG levels after 30 days of the intervention. Moreover, decreased LDL-C level and increased HDL-C level were also observed in these patients after 90 days of the intervention.

Based on the previous studies, although there was no specific dietary intervention guideline for HIV-infected with metabolic syndrome, the studies of dietary intervention in these patients showed the beneficial effects of dietary advice on metabolic components such as blood lipid profiles and anthropometric parameters. Thus, the dietary advice could also be applied in the therapeutic plan for HIV/AIDs patients with metabolic syndrome. The healthcare provider should suggest the lifestyle modification for HIV-infected patients with metabolic syndrome with or without medication.

CHAPTER III
MATERIALS AND METHODS

3.1 Participants

HIV-infected patients (both males and females) aged 18 years old and over from HIV-outpatient clinic at Banbung Hospital, Chonburi Province who had received stable combination HAART for at least 3 months were recruited into this study. All of them had been diagnosed with metabolic syndrome or having central obesity plus any two of followings: TG level at least 150 mg/dL or on dyslipidemia treatment, HDL-C less than 40 mg/dL in men or less than 50 mg/dL in women or on drug treatment for reduced HDL-C, systolic blood pressure (SBP) or diastolic blood pressure (DBP) more than or equal to 130 mmHg and 85 mmHg respectively, or on drug treatment for hypertension and fasting blood sugar (FBS) greater than or equal to 100 mg/dL or previously diagnosed with diabetes mellitus. The patients who were pregnant, changed medical use for HIV/AIDs and metabolic syndrome treatment or discontinued antiviral therapy were excluded.

The study protocol was approved by the Ethics Committee of the Faculty of Chonburi Provincial Health Office (Appendix A). Participants received oral and written information about the experimental protocol and signed consent form before they participated in the study (Appendix B).

3.1.1 sample size calculation

$$N = [(Z\alpha+Z\beta)(SD)/D]^2$$

According to Reis et al. (2014), TG level of metabolic syndrome women was decreased by 36.7 $\pm$ 51.1 mg/dL after receiving dietary advice according to dietary

guidelines based on NCEP ATP III for the diagnosis and treatment of metabolic syndrome for 16 weeks.

α = 0.05 (two-sided); Z_α = 1.96

β = 0.10 (0ne-sided); Z_β = 1.28

D = the different of TG level between baseline and the end of study

= 36.7

$N = [(1.96+1.28)(51.1)/36.7]^2$

= 21

Thirty percent of the number (N) was added to adjust the sample size for dropouts.

N = 21/(1-0.3) = 30

Therefore, the number of participants recruited in each group was 30, and the total number of participants in this study was 60.

3.2 Study design

This study was an experimental research. The participants were match-paired by WC, frequency of exercise per week and times of exercise at a time. The study design and experimental details are shown in the Figure 1. The patients participated in a 24-week study. At the beginning of the study (baseline), each patient was interviewed for general information (Appendix C), and dietary intake of the patient was assessed by 24-hr dietary recall (Appendix D) and food frequency questionnaire (FFQ) (Appendix E). Blood samples were collected for measuring lipid profiles including LDL-C, TC, TG, and HDL-C. In addition, FBS, CD4+ and viral loads were determined. Weight, height, WC, hip circumference (HC), and blood pressure were measured. Total daily energy expenditure and BMI were calculated.

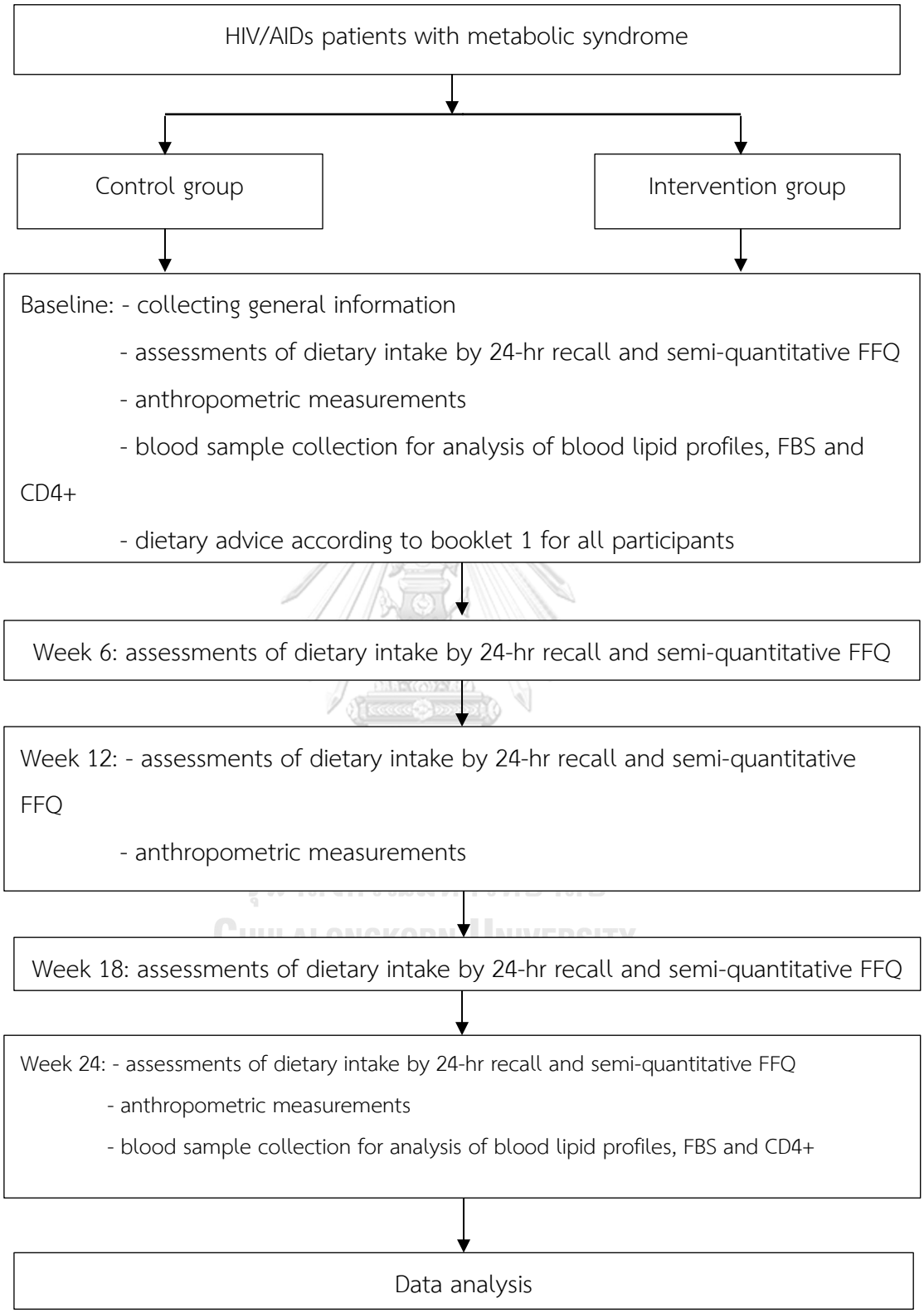

Figure 1 Study design and experimrntal procedure

All participants received the dietary intervention booklet 1 with instruction (Appendix F). The dietary intervention booklet 1 is a general booklet providing the advice on a healthy diet according to Thai nutrition flag. Then the participants were randomly assigned into the intervention and control groups. Only the participants in the intervention group were additionally given the dietary intervention booklet 2 (Appendix G), which provides the advice on appropriate diet for HIV/AIDS patients with metabolic syndrome. The dietary advice in this booklet was appropriately modified for Thai people based on the recommendations from NCEP ATP III, EACS and Mediterranean diet (the modified NEM diet). Dietary intake was assessed by 24-hr dietary recall and FFQ at baseline, week 6, week 12, week 18, and week 24. At the end of the study (week 24), anthropometric measurements were performed, and blood pressure and biochemical parameters were determined again. During the study, the participants were also phoned once a week to ensure that they properly followed the dietary advices.

3.3 Dietary intervention

At baseline, all participants were given the dietary intervention booklet 1 with instruction. It is a general booklet providing the suggestion on a healthy diet for Thai people according to Thai nutrition flag. Meanwhile, only the intervention group received the dietary intervention booklet 2, which provides the information about the modified NEM diet derived from the dietary recommendations following NCEP ATP III, EACS guidelines and Mediterranean diet and was appropriately modified for Thai people. The characteristics of the modified NEM diet compared with these guidelines is shown in Table 2. The dietary advice included consideration of energy intake and the suitable proportion of carbohydrate, protein, fat, dietary fiber, and other nutrients for each participant. The participants received the food exchange list with the information of suitable foods including the types of carbohydrate, protein, fat, and

dietary fiber, as well as the amount of total fat, saturated fat and cholesterol in 100-g of food cooked without added fat. The classification of foods that contain similar nutrients and nearly the same energy value per serving were gathered into one list (the food exchange list). The list comprises of six food groups including milk and product, vegetables, fruits, grains and starches, meats and products, and oils and fat. This tool provides the healthy food choices for the patients so that they could plan a wide variety of menu within their daily food allowances. At week 12, only the intervention group received dietary advice according to dietary intervention booklet 2 again.

Table 2 The characteristics of the modified NEM diet compared with the dietary recommendations following NCEP ATP III, EACS guidelines and Mediterranean diet

Parameters	NCEP ATP III guidelines[1]	EACS guideline[2]	Mediterranean Diet[3]	The Modified NEM diet
Carbohydrate	50 % - 60 % of total calories		High consumption of cereals and whole grain	- 55 - 60 % of total calories - Choosing low glycemic index foods
Protein	Approximately 15 % of total calories	Emphasis on intake of lean meat and fish	- High consumption of nut - Moderate consumption of fish and poultry - Low consumption of red meat	- 15 - 20 % of total calories - High consumption in lean meat, fish and meat with enriched ω-3 fatty acids - Restriction fatty meat and processed meat
Fat - Total fat - Saturated fat - Cholesterol	25%-35% of total calories < 7% of total calories < 200 mg/day	< 30% of total calories Limited intake < 300 mg/day	Olive oil as a primary fat source	25% of total calories < 7% of total calories < 200 mg/day
Fruit and vegetable		Emphasis on intake	High consumption	High consumption
others	Balance energy intake and energy expenditure to maintain desirable body weight/prevent weight gain	Keep caloric intake balanced with energy expenditure	Moderate consumption of red wine	- Maintain caloric intake balanced with energy expenditure - Individuals who obese or overweight were advised to lose weight. - Limited intake of vegetable oil, sugar and salt

[1]The characteristic of diet according to NCEP ATP III guidelines (Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults, 2001)

[2]The characteristic of diet according to EACS guidelines (Lundgren, 2008)

[3]The characteristic of Mediterranean diet (Altomare et al., 2013)

3.4 Study measurements and data collection

3.4.1 Dietary assessment

The habitual dietary intake of each participant was assessed by 24-hr recall and FFQ at baseline, week 8, week 12, week 16, and week 24. The 24-hr recall form contained the dates on which data were recorded, all items and portions of food consumed. The records were evaluated for daily dietary intake including carbohydrate, protein, fat, cholesterol, and dietary fiber by the software INMUCAL Nutrients Database (Institute of Nutrition, Mahidol University, 2013). The FFQ used in this study was the semi-quantitative FFQ that included the frequency of various foods and beverages consumed with the clearly described serving sizes as standardized portions for every item. The participants were interviewed how often each item they consumed in a week.

3.4.2 Anthropometric measurements

Body weight was measured to the nearest 0.1 kg by weight meter while the patients were wearing light clothing without shoes. Height was measured to the nearest 0.1 cm scale by height meter while they were not wearing shoes and stood with their heels against the wall. BMI was calculated from body weight in kilograms divided by the square of height in meter (kg/m^2). The patients were categorized according to the WHO Asia-Pacific guidelines for Asian adults (International Obesity Task Force, 2000) as followed:

BMI (kg/m^2)	Nutritional status
$<$ 18.5	underweight
18.5 - 22.9	normal weight
23.0 - 24.9	overweight
$\geq$ 25	obese

WC was obtained by measuring the distance around the smallest area below the rib cage and above the umbilicus, and hip circumference (HC) was obtained by measure the distance around the largest part of your hips that is the widest part of your buttocks with the use of a non-stretchable measuring tape. Waist to hip circumference ratio (WHR) was then calculated from the WC divided by HC. All anthropometric measurements were assessed at baseline, week 12 and week 24.

3.4.3 Assessments of biochemical parameters and blood pressure

At baseline and the end of study, venous blood samples were obtained from the patients after 12-hour fast. The samples were collected for determining LDL-C, TC, TG, HDL-C, FBS, CD4+, and viral load. These parameters were measured at laboratory department of Banbung hospital. Blood pressure was measured at baseline, week 12 and week 24.

3.5 Statistical analysis

Continuous data were presented as mean ± standard deviation (SD). Distribution of each parameter was tested by Shapiro-Wilk test. Demographic data between the two groups were compared by Chi-square tests. Independent t-test was used to compare the mean difference of normally distribution data between groups while Mann-Whitney *U* test was used to compare the difference between groups when the data was not normally distributed. The difference within group was compared by paired t test for normally distribution data, and Wilcoxon Signed Rank test was used to compare the difference within groups when the data was not normally distributed. When the values of more than two time points were compared, the repeated measures ANOVA was used. For each analysis conducted, the significance level was set at the p-value < 0.05.

CHAPTER IV
RESULTS

4.1 Baseline characteristics of the participants

There were 60 HIV-infected patients with metabolic syndrome participating in this study. The characteristics of the participants are shown in Table 3. Most of them were female (68.3 %). The average age and duration of HIV infection were 46.97 ± 8.44 and 8.40 ± 3.60 years, respectively. Most of the participants had at least one comorbid disease (53.3%). The comorbid diseases found in this study were dyslipidemia (75.0 %), hypertension (21.7 %) and diabetes mellitus (6.7 %). The combination of tenofovir, emtricitabine and efavirenz were the most common antiretroviral regimen used in these participants (50%). Most of the participants had BMI more than 25 kg/m^2 (51.7 %). The education level of most participants was primary school (53.0 %), and 20.0 % of the participants were illiterate. Most of them were merchant or having their own business (46.7 %).

In this study, most of the participants (95.0 %) did not smoke. Rights of medical expenses in the participants were universal health coverage (71.7 %) and social security treatment rights (28.3 %). All the participants did not use dietary supplements and had never received metabolic syndrome information before participating in this study. Most of the participants did not exercise (66.7 %), and the patients who did exercise mostly exercised for 15 - 30 minutes/times (40 %). The results showed that most of the participants ate home-cooked meal (51.0 %) and consumed less than 3 meals per day (58.3 %). Baseline characteristics of the participants in the control and intervention groups were not different.

Table 3 Baseline characteristics of the participants

Parameters	**Total (n = 60) N (%)**	**Control group (n = 30) N (%)**	**Interventio n group (n = 30) N (%)**	p^a
Gender				
Male	19 (31.7)	10 (33.3)	9 (30.0)	0.781
Female	41 (68.3)	20 (66.7)	21 (70.0)	
Age (year)				
21-35	4 (6.7)	2 (6.7)	2 (6.7)	0.961
36-50	37 (61.7)	18 (60.0)	19 (63.3)	
51-65	19 (31.7)	10 (33.3)	9 (30.0)	
Average	47.0 ± 8.4	47.8 ± 8.3	46.1 ± 8.6	0.584
Duration of infection (year)				
< 5	11 (18.3)	6 (20.0)	5 (16.7)	0.361
5 - 10	27 (45.0)	16 (53.3)	11 (18.3)	
11 - 15	21 (35.0)	8 (26.7)	13 (43.3)	
16 - 20	1 (1.7)	0 (0.0)	1 (1.7)	
Average	8.40 ± 3.60	7.60 ± 3.30	9.20 ± 3.77	0.095
Number of comorbid diseases				
0	14 (23.3)	9 (30.0)	5 (16.7)	0.352
1	32 (53.3)	15 (50.0)	17 (56.7)	
2	12 (20.0)	6 (20.0)	6 (20.0)	
3	2 (3.3)	0 (0.0)	2 (6.7)	
Comorbid disease				
Dyslipidemia	45 (75.0)	20 (66.7)	25 (83.3)	0.489
Hypertension	13 (21.7)	6 (20.0)	7 (23.3)	
Diabetes mellitus	4 (6.7)	1 (3.3)	3 (10.0)	

Table 3. Baseline characteristics of the participants (continue)

Parameters	**Total (n = 60) N (%)**	**Control group (n = 30) N (%)**	**Interventio n group (n = 30) N (%)**	***p*[a]**
Medication use				
TDF + FTC + EFV	30 (50.0)	16 (53.3)	14 (46.7)	0.648
TDF + FTC + NVP	6 (10.0)	3 (10.0)	3 (10.0)	
AZT + 3TC + LPV/r	1 (1.7)	0 (0.0)	1 (3.3)	
AZT + 3TC + NVP	14 (23.3)	7 (23.3)	7 (23.3)	
AZT + 3TC + EFV	2 (3.3)	0 (0.0)	2 (6.7)	
TDF + AZT + LPV/r	3 (5.0)	0 (0.0)	1 (3.3)	
TDF + 3TC + NVP	3 (5.0)	2 (6.7)	1 (3.3)	
TDF + 3TC + LPV/r	3 (5.0)	2 (6.7)	1 (3.3)	
Body mass index (kg/m^2)				
18.5 - 22.9	14 (23.3)	7 (23.3)	7 (23.3)	0.089
23.0 - 24.9	15 (25.0)	4 (13.3)	11 (36.7)	
> 25.0	31 (51.7)	19 (63.3)	12 (40.0)	
Education				
Less than primary school	12 (20.0)	6 (20.0)	6 (20.0)	0.803
Primary school degree	32 (53.0)	16 (53.3)	16 (53.3)	
High school degree	10 (16.7)	4 (13.3)	6 (20.0)	
Vocational/technical/Diploma	6 (10.0)	4 (13.3)	2 (6.7)	
Occupation				
No occupation/housewife	22 (36.7)	12 (40.0)	10 (33.3)	0.743
Merchant/own business	28 (46.7)	14 (46.7)	14 (46.7)	
Others	10 (16.7)	4 (13.3)	6 (20.0)	
Cigarette smoking				
Nonsmoker	57 (95.0)	29 (96.7)	28 (93.3)	0.587
Current smoker	3 (5.0)	1 (3.3)	2 (6.7)	

Table 3. Baseline characteristics of the participants (continue)

Parameters	Total (n = 60) N (%)	Control group (n = 30) N (%)	Interventio n group (n = 30) N (%)	*p*[a]
Right of medical expenses				
Universal health coverage	43 (71.7)	23 (76.7)	20 (66.7)	0.567
Social security treatment	17 (28.3)	7 (23.3)	10 (33.3)	
Dietary supplement using before study				
No	60 (100.0)	30 (100.0)	30 (100.0)	
Yes	0 (0.0)	0 (0.0)	0 (0.0)	
Receiving metabolic syndrome information before study				
No	60 (100.0)	30 (100.0)	30 (100.0)	
Yes	0 (0.0)	0 (0.0)	0 (0.0)	
Exercise				
No exercise	40 (66.7)	20 (66.7)	20 (66.7)	> 0.999
1 - 2 times/week	14 (23.3)	7 (23.3)	7 (23.3)	
3 - 5 times/week	2 (3.3)	1 (3.3)	1 (3.3)	
> 5 times/week	4 (6.7)	2 (6.7)	2 (6.7)	
Times of exercise at a time				
15 minutes	8 (40.0)	4 (40.0)	4 (40.0)	> 0.999
30 minutes	8 (40.0)	4 (40.0)	4 (40.0)	
60 minutes	4 (20.0)	2 (20.0)	2 (20.0)	
Type of food usually consumed				
Home-cooked meal	31 (51.7)	16 (53.3)	15 (50.0)	0.963
Food cooked to order or food served in pits	6 (10.0)	3 (10.0)	3 (10.0)	
Both	23 (38.3)	11 (36.7)	12 (40.0)	

Table 3. Baseline characteristics of the participants (continue)

Parameters	Total (n = 60) N (%)	Control group (n = 30) N (%)	Interventio n group (n = 30) N (%)	p^a
Number of meals per day				
< 3 times/day	35 (58.3)	16 (53.3)	19 (63.3)	0.43
3 times/day	25 (41.7)	14 (46.7)	11 (36.7)	2

[a]Significant relationship between categorical variables was analyzed by χ^2 test, and means between groups were compared by Mann-Whitney *U* test ($p < 0.05$).

HIV = human immunodeficiency virus; BMI = Body mass index; TDF = Tenofovir; FTC = Emtricitabine; EFV = Efavirenz; NVP = Nevirapine; AZT = Zidovudine; 3TC = Lamivudine; LPV/r = Lopinavir/ritonavir

4.2 Baseline dietary requirement and intake of the participants

Baseline daily dietary intakes of the participants are shown in Table 4. Calculated energy requirement of the participants in the control and intervention groups were 2498.16 ± 456.92 kcal/day and 2148.39 ± 439.11 kcal/day, respectively. The participants in the control group had significantly higher energy requirement than those in the intervention group ($p < 0.05$); however, total energy intake of the two groups was not different. Total energy intake was 1998.54 ± 488.76 kcal/day in the control group and was 2033.97 ± 475.98 kcal/day in the intervention group. Amount and energy from the macronutrients including protein, carbohydrate and fat were not different between groups. The ratio of the energy distribution from protein, carbohydrate and fat in the control group was 16 : 56 : 28 while that in the intervention group was 17 : 57 : 26. The participants in the control group had cholesterol intake lower than those in the intervention group (222.34 ± 287.53 mg and 353.12 ± 350.46 mg, respectively) while the intake of saturated fat, sugar and dietary fiber was not significantly different between groups.

Table 4 Daily dietary intakes of the participants at baseline

Parameters	Control group (n = 30)	Intervention group (n = 30)	P^a
Energy requirement (Kcal/day)	2498.16 ± 456.92	2148.39 ± 439.11	0.004
Total energy intake (kcal/day)	1998.54 ± 488.76	2033.97 ± 475.98	0.647[b]
Protein			
g/day	80.95 ± 38.58	85.87 ± 31.60	0.287
Kcal/day	323.81 ± 154.33	343.27 ± 126.38	0.287
% Total calories	15.62 ± 4.43	16.64 ± 4.15	0.359[b]
Carbohydrate			
g/day	275.71 ± 52.98	287.45 ± 76.70	0.367[b]
Kcal/day	1102.84 ± 211.92	1149.78 ± 306.81	0.367
% Total calories	56.11 ± 6.73	57.13 ± 11.09	0.666
Fat			
g/day	63.97 ± 26.52	59.92 ± 28.82	0.367
Kcal/day	575.69 ± 238.64	539.35 ± 259.41	0.367
% Total calories	28.27 ± 7.00	26.22 ± 9.90	0.358[b]
% caloric distribution protein : carbohydrate : fat	16 : 56 : 28	17 : 57 : 26	
Cholesterol (mg)	222.34 ± 287.53	353.12 ± 350.46	0.028
Saturated fat (g)	10.27 ± 9.67	12.33 ± 10.14	0.268
Sugar (g)	39.69 ± 25.58	48.38 ± 27.10	0.186
Dietary fiber (g)	7.38 ± 4.30	10.66 ± 18.34	0.802

[1]Data are expressed as mean ± SD.

[a]Significant difference between groups analyzed by Independent t-test ($p < 0.05$)

[b]Significant difference between groups analyzed by Mann-Whitney *U* test ($p < 0.05$)

4.3 Effect of dietary advice on laboratory parameters

Laboratory parameters of the participants are shown in Table 5. Baseline TC levels in the control group and the intervention group were 197.30 ± 29.59 mg/dL and 203.90 ± 41.79 mg/dL, respectively. TG levels at baseline in the control group and the intervention group were 149.93 ± 62.23 mg/dL and 147.23 ± 71.42 mg/dL, respectively. In the control group, baseline HDL-C levels were 47.00 ± 10.89 mg/dL in males and 49.85 ± 11.34 mg/dL in females while those in the intervention group were 48.00 ± 18.99 mg/dL in males and 49.71 ± 13.74 mg/dL in females. It was found that baseline FBS levels were 99.70 ± 26.18 mg/dL in the control group and 108.83 ± 33.12 mg/dL in the intervention group. In this study, CD4 number of the participants in the control group was 582.20 ± 205.08 cell/mm^3, and in the intervention group was 657.90 ± 265.96 cell/mm^3. Viral load levels at baseline in the control group and the intervention group were 21.03 ± 5.66 copies/mL and 20.17 ± 0.91 copies/mL, respectively All blood parameters at baseline did not differ between groups. At the end of the study, the participants in the intervention group had significantly lower TG and FBS levels when compared with baseline (p = 0.008 and p <0.001, respectively). In addition, it appeared that the participants in the intervention group had significantly lower TG level than those in the control group at week 24 (p = 0.014).

Table 5 Effect of dietary advice on laboratory parameters

Parameters	Control group (n = 30)			Intervention group (n = 30)			*P* between group at baseline	*P* between group at week 24
	Baseline	Week 24	*P* within group	Baseline	Week 24	*P* within group		
TC (mg/dL)	197.30 ± 29.59	193.37 ± 29.04	0.387	203.90 ± 41.79	193.47 ± 35.69	0.074	0.483	0.991
TG (mg/dL)	149.93 ± 62.23	163.00 ± 73.37	0.156	147.23 ± 71.42	115.57 ± 44.87	0.008[a]	0.636	0.014[b]
HDL-C (mg/dL)	48.90 ± 10.85	46.70 ± 11.03	0.122	49.20 ± 15.18	51.20 ± 11.35	0.217	0.728	0.125
Male	47.00 ± 10.89	44.80 ± 12.52	0.206	48.00 ± 18.99	48.33 ± 15.55	1.000	0.886	0.780
Female	49.85 ± 11.34	47.65 ± 10.42	0.157	49.71 ± 13.74	52.43 ± 9.21	0.180	0.973	0.147
LDL-C (mg/dL)	118.37 ± 27.89	114.02 ± 21.90	0.296	125.19 ± 38.05	119.15 ± 30.01	0.272	0.432	0.453
FBS (mg/dL)	99.70 ± 26.18	100.77 ± 23.29	0.845	108.83 ± 33.12	101.90 ± 27.78	< 0.001[a]	0.101	0.842
CD4 (cell/mm^3)	582.20 ± 205.08	591.03 ± 191.06	0.560	657.90 ± 265.96	674.00 ± 218.35	0.537	0.222	0.123
Viral load (copies/mL)	21.03 ± 5.66	20.00 ± 0.00	0.317	20.17 ± 0.91	20.00 ± 0.00	0.317	0.981	> 0.999

[1]Data are expressed as mean ± SD., TC = total cholesterol; TG = triglyceride; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; FBS = fasting blood sugar; CD = cluster of differentiation

[a]Significant difference within group at week 24 analyzed by Wilcoxon Signed Ranks test ($p < 0.05$)

[b]Significant difference between groups at week 24 analyzed by Mann-Whitney *U* test ($p < 0.05$)

4.4 Effect of dietary advice on anthropometry and blood pressure

Anthropometric parameters and blood pressure are shown in Table 6 Baseline BMI of the patients in the control and the intervention groups were 26.48 ± 4.35 kg/m^2 and 25.59 ± 4.14 kg/m^2, respectively. The participants in both groups had similar average waist circumference at baseline (90.90 ± 6.13 cm). Regarding of gender, waist circumference of male in the control and the intervention groups were 95.40 ± 4.06 cm and 96.44 ± 4.16 cm, respectively, and in female were 88.65 ± 5.80 cm and 88.52 ± 5.28 cm, respectively. Baseline mean SBP in the control and the intervention groups were 138.53 ± 12.14 mmHg and 136.63 ± 10.59 mmHg, respectively. Mean DBP in the control and the intervention groups were 84.83 ± 8.58 mmHg and 80.60 ± 13.36 mmHg, respectively. All baseline anthropometric parameters and blood pressure did not differ between groups. The results showed that after receiving the advice based on the modified NEM diet, the participants in the intervention group had significantly decreased weight at week 12 and week 24 when compared with baseline. In the intervention group, BMI, WC and systolic blood pressure were significantly decreased at week 24 when compared with baseline while diastolic blood pressure did not change. There were no changes in any parameters in the control group throughout study. It was found that at the end of the study, blood pressure, both systolic and diastolic, in the intervention group was significantly lower than those in the control group ($p < 0.05$).

Table 6 Effect of dietary advice on anthropometric parameters and blood pressure

Parameters	Control group (n = 30)			Intervention group (n = 30)		
	Baseline	Week 12	Week 24	Baseline	Week 12	Week 24
Weight (kg)	68.90 ± 15.47[a]	69.13 ± 15.29[a]	69.10 ± 15.39[a]	66.33 ± 12.41[a]	65.57 ± 11.52[b]	64.60 ± 11.27[c]
BMI (kg/m^2)	26.48 ± 4.35[a]	26.60 ± 4.31[a]	26.58 ± 4.34[a]	25.59 ± 4.14[a]	25.31 ± 3.92[a]	24.95 ± 3.90[b]
Waist circumference (cm)	90.90 ± 6.13[a]	91.27 ± 6.28[a]	91.20 ± 6.70[a]	90.90 ± 6.13[a]	90.40 ± 5.96[a]	88.83 ± 6.57[b]
Male	95.40 ± 4.06[a]	95.70 ± 4.37[a]	96.00 ± 5.33[a]	96.44 ± 4.16[a]	95.33 ± 4.39[a]	93.22 ± 5.29[b]
Female	88.65 ± 5.80[a]	89.05 ± 5.97[a]	88.80 ± 6.07[a]	88.52 ± 5.28[a]	88.29 ± 5.30[ab]	86.95 ± 6.25[b]
Blood pressure						
Systolic	138.53 ± 12.14[a]	137.40 ± 11.60[a]	137.13 ± 11.48[a]	136.63 ± 10.59[a]	133.67 ± 9.02[b]	127.43 ± 10.39[c,*]
Diastolic	84.83 ± 8.58[a]	84.20 ± 6.90[a]	84.33 ± 8.52[a]	80.60 ± 13.36[a]	80.73 ± 8.70[a]	79.23 ± 7.81[a,*]

[1]Data are expressed as means ± SD.

BMI = body mass index

[a,b,c]Means with different superscripts in the same row indicate significant differences among time points in each group ($p < 0.05$).

*Significant difference between groups at the same time points analyzed by Independent t- test ($p<0.05$)

4.5 Effect of dietary advice on daily dietary intake

4.5.1 Dietary intake evaluated by 24-hr recall

Effects of dietary advice on daily dietary intake data from 24-hr recall are shown in Table 7. There was no difference in any dietary intake at baseline between groups. At the end of the study, the participants in the intervention group had lowered total energy intake at week 24 (from 2033.97 ± 475.98 kcal/day at baseline to 1416.34 ± 283.48 kcal/day at week 24) ($p < 0.001$). When compared between groups, the participants in the intervention group had significantly lower total energy intake than those in the control group at week 6, week 12, week 18, and week 24 ($p = 0.014$, 0.004, 0.002, and < 0.001, respectively). Total energy intake in the intervention group was significantly decreased at all time points when compared with baselines ($p < 0.05$).

There was no change in amount and calories of protein intake throughout the study in both groups. However, significantly higher amount of protein intake was found in the intervention group than the control group at week 18 ($p = 0.001$) and week 24 ($p = 0.042$). The calories from protein was also significantly higher in the intervention group than in the control group at week 18 ($p = 0.001$). After receiving the advice based on the modified NEM diet, the participants in the intervention group had significant increase in percentage of total caloric intake from protein at every time point ($p < 0.05$).

For carbohydrate intake, amount of carbohydrate intake in both groups was significantly decreased at week 6, week 12, week 18, and week 24 when compared with baseline ($p = 0.006$, 0.005, 0.005, < 0.001 in the control group and $p < 0.001$ at all time points in the intervention group, respectively). Similar results were also found for the calories from carbohydrate intake. The significant differences in amount of carbohydrate intake between groups were found at week 12, week 18 and week 24 (p

= 0.001, 0.010 and 0.024, respectively). When compared with baseline, the percentage of total caloric intake from carbohydrate in the control group was significantly decreased at week 6, week 12, week 18, and week 24 (p = 0.023, 0.014, 0.005, and 0.002, respectively) while that in the intervention group was significantly decreased at week 12 and week 18 (p = 0.010 and 0.025). The percentage of total caloric intake from carbohydrate in the intervention group was significantly higher than the control group was at week 24 (p = 0.025).

In this study, amount of fat intake in the intervention group was significantly decreased at week 12, week 18 and week 24 (p = 0.024, 0.010 and < 0.001) while no difference in amount of fat intake was observed throughout the study in the control group. When compared between groups, the participants in the intervention group had significantly lower fat intake than those in the control group at week 6, week 12, week 18, and week 24 (p < 0.001, 0.001, < 0.001, and < 0.001, respectively). The results showed that the participants in the control group had significantly decreased cholesterol intake at week 24 compared with week 6, week 12 and week 18 (p = 0.005, 0.033 and 0.015). There was no change in cholesterol intake of the participants in the intervention group throughout the study; however, the amount of cholesterol consumed was significantly higher in the intervention group than the control group at all time points (p = 0.028, 0.005, 0.076, 0.006 and < 0.001). When compared within group, the participants in the control group had significantly increased saturated fat intake from baseline at week 6 and week 18 (p = 0.014 and 0.003) while those in the intervention group had significantly decreased saturated fat intake from baseline at week 24 (p = 0.047). It appeared that the participants in the intervention group had significantly lowered saturated fatty acid intake than those in the control group at week 12, week 18 and week 24 (p = 0.027, < 0.001 and 0.035, respectively).

Sugar intake were not different in the control group at all time points when compared with baseline while it was significantly decreased at week 6, week 12, week 18 and week 24 ($p < 0.001$ for all time points) in the intervention group. Sugar intake between groups was not different at baseline but significant different was found at week 12, week 18 and week 24 ($p = 0.006$, 0.006 and 0.005, respectively). At the end of study, the change in dietary fiber intake was not observed in the control group while significant increase in dietary fiber intake was found in the intervention group at week 6, week 12, week 18 and week 24 ($p < 0.001$ for all time points).

Table 7 Effects of dietary advice on daily dietary intake evaluated by 24-hr recall

Parameters	Control group (n = 30)	Intervention group (n = 30)	*P*
Total energy (Kcal)			
Baseline	1998.54 ± 488.76[a]	2033.97 ± 475.98[a]	0.777
Week 6	1872.67 ± 356.08[a]	1644.18 ± 343.83[b]	0.014*
Week 12	1812.79 ± 432.99[a]	1518.25 ± 305.60[bc]	0.004*
Week 18	1850.68 ± 351.61[a]	1565.09 ± 330.95[b]	0.002*
Week 24	1716.56 ± 246.13[a]	1416.34 ± 283.48[cd]	< 0.001*
Protein			
g			
Baseline	80.95 ± 38.58[a]	85.87 ± 31.60[a]	0.595
Week 6	71.59 ± 26.54[a]	83.58 ± 25.94[a]	0.082
Week 12	70.85 ± 24.68[a]	77.84 ± 26.19[a]	0.225
Week 18	65.67 ± 16.40[a]	88.77 ± 29.86[a]	0.001*
Week 24	67.11 ± 14.66[a]	77.82 ± 23.97[a]	0.042*
Kcal			
Baseline	323.81 ± 154.33[a]	343.27 ± 126.38[a]	0.595
Week 6	286.35 ± 106.17[a]	334.32 ± 103.75[a]	0.082
Week 12	283.40 ± 98.71[a]	311.37 ± 104.75[a]	0.225
Week 18	262.66 ± 65.59[a]	355.09 ± 119.45[a]	0.001*
Week 24	268.46 ± 58.62[a]	311.28 ± 95.90[a]	0.076
% total calories			
Baseline	15.62 ± 4.43[a]	16.65 ± 4.15[a]	0.359
Week 6	15.06 ± 3.65[a]	20.48 ± 5.67[b]	< 0.001[#]
Week 12	15.52 ± 3.59[a]	20.66 ± 6.53[b]	< 0.001[#]
Week 18	14.54 ± 4.29[a]	22.39 ± 4.28[b]	< 0.001*
Week 24	15.70 ± 2.97[a]	22.15 ± 5.75[b]	< 0.001[#]

Table 7 Effects of dietary advice on daily dietary intake evaluated by 24-hr recall (continue)

Parameters	Control group (n = 30)	Intervention group (n = 30)	*P*
Carbohydrate			
g			
Baseline	275.71 ± 52.98[a]	287.45 ± 76.70[a]	0.493
Week 6	239.02 ± 50.00[b]	215.48 ± 44.10[b]	0.058
Week 12	235.15 ± 55.89[bc]	192.24 ± 35.68[c]	0.001*
Week 18	235.59 ± 64.04[bc]	199.64 ± 35.27[bc]	0.010*
Week 24	215.73 ± 34.13[c]	190.42 ± 48.99[bc]	0.024*
Kcal			
Baseline	1102.84 ± 211.92[a]	1149.78 ± 306.81[a]	0.493
Week 6	956.07 ± 200.00[b]	861.94 ± 176.38[b]	0.058
Week 12	940.58 ± 223.56[bc]	768.97 ± 142.71[c]	0.001*
Week 18	942.35 ± 256.14[bc]	798.57 ± 141.10[bc]	0.010*
Week 24	862.92 ± 136.50[c]	761.67 ± 195.98[bc]	0.024*
% total calories			
Baseline	56.11 ± 6.73[a]	57.13 ± 11.09[ab]	0.525
Week 6	51.42 ± 9.15[b]	53.00 ± 7.53[bc]	0.225
Week 12	52.04 ± 6.18[b]	51.30 ± 6.70[cd]	0.664
Week 18	50.27 ± 6.73[b]	52.03 ± 7.80[ce]	0.353
Week 24	50.43 ± 6.26[b]	53.47 ± 6.19[be]	0.025[#]
Fat			
g			
Baseline	63.97 ± 26.52[a]	59.92 ± 28.82[a]	0.367
Week 6	70.44 ± 21.11[a]	49.58 ± 19.66[ab]	< 0.001*
Week 12	81.36 ± 85.00[a]	48.36 ± 19.89[b]	0.001[#]
Week 18	72.46 ± 17.91[a]	45.39 ± 19.21[bd]	< 0.001*
Week 24	65.40 ± 17.42[a]	37.91 ± 8.95[cd]	< 0.001[#]

Table 7 Effects of dietary advice on daily dietary intake evaluated by 24-hr recall (continue)[1]

Parameters	Control group (n = 30)	Intervention group (n = 30)	*P*
Fat			
Kcal			
Baseline	575.69 ± 238.64[a]	539.35 ± 259.41[a]	0.367
Week 6	633.94 ± 189.94[a]	446.21 ± 176.92[ab]	< 0.001*
Week 12	732.20 ± 765.01[a]	435.27 ± 179.05[b]	0.001[#]
Week 18	652.16 ± 161.24[a]	408.49 ± 172.86[bd]	< 0.001*
Week 24	588.64 ± 156.75[a]	341.20 ± 80.55[cd]	< 0.001[#]
% total calories			
Baseline	28.27 ± 7.00[a]	26.22 ± 9.90[ac]	0.344
Week 6	33.52 ± 7.59[a]	26.53 ± 6.67[ac]	< 0.001*
Week 12	32.43 ± 5.82[a]	28.04 ± 7.48[ab]	0.014*
Week 18	35.19 ± 6.46[a]	25.58 ± 7.88[ac]	< 0.001*
Week 24	33.87 ± 6.19[a]	24.38 ± 4.90[c]	< 0.001*
Cholesterol (mg)			
Baseline	223.34 ± 287.53[ab]	353.12 ± 350.46[a]	0.028[#]
Week 6	240.13 ± 136.75[b]	353.02 ± 160.43[a]	0.005*
Week 12	269.67 ± 239.20[bc]	346.27 ± 211.73[a]	0.076
Week 18	228.80 ± 173.51[bd]	359.19 ± 178.16[a]	0.006*
Week 24	149.30 ± 92.85[ae]	375.55 ± 182.15[a]	< 0.001*
Saturated fat (g)			
Baseline	10.27 ± 9.67[ab]	12.33 ± 10.14[ab]	0.268
Week 6	17.43 ± 13.31[cd]	13.00 ± 11.77[bc]	0.121
Week 12	14.00 ± 11.01[ac]	8.74 ± 7.47[ad]	0.027[#]
Week 18	19.63 ± 13.18[c]	9.20 ± 7.34[abd]	< 0.001[#]
Week 24	14.06 ± 11.31[ad]	7.61 ± 4.54[de]	0.035[#]

Table 7 Effects of dietary advice on daily dietary intake evaluated by 24-hr recall (continue)[1]

Parameters	Control group (n = 30)	Intervention group (n = 30)	*P*
Sugar (g)			
Baseline	39.69 ± 25.58[a]	48.38 ± 27.10[a]	0.186
Week 6	33.92 ± 24.11[a]	29.08 ± 18.84[b]	0.469
Week 12	37.36 ± 19.74[a]	24.07 ± 15.26[bc]	0.006[#]
Week 18	45.60 ± 33.27[a]	25.53 ± 15.63[b]	0.006[#]
Week 24	32.29 ± 18.61[a]	19.18 ± 11.22[c]	0.005[#]
Dietary fiber (g)			
Baseline	7.38 ± 4.30[a]	10.66 ± 18.34[a]	0.802
Week 6	6.63 ± 4.49[a]	12.37 ± 5.23[bc]	< 0.001*
Week 12	6.04 ± 5.28[a]	10.97 ± 4.08[b]	< 0.001*
Week 18	7.39 ± 5.14[a]	14.70 ± 4.58[cd]	< 0.001*
Week 24	6.90 ± 3.79[a]	14.26 ± 4.30[d]	< 0.001*

[1]Data are expressed as mean ± SD.

[a,b,c]Means with different superscripts in the same column indicate significant differences among time points in each group ($p < 0.05$).

*Significant difference between groups analyzed by Independent t- test ($p < 0.05$)

[#]Significant difference between groups analyzed by Mann-Whitney *U* test ($p < 0.05$)

4.5.2 Dietary intake evaluated by semi-quantitative FFQ

Effects of dietary advice on amount of nutrient intake from semi-quantitative FFQ are shown in Table 8, and the frequencies of food items consumed per week are shown in Table 9. There was no difference in any nutrient intake at baseline between groups. At the end of the study, the participants in the intervention group had lowered total energy intake at week 24 (from 1938.38 ± 333.29 kcal/day at baseline to 1702.67 ± 183.58 kcal/day at week 24) ($p < 0.001$). When compared between groups, the participants in the intervention group had significantly lower total energy intake than those in the control group at week 6, week 12, week 18, and week 24 ($p = 0.046$, 0.024, 0.001, and 0.001, respectively). Total energy intake in the intervention group was significantly decreased at all time points when compared with baseline ($p < 0.05$), while total energy intake in the control group did not change throughout the study.

There was no change in amount and calories of protein intake throughout the study in the control group. However, significantly higher amount of protein intake was found in the intervention group when compared with baseline at all time points ($p < 0.05$). The calories from protein was also significantly higher in the intervention group than in the control group at week 6, week 12, week 18, and week 24 ($p = 0.003$, < 0.001, < 0.001, and < 0.001, respectively). After following the advice based on the modified NEM diet, the participants in the intervention group had significant increase in percentage of total caloric intake from protein at every time point ($p < 0.05$), compared with baseline. The data from food frequency questionnaires showed that protein consumption of the participants in both groups was not different at baseline but the difference was observed after 24 weeks of the study. The participants in intervention group had decreased fatty meat consumption and increased consumption of lean meat and meat rich in omega-3 fatty acids. The consumption of whole milk and low-fat milk was similar between both groups.

For carbohydrate intake, there was no change in amount of carbohydrate intake throughout the study in both groups, except at week 18 that the participants in the intervention group had significantly increased amount of carbohydrate when compared with baseline ($p < 0.05$). Similar results were also found for the calories from carbohydrate intake. The significant differences in amount of carbohydrate intake between groups were not found at any time points. When compared with baseline, the percentage of total caloric intake from carbohydrate in the control group was not changed throughout the study while that in the intervention group was significantly increased at every time points ($p < 0.05$). The percentage of total caloric intake from carbohydrate in the intervention group was significantly higher than that of the control group at week 6, week 12, week 18, and week 24 ($p = 0.004$, < 0.001, < 0.001, and < 0.001, respectively). At the end of study, the participants in the intervention group had increased frequency of brown rice consumption while most of the participants in the control group still consumed white rice every day.

In this study, amount of fat intake in the intervention group was significantly decreased at week 6, week 12, week 18 and week 24 ($p < 0.05$) while significantly increased amount of fat intake was observed in the control group at week 12 ($p < 0.05$). When compared between groups, the participants in the intervention group had significantly lower fat intake than those in the control group at week 6, week 12, week 18, and week 24 ($p < 0.001$, 0.001, < 0.001 and < 0.001, respectively). The results showed no change in cholesterol intake of the participants in the control group throughout the study. In contrast, cholesterol intake in the intervention group was significantly increased at all time points when compared with baseline ($p < 0.05$). The amount of cholesterol consumed was not different between groups at baseline but significantly higher in the intervention group than the control group at week 6, week 12, week 18, and week 24 ($p = 0.043$, < 0.001, < 0.001 and < 0.001). When compared

within group, there was no change in amount of saturated fat intake throughout the study in the control group. However, the participants in the intervention group had significantly decreased saturated fat intake from baseline at week 6, week 12, week 18 and week 24 ($p < 0.05$ for all time points). It appeared that the participants in the intervention group had significantly lowered saturated fat intake than those in the control group at week 6, week 12, week 18 and week 24 ($p < 0.001$ at every time point). The frequencies of animal oil/palm oil and vegetable oil consumption in the participants in both groups were similar, but after 24 weeks of the dietary advice based on the modified NEM diet, the participant in the intervention group had decreased frequency of animal oil/palm oil intake.

Sugar intake were not different in the control group at all time points when compared with baseline while it was significantly increased at week 12 and week 18 ($p < 0.05$) in the intervention group. Sugar intake between groups was not different at baseline, but significant difference was found at week 6, week 12, week 18 and week 24 ($p = 0.046$, < 0.001, 0.004 and 0.025, respectively). At the end of study, the change in dietary fiber intake was not observed in the control group while significant increase in dietary fiber intake was found in the intervention group at week 6, week 12, week 18 and week 24 ($p < 0.001$ for all time points). At baseline, there was no difference in fruit and vegetable consumptions of the participants in both groups. After 24 weeks of the dietary advice, it appeared that most of the participants in the intervention group consumed fruits and vegetables everyday (56.7 % and 96.7 %, respectively). The results of the study showed that the participants in the intervention group generally well followed the advice based on the modified NEM diet (Table 10).

Table 8 Effects of dietary advice on dietary intake from semi-quantitative food frequency questionaire

Parameters	Control group (n = 30)	Intervention group (n = 30)	*P*
Total energy (Kcal)			
Baseline	1889.98 ± 231.87[a]	1938.38 ± 333.29[a]	0.517
Week 6	1980.01 ± 308.73[a]	1840.24 ± 211.28[b]	0.046*
Week 12	1949.61 ± 276.05[a]	1793.62 ± 245.72[bc]	0.024*
Week 18	1964.29 ± 259.33[a]	1770.19 ± 167.48[b]	0.001*
Week 24	1921.48 ± 277.59[a]	1702.67 ± 183.58[c]	0.001*
Protein			
g			
Baseline	64.90 ± 7.88[a]	68.52 ± 17.99[a]	0.700
Week 6	69.88 ± 16.98[a]	81.56 ± 19.17[b]	0.003[#]
Week 12	67.97 ± 12.99[a]	90.35 ± 19.29[c]	< 0.001[#]
Week 18	69.83 ± 16.41[a]	98.51 ± 19.89[d]	< 0.001[#]
Week 24	66.54 ± 7.66[a]	98.46 ± 15.70[d]	< 0.001[#]
Kcal			
Baseline	259.59 ± 31.52[a]	274.10 ± 71.94[a]	0.700
Week 6	279.52 ± 67.93[a]	326.23 ± 76.67[b]	0.003[#]
Week 12	271.87 ± 51.95[a]	361.39 ± 77.17[c]	< 0.001[#]
Week 18	279.31 ± 65.62[a]	394.05 ± 79.55[d]	< 0.001[#]
Week 24	266.16 ± 30.65[a]	393.83 ± 62.78[d]	< 0.001[#]
% total calories			
Baseline	13.90 ± 1.74[a]	14.22 ± 2.65[a]	0.756
Week 6	14.24 ± 2.70[a]	17.76 ± 3.08[b]	< 0.001[#]
Week 12	14.12 ± 2.51[a]	20.53 ± 4.08[c]	< 0.001[#]
Week 18	14.28 ± 2.45[a]	22.60 ± 4.29[d]	< 0.001[#]
Week 24	14.11 ± 2.11[a]	23.52 ± 3.13[d]	< 0.001[#]

Table 8 Effects of dietary advice on dietary intake from semi-quantitative food frequency questionnaire (continue)[1]

Parameters	Control group (n = 30)	Intervention group (n = 30)	*P*
Carbohydrate			
g			
Baseline	228.70 ± 34.75[a]	223.81 ± 38.52[a]	0.515
Week 6	229.86 ± 39.45[a]	237.22 ± 30.91[ab]	0.274
Week 12	224.21 ± 35.67[a]	235.19 ± 39.12[ab]	0.104
Week 18	227.69 ± 34.39[a]	240.67 ± 33.57[b]	0.141
Week 24	225.84 ± 36.18[a]	232.65 ± 31.86[ab]	0.203
Kcal			
Baseline	914.80 ± 139.01[a]	895.22 ±154.07[a]	0.515
Week 6	919.46 ± 157.79[a]	948.86 ± 123.64[ab]	0.274
Week 12	896.85 ± 142.67[a]	940.76 ± 156.46[ab]	0.104
Week 18	910.74 ± 137.55[a]	962.51 ± 134.28[b]	0.141
Week 24	903.36 ± 144.72[a]	930.58 ± 127.44[ab]	0.203
% total calories			
Baseline	48.86 ± 6.14[a]	46.79 ± 5.70[a]	0.203
Week 6	47.00 ± 6.25[a]	52.27 ± 6.00[b]	0.004[#]
Week 12	46.49 ± 5.83[a]	53.02 ± 5.01[bd]	< 0.001[#]
Week 18	46.87 ± 6.02[a]	55.05 ± 3.83[c]	< 0.001[#]
Week 24	47.53 ± 5.87[a]	55.47 ± 4.00[cd]	< 0.001[#]
Fat			
g			
Baseline	78.49 ± 20.08[a]	84.44 ± 22.24[a]	0.280
Week 6	85.71 ± 22.60[ab]	60.88 ± 15.12[b]	< 0.001[#]
Week 12	85.80 ± 21.45[b]	52.05 ± 13.74[c]	< 0.001[#]
Week 18	84.97 ± 21.45[ab]	42.96 ± 9.27[d]	< 0.001[#]
Week 24	82.55 ± 22.12[ab]	39.17 ± 7.39[e]	< 0.001[#]

Table 8 Effects of dietary advice on daily dietary intake from semi-quantitative food frequency questionnaire (continue)[1]

Parameters	Control group (n = 30)	Intervention group (n = 30)	*P*
Fat			
Kcal			
Baseline	706.40 ± 180.68[a]	759.94 ± 200.13[a]	0.280
Week 6	771.40 ± 203.38[ab]	547.93 ± 136.04[b]	< 0.001[#]
Week 12	772.18 ± 193.05[b]	468.45 ± 123.67[c]	< 0.001[#]
Week 18	764.70 ± 180.01[ab]	386.70 ± 83.45[d]	< 0.001[#]
Week 24	742.99 ± 199.08[ab]	352.56 ± 66.49[e]	< 0.001[#]
% total calories			
Baseline	37.24 ± 6.81[a]	38.99 ± 5.91[a]	0.329
Week 6	38.76 ± 6.69[a]	29.96 ± 6.05[b]	< 0.001[#]
Week 12	39.38 ± 6.45[a]	26.45 ± 5.52[c]	< 0.001[#]
Week 18	38.85 ± 6.26[a]	22.35 ± 5.36[d]	< 0.001[#]
Week 24	38.36 ± 6.63[a]	21.01 ± 3.24[d]	< 0.001[#]
Cholesterol (mg)			
Baseline	108.52 ± 22.90[a]	120.35 ±41.12[a]	0.342
Week 6	121.48 ± 39.21[a]	143.54 ± 48.89[b]	0.043[#]
Week 12	118.76 ± 29.82[a]	162.71 ± 47.92[c]	< 0.001[#]
Week 18	123.29 ± 39.07[a]	182.64 ± 48.12[d]	< 0.001[#]
Week 24	113.77 ± 20.73[a]	181.15 ± 46.89[cd]	< 0.001[#]
Saturated fat (g)			
Baseline	32.00 ± 8.26[a]	34.19 ± 8.58[a]	0.280
Week 6	34.53 ± 8.54[a]	23.40 ± 6.07[b]	< 0.001[#]
Week 12	34.51 ± 8.21[a]	19.00 ± 6.54[c]	< 0.001[#]
Week 18	34.40 ± 8.24[a]	14.77 ± 5.04[d]	< 0.001[#]
Week 24	33.16 ± 8.51[a]	13.10 ± 3.14[d]	< 0.001[#]

Table 8 Effects of dietary advice on daily dietary intake from semi-quantitative food frequency questionnaire (continue)[1]

Parameters	Control group (n = 30)	Intervention group (N = 30)	*P*
Sugar (g)			
Baseline	49.97 ± 27.09[a]	48.66 ± 24.47[ab]	0.773
Week 6	51.17 ± 28.61[a]	55.03 ± 20.37[ab]	0.046[#]
Week 12	47.25 ± 24.40[a]	61.29 ± 16.59[c]	< 0.001[#]
Week 18	49.23 ± 24.57[a]	62.58 ± 19.81[c]	0.004[#]
Week 24	48.43 ± 25.35[a]	56.26 ± 19.07[ac]	0.025[#]
Dietary fiber (g)			
Baseline	10.69 ± 3.42[a]	11.36 ± 4.67[a]	0.536
Week 6	11.77 ± 4.78[a]	17.81 ± 4.90[b]	< 0.001[#]
Week 12	10.94 ± 4.33[a]	21.55 ± 6.14[c]	< 0.001[#]
Week 18	11.33 ± 4.63[a]	24.30 ± 5.45[d]	< 0.001[#]
Week 24	10.72 ± 3.75[a]	25.45 ± 2.32[d]	< 0.001[#]

[1]Data are expressed as mean ± SD.

[a,b,c]Means with different superscripts in the same column indicate significant differences among time points in each group ($p < 0.05$).

*Significant difference between groups analyzed by Independent t- test ($p < 0.05$)

[#]Significant difference between groups analyzed by Mann-Whitney *U* test ($p < 0.05$)

Table 9 Effect of dietary advice on the frequency of dietary food intake per week

Items	Control group (n = 30) N (%)					Intervention group (n = 30) N (%)					P^a between group at baseline	P^a between group at week 24
	Baseline	Week 6	Week 12	Week 18	Week 24	Baseline	Week 6	Week 12	Week 18	Week 24		
Meat												
Fatty meat												
Not consumed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (16.7)	20(66.7)	23 (76.7)	0.693	< 0.001
≤ 3 days/week	4 (13.3)	4 (13.3)	6 (20.0)	5 (16.7)	5 (16.7)	6 (20.0)	17 (56.7)	20 (66.7)	8 (26.7)	7 (23.3)		
4-6 days/week	7 (23.3)	4 (13.3)	2 (6.7)	6 (20.0)	3 (10.0)	5 (16.7)	6 (20.0)	4 (13.3)	2 (6.7)	0 (0.0)		
7 days/week	19 (63.3)	22 (73.3)	22 (73.3)	19 (63.3)	22 (73.3)	19 (63.3)	7 (23.3)	1 (3.3)	0 (0.0)	0 (0.0)		
Lean meat												
Not consumed	1 (3.3)	2 (6.7)	1 (3.3)	1 (3.3)	1 (3.3)	1 (3.3)	1 (3.3)	0 (0.0)	0 (0.0)	0 (0.0)	0.989	< 0.001
≤ 3 days/week	17 (56.7)	16 (53.3)	17 (56.7)	17 (56.7)	17 (56.7)	18 (60.0)	8 (26.7)	5 (16.7)	3 (10.0)	0 (0.0)		
4-6 days/week	6 (20.0)	5 (16.7)	5 (16.7)	5 (16.7)	6 (20.0)	5 (16.7)	7 (23.3)	7 (23.3)	3 (10.0)	6 (20.0)		
7 days/week	6 (20.0)	7 (23.3)	7 (23.3)	7 (23.3)	6 (20.0)	6 (20.0)	14 (46.7)	18 (60.0)	24 (80.0)	24 (80.0)		
Rich in omega-3 fatty acids												
Not consumed	4 (13.3)	3 (10.0)	2 (6.7)	3 (10.0)	3 (10.0)	3 (10.0)	1 (3.3)	2 (6.7)	0 (0.0)	0 (0.0)	0.356	< 0.001
≤ 3 days/week	20 (66.7)	23 (76.7)	24 (80.0)	21 (70.0)	23 (76.7)	22 (73.3)	8 (26.7)	3 (10.0)	2 (6.7)	0 (0.0)		
4-6 days/week	6 (20.0)	2 (6.7)	3 (10.0)	4 (13.3)	4 (13.3)	3 (10.0)	11 (36.7)	8 (26.7)	4 (13.3)	6 (20.0)		
7 days/week	0 (0.0)	2 (6.7)	1 (3.3)	2 (6.7)	0 (0.0)	2 (6.7)	10 (33.3)	17 (56.7)	24 (80.0)	24 (80.0)		

Table 9 Effect of dietary advice on the frequency of dietary food intake per week (continued)

Items	Control group (n = 30) N (%)					Intervention group (n = 30) N (%)					P^a between group at baseline	P^a between group at week 24
	Baseline	Week 6	Week 12	Week 18	Week 24	Baseline	Week 6	Week 12	Week 18	Week 24		
Whole milk												
Not consumed	10 (33.3)	10 (33.3)	10 (33.3)	10 (33.3)	11 (36.7)	10 (33.3)	11 (36.7)	17 (56.7)	15 (50.0)	14 (46.7)	0.774	0.393
≤ 3 days/week	8 (26.7)	8 (26.7)	8 (26.7)	6 (20.0)	7 (23.3)	7 (23.3)	6 (20.0)	3 (10.0)	3 (10.0)	4 (13.3)		
4-6 days/week	1 (3.3)	2 (6.7)	2 (6.7)	3 (10.0)	2 (6.7)	3 (10.0)	4 (13.3)	4 (13.3)	3 (10.0)	5 (16.7)		
7 days/week	11 (36.7)	10 (33.3)	10 (33.3)	11 (36.7)	10 (33.3)	10 (33.3)	9 (30.0)	6 (20.0)	9 (30.0)	7 (23.3)		
Fat free /low fat milk												
Not consumed	25 (83.3)	24 (80.0)	25 (83.3)	24 (80.0)	25 (83.3)	24 (80.0)	25 (83.3)	23 (76.7)	22 (73.3)	25 (83.3)	0.546	0.072
≤ 3 days/week	5 (16.7)	4 (13.3)	4 (13.3)	5 (16.7)	4 (13.3)	4 (13.3)	3 (10.0)	2 (6.7)	2 (6.7)	0 (0.0)		
4-6 days/week	0 (0.0)	1 (3.3)	0 (0.0)	1 (3.3)	0 (0.0)	1 (3.3)	2 (6.7)	3 (10.0)	2 (6.7)	2 (6.7)		
7 days/week	0 (0.0)	1 (3.3)	1 (3.3)	0 (0.0)	1 (3.3)	1 (3.3)	0 (0.0)	2 (6.7)	4 (13.3)	3 (10.0)		
Dairy products												
Not consumed	12 (40.0)	15 (50.0)	13 (43.3)	13 (43.3)	12 (40.0)	15 (50.0)	23 (76.7)	28 (93.3)	28 (93.3)	28 (93.3)	0.748	< 0.001
≤ 3 days/week	7 (23.3)	5 (16.7)	5 (16.7)	5 (16.7)	6 (20.0)	5 (16.7)	6 (20.0)	0 (0.0)	2 (6.7)	2 (6.7)		
4-6 days/week	1 (3.3)	2 (6.7)	2 (6.7)	2 (6.7)	1 (3.3)	2 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
7 days/week	10 (33.3)	8 (26.7)	10 (33.3)	10 (33.3)	11 (36.7)	8 (26.7)	1 (3.3)	2 (6.7)	0 (0.0)	0 (0.0)		

Table 9 Effect of dietary advice on the frequency of dietary food intake per week (continued)

Items	Control group (n = 30) N (%)					Intervention group (n = 30) N (%)					P^a between group at baseline	P^a between group at week 24
	Baseline	Week 6	Week 12	Week 18	Week 24	Baseline	Week 6	Week 12	Week 18	Week 24		
Animal 0il/ Palm oil												
Not consumed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (23.3)	7 (23.3)	0.819	< 0.001
≤ 3 days/week	2 (6.7)	1 (3.3)	1 (3.3)	0 (0.0)	2 (6.7)	1 (3.3)	11 (36.7)	20 (66.7)	17 (56.7)	20 (66.7)		
4-6 days/week	7 (23.3)	8 (26.7)	6 (20.0)	8 (26.7)	6 (20.0)	8 (26.7)	8 (26.7)	7 (23.3)	4 (13.3)	3 (10.0)		
7 days/week	21 (70.0)	21 (70.0)	23 (76.7)	22 (73.3)	22 (73.3)	21 (70.0)	11 (36.7)	3 (10.0)	2 (6.7)	0 (0.0)		
Vegetable oil												
Not consumed	10 (33.3)	10 (33.3)	8 (26.7)	8 (26.7)	8 (26.7)	9 (30.0)	10 (33.3)	6 (20.0)	5 (16.7)	6 (20.0)	0.676	0.205
≤ 3 days/week	8 (26.7)	9 (30.0)	10 (33.3)	12 (40.0)	8 (26.7)	11 (36.7)	6 (20.0)	12 (40.0)	15 (50.0)	14 (46.7)		
4-6 days/week	3 (10.0)	1 (3.3)	1 (3.3)	2 (6.7)	2 (6.7)	1 (3.3)	7 (23.3)	9 (30.0)	5 (16.7)	4 (13.3)		
7 days/week	9 (30.0)	10 (33.3)	11 (36.7)	8 (26.7)	12 (40.0)	9 (30.0)	7 (23.3)	3 (10.0)	5 (16.7)	6 (20.0)		

Table 9 Effect of dietary advice on the frequency of dietary food intake per week (continued)

Items	Control group (n = 30) N (%)					Intervention group (n = 30) N (%)					P^a between group at baseline	P^a between group at week 24
	Baseline	Week 6	Week 12	Week 18	Week 24	Baseline	Week 6	Week 12	Week 18	Week 24		
White rice												
Not consumed	0 (0.0)	1 (3.3)	0 (0.0)	1 (3.3)	0 (0.0)	1 (3.3)	4 (13.3)	18 (60.0)	24 (80.0)	27 (90.0)	0.529	< 0.001
≤ 3 days/week	2 (6.7)	3 (10.0)	4 (13.3)	3 (10.0)	3 (10.0)	3 (10.0)	11 (36.7)	5 (16.7)	3 (10.0)	3 (10.0)		
4-6 days/week	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)		
7 days/week	28 (93.3)	26 (86.7)	26 (86.7)	28 (93.3)	27 (90.0)	26 (86.7)	12 (40.0)	7 (23.3)	3 (10.0)	0 (0.0)		
Brown rice												
Not consumed	28 (93.3)	25 (83.3)	26 (86.7)	25 (83.3)	27 (90.0)	25 (83.3)	12 (40.0)	7 (23.3)	3 (10.0)	0 (0.0)	0.228	< 0.001
≤ 3 days/week	2 (6.7)	5 (16.7)	4 (13.3)	5 (16.7)	3 (10.0)	5 (16.7)	3 (10.0)	1 (3.3)	0 (0.0)	0 (0.0)		
4-6 days/week	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (36.7)	4 (13.3)	3 (10.0)	3 (10.0)		
7 days/week	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (13.3)	17 (56.7)	24 (80.0)	27 (90.0)		

Table 9 Effect of dietary advice on the frequency of dietary food intake per week (continued)

Items	Control group (n = 30) N (%)					Intervention group (n = 30) N (%)					*P*[a] between group at baseline	*P*[a] between group a week 2
	Baseline	Week 6	Week 12	Week 18	Week 24	Baseline	Week 6	Week 12	Week 18	Week 24		
Fruit												
Not consumed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.577	< 0.001
≤ 3 days/week	22 (73.3)	22 (73.3)	23 (76.7)	22 (73.3)	22 (73.3)	21 (70.0)	15 (50.0)	9 (30.0)	4 (13.3)	3 (10.0)		
4-6 days/week	1 (3.3)	2 (6.7)	2 (6.7)	3 (10.0)	2 (6.7)	3 (10.0)	9 (30.0)	13 (43.3)	14 (46.7)	10 (33.3)		
7 days/week	7 (23.3)	6 (20.0)	5 (16.7)	5 (16.7)	6 (20.0)	6 (20.0)	6 (20.0)	8 (26.7)	12 (40.0)	17 (56.7)		
Non-starchy vegetables												
Not consumed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.670	< 0.001
≤ 3 days/week	15 (50.0)	18 (60.0)	18 (60.0)	17 (56.7)	18 (60.0)	18 (60.0)	2 (6.7)	2 (6.7)	1 (3.3)	0 (0.0)		
4-6 days/week	5 (16.7)	4 (13.3)	5 (16.7)	4 (13.3)	6 (20.0)	5 (16.7)	16 (53.3)	6 (20.0)	3 (10.0)	1 (3.3)		
7 days/week	10 (33.3)	8 (26.7)	7 (23.3)	9 (30.0)	6 (20.0)	7 (23.3)	12 (40.0)	22 (73.3)	26 (86.7)	29 (96.7)		
Starchy vegetables												
Not consumed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.158	< 0.001
≤ 3 days/week	26 (86.7)	24 (80.0)	24 (80.0)	28 (93.3)	24 (80.0)	25 (83.3)	4 (13.3)	3 (10.0)	3 (10.0)	0 (0.0)		
4-6 days/week	0 (0.0)	3 (10.0)	3 (10.0)	0 (0.0)	3 (10.0)	3 (10.0)	14 (46.7)	4 (13.3)	1 (3.3)	1 (3.3)		
7 days/week	4 (13.3)	3 (10.0)	3 (10.0)	2 (6.7)	3 (10.0)	2 (6.7)	12 (40.0)	23 (76.7)	26 (86.7)	29 (96.7)		

[a]Significant relationship between categorical variables at week 0 and week 24 was analyzed by χ^2 test.

Table 10 Adherence of participants in the intervention group to the modified NEM diet

Characteristics	**The Modified NEM diet**	**Adherence of the participants to the modified NEM diet**
Carbohydrate	- 55 - 60 % of total calories	- Yes
	- Choosing low glycemic index foods	- Yes
Protein	- 15 - 20 % of total calories	- 22 - 23 % of total calories
	- High consumption in lean meat, fish and meat with enriched omega 3 fatty acids	- Yes
	- Restriction fatty meat and processed meat	- Yes
Fat		
Total fat	25 % of total calories	- Yes
Saturated fat	< 7 % of total calories	- Yes
Cholesterol	< 200 mg/day	- the amount was increased after receiving dietary advice
Fruit and vegetable	High consumption	- Yes
Others	- Maintaining caloric intake balanced with energy expenditure	- Yes
	- Weight loss advice for participants who were obese or overweight	- Yes
	- Limit intake of vegetable oil, sugar and salt	- Yes (for vegetable oil and sugar, but no report for salt intake)

4.6 Effect of dietary advice on components of metabolic syndrome

Table 11 shows the effects of dietary advice on components of metabolic syndrome. At baseline all participants had WC less than 90 cm (male) and 80 cm (female). The results showed that all components of metabolic syndrome at baseline did not differ between group. The number of participants who had TG level more than or equal to 150 mg/dL or on specific treatment for this lipid abnormality were decreased from 13 (43.3 %) at baseline to 12 (40.0 %) at week 24 in the control group and from 13 (43.3 %) at baseline to 5 (16.7 %) at week 24 in the intervention group. The number of participants who had BP higher or equal to 130/85 mmHg or on treatment of previously diagnosed hypertension were decreased from 28 (93.3 %) at baseline to 27 (90.0 %) at week 24 in the control group, while those in the intervention group were decreased from 26 (86.7 %) to 16 (53.3 %).

At baseline, every participant had at least 3 components of metabolic syndrome (central obesity plus two other metabolic components) according to IDF criteria. However, after receiving dietary advice, the number of participants who had at least 3 components of metabolic components in both groups were less than those at baseline. In addition, the number of participants with metabolic syndrome according to IDF criteria was decreased from 30 (100 %) at baseline to 24 (20.0 %) at week 24 in the control group and from 30 (100 %) at baseline to 15 (50 %) at week 24 in the intervention group.

Table 11 Effect of dietary advice on components of metabolic syndrome

Parameters	Control group (n = 30) N (%)		Intervention group (n = 30) N (%)		*P* between group at baseline	*P* between group at week 24
	Baseline	Week 24	Baseline	Week 24		
Waist circumference						
< 90 cm (male) or 80 cm (female)	0 (0.0)	1 (3.3)	0 (0.0)	3 (10.0)	> 0.999	0.301
≥ 90 cm (male) or 80 cm (female)	30 (100.0)	29 (96.7)	30 (0.0)	27 (90.0)		
Triglyceride						
< 150 mg/dL	17 (56.7)	18 (60.0)	17 (56.7)	25 (83.3)	0.793	0.024
≥ 150 mg/dL or specific treatment for this lipid abnormality	13 (43.3)	12 (40.0)	13 (43.3)	5 (16.7)		
HDL-C						
> 40 mg/dL (male) or 50 mg/dl (female)	16 (53.3)	14 (46.7)	10 (33.3)	18 (60.0)	0.118	0.301
≤ 40 mg/dL (male) or 50 mg/dl (female) or specific treatment for this lipid abnormality	14 (46.7)	16 (53.3)	20 (66.7)	12 (40.0)		
Blood pressure						
< 130/85 mmHg	2 (6.7)	3 (10.0)	4 (13.3)	14 (46.7)	0.389	0.002
≥ 130/85 mmHg or treatment of previously diagnosed hypertension	28 (93.3)	27 (90.0)	26 (86.7)	16 (53.3)		

Table 11 Effect of dietary advice on components of metabolic syndrome (continued)

Parameters	Control group (n = 30) N (%)		Intervention group (n = 30) N (%)		P^a between group at baseline	P^a between group at week 24
	Baseline	Week 24	Baseline	Week 24		
Fasting blood sugar						
< 100 mg/dL	19 (63.3)	16 (53.3)	15 (50.0)	17 (56.7)	0.297	0.795
≥ 100 mg/dL or previously diagnosed type 2 diabetes	11 (36.7)	14 (46.7)	15 (50.0)	13 (43.3)		
Number of metabolic components						
1	0 (0.0)	0 (0.0)	0 (0.0)	5 (16.7)	0.341	0.051
2	0 (0.0)	6 (20.0)	0 (0.0)	10 (33.3)		
3	21 (70.0)	12 (14.0)	16 (53.3)	9 (30.0)		
4	8 (26.7)	7 (23.3)	11 (36.7)	5 (16.7)		
5	1 (3.3)	5 (16.7)	3 (10.0)	1 (3.3)		
Number of HIV/AIDS patients						
metabolic syndrome	30 (100.0)	24 (80.0)	30 (100.0)	15 (50.0)	> 0.999	0.015
without metabolic syndrome	0 (0.0)	6 (20.0)	0 (0.0.)	15 (50.0)		

HDL-C = high-density lipoprotein cholesterol; HIV/AIDS = Human Immunodeficiency Virus/Acquired Immune Deficiency

[a]Significant relationship between categorical variables was analyzed by χ^2 test.

CHAPTER V
DISCUSSION

The present study aimed to investigate the effect of dietary advice on the components of metabolic syndrome including anthropometric parameters, lipid profiles, fasting blood sugar, and blood pressure in HIV/AIDS patients.

5.1 Characteristics of the participants

In this present study, most of the participants were females. Gender was found to be associated with metabolic syndrome. Previous studies demonstrated that the female HIV/AIDS patients had a higher prevalence of metabolic syndrome than males (Jantarapakde et al., 2014; Samaras et al., 2007). However, this still could not be conclusive as Pongthananikorn et al. (2018) found higher prevalence of metabolic syndrome in male than female, and Jerico et al. (2005) found no association between gender and metabolic syndrome. The average age of the participants in this study was 46.97 $\pm$ 8.44 years corresponded to the data from World Health Organization that the patients aged 15 - 49 years were the most affected group for metabolic syndrome (WHO, 2019). In addition, increasing age is one of the risk factors of metabolic syndrome (Ayodele et al., 2012). The prevalence of metabolic syndrome in the patients who were 41 years and older was twice higher than the younger patients (Bonfanti et al., 2010; Wand et al., 2007).

The duration of HIV treatment in the present study was 8.40 $\pm$ 3.60 years. It was reported that the patients who had duration of treatment longer than 60 months had three times higher risk for metabolic syndrome, compared with the patients who had shorter duration of treatment (Malangu, 2014). Most of the participants in this study had at least one comorbid disease. The comorbid disease found in this study included

dyslipidemia, hypertension and diabetes mellitus. These diseases were the most common co-morbidities among patients with HIV (Lorence et al., 2014), and they can be caused by many reasons including HIV infection itself and antiretroviral drugs (Khan et al., 2014). HIV infection and antiretroviral therapy can alter lipid profiles (high TC, LDL-C and TG levels but low HDL-C level) in HIV-infected patient (Nicholas et al., 2016).

In HIV-infected individuals, the rate of hepatic lipid production and basal lipolysis are increased, peripheral fatty acid trapping is impaired, and ability of insulin to suppress lipolysis in adipocytes is decreased (Hemkens and Bucher, 2014). Adverse effects of antiretroviral are represented by an alteration of fat distribution and metabolic complications. Lipodystrophy, the main clinical feature, refers to peripheral fat loss (lipoatrophy) in the face, limbs and buttocks, or abnormal fat accumulation in breasts abdomen and dorsocervical adipose tissue or a combination of these two problems (Montessori et al., 2004; Florentina et al., 2016). Protease Inhibitors class was linked to lipohypertrophy while NRTIs class was linked to lipoatrophy (Hoffmann et al., 2015). The prevalence of lipodystrophy has been estimated about 50 % after treated with antiretroviral drug more than one year (Carr et al., 1999). Further adverse effects of antiretroviral therapy are dyslipidemia, glucose metabolism disorder and high levels of inflammatory cytokines (Hemkens et al., 2014).

Antiretroviral therapy was induced dyslipidemia (Mills et al., 2009). PIs used, especially Lopinavir/ritonavir, has been associated with hypercholesterolemia, hypertriglyceridemia and low HDL-C level (Acosta et al., 2002; Shafran et al., 2005; Lee et al., 2004), Some of PIs regimen affects lipid profiles but not class regimen effect. The newer PIs, atazanavir and darunavir had minor effect on serum lipids (Murphy et al., 2003; Mills et al., 2009). PIs affect fat metabolism in liver and adipose tissue. In adipose tissue, PIs inhibit lipolysis by impairing lipoprotein lipase activity resulting in impaired uptake of TGs into adipocytes which may associate to increased plasma TGs.

(den Boer et al., 2006). In liver, PIs inhibit the proteosomal degradation of pre-secretory apolipoprotein B, the protein component of LDL particles, in hepatocytes (Liang et al., 2001). Among NNRTIs, efavirenz provided more TG increasing effect than nevirapine (van Leth et al., 2004; Young et al., 2005). NRTIs regimen was also found to alter lipid profiles. The uses of abacavir and stavudine were associated with increase in TG and TC levels (Gallant et al., 2004; Smith et al., 2009). In this study, most of the participants used the combination of two NRTIs (tenofovir and emtricitabine) and one NNRTIs (efavirenz) while, only few of them used PIs. Therefore, ART used may be the cause of dyslipidemia in these participants.

Most of the participants in this study were obese based on the BMI and did not exercise. In the participants who did exercise, duration of exercise per time was 15 to 30 minutes. Physical inactivity was independently associated with metabolic syndrome in male HIV-infected patients (Alencastro et al., 2011). Light to moderate physical activity (< 7 kcal/min expended) was associated with decreased prevalence of the metabolic syndrome in the general population, and intensive exercise was associated with much greater reduction (Panagiotakos et al., 2004). The increased prevalence of obese and overweight in HIV-infected patients has been observed in many countries (De Carvalho et al., 2015; Paton 2006; Crum-Cianflone et al., 2010; Gomes et al., 2016). Overweight and obesity are associated with diabetes and cardiovascular disease in HIV-infected patients (Gomes et al., 2016; Bray et al., 1985; Wilson et al., 2002; Eeg-Olofsson et al., 2009). Koethe et al. (2016) showed that white HIV-infected women had a higher BMI after three years of ART than control. In this study the participants had mean CD4 cell more than 350 cell/mm^3. This finding agreed with the results from Castro (2016) that the patients who had CD4 cell more than 350 cell/mm^3 and were treated with HAART may have favored the higher prevalence of overweight.

The participants in this study had total energy intake less than energy requirement. This problem was consistent with that of other study (Onyango et al., 2012). WHO (2005) suggested that HIV-infected patients had increased resting metabolic rate around 10 %. Total energy intake in HIV-infected patients was reduced from loss of appetite (Macallan et al, 1995). The other causes may involve anorexia, lack of food in the household and ulceration at mouth (Beisel et al., 1996). Energy balance in HIV-infected patients was caused by increased the resting metabolic rate and decreased in total energy intake. In this study, percentages of energy distribution from carbohydrate and fat intake were in the ranges recommended by NCEP ATP III, but percentage of energy distribution from protein and cholesterol intake were higher than the recommendation. It was found that dietary fiber intake of the participants in this study was lower than the recommendation.

5.2 Effect of dietary advice on laboratory parameters

In this study, at baseline the participants in the intervention group had TC and FBS slightly higher than the recommended range (normal ranges of TC and FBS were less than 200 mg/dL and 70 - 100 mg/dL, respectively). In addition, HDL-C in females of both groups was lower than the recommended range (normal range was 50 - 59 mg/dL). At the end of study, there was no change in TC and HDL-C level in both groups, but the participants in the intervention group had significantly decreased TG and FBS, compared to baseline, and the level of their TG was significantly lower than that of the participants in the control group. This finding may result from decreased consumption of total energy, amount of carbohydrate, fat, saturated fatty acid, and sugar, but increased dietary fiber intake after following the modified NEM diet. Restriction of total energy intake was recommended for weight reduction in the participants who obese. At baseline, the participants in both groups had the percentage of total caloric intake from carbohydrate and fat higher than the recommendation;

however, after following dietary advice based on the modified NEM diet for 24 weeks, the participants in the intervention group had lower percentages of calories from carbohydrate and fat intake. These results indicated the success of eating behavior modification in these participants, and thus providing beneficial effects on TG and FBS levels.

After the dietary advice, the participants in the intervention group consumed complex carbohydrate more often than simple carbohydrate. Furthermore, they had lower sugar intake and higher dietary fiber intake compared to baseline. The long-term intake of simple carbohydrate caused weight gain and decreased insulin sensitivity leading to the development of type 2 diabetes and metabolic syndrome (Bray et al., 2004). Previous study also showed that long-term consumption of fructose resulted in decreased insulin sensitivity and increased weight (Bray et al., 2004). In contrast, low glycemic index foods led to slower and lower increase in blood glucose and insulin levels (Liu et al., 2000; Burger et al., 2011), and they were recommended for the patients with metabolic syndrome (McMillan-Price et al., 2006; Hoton, 2009). Foods with glycemic index of less than or equal to 55 caused slower increase or lower in blood glucose and insulin level than higher glycemic index foods (Hoyas et al., 2019). In addition, diet with low glycemic index produced lower concentrations of TG (Jarvi et al., 1999). Thus, consumption of complex carbohydrate rather than simple carbohydrate and decreased sugar intake of the participants in the intervention group could be the reasons of decreased TG and FBS at the end of the study.

The percentage of calories from fat intake in the intervention group was reduced to less than 25 % in this study, and the consumption of saturated fat was decreased. Dietary fat intake greater than 35-40% of total energy intake affected insulin sensitivity and increased the risk of developing type 2 diabetes (Vessby et al., 2001). The saturated fat intake was decreased in the present study because of the dietary

advice on choosing suitable meat and suitable types of oils for cooking process. The participants were recommended to choose lean meat and non-processed meat for their daily diet, and the consumption of fish that higher of omega-3 fatty acids was also promoted. The other dietary advice was about the use of suitable oils for each cooking methods. The animal oil or palm oil should be used for frying and vegetable oil should be used for stirring foods. The amount of oil was recommended for optimal daily use. At the end of the study, only the participants in the intervention group had reduced TG level. This could be due to higher consumption of the diets enriched in monounsaturated fats that improve TG and LDL-C levels (Rivellese et al., 2003; Thomsen et al., 1999; Rasmussen et al., 2006).

5.3 Effect of dietary advice on anthropometry and blood pressure

Most of the participants in this study were obese according to BMI. The participants who were obese were advised to reduce their weight. After the dietary advice for 24 weeks, the participants in the intervention group had weight loss. Their BMI and WC were also decreased. Weight loss was affected from energy intake restriction in the modified NEM diet. Hoyas (2019) was recommended weight reduction for the participants weight loss about 7 % resulted in reductions in TG, TC and FBS levels (Case et al., 2002; Phelan et al., 2007).

In this study, the participants in both groups had baseline systolic and diastolic blood pressure higher than normal range. These were normal findings in metabolic syndrome patients. At the end of the study, blood pressure was decreased from baseline in the participants who followed the advice based on the modified NEM diet. In addition, the blood pressure at week 24 of the participants in the intervention group was also lower than that of the participants in the control group. These results may be due to decreased energy intake, increased consumption of complex carbohydrate,

vegetable and fruit, weight loss, and decreased saturated fatty acid intake after following the dietary advice based on the modified NEM diet. Reeds (2019) showed that the women who had 7.7 % weight loss by energy deficit 1000 kcal/day had decreased systolic and diastolic blood pressure and decreased visceral adipose tissue. These results agreed with the study of Duncan (2019) that showed decreased blood pressure in HIV patients with impaired fasting glucose after receiving the dietary advice for 24 weeks to achieve 7 % weight loss, restrict saturated fat to less than 10 % of total daily energy intake, and limit sugar and sodium intake. The present study suggested that following the advice based on modified NEM diet for 24 weeks could improve weight, WC, systolic and diastolic blood pressure in the HIV/AIDS patients with metabolic syndrome.

5.4 Effect of dietary advice on dietary intake

The participants in the intervention group received the advice about the diet that modified from dietary recommendation of NCEP ATP III, EACS and the Mediterranean diet (the modified NEM diet) in addition to the dietary advice following the Thai nutrition flag. The modified NEM dietary advice included maintaining caloric intake balanced with energy expenditure. The participants who were obese or overweight were advised to lose weight without starvation. The percentages of caloric intake from carbohydrate, protein and fat intake were 55 to 60, 15 to 20 and 25 %. The intake of saturated fat and cholesterol were limited, and trans-fat intake was avoided. The intake of vegetable oil, sugar and salt were limited as well. The participants were advised to emphasize the intake of vegetables, fruits and fiber. Consumption of fish (the source of omega-3 fatty acids), white meat and complex carbohydrate was promoted. The recommendation for decreased processed meat intake was advised. According to the results of dietary intake, this study revealed that the participants can well follow the advice based on the modified NEM diet.

In the present study, the results from 24-hr recall and semi-quantitative FFQ showed lowered total energy intake in the participants who received dietary advice on the modified NEM diet compared to their baseline and those in the control group. These results were different from the study on the effect of a Mediterranean diet in type 2 diabetes patients (Esposito et al., 2014). In the type 2 diabetic patients in that previous study, their daily energy intake either following a low-carbohydrate Mediterranean diet or a low-fat diet for 4 years was not different. The percentage of caloric intake from protein was significant increased from less than 20 % (14.22 - 16.65 %) at baseline to more than 20 % (22.15 - 23.52 %) at the end of study while there was no difference in amount and total calories of protein intake throughout the study. This may be the result of decreased consumption of carbohydrate and fat, and thus increased the proportion of total caloric intake from protein. Although the participants who received the advice on the modified NEM diet seemed to consume protein higher than the advice in this study (20 %), it was still acceptable as the recommended guideline of energy intake from protein was ranges from 10 - 35 % for adults or 0.8 g/kg per day. The participants who followed the advice on the modified NEM diet also increased consumption of lean meat and meat with high -3 fatty acids and decreased consumption of fatty meat. High protein intake was associated with the preservation of lean body mass during weight loss and increased satiety (Hoyas and Leon-Sanz, 2019).

After following the dietary advice based on the modified NEM diet, the consumption of complex carbohydrate and dietary fiber was increased while the amount and total consumption of fat and saturated fat was decreased. The results indicated that the participants consumed appropriate amount of carbohydrate, fat and dietary fiber according to the dietary advice in this study. The information of proper foods and the amount of total fat, saturated fat and cholesterol in 100-g of food

cooked provided in the booklet could help the participants in choosing healthy foods for their regular meals. However, in this present study, the participants in the intervention group had increased cholesterol intake after receiving dietary advice. The increased cholesterol intake in these patients may be due to increase in seafood consumption that replaced the fatty meat.

Sugar intake was decreased when evaluated by 24-hr recall but was increased when evaluated by semi-quantitative FFQ. The conflict results may be due to the percentage of the participants with increased frequency of fruit consumption was increased, and thus the sugar intake from semi-quantitative FFQ was increased. In this study, it appeared that the participants in the intervention group had increased dietary fiber intake after following the advice based on the Modified NEM diet. The increased fiber intake could be a result from high frequency of fruit and vegetable consumption. This was corresponded to the Mediteranean diet that rich in fruits and vegetables (Meslier et al., 2020).

This study showed that the advice along with the booklet providing the information on the modified NEM diet can be achieved, as demonstrated by the participants' overall dietary intake consistent with the advice at the end of the study. Following the advice could be the reason of improved components of metabolic syndrome and decreased number of the participants with metabolic syndrome in this 24-week study. This suggested the benefit of such advice for HIV/AIDS patients with metabolic syndrome. A longer study may be required to investigate whether patients can still follow the advice.

CHAPTER VI
CONCLUSION

The present study was conducted to investigate the effects of dietary advice on the components of metabolic syndrome in Thai HIV/AIDS patients with metabolic syndrome. The participants in the intervention group received the individual dietary advice based on the modified NEM diet, which was developed according to NCEP ATP III guideline, EACs guideline and Mediterranean diet. After following the advice for 24 weeks, the participants had reduced weight, WC, BMI, TG and FBS levels, systolic and diastolic blood pressure. In addition, the number of the participants who had metabolic syndrome were decreased at the end of the study. These results could be due to the fact that these participants can well follow the dietary advice in this study as their total energy intake, amount and calories from carbohydrate and fat were decreased while the consumption and frequency of white meat and fish that rich in omega-3 fatty acids were increased after following the advice. These findings suggested the benefit of such dietary advice in improving the components of metabolic syndrome in Thai HIV/AIDS patients with metabolic syndrome. The booklet containing the advice based on the modified NEM diet would be the useful tool for Thai HIV/AIDS patients in management of metabolic syndrome.

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APPENDICES

APPENDIX A

CBO REC No. 01.0

สำนักงานสาธารณสุขจังหวัดชลบุรี
กระทรวงสาธารณสุข
ที่อยู่ 29/9 หมู่ 4 ถนนวชิรปราการ อำเภอเมืองชลบุรี จังหวัดชลบุรี รหัสไปรษณีย์ 20000
โทร. 038-932-491-2

เอกสารรับรองโครงการวิจัย

คณะกรรมการจริยธรรมการวิจัยในมนุษย์ สำนักงานสาธารณสุขจังหวัดชลบุรี ดำเนินการให้การรับรองโครงการวิจัยตามแนวทางหลักจริยธรรมการวิจัยในมนุษย์ที่เป็นมาตรฐานสากลได้แก่ Declaration of Helsinki, The Belmont Report, CIOMS Guideline และ International Conference on Harmonization in Good Clinical Practice หรือ ICH-GCP

ชื่อโครงการ : ผลของการให้คำแนะนำเกี่ยวกับอาหารต่อองค์ประกอบของกลุ่มอาการเมแทบอลิกในผู้ป่วยติดเชื้อเอชไอวีหรือผู้ป่วยเอดส์ ที่มีกลุ่มอาการเมแทบอลิก

เลขที่โครงการวิจัย : 04/62

ผู้วิจัยหลัก : นางสาวพัชรี เกลุเลียว

สังกัดหน่วยงาน : โรงพยาบาลบ้านบึง จังหวัดชลบุรี

วิธีทบทวน : คณะกรรมการเต็มชุด (Full board)

รายงานความก้าวหน้า : ส่งรายงานวิจัยฉบับสมบูรณ์เมื่อดำเนินการเสร็จสิ้น

เอกสารรับรอง :โครงร่างการวิจัย,เอกสารชี้แจง,หนังสือแสดงความยินยอม,เครื่องมือวิจัย

ลงนาม ..... ลงนาม .....

(นางจุฬิวา พานิชสุโข)
ประธาน
คณะกรรมการจริยธรรมการวิจัยในมนุษย์

(นางวิจิตรา นวลรัตน์สกุล)
กรรมการและเลขานุการ
คณะกรรมการจริยธรรมการวิจัยในมนุษย์

วันที่รับรอง : 1 มีนาคม 2562
วันหมดอายุ : 28 กุมภาพันธ์ 2563
ทั้งนี้ การรับรองนี้มีเงื่อนไขดังที่ระบุไว้ด้านหลังทุกข้อ (ดูด้านหลังของเอกสารรับรองโครงการวิจัย)

APPENDIX B

หนังสือแสดงความยินยอม

(Consent Form)

การศึกษาวิจัยเรื่อง (ภาษาไทย) ผลของการให้คำแนะนำเกี่ยวกับอาหารต่อองค์ประกอบของกลุ่มอาการเมแทบอลิกในผู้ป่วยติดเชื้อเอชไอวีหรือผู้ป่วยเอดส์ที่มีกลุ่มอาการทางเมแทบอลิก

ผู้วิจัยหลัก นางสาวพัชรี เกตุแสงวิ

สถานที่ติดต่อ ฝ่ายเภสัชกรรมและการคุ้มครองผู้บริโภค โรงพยาบาลบ้านบึง จังหวัดชลบุรี
โทรศัพท์ 087-5033335, 038-442200 ต่อ 305, 306

ผู้วิจัยหลักร่วม/อาจารย์ที่ปรึกษา รองศาสตราจารย์ เภสัชกรหญิง ดร.กุลวรา แสงสวรรค์
ภาควิชาอาหารและเภสัชเคมี คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
โทรศัพท์ 089-7796084, 02-2188295

วันให้คำยินยอม วันที่..... เดือน..... พ.ศ. .....

ข้าพเจ้า (นาย/ นาง/ นางสาว) ..... **นามสกุล** .....
อยู่บ้านเลขที่ ..... **ซอย** ..... **ถนน** ..... **แขวง/ ตำบล** .....
เขต/ อำเภอ ..... **จังหวัด** ..... **รหัสไปรษณีย์** .....

ก่อนที่จะลงนามในใบยินยอมให้ทำการวิจัยนี้ **ข้าพเจ้าได้รับเอกสารข้อมูลคำอธิบาย/คำชี้แจงสำหรับอาสาสมัครที่เข้าร่วมการวิจัย** จากผู้วิจัยให้ทราบถึงวัตถุประสงค์ของการวิจัย วิธีวิจัย อันตรายหรืออาการข้างเคียงที่อาจเกิดขึ้นจากการวิจัย รวมทั้งประโยชน์ที่เกิดขึ้นจากการวิจัยอย่างละเอียด และมีความเข้าใจดีแล้ว

ผู้วิจัยได้ตอบคำถามต่างๆ ที่ข้าพเจ้าสงสัยด้วยความเต็มใจ ไม่ปิดบัง ซ่อนเร้น จนข้าพเจ้าพอใจ

ข้าพเจ้าเข้าร่วมโครงการนี้โดยความสมัครใจ และยินยอมให้ผู้วิจัยทำการทดลองเก็บข้อมูลและสรุปผลการวิจัยเรื่องผลของการให้คำแนะนำเกี่ยวกับอาหารต่อองค์ประกอบของกลุ่มอาการเมแทบอลิกในผู้ติดเชื้อเอชไอวีหรือผู้ป่วยเอดส์ที่มีกลุ่มอาการทางเมแทบอลิกที่โรงพยาบาลบ้านบึง จังหวัดชลบุรี ตามที่ระบุไว้ในเอกสารชี้แจงผู้ร่วมโครงการวิจัยโดยข้าพเจ้ายินยอมตอบแบบสอบถามข้อมูลทั่วไป แบบสอบถามการรับประทานอาหารใน 24 ชั่วโมง จำนวน 5 ครั้งได้แก่ ในสัปดาห์ที่ 0, 6, 12, 18 และ 24 เข้ารับฟังการให้คำแนะนำเกี่ยวกับอาหารทั้งหมด 2 ครั้ง เจาะเลือดจากเส้นเลือดดำ 2 ครั้ง ประมาณครั้งละ 3 ช้อนชา ในสัปดาห์ที่ 0 และ 24 เมื่อเสร็จสิ้นการวิจัยแล้ว ตัวอย่างเลือดที่เหลือหลังการวิเคราะห์ต่างๆ ของข้าพเจ้าจะถูกทำลาย และการเข้าร่วมโครงการนี้ข้าพเจ้าทราบดีว่าจะไม่ได้รับค่าตอบแทนใดๆ ทั้งในรูปแบบของเงินและสิ่งของ

ข้าพเจ้าสามารถถอนจากการวิจัยได้ตลอดโดยการบอกเลิกการเข้าร่วมโครงการวิจัย จะไม่มีผลต่อการรักษาโรคที่ข้าพเจ้าจะได้รับต่อไป

ผู้วิจัยรับรองว่า **"จะเก็บข้อมูลเฉพาะเกี่ยวกับตัวข้าพเจ้าไว้เป็นความลับ และจะเปิดเผยได้เฉพาะในรูปที่เป็นสรุปผลการวิจัย"** เท่านั้น

APPENDIX C

เลขที่บันทึก/แบบสอบถาม.....

วันที่บันทึก.....

แบบบันทึกประวัติผู้ป่วย

ส่วนที่ 1 ข้อมูลทั่วไป

1. อายุ ..... ปี
2. เพศ

❑ 1. ชาย ❑ 2. หญิง

3. ระดับการศึกษาสูงสุด

❑ 1. ไม่ได้เรียนหนังสือ ❑ 2. ประถมศึกษา

❑ 3. มัธยมศึกษา ❑ 4. ปวช./ปวส./อนุปริญญา

❑ 5. ปริญญาตรี/สูงกว่าปริญญาตรี

4. อาชีพ

❑ 1. ไม่ได้ประกอบอาชีพ ❑ 2. รับราชการ

❑ 3. พนักงานรัฐวิสาหกิจ ❑ 4. ค้าขาย/ธุรกิจส่วนตัว

❑ 5. อื่นๆโปรดระบุ.....

5. สิทธิการรักษา

❑ 1. ชำระเงินสด ❑ 2. บัตรทอง

❑ 3. เบิกต้นสังกัด/โครงการเบิกจ่ายตรง ❑ 4. ประกันสังคม

❑ 5. อื่นๆโปรดระบุ.....

6. ท่านเคยได้รับความรู้เกี่ยวกับกลุ่มอาการเมแทบอลิกหรือไม่

❑ 1. ไม่เคย ❑ 2. เคย

7. ท่านรับประทานผลิตภัณฑ์เสริมอาหารอยู่หรือไม่

- ❑ 1. ไม่ได้รับประทาน
- ❑ 2. รับประทาน (ระบุ).....

8. ท่านสูบบุหรี่หรือไม่

- ❑ 1. ไม่สูบ
- ❑ 2. สูบ (ระบุความถี่และจำนวน) .....

9. ท่านออกกำลังกายกี่ครั้งใน 1 สัปดาห์ (โปรดระบุเวลาที่ออกกำลังกายในแต่ละครั้ง)

- ❑ 1. ไม่ได้ออกกำลังกายเลย
- ❑ 2. ออกกำลัง 1-2 ครั้งต่อสัปดาห์ แต่ละครั้งใช้เวลาประมาณ.....นาที
- ❑ 3. ออกกำลัง 3-5 ครั้งต่อสัปดาห์ แต่ละครั้งใช้เวลาประมาณ.....นาที
- ❑ 4. ออกกำลังมากกว่า 5 ครั้งต่อสัปดาห์ แต่ละครั้งใช้เวลาประมาณ.....นาที

10. ปกติท่านกินอาหารประเภทใด

- ❑ 1. อาหารที่ทำเอง
- ❑ 2. อาหารสำเร็จรูป

11. ปกติท่านกินอาหารครบ 3 มื้อ หรือไม่

- ❑ 1. ครบ 3 มื้อ
- ❑ 2. ไม่ครบ 3 มื้อ ส่วนใหญ่ไม่ได้กินอาหารมื้อใด (โปรดระบุ) .....

ส่วนที่ 2 ประวัติผู้ป่วย

1. ได้รับการวินิจฉัยว่าติดเชื้อเอชไอวี เป็นระยะเวลา ..... ปี
2. ประวัติการแพ้ยา

   ☐ 1. ไม่มี

   ☐ 2. มี (ระบุชื่อยาและอาการ).....

3. ประวัติการแพ้อาหาร

   ☐ 1. ไม่มี

   ☐ 2. มี (ระบุชื่ออาหารและอาการ).....

4. ประวัติการเจ็บป่วยหรือผ่าตัด

   ☐ 1. ไม่มี

   ☐ 2. มี.....

5. ประวัติการใช้ยาต้านเชื้อเอชไอวี (เก็บข้อมูลย้อนหลัง 3 เดือน และระหว่างวิจัยทุก 2 เดือน)

วันเดือนปี	ขนาดยาที่ได้รับ	หมายเหตุ

6. ประวัติการใช้ยารักษาโรคความดันโลหิตสูง โรคเบาหวาน ภาวะไขมันในเลือดผิดปกติ (เก็บข้อมูลย้อนหลัง 3 เดือน และระหว่างวิจัยทุก 2 เดือน)

วันเดือนปี	ขนาดยาที่ได้รับ	หมายเหตุ

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APPENDIX D

เลขที่แบบสอบถาม.....

วันที่ตอบแบบสอบถาม.....

ครั้งที่ตอบแบบสอบถาม.....

แบบบันทึกการรับประทานอาหารใน 24 ชั่วโมง

มื้ออาหาร	ระบุชื่ออาหารและปริมาณที่รับประทาน								
	แป้ง ข้าว (ทัพพี)	เนื้อสัตว์ (ช้อนโต๊ะ)	ถั่ว/ธัญพืช (ช้อนโต๊ะ)	ไข่ (ฟอง)	นม (มิลลิลิตร)	ผัก (ถ้วยตวง)	ผลไม้ (ผล)	น้ำมัน/ไขมัน	น้ำตาล/น้ำปลา (ที่เติมเพิ่ม)

APPENDIX E

เลขที่แบบสอบถาม.....

วันที่ตอบแบบสอบถาม.....

ครั้งที่ตอบแบบสอบถาม.....

แบบสอบถามความถี่ในการรับประทานอาหารของผู้ป่วยที่มีกลุ่มอาการเมแทบอลิก

หมวดเนื้อสัตว์: 1 ส่วนแลกเปลี่ยน = 30 กรัม = 2 ช้อนโต๊ะ							
ประเภทอาหาร	ขนาดการบริโภคต่อวัน (ส่วนแลกเปลี่ยน)				จำนวนวันที่บริโภคต่อสัปดาห์		
	3	4-5	6	≥7	3	4-6	7
เนื้อสัตว์ประเภทไขมันปานกลางถึงสูง ได้แก่ เนื้อสัตว์ (หมู วัว ควาย แพะ แกะ) ปนเปื้อ เครื่องในสัตว์ทุกชนิด เนื้อไก่ เป็ด ติดหนัง ปลาทุกชนิดทอด ปลาหมึก มันปู มันกุ้ง หอยนางรม ไส้กรอก เบคอน กุนเชียง							
เนื้อสัตว์ประเภทไขมันต่ำถึงต่ำมาก ได้แก่ เนื้อวัว หมู แพะ แกะ ควาย เป็นเนื้อล้วนไม่ติดมัน เป็ด ไก่ เนื้อล้วนลอกหนังออก ปลา ปู (ยกเว้นมันปู) หอย (ยกเว้นหอยนางรม)							
เนื้อปลาที่มีกรดไขมันโอเมก้า 3 ปริมาณสูง ได้แก่ ปลาทู ปลาจาละเม็ดขาว ปลาสำลี ปลากะพงขาว ปลาแก้ว ปลาตุก ปลาสวาย ปลาช่อน ปลานิล ปลาน้ำดอกไม้ ปลากราย ปลาทูน่า ปลาแซลมอน และปลาซาร์ดีน							

หมวดนมและผลิตภัณฑ์นม: 1 ส่วนแลกเปลี่ยน = 240 มิลลิลิตร = 1 กล่อง หรือโยเกิร์ตพร่องมันเนย						
ประเภทอาหาร	ขนาดการบริโภคต่อวัน (ส่วนแลกเปลี่ยน)			จำนวนวันที่บริโภคต่อสัปดาห์		
	< 1	1	> 1	3	4-6	7
นมที่มีไขมัน ได้แก่ นมสด (whole milk) นมข้นจืด นมเปรี้ยวทำจากนมสด นมข้นหวาน						
นมไขมันต่ำ (fat free หรือ low-fat) ได้แก่ นมสดขาด (พร่อง) มันเนย นมข้นขาด (พร่อง) มันเนย นมเปรี้ยวทำจากนมขาดมันเนย) (โยเกิร์ตพร่องมันเนย) นมถั่วเหลือง						
ผลิตภัณฑ์จากนมที่มีไขมัน ได้แก่ เนยแข็ง ครีมเทียม (2 ช้อนชา) ไอศกรีม (ขนาดปกติ ½ ถ้วย)						
หมวดน้ำมันและไขมันสำหรับปรุงอาหาร: 1 ส่วนแลกเปลี่ยน = น้ำมัน 1 ช้อนชา						
ประเภทอาหาร	ขนาดการบริโภคต่อวัน (ส่วนแลกเปลี่ยน)				จำนวนวันที่บริโภคต่อสัปดาห์		
	3	4-5	6	≥7	3	4-6	7
เนยแข็ง มายองเนส น้ำมันมะพร้าว น้ำมันปาล์ม กะทิ น้ำมันจากสัตว์							
น้ำมัน (ข้าวโพด ฝ้าย คอกคำฝอย คอกทานตะวัน) น้ำมันมะกอก น้ำมันถั่วลิสง							

หมวดข้าว-แป้ง: 1 ส่วนแลกเปลี่ยน = ข้าว 1 ทัพพี ขนมปัง 1 แผ่น เส้นก๋วยเตี๋ยวสุก 1 ทัพพี หรือ ½ ถ้วย								
ประเภทอาหาร	ขนาดการบริโภคต่อวัน (ส่วนแลกเปลี่ยน)					จำนวนวันที่บริโภคต่อสัปดาห์		
	≤ 7	8	10	12	≥ 13	3	4-6	7
ข้าวขาว เส้นก๋วยเตี๋ยว บักเทส								
ข้าวซ้อมมือ ขนมปังโฮลวีท เมี่ยงคำ วุ้นเส้น ข้าวโพดหวาน มักกะโรนี สปาเกตตี								
หมวดผลไม้: 1 ส่วนแลกเปลี่ยน = ผลไม้ขนาดใหญ่ 8 ชิ้นคำ ขนาดกลาง 1-2 ผล ขนาดเล็ก 3-5 ผล								
ประเภทอาหาร	ขนาดการบริโภคต่อวัน (ส่วนแลกเปลี่ยน)					จำนวนวันที่บริโภคต่อสัปดาห์		
	≤ 3	4	5	≥ 6		3	4-6	7
ผลไม้								
หมวดผัก: 1 ส่วนแลกเปลี่ยน = ผักดิบ 1 ถ้วยตวง ผักสุก ½ ถ้วยตวง								
ประเภทอาหาร	ขนาดการบริโภคต่อวัน (ส่วนแลกเปลี่ยน)					จำนวนวันที่บริโภคต่อสัปดาห์		
	≤ 4	5	6	≥7		3	4-6	7
หมวด ก. ผักกาดขาว กะหล่ำปลี ผักบุ้งจีน และไทย ดอกกุยช่าย แตงกวา สายบัว ตั้งโอ๋ ผักสลัด ผักกระแยง ผักกาดเขียว ผักกาดหอม ผักกวางตุ้ง ผักคื่นฉ่าย ผักคะน้า								
หมวด ข. มะเขือเทศ ถั่วลันเตา รากบัว แครอท น้ำเต้า มะเขือยาว บรอกโคลี่ มะระ ดอกโสน ยอดมะยม ยอดกระถิน ผักหวาน ใบยอ ถั่วฝักยาว กะหล่ำดอก ถั่วแขก ถั่วฝักยาว พริกเขียว ผักชม ฟักทอง ข้าวโพดอ่อน								

APPENDIX F

คู่มือการดูแลตนเองด้านโภชนาการ

จัดทำโดย
น.ส. พัชรี เกตุเฉลียว
นิสิตปริญญาโท
สาขาอาหารเคมีและโภชนศาสตร์ทางการแพทย์
ภาควิชาอาหารและเภสัชเคมี
คณะเภสัชศาสตร์
จุฬาลงกรณ์มหาวิทยาลัย

APPENDIX G

คู่มือการดูแลตนเองด้านโภชนาการ

(Supplement)

จัดทำโดย
น.ส. พัชรี เกตุเฉลียว
นิสิตปริญญาโท
สาขาอาหารเคมีและโภชนศาสตร์ทางการแพทย์
ภาควิชาอาหารและเภสัชเคมี
คณะเภสัชศาสตร์
จุฬาลงกรณ์มหาวิทยาลัย

VITA

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