國立臺灣大學公共衛生學院流行病學與預防醫學研究所

博士論文

Graduate Institute of Epidemiology and Preventive Medicine,
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Doctoral Dissertation

台灣素食與代謝風險：糖尿病與非酒精性脂肪肝

Taiwanese Vegetarian Diet and Metabolic Risk: Diabetes and Nonalcoholic Fatty Liver

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國立臺灣大學博士學位論文
口試委員會審定書

台灣素食與代謝風險：糖尿病與非酒精性肝炎
Taiwanese Vegetarian Diet and Metabolic Risk: Diabetes and Nonalcoholic Fatty Liver

本論文係　邱雪婷　君（學號 D02849001　）在國立臺灣大學流行病學與預防醫學研究所完成之博士學位論文，於民國 106 年 2 月 6 日承下列考試委員審查通過及口試及格，特此證明。

口試委員：潘文涵　程蘊菁（簽名）
（指導教授）

黃青真　杜裕康

林名男　黃暉庭

邱思穎

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邱雪婷 謹致

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中文摘要

背景:素食含有較低的飽和脂肪酸與血鐵質，及較高的纖維及植物生化素，這些可能影響幾個糖尿病致病機轉，然而目前很少研究探討亞洲素食飲食型態對糖尿病的影響。

目的: 了解台灣素食飲食對糖尿病發生率及其相關代謝危險因子，包含脂肪肝、代謝症候群、及葡萄糖代謝異常的影響。

方法: 慈濟健康研究於 2007–2009 年之間招募了 4625 名慈濟志工，其中約 1/3 為素食者，2/3 為葷食者。所有參予者在大林慈濟醫院進行完整的健康檢查，並接受問卷訪問基本資料、疾病及健康史、生活型態、與飲食。並於 2010–2012 及 2013–2016 年追蹤疾病狀況及飲食改變。參予者每三年被邀請回醫院作追蹤檢查。從沒回來接受追蹤檢查者以郵寄問卷追蹤。

結果: 台灣素食飲食除了不含肉類及魚類，也包含較高的黃豆、蔬菜、全穀、堅果種子，其與較低的代謝症候群(以 ATP III 定義: OR: 0.84, 95% CI: 0.70 – 1.00; 以 International Federation of Diabetes 定義: OR: 0.62, 95% CI: 0.49 – 0.77)，較低的脂肪肝(OR: 0.79, 95% CI: 0.68, 0.91)，以及較低的肝臟纖維化有相關性。在平均 5 年的追蹤期間，有 183 名糖尿病新案例，與葷食者比較且校正可能干擾因子後，長期素食者與葷食轉素食者大幅降低糖尿病風險，危險率分別為 HR: 0.52 (95% CI: 0.37, 0.73)及 HR: 0.43 (95% CI: 0.28, 0.66)。

結論： 台灣素食飲食與較低的代謝危險因子及非酒精性脂肪肝有相關性，同時對糖尿病的發生有保護效果。增加植物性蛋白質、全穀、及堅果種子可能有助代謝相關疾病。

關鍵字： 糖尿病、非酒精性脂肪肝、代謝症候群、素食、前瞻性世代追蹤研究

ENGLISH ABSTRACT

Background: Vegetarian diets contain lower levels of saturated fat and heme iron, and higher levels of fiber and phytochemicals, which may ameliorate several underlying pathophysiological pathways of type 2 diabetes. However, the effect of Asian vegetarian diets on diabetes has not been carefully investigated.

Aim: To examine whether a Taiwanese vegetarian diet affects incidence of diabetes and its related metabolic risk factors, including fatty liver, metabolic syndrome, and impaired glucose metabolism.

Methods: The Tzu Chi Health Study recruited 4625 devoted Buddhist volunteers of the Buddhist Tzu Chi Foundation, with 1/3 vegetarians and 2/3 nonvegetarians. All participants received a health examination and were interviewed on basic demographics, medical history, diet (through a validated food frequency questionnaire) and lifestyle at the Buddhist Dalin Tzu Chi Hospital from 2007 to 2009, and followed from 2010 to 2012, and from 2013 to 2016. Participants were invited back for follow-up health examinations every 3 years. Those who never returned for follow-ups were sent a follow-up questionnaire to assess their diet and disease conditions.

Results: Taiwanese vegetarian diets were characterized by higher intake of soy, vegetables, whole grains, nuts and seeds, and avoidance of meat and fish. This dietary

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pattern was associated with lower risk of metabolic syndrome (Adult Panel Treatment III definition, OR: 0.84, 95% CI: 0.70 – 1.00; International Federation of Diabetes definition, OR: 0.62, 95% CI: 0.49 – 0.77), nonalcoholic fatty liver (OR: 0.79, 95% CI: 0.68, 0.91) and liver fibrosis. In the 5-year (median) follow-up, 183 incident cases of diabetes were identified. Long-term vegetarians and the converted (nonvegetarians converted to vegetarians) experienced lower risk of diabetes, HR= 0.52 (95% CI: 0.37, 0.73) and HR = 0.43 (95% CI: 0.28, 0.66), respectively, when compared with the nonvegetarians.

Conclusion: Taiwanese vegetarian diet was inversely associated with cardiometabolic risk factors, nonalcoholic fatty liver, and risk of developing diabetes. Increasing consumption of plant protein, whole grains, seeds, and nuts may improve cardiometabolic health.

Key words: diabetes, nonalcoholic fatty liver, metabolic syndrome, vegetarian diets, prospective cohort study

CHAPTER 1. INTRODUCTION

Vegetarian diets exclude meat, fish, and seafood, and vegan diets further exclude dairy and eggs(1). Such diets tend to make up for calories by including more plant foods such as grains, beans, soy, nuts, seeds, fruits, and vegetables(2), resulting in higher intakes of fiber, antioxidants, phytochemicals, magnesium, potassium, vitamin E, vitamin C, folate, and carotenoids, and lower intakes of saturated fat, cholesterol, heme iron, and contaminants associated with animal products such as heavy metals and antibiotic residues(3,4,5,6). Such a diet may reduce oxidative stress, inflammation, lower blood pressures and cholesterol, and change gut microbiota composition, thus holding a great potential for prevention of multiple chronic diseases.

Diabetes prevalence has nearly doubled from 1980 to 2014(7). It affects 415 million individuals (1 in 11) worldwide, and projected to increase to 642 million (1 in 10) by 2040(8). In Taiwan, diabetes patients incur 2.8 times more medical expenses than matched non-diabetes individuals, and used up 29% of total healthcare dollars(9). Nonalcoholic fatty liver disease (NAFLD), a related metabolic disorder, is also emerging to be the most common chronic liver disease, affecting 20 – 40% of the population(10,11). Asians tend to develop both diabetes and NAFLD at a lower body mass index (BMI) than Westerners, possibly due to genetics and environmental factors(12,13,14).

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Diabetes is defined by elevation of glucose(15), but elevation of glucose is only the tip of the iceberg (**Figure 1 – 1**). Multiple pathways and organ systems, detailed as follows, fuel the elevation of glucose(16): Pancreas produces more glucagon and less insulin. A fatty liver contributes to insulin resistance and increases hepatic glucose production. Muscles become resistance to insulin thus reduce glucose uptake. Intestinal L-cell and K-cells fail to produce sufficient incretin to regulate insulin and glucagon secretion. Fat cells release more free fatty acids and intermediate fatty acid oxidation metabolites, which exacerbate insulin resistance. Failure of appetite control and satiety response lead to caloric overconsumption and obesity. As multiple organ systems work in conjunction to raise glucose, an ideal preventive strategy should simultaneously target all the underlying pathophysiology.

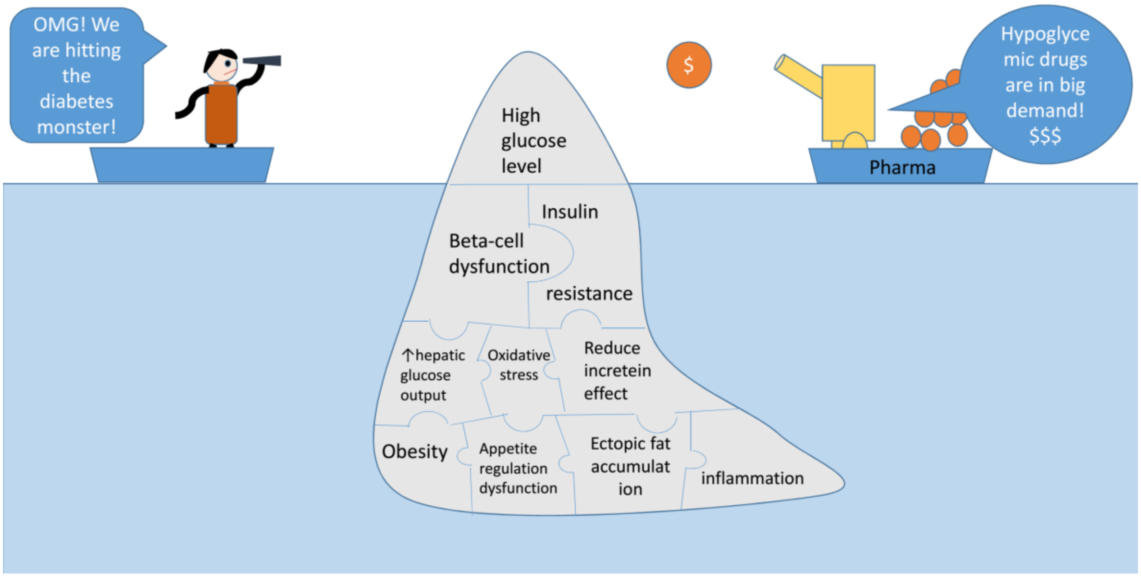

Figure 1 – 1. The iceberg of diabetes.

Dietary approaches with multiple beneficial components such as vegetarian diet may provide a total solution. The lower saturated fat and iron may respectively reduce endoplasmic reticulum (ER) stress and oxidative stress, protecting against β-cell failure(17,18,19). The higher magnesium and other phytochemicals from plant foods may reduce insulin resistance(20,21,22). In addition, Short Chain Fatty Acids (SCFA, from microbial fermentation of fiber) and plant polyphenol may stimulate incretin secretion leading to improved β-cell function and glucose metabolism(23). SCFA has also been shown to suppress desire for high energy foods(24), which may halt the vicious cycle of excess energy intake and obesity in the long term.

Despite promising potentials, the effect of vegetarian diets on diabetes risk has not been carefully investigated in Asians. This dissertation aims to examine whether vegetarian diets affect diabetes incidence and its associated metabolic risk factors, including metabolic syndrome, impair glucose metabolism, and nonalcoholic fatty liver **(Figure 1 – 2)**.

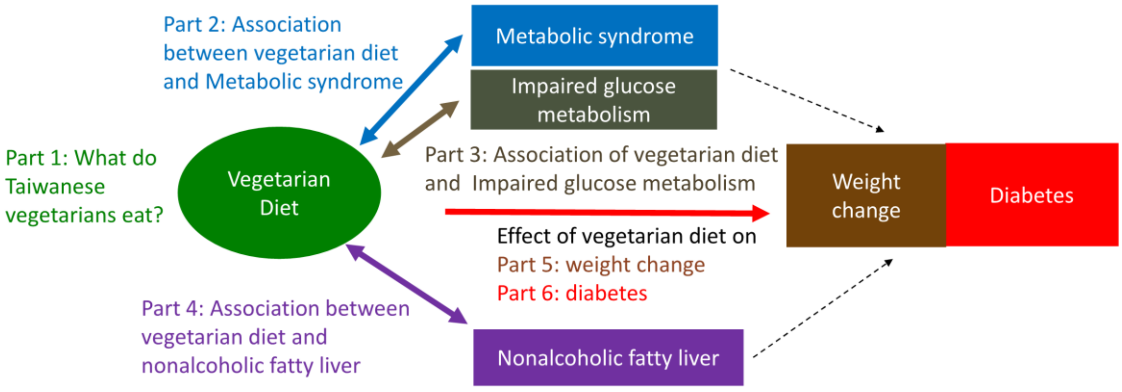

Figure 1 – 2. Overview of the study

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CHAPTER 2. LITERATURE REVIEW

Vegetarian diets are defined by avoidance of animal flesh (including meat, fish, and sea food). There are a wide range of dietary practices: vegans (avoiding eggs and dairy, and honey in addition to animal flesh), raw vegans (avoiding all cooked foods in addition to animal products), lacto-vegetarians (including dairy), ovo-vegetarians (including eggs), and lacto-ovo vegetarians (including both dairy and eggs)(25). Some individuals who avoid meat but eat fish and sea food are named as pesco-vegetarians in literature (3,4). While avoiding or reducing foods of animal origins, vegetarians tend to consume more plant foods, including whole grains, fruits, vegetables, beans, soy, nuts and seeds(2,26).

2.1 Health effects of vegetarian diets

Potential disadvantages of vegetarian diets may include lower protein, vitamin B12, vitamin D, iron, zinc, calcium (for vegans), and long chain omega-3 fatty acids(25). Low vitamin B12 could raise homocysteine(27), a risk factor for cardiovascular diseases(28). Low vitamin D and calcium may be associated with lower bone mineral density, together with low protein and vitamin B12 status, may increase risk for fracture(29). However, since these nutritional needs could be easily met by a more mindful meal planning and supplementation, the Academy of Nutrition and Dietetics (previously the American Dietetics Association) has repeatedly released position statements to support the nutritional adequacy (through appropriate planning) and health benefits of vegetarian diets(1,25).

The advantages of a balanced vegetarian diet include lower saturated fat and heme iron, higher plant protein, fiber, vitamin C, vitamin E, folate, magnesium, potassium, and a wide array of phytochemicals. These dietary compounds may contribute to lowering of cholesterol, blood pressures, chronic low grade inflammation, oxidative stress, all of which play key mechanistic roles in the etiology of multiple chronic diseases including cardiovascular diseases, diabetes, cancer, cataract, dementia, and even cancer(30).

In fact, prospective cohorts from Western populations have shown that vegetarian diets decrease the risk of obesity(31), ischemic heart diseases(32,33), cerebrovascular diseases(34), cancer of lymphatic and hematopoietic tissue(35), prostate cancer(36), colorectal cancer(37), diverticular diseases(38), diabetes(39), cataract(40), and dementia(41) compared with a nonvegetarian diet. In the EPIC-Oxford cohort, the risk of bone fracture is higher in vegan with calcium intake less 525 mg/day, but similar for meat eaters, fish eaters, vegetarians, and vegans with calcium intake greater than 525 mg/day (42).

The lower incidence of chronic diseases also translates into lower healthcare expenditures. A study found that vegetarians have lower hospitalization and surgery rates than omnivores in the Seventh-day Adventist populations(43). Barnard et al estimated that the medical cost in the US attributable to meat consumption amounts to 28.6 – 61.4 billion US dollars in the year 1992(44). A recent study linking the Nutrition and Health Survey in Taiwan (NAHSIT) with the National Health Insurance Database also found elderly who spend more on fruits and vegetables and less on animal based foods incurred lower medial expenditure (45).

Despite ample evidences from Western populations, there is very little investigations on Asian and Taiwanese vegetarian diet and its long term effect, with most research limited to cross-sectional studies(46,47,48,49), and only a few prospective studies on metabolic syndrome and hypertension(50,51). Vegetarianism in Taiwan is typically associated with religion (Buddhism, Taoism). Since religious activity itself may influence health outcome(52), studies that did not control for religion may be prone to confounding bias. Moreover, research from Western populations may not be applicable to Asian and Taiwanese population due to the difference in contents of vegetarian diets. While Western vegetarians tend to consume more beans, seeds, nuts, raw vegetables (in the form of salads), and were more likely to use foods fortified with vitamin B12 and vitamin D(2,4), Taiwanese vegetarians tend to consume more soy, and cooked vegetables, with little fortified foods available. Studies of Taiwanese vegetarians

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using a prospective design and controlling for religion are desperately needed to delineate the impact of vegetarian diets on health and disease outcome.

2.2 The pathophysiology of diabetes and nonalcoholic fatty liver

Diabetes is defined as fasting glucose≧126 mg/dL or HbA1C≧6.5(15). It is manifested by the combination of two physiological features: insulin resistance and β-cell dysfunction(16). While insulin resistance is the traditional hallmark of type 2 diabetes, progression from prediabetes to overt type 2 diabetes typically occurs when β-cell is unable to secrete enough insulin to keep up with the rising insulin resistance(16). In fact, studies have shown that by the time type 2 diabetes occurs, patients have already lost 80% of the β-cell function(53,54,55). Obesity causes insulin resistance and fuels the diabetes epidemic(56,57). Those developed type 2 diabetes despite normal weight tend to have problems with β-cell dysfunction, possibly due to genetics(58). Genetic loci found to influence risk of type 2 diabetes tend to be associated with insulin secretion rather than obesity(58). While diabetes in Caucasian is highly attributed to obesity and insulin resistance, emerging evidence suggests that β-cell dysfunction is more predictive diabetes in Asians(59); this may explain why Asians tend to develop diabetes despite lower BMI.

Many organs systems – pancreas, liver, muscle, adipose tissue, gastrointestinal tract, kidney, and brain – contribute to the elevation of glucose and work in concerto to induce hyperglycemia (**Figure 2 – 1**)(16). Glucolipotoxicity damages β-cell through ER stress, oxidative stress, and inflammation in type 2 diabetes(17). The gastrointestinal track also plays an important role in regulating blood glucose through the gut hormone incretins, including the glucagon-like-peptide-1 (GLP-1, secreted by L-cell in distal small intestine) and the gastric inhibitory peptide (GIP, secreted by K-cells in the proximal small intestine)(60). GIP stimulates insulin secretion while GLP-1 inhibits glucagon secretion(60). Diabetic individuals became resistant to GIP, and have decreased secretion of GLP-1(61,62). Ectopic fat accumulation in liver and muscle, and release of intermediate fatty acid metabolites (such free fatty acids, diacyl glycerol, acyl caritines) from adipose tissue all contribute to insulin resistance, and result in increased hepatic glucose production and decreased glucose uptake in muscle cells(63). Among diabetes patients, the kidney may contribute to glucose elevation through glucose reabsorption. Finally, impaired appetite regulation in the brain may contribute to overeating, leading to obesity, which worsens insulin resistance, and drives forth the vicious cycle. The joint effect of multiple organs has driven to the trend of using multiple drugs targeting different organs to manage diabetes (**Figure 2 – 2**): Metformin and TZDs lower insulin resistance and suppress hepatic glucose production. GLP-1 analogues and DPP-IV inhibitors (prevents degradation of GIP and GLP-1) work through the incretin effect to

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increase insulin secretion; sulfonylurea further stimulates insulin secretion, and TZDs reduces lipolysis$^{(16)}$. Other diabetes drugs: Alpha glucosidase inhibitors reduces digestion and absorption of complex carbohydrates. Sodium glucose-limiting cotransporter 2 inhibitors (SGLT2) promote glucose loss through urine.

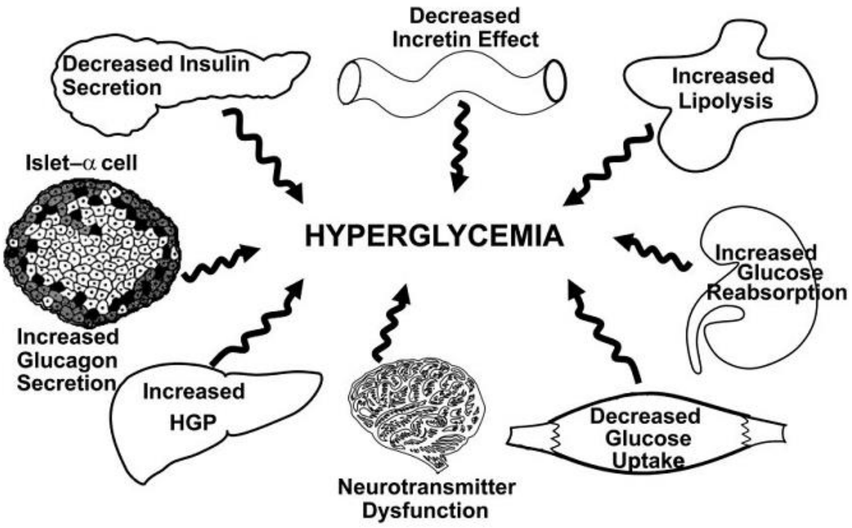

Figure 2 – 1. The ominous octet of diabetes. Adopted from DeFronzo (2009)$^{(16)}$.

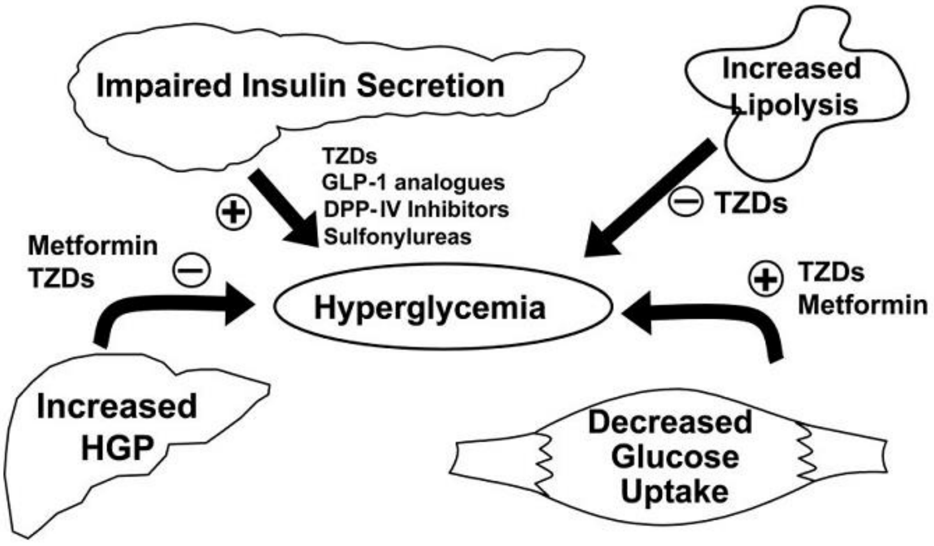

Figure 2 – 2. Multiple pharmaceutical therapies targeting pathophysiology of diabetes. Adopted from DeFronzo (2009)$^{(16)}$.

NAFLD encompasses a wide range of conditions from simple steatosis, nonalcoholic steatohepatitis (NASH), fibrosis, to cirrhosis. Simple steatosis is generally benign, while NASH is more likely to progress to advance liver diseases characterized by fibrosis and cirrhosis(64). NAFLD is caused by excess energy intake(64). Oxidative stress and insulin resistance are important contributors to NAFLD progression(65).

Taylor proposed and provided experimental evidence to support the twin cycles hypothesis of type 2 diabetes (**Figure 2 – 3**), that tights together fatty liver and diabetes(66).

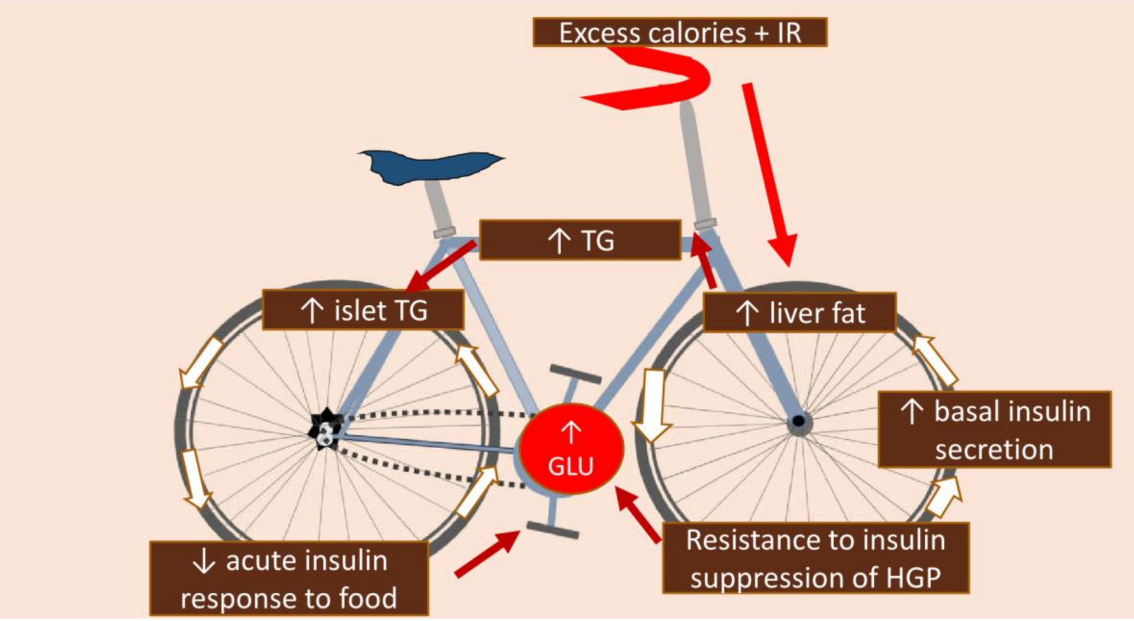

Figure 2 – 3. The twin cycles of Type 2 diabetes. Idea proposed by Taylor at the Banting Memorial (66). IR = insulin resistance, TG = triglyceride, Glu = glucose. HGP = hepatic glucose production.

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As demonstrated in **Figure 2 – 3**, excess calories causes accumulation of fat in the liver, making the liver resistant to insulin suppression of hepatic glucose production. The excess fat eventually – via increasing triglyceride (TG) – spills over to the pancreas, and the accumulation of fat in pancreas impairs insulin secretion. Hence, weight reduction, and taking control of the diet (handle of the bicycle that determines the direction) is important. It is why a very low caloric diets reduces hepatic and pancreatic fat, improves glucose control, and could even put diabetes under remission(67). Taylor has also suggested that type 2 diabetes with normal BMI – typically seen in Asians – may also be reversed via this pathway, as these individuals tend to have relatively high liver fat contents(66).

Currently, the most effective cure for diabetes among the morbidly obese is bariatric surgery. A study showed 88% diabetes remission after bariatric surgery(68). Within days of the surgery and even before weight loss, insulin sensitivity greatly improved, with drop in hepatic and pancreatic fat(69), suggesting the role of the gut in the pathophysiology of both diabetes and NAFLD.

Gut microbiota may play an important role in both diabetes(70) and NAFLD(71). Gut microbes produce a wide array of metabolites that could influence multiple biochemical and disease pathways. SCFA produced by gut microbes, could regulate incretin secretion, and yet may also contribute to extra energy. Diet has a strong influence on gut

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microbiota. Consumption of complete plant based diet versus complete animal based diet substantially changes gut microbiota composition in as short as one day (72).

2.3 Diet and diabetes

Diet may potentially be a powerful tool to prevent diabetes, as a healthy diet may simultaneously target multiple pathways, and affect multiple organ systems in the pathophysiology of diabetes. Diet and lifestyle intervention aiming at weight loss had been shown to be more effective than metformin in preventing type 2 diabetes among overweight individuals with impaired glucose tolerance, in the Diabetes Prevention Program (DPP) trial(73). Besides reducing weights through energy restriction, components from vegetarian diets may potentially work through other underlying pathophysiology – insulin resistance, β-cell dysfunction, incretin effect, appetite regulation – to prevent diabetes.

Insulin resistance

Cross-sectional studies have consistently shown that vegetarians have lower insulin resistance than nonvegetarians(46,47,48). A recent randomized controlled trial also showed that a vegetarian diet improves insulin resistance to a greater extent than conventional diabetes diet among diabetes individuals in an isocaloric setting (74).

Vegetarian diets tend to be higher in carbohydrates and lower in fat. High fat diets and intermediate fatty acid oxidation products such free fatty acids, diacylglycerol, and acyl carnitines, have been shown to induce insulin resistance(63,75,76). Vegetarians in the EPIC-Oxford were found to have lower acyl carnitines than nonvegetarians(77). A trial also shows that type 2 diabetes patients have higher post-prandial free fatty acids after a hamburger meal than a high carbohydrate vegan meal(78). In addition, gut microbiota may influence insulin resistance through metabolites such as branch chain amino acids (BCAA)(79). BCAA have been associated with insulin resistance and predict the development of diabetes, and may interact synergistically with fatty acid metabolite to induce insulin resistance(80,81). Taiwanese vegetarians were found to have lower BCAA than their omnivore counterparts(82). Replacing meat with soy has also been shown to improve insulin resistance in randomized controlled trials.(83,84)

Salicylates may prevent fat-induced insulin resistance(85), and salicylates is found to be naturally present in a wide range of plant foods, with the highest amount found in spices and herbs(86).Whole grains and leafy green vegetables are major sources of magnesium, which is a co-factor in phosphorylation, and its deficiency impairs insulin signaling(87). Bitter melon has been hypothesized to activate AMP-activated kinase (similar manner as metformin)(22). Cinnamon extracts improves insulin sensitivity through activation of insulin receptor kinas and inhibition of insulin receptor

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phosphatase(88). On the other hand, heme iron from meat are highly bioavailable, and iron overload may contribute to insulin resistance through several different pathways(19).

Β-cell dysfunction and incretin effects

Glucolipotoxicity may cause β-cell failure in type 2 diabetes through inducing ER stress, oxidative stresss, and islet inflammation(17). Saturated fat has been shown to trigger β-cell apoptosis through ER stress in vitro and in vivo(18). Fatty acids from meat have been adversely associated with insulin secretion in a Dutch population(89). Nitrites found in processed meat could damage β-cells(90,91). A randomized trial found that while a fish-based diet rich in long chain omega-3 fatty acids reduces β-cell function, a diet rich in plant polyphenols improves β-cell function and increases GLP-1 secretion(92).

Consumption of plant based diet increase production of SCFA and shift the intestinal microbiome to favor those that metabolize carbohydrates(72). SCFA and plant polyphenol have been shown to stimulate the secretion of GLP-1(93). In a randomized cross-over trial, type 2 diabetes patients secreted more GIP and GLP-1 after a vegan meal than a hamburger meal, though this is not observed in healthy individuals(78).

Weight and appetite regulation

Fiber may also assist in energy homeostasis. Besides its potential effect on GLP-1,

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increased colonic propionate (a SCFA) has also been shown to increase peptide YY, and reduce anticipatory reward responses from high-energy food, resulting in lower ad libitum energy intake in a randomized cross-over trial of healthy human(24). Peptide YY has been shown to regulate appetite and weights in both rodent and human(94).

Consumption of fiber rich foods, such as whole grains, vegetables, and fruits have been associated with long term weight reduction among US nurses and health professionals(95). Vegetarians have consistently been shown to have lower BMI than nonvegetarians across cultures(31,46,96). In a randomized controlled trial of type 2 diabetic patients, those on vegan diet with no caloric restriction experienced a greater weight reduction than those on the standard diabetes diet(97).

Epidemiological studies on dietary patterns and diabetes risk

Dietary patterns associated with diabetes protection typically centered on plant based foods with limited red meat, such as the Mediterranean diet(98), the DASH diet(99,100) and dietary patterns in accordance with the dietary guideline(100). Among populations of Chinese ethnicity, dietary patterns characterized by beans, soy, and vegetables are also associated with lower risk of diabetes(101,102,103).

In the Adventist Health Study – 2 (AHS-2), vegan, lacto-ovo, pesco, and semi-vegetarians are associated with 62%, 38%, 21%, and 51% reduction (BMI adjusted) in

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diabetes, respectively, compared with nonvegetarians(39). Among US nurses and health professionals, increasing degree of healthy plant based dietary pattern is associated with decreasing diabetes risk in a dose-dependent trend(104).

2.4 Diet and nonalcoholic fatty liver

Nonalcoholic fatty liver is strongly influenced by body weight, and weight loss is associated with resolution of NAFLD and histological improvement(64). Soft drinks and meat have been found to be associated with NAFLD(105), while saturated fat and cholesterol are associated with nonalcoholic steatohepatitis (NASH)(106), a more severe form of NAFLD characterized by inflammation. High intake of meat and saturated fat increase cholesterol level, and high concentration of cholesterol in liver may play a role in the pathogenesis of NASH(107). On the other hand, Mediterranean diet and carbohydrate restriction have both been shown to reduce hepatic fat in randomized controlled trials(108,109).

Several nutrients are found to play a role in hepatic steatosis. Choline is essential for forming phosphatidylcholine, which is an important component for VLDL-C (very low density lipoprotein) cholesterol needed for exporting TG from the liver(110). Choline intake is inversely associated with nonalcoholic fatty liver in a Chinese population, and effect seems to be more pronounced in men with low saturated fat intake than those

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with high intake(111). Low serum levels of vitamin D has been associated with NAFLD(112), and vitamin D has been speculated to affect hepatic lipogenesis and gluconeogenesis though further research is needed(113).

In vitro and animal studies have shown that polyphenols found in plants, such as EGCG, resveratrol, genistein, quercetin, and anthocyanin, may reduce de novo lipogenesis and increase beta oxidation of fatty acids(114). Other compounds found to reduce lipid fat synthesis and accumulation include betain, myo-inositol, methionine, carnitine(110).

The association between vegetarian diet and nonalcoholic fatty liver had been examined in two studies. Choi et al compared Korean vegetarian monks with individuals from health screening matched for metabolic syndrome and BMI, and found no cross-sectional association(115). However, since nonalcoholic fatty liver and metabolic syndrome are “essentially two definitions of the same problem”(116), the matching procedure would have dismissed potential association altogether. Another case control study in Indians found an inverse association between vegetarian diet and nonalcoholic fatty liver(117).

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CHAPTER 3. METHODS

3.1 Study population

The Tzu Chi Health Study (TCHS) recruited 4625 (age 18 to 87) Tzu Chi volunteers – devoted Buddhists of the Tzu Chi Foundation. Tzu Chi volunteers had at least two years of training, and spent substantial amount of time volunteering for various projects hosted by the Buddhist Tzu Chi Foundation: charity and community services, hospital voluntary work, environmental protection and recycling projects, fund raising, recruiting candidates for Tzu Chi bone marrow registry, and emergency aids during natural disaster in Taiwan and worldwide. Tzu Chi volunteers are required to abstain from alcohol, tobacco, gambling, and encouraged to consume a vegetarian diet. The ratio of men to women is 1:2. Many nonvegetarian volunteers converted to vegetarian in the year 2011 due to a large effort in promoting vegetarian diet, in preparation of the special “water-repentance” activity, in which many took pledge to switch to vegetarian diets.

3.2 Study design

Participants were recruited from October, 2007 to December, 2009. All participants received a comprehensive health examination at the Buddhist Dalin Tzu Chi General Hospital, including anthropometrics, blood chemistry, and abdominal sonography; in

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addition to completing a questionnaire that included basic demographics, medical history, lifestyle, and diet (Appendix A). Participants were followed from 2010 to 2012 (first follow-up), and from 2013 to mid-2016 (second follow-up). Every three years, a post card was sent to invite each participant for a follow-up health examination. At the follow-up, participants answered a questionnaire on diagnosed disease and dietary habits (Appendix C), while receiving a health examination similar to the one at baseline, but with additional HbA1C test. Participants who did not return for health examination by the end of 2015 would receive a follow-up questionnaire in May 2016 to assess their dietary practice and disease conditions (Appendix D). For each disease, choices include: “no”, “yes”, “not sure”, and the time of diagnosis. If the questionnaire was not returned within a month, a research assistant would call the participant to administer this questionnaire. The study was approved by the Institutional Review Board at the Dalin Tzu Chi Hospital (Project numbers: B09602032 and B104030021), and all participants gave written informed consents.

3.3 Assessments of demographics, lifestyle, and diet

At baseline, one of two trained research assistants interviewed each participant on demographics, family history of diseases, personal medical and surgical history, lifestyles including smoking, alcohol drinking, and leisure time physical activities

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(LTPA). Women were additionally interviewed on menstrual cycle and pregnancy related issues. The diet section (Food Frequency Questionnaire – FFQ) included 64 food-group items, in addition to cooking methods, use of sauces, condiments, and dietary supplements. The diet section includes a few questions on vegetarian diet: diet duration and reasons for switching to vegetarian diet. Meat section was skipped for vegetarians to lessen participant burden. Besides frequency, participants were also asked about the portion size they typically consume with reference to pictures and measuring equipment.

Taiwan's food composition table(118) and the United States Department of Agriculture's nutrient database(119) were used to estimated intakes levels of energy and nutrients. Vitamin D and folate contents were previously compiled by Taiwanese experts (120,121). The reliability and validity of the FFQ had been tested in a sub-cohort of the study participants and showed good reliability and moderate to good validity for energy and selected nutrients(122). The correlation coefficients between FFQ and dietary records for vegetables, fruits, soy, meat, fish, eggs and dairy are 0.47, 0.30, 0.41, 0.46, 0.55, 0.47, and 0.39 respectively (unpublished data). The FFQ and detailed grouping of FFQ items into food groups are shown in Appendix A and B, respectively. Nutrients intakes were compared with the 7th Dietary Reference Intakes (DRIs) for Taiwan (Appendix E)(123).

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At follow-up health examination, all participants answered a simple questionnaire (Appendix C) on whether they are vegetarians (choices including: not vegetarian, breakfast vegetarian, vegetarian on 1st and 15th day of each lunar month [a cultural practice for many Asian Buddhists], irregular dates of vegetarian diets, full time vegetarian), and the types of vegetarian diet (vegan, lacto-ovo vegetarian, lacto-vegetarian, ovo-vegetarian). Only full time vegetarians who completely avoid meat, fish, and sea foods were considered vegetarians in our analysis.

For prospective analyses, dietary patterns are divided into 4 types: (1) “vegetarians” are defined as those who have been following vegetarian diets at baseline and all the follow-ups; (2) “the reverted” are those who were initially vegetarians but became nonvegetarians at one of the follow-ups; (3) “the converted” are those who were initially nonvegetarians but converted to vegetarians later; and (4) “nonvegetarians” are those who had consistently reported eating nonvegetarian diet at baseline and follow-up questionnaires.

3.4 Assessment of glucose and metabolic risk factors

Height and weight were measured using a digital scale with participants in light clothes and standing without shoes. Body mass index (BMI) was calculated by dividing weight (kg) by the square of height (m^2). Waist circumference was measured at navel while the participants stood in an upright position. Fasting glucose and blood lipids were assessed using INTEGRA 800 system (Roche, Holliston, MA) at baseline, and Dimension RxL Max (Siemens, Washington, DC) at follow-ups, HbA1C was assessed by Variant Turbo (BIO-RAD, Hercules, CA). Two definitions of metabolic syndrome (MS) were used: (1) the third report of the National Cholesterol Education Program, Adult Treatment Panel (ATP III)(124), which defines MS by presence of any three of the risk criteria: fasting glucose≧100 mg/dL or on hypoglycemic medication, systolic blood pressure (SBP)≧130 mmHg or diastolic blood pressure (DBP)≧85 mmHg or on antihypertensive medication, HDL-C < 40mg/dL for men or <50 mg/dL for women, triglyceride (TG)≧150mg/dL, waist circumference≧90 cm for men or ≧80 cm for women (waist circumference using Asian criteria). (2) the International Diabetes Federation Criteria (IDF)(125), which includes elevated waist circumference, plus two additional risk factors.

3.5 Assessment of liver associated conditions

Fatty liver was evaluated through ultrasound performed by gastroenterologists at the Dalin Tzu Chi Hospital. For those with fatty liver defined by ultrasound, liver fibrosis was further assessed through the Nonalcoholic Fatty Liver Disease (NAFLD) Fibrosis Score(126) according to the following formula:

-1.675 + 0.037 x age + 0.094 x BMI (kg/m^2) + 1.13 x impaired fasting glucose or diabetes (yes=1, no=0) + 0.99 x (AST / ALT) – 0.013 x platelet count (10^9/L) – 0.66 albumin (g/dL)

NAFLD score less than -1.455 is considered to be no fibrosis to fibrosis stage2; -1.455 to 0.675 is considered indeterminate fibrosis, while greater than 0.676 is considered advance fibrosis (stage 3 and 4). These cut off points have been shown to have high accuracy in determining stages of liver fibrosis compared with liver biopsy(126).

Liver enzymes, including gamma-glutamyl-transferase (GGT), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were assessed were assessed using the INTEGRA 800 system (Roche, Holliston, MA). Hepatitis B virus surface antigen and hepatitis C virus antibody were assessed using the Vitro Eci System (Abbott Laboratories, Abbott Park, IL).

3.6 Diabetes ascertainment

Incident cases of diabetes were identified if participants reported diabetes diagnosis at follow-up questionnaire, or if their HbA1C is greater than 6.5%. Participants with only one fasting blood glucose≧126 mg/dL were identified as possible diabetes cases. For these possible diabetes cases, a physician further reviewed their medical records (in October 2016) to check if they have additional blood tests or prescription of diabetes medication to confirm their diabetes status. Participants without further tests or available medical records were considered unconfirmed diabetes events (n=25) and were excluded in main analysis but included in a sensitivity analysis.

	Analysis topics	Elimination criteria	n
1	Food and nutrient intakes	Extreme caloric intakes (men > 4000 kcal or < 800 kcal, women > 3500 kcal or < 500 kcal), n=165	4460
2	Metabolic syndrome	Self-reported history of coronary heart disease and stroke (n=218), smoker (n=79), alcohol drinker (n=169)	4197
3	Impaired glucose metabolism	Extreme caloric intake (n = 165), switched to vegetarian diet after diabetes diagnosis (n=35), uncertain diabetes status (n=10)	4384
4	Fatty liver	(1) Alcohol drinking (n=169), smoking (n=79), hepatitis B (n=818), hepatitis C (n=233), history of cancer (n=172)	3400
		(2) Further exclusion of extreme caloric intakes (n=121) for food vs fatty liver	3279
5	Diabetes incidence	Self reported diabetes or fasting glucose >= 126 at baseline (n=322), history of cancer (n=172), coronary heart disease (n=194), stroke (n=26), ever smokers (n=691) or habitual alcohol drinkers (n=606). Loss to follow-up (n=210), missing in diabetes item in questionnaire (n=42). 25 unconfirmed diabetes.	2918
6	Weight change	Same as (5) diabetes incidence, but additionally excluded those without follow-up weight measurement	2375

Table 3-1. Exclusion criteria and number of participants in each analysis.

3.7 Statistical analysis

The number of participants excluded in each analyses are detailed in **Table 3-1**. We excluded those with extreme energy intake (men: <800kcal/d or >4000kcal/d; women: <500 kcal/d or >3500kcal/d) when analyzing dietary components assessed by FFQ, as

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extreme energy intake may indicate inaccurate response to FFQ or inability of the FFQ to capture the actual diet of the participants. Smokers and habitual alcohol drinkers were excluded from the analysis as smoking may modify the effect of diet on diabetes(101), and alcohol drinking tend to be closely associated with smoking. Those with self-reported history of cancer, coronary heart disease, and stroke were excluded because diet therapy is likely initiated after the diagnosis of these diseases. For analyses on nonalcoholic fatty liver, those with hepatitis B and hepatitis C were further excluded because these conditions may also influence fatty liver(127,128).

For comparison of baseline demographic characteristics, continuous variable were compared using independent sample t-tests (for two groups) or analysis of variance (for more than two groups); categorical variables were compared using Chi-square test or Fisher's exact test (for any cell value less than 5). Nutrient and food intakes were compared using Wilcoxon two sample tests due to the non-normal distribution.

Binary logistic regression was used to study the association between vegetarian diet and metabolic syndrome, while adjusting for age, sex, education, and LTPA, smoking and alcohol drinking. Subgroup analyses on men, premenopausal women, and post-menopausal women were also performed.

Polytomous logistic regression was used to compare the cross-sectional association between vegetarian diet and three stages of glucose metabolism: normal (fasting glucose

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< 100 mg/dL), impaired fasting glucose (IFG, fasting glucose: 100mg/dL to 125 mg/dL), and diabetes (two fasting glucose≧126 mg/dL or self-reported diabetes), while adjusting for age, family history of diabetes, education, LTPA, smoking (men only) and alcohol (men only) in Model 1. Model 2 additionally adjusted for BMI. Analysis were conducted separately for men, premenopausal women, and post-menopausal women.

For the association between nonalcoholic fatty liver and vegetarian diet / food groups, we used binary logistic regression while adjusting for age, gender, education, history of smoking, history of alcohol drinking in Model 1. Model 2 additionally adjusted for BMI. The effect of substituting one food for another on nonalcoholic fatty liver is also performed using logistic regression, in which one of the foods, and the sum of both foods were included as independent, continuous variables in the model, while adjusting for potential confounders(129):

$$\text{Logit (P)} = \beta_0 + \beta_1 * \text{meat} + \beta_2 * (\text{soy} + \text{meat}) + \sum_i \alpha_i z_i$$

where P is the probability for a person to have fatty liver, z_i is covariate i.

In the above model, β_1 is equivalent to increasing 1 serving of meat while holding the total of meat and soy constant (as this value is controlled for in the model). Since the total of meat and soy is held constant, increasing 1 serving of meat means simultaneously decreasing 1 serving of soy. Therefore, β_1 represents the effect of

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substituting a serving of soy (7g protein equivalent) with a serving of meat (7g protein equivalent) on $\log_e$ (P/(1-P)). The same method was applied to all substitution analyses.

General linear model was used to compare change in weight between different dietary patterns while adjusting for baseline age, and education, LTPA, and followed months. Analysis for men and women were conducted separately.

Stratified Cox proportional hazards regression (stratified by follow-up methods and LTPA as the interaction term of these variables and time violated the proportional hazard assumption) was used to analyze the association between dietary patterns and risk of diabetes, with follow-up time as the underlying time scale, while adjusting for age sex, education, family history of diabetes, LTPA, methods of follow-up (questionnaire only vs health examination) in Model 1. Model 2 additionally adjusts for BMI to estimate the protective effect independent of BMI (a mediator). Time of disease occurrence was set to be the time that the first abnormal glucose was identified (HbA1c ≧ 6.5% or fasting blood glucose ≧ 126 mg/dL). For participants who reported diagnosis of diabetes at questionnaire but could not remember the time of diabetes diagnosis, censor time was set to be half-way between the previous known disease-free time point and the follow-up time in which diabetes was reported. For those who did not report having diabetes in the questionnaire, but were found to have diabetes during health examination, the date of health examination was used as the date of disease onset.

Several sensitivity analyses were performed: (1) 25 unconfirmed diabetes event were treated as diabetes cases. (2) To ensure our result was not affected by detection bias from different follow-up methods (health examination vs questionnaire-only), we performed another sensitivity analysis in which only self-reported diabetes were counted as cases. (3) We adjusted for metabolic syndrome in addition to Model 2. (4) Among those with weight measurements at follow-up, we additionally adjusted for change in weight or change in BMI on top of Model 2, to test whether weight change has any effect on diabetes risk.

Among those with consistent diets (included consistent vegetarians and nonvegetarians; excluded the reverted and the converted), we conducted additional analyses on the association between diabetes and food groups (meat, fish, soy, eggs, dairy, whole grains, refined grains, vegetables, fruits). All these food groups were adjusted for energy using residual method(129) and put simultaneously as independent continuous variables into Cox regression model, adjusting for sex, education, family history of diabetes, LTPA, follow-up methods, calories, and BMI, while excluding participants with extreme caloric intakes and participants with censor age <50 years old (to prevent violation of proportional hazard assumption). All analysis were conducted using SAS Statistical Software (version 9.4, SAS Institute, Cary, NC).

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CHAPTER 4. RESULTS

4.1 Food and nutrient intakes

Distribution of nutrient intake for men, pre-menopausal women, and postmenopausal women are shown in **Table 4-1**, **4-2** and **4-3**, respectively. Compared with nonvegetarians, vegetarians tend to consume higher proportion of energy from carbohydrates and lower from fat and protein; higher fiber and lower cholesterol, saturated fat, and vitamin D; higher calcium, magnesium, total iron, thiamin, folate, vitamin A and lower vitamin B12. Among women, vegetarians tend to consume higher energy. When controlling for energy intake by standardizing all participants to 2000 kcal, we found that the difference in calcium and folate intake became statistically insignificant in women.

Distribution of food intakes for men, pre-menopausal women, and post menopausal women are shown in **Table 4-4**, **4-5** and **4-6**, respectively. Compared with nonvegetarians, vegetarians consumed more whole grains, vegetables, nuts, soy, similar amount of fruits, dairy, eggs, and less tea, while completely avoiding meat and fish. Nonvegetarians generally eat a predominantly plant based diet, with the majority consuming less than 1 serving (7g protein equivalent) of meat and 1 serving (7g protein equivalent) of fish per day. Intake of nuts and dairy product is less than a serving per day for 75% of the population. Consumption of sweet beverage is rare.

Table 4-1. Comparison of nutrient intakes between non-vegetarian and vegetarian men

	Crude intake							Standardized to 2000kcal						
	Nonvegetarians (n=1279)			Vegetarians (n=384)			P	Nonvegetarians (n=1279)			Vegetarians (n=384)			P
	Median	P25	P75	Median	P25	P75		Median	P25	P75	Median	P25	P75	
Energy, kcal	2027	1584	2553	2113	1602	2697	0.07							
Protein %	12	11	14	12	10	13	<.001							
CHO %	63	56	69	67	61	72	<.001							
Fat %	25	19	31	22	17	28	<.001							
Protein, g	63	49	82	61	45	78	0.020	62	56	72	58	51	65	<.001
Animal protein, g	19	12	31	4	2	8	<.001	20	12	30	4	2	7	<.001
Plant protein, g	43	33	55	55	41	72	<.001	43	38	48	52	46	59	<.001
Fat, g	53	37	76	50	34	74	0.10	55	42	68	49	39	63	<.001
SFA, g	12	8	17	10	6	14	<.001	12	9	15	10	7	13	<.001
MUFA, g	16	11	25	14	8	20	<.001	17	12	23	13	9	18	<.001
PUFA, g	12	8	21	12	7	21	0.31	13	9	19	12	8	18	0.020
CHO, g	307	243	404	344	257	441	<.001	314	280	346	333	304	358	<.001
Dietary fiber, g	20	15	26	24	18	33	<.001	20	16	25	24	19	29	<.001
Cholesterol, g	158	102	257	92	36	159	<.001	163	105	243	87	36	143	<.001
Ca, mg	540	376	785	649	453	914	<.001	535	376	770	607	446	828	<.001
K, mg	2208	1668	2878	2403	1746	3132	0.004	2217	1705	2766	2297	1793	2835	0.0463
Mg, mg	277	209	370	322	232	437	<.001	270	210	354	305	238	407	<.001
Total iron, mg	11	8	16	14	10	19	<.001	11	9	15	13	10	17	<.001
Heme iron, mg	0.2	0.1	0.4	0	0	0	<.001	0.2	0.1	0.4	0	0	0	<.001
Zinc, mg	10.5	7.9	14.8	10.6	8.2	14.3	0.79	9.7	8.6	12.6	9.4	8.4	11.4	0.0153
Thiamine, mg	1.3	0.8	2.3	1.9	1.1	3.4	<.001	1.3	0.8	2.3	1.8	1.0	3.4	<.001
Riboflavin, mg	1.2	0.8	2.0	1.1	0.7	2.0	0.60	1.1	0.8	1.9	1.0	0.7	1.8	0.0505
Niacin, mg	23	15	33	21	14	31	0.06	21.9	15.4	30.8	19.2	13.3	28.4	<.001
Vitamin B6, mg	1.4	1.0	2.3	1.4	1.0	2.2	0.29	1.3	1.1	2.1	1.2	1.0	1.8	<.001
Folate, µg	417	283	612	506	330	714	<.001	407	279	591	458	331	670	<.001
Vitamin B12, µg	4.0	1.9	9.7	1.2	0.6	3.6	<.001	3.9	2.0	9.0	1.1	0.6	3.3	<.001
Vitamin C, mg	165	116	223	176	122	250	0.006	162	117	223	172	117	236	0.12
Vitamin D, µg	5.5	2.9	59.0	3.5	1.8	13.7	<.001	5.5	2.8	58.6	3.2	1.7	9.4	<.001
Vitamin A, µg RE	2056	1342	3177	2645	1604	3792	<.001	2084	1377	3162	2519	1582	3638	<.001

P25= 25th percentile, P75=75th percentile, SFA= saturated fat, MUFA=monounsaturated fat, PUFA= polyunsaturated fat, CHO= carbohydrates, Ca= calcium, K=potassium, Mg=magnesium, RE=retinol equivalent.

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Table 4-2. Comparison of nutrient intakes between non-vegetarian and vegetarian pre-menopausal women

	Crude intake							Standardized to 2000kcal						
	Non-vegetarians (n=592)			Vegetarians (n=376)			P-value	Non-vegetarians (n=592			Vegetarians (n=376)			P-value
	Median	P25	P75	Median	P25	P75		Median	P25	P75	Median	P25	P75	
Energy, kcal	1472	1129	1954	1680	1268	2119	<.001							
Protein %	13	12	15	12	11	14	<.001							
CHO %	59	53	64	62	56	67	<.001							
Fat %	30	24	35	27	22	32	<.001							
Protein, g	48	36	66	51	38	65	0.30	66	58	74	61	55	68	<.001
Animal protein, g	14	8	21	4	2	7	<.001	19	12	29	5	2	9	<.001
Plant protein, g	34	25	45	46	33	59	<.001	46	41	52	54	49	61	<.001
Fat, g	48	32	67	48	34	67	0.52	66	54	77	59	50	72	<.001
SFA, g	10	7	14	9	6	13	0.00	14	10	17	11	9	14	<.001
MUFA, g	14	9	21	12	9	19	0.01	19	14	26	16	11	21	<.001
PUFA, g	11	6	17	11	7	18	0.25	15	10	21	14	9	20	0.27
CHO, g	213	163	283	258	191	319	<.001	293	263	321	310	281	333	<.001
Dietary fiber, g	19	14	26	22	16	30	<.001	25	20	32	27	22	34	<.001
Cholesterol, g	152	90	231	105	45	163	<.001	208	123	293	125	55	210	<.001
Ca, mg	515	355	773	599	404	865	0.002	688	489	960	715	536	942	0.41
K, mg	2049	1469	2765	2154	1619	2877	0.05	2749	2123	3540	2658	2105	3339	0.23
Mg, mg	236	174	311	280	206	370	<.001	310	243	393	333	263	413	0.002
Total iron, mg	11	8	16	13	9	19	<.001	14	11	19	15	12	20	0.003
Heme iron, mg	0.1	0.0	0.3	0	0	0	<.001	0.2	0.1	0.4	0	0	0	<.001
Zinc, mg	7.7	5.6	11.1	8.2	6.0	11.9	0.09	9.7	8.4	12.5	9.4	8.3	11.9	0.08
Thiamine, mg	1.0	0.6	1.9	1.4	0.8	2.9	<.001	1.3	0.8	2.3	1.7	1.0	3.4	<.001
Riboflavin, mg	1.1	0.7	1.8	1.1	0.7	2.0	0.65	1.4	1.0	2.2	1.3	0.9	2.2	0.12
Niacin, mg	21	13	30	21	14	31	0.44	26	19	37	24	17	35	0.05
Vitamin B6, mg	1.2	0.8	1.8	1.2	0.8	2.1	0.45	1.4	1.1	2.1	1.4	1.0	2.4	0.06
Folate, µg	414	265	607	453	312	708	0.004	533	368	824	541	398	769	0.48
Vitamin B12, µg	2.7	1.4	5.8	1.2	0.6	4.3	<.001	3.5	2.0	7.5	1.6	0.8	4.3	<.001
Vitamin C, mg	160	109	227	164	114	244	0.13	221	146	300	207	144	289	0.29
Vitamin D, µg	4.7	2.3	16.1	4.6	2.3	27.4	0.97	6.2	3.3	21.1	5.7	2.9	32.4	0.29
Vitamin A, µg RE	2057	1181	3283	2296	1459	3463	0.004	2683	1731	4257	2730	1853	4272	0.44

P25= 25th percentile, P75=75th percentile, SFA= saturated fat, MUFA=monounsaturated fat, PUFA= polyunsaturated fat, CHO= carbohydrates, Ca= calcium, K=potassium, Mg=magnesium, RE=retinol equivalent.

Table 4-3. Comparison of nutrient intakes between non-vegetarian and vegetarian post-menopausal women

	Crude intake							Standardized to 2000kcal						
	Nonvegetarians (n=964)			Vegetarians (n=865)			P	Nonvegetarians (n=964)			Vegetarians (n=865)			P
	Median	P25	P75	Median	P25	P75		Median	P25	P75	Median	P25	P75	
Energy, kcal	1416	1071	1784	1575	1218	1933	<.001							
Protein %	13	12	15	12	11	13	<.001							
CHO %	62	56	68	65	59	70	<.001							
Fat %	26	20	31	24	19	29	<.001							
Protein, g	46	36	59	47	36	59	0.34	65	58	74	60	54	67	<.001
Animal protein, g	12	7	19	3	1	7	<.001	18	11	28	4	2	9	<.001
Plant protein, g	34	26	43	42	33	53	<.001	48	42	54	54	49	61	<.001
Fat, g	39	27	55	40	29	56	0.22	57	45	69	54	42	65	<.001
SFA, g	8	5	12	7	5	11	<.001	12	9	15	10	7	12	<.001
MUFA, g	12	7	18	11	7	17	0.18	17	12	23	15	10	21	<.001
PUFA, g	9	5	14	9	5	15	0.06	12	8	18	12	8	18	0.22
CHO, g	218	161	275	254	195	312	<.001	312	281	340	324	296	350	<.001
Dietary fiber, g	18	14	25	21	16	29	<.001	27	21	34	28	22	35	0.0446
Cholesterol, g	107	59	168	73	27	122	<.001	155	90	230	91	36	155	<.001
Ca, mg	572	379	836	630	428	938	<.001	783	567	1177	819	575	1173	0.45
K, mg	2020	1527	2740	2140	1591	2833	0.043	2909	2306	3690	2773	2189	3443	<.001
Mg, mg	249	180	347	289	209	384	<.001	357	270	462	370	283	477	0.06
Total iron, mg	10	7	15	12	8	17	<.001	14	11	19	15	12	20	<.001
Heme iron, mg	0.1	0.0	0.2	0	0	0	<.001	0.1	0.0	0.3	0	0	0	<.001
Zinc, mg	8.3	6.1	13.5	9.1	6.4	15.0	0.009	10.8	9.1	17.2	10.5	9.0	17.5	0.1499
Thiamine, mg	1.2	0.7	2.2	1.6	0.8	3.1	<.001	1.6	1.0	3.1	2.1	1.1	4.1	<.001
Riboflavin, mg	1.2	0.7	2.2	1.2	0.7	2.3	0.54	1.6	1.0	3.0	1.5	1.0	2.8	0.042
Niacin, mg	20	13	31	19	12	32	0.90	27	19	43	25	16	39	<.001
Vitamin B6, mg	1.2	0.8	2.6	1.2	0.8	2.9	0.34	1.5	1.2	3.5	1.4	1.1	3.4	<.001
Folate, μg	441	292	673	500	325	728	<.001	613	417	932	630	447	916	0.38
Vitamin B12, μg	3.0	1.2	9.4	1.4	0.6	7.6	<.001	4.0	1.8	12.8	1.8	0.8	10.9	<.001
Vitamin C, mg	164	116	239	165	116	234	0.71	236	170	327	217	155	305	<.001
Vitamin D, μg	5.5	2.4	145.7	4.1	1.5	171.7	0.001	7.4	3.5	202.0	5.2	2.1	192.6	<.001
Vitamin A, μg RE	2193	1387	3390	2447	1624	3756	<.001	3059	2028	4756	3105	2186	4699	0.44

P25= 25th percentile, P75=75th percentile, SFA= saturated fat, MUFA=monounsaturated fat, PUFA= polyunsaturated fat, CHO= carbohydrates, Ca= calcium, K=potassium, Mg=magnesium, RE=retinol equivalent.

Table 4-4. Comparison of food intakes between non-vegetarian and vegetarian men

	Crude intake							Standardized to 2000kcal						
	Nonvegetarians (n=1279)			Vegetarians (n=384)			P	Nonvegetarians (n=1279)			Vegetarians (n=384)			P
	Median	P25	P75	Median	P25	P75		Median	P25	P75	Median	P25	P75	
Whole grain	1.7	0.5	4.2	2.7	1.1	5.9	<.001	1.7	0.5	4.3	2.6	0.9	6.0	<.001
Refined grain	10.0	6.7	14.1	10.7	6.3	14.8	0.38	10.4	7.5	13.0	10.4	7.4	13.6	1.00
Vegetables	3.7	2.3	5.4	4.7	3.0	6.7	<.001	3.7	2.4	5.4	4.5	2.9	6.5	<.001
Fruits	1.0	0.5	2.0	1.0	0.6	2.0	0.22	1.0	0.5	1.8	1.0	0.5	1.8	0.61
Nuts	0.2	0.1	0.7	0.4	0.1	1.1	<.001	0.2	0.1	0.7	0.4	0.1	1.0	<.001
Dairy	0.2	0.0	0.7	0.2	0.0	0.7	0.70	0.2	0.0	0.6	0.2	0.0	0.6	0.50
Soy	1.0	0.5	1.7	1.5	0.9	2.6	<.001	1.0	0.6	1.6	1.5	0.9	2.4	<.001
Meat	0.6	0.3	1.5	0	0	0	-	0.6	0.2	1.5	0.0	0.0	0.0	-
Fish	0.6	0.2	1.2	0	0	0	-	0.5	0.2	1.2	0.0	0.0	0.0	-
Egg	0.32	0.14	0.57	0.29	0.08	0.46	<.001	0.34	0.17	0.58	0.27	0.09	0.50	<.001
Coffee	8	0	60	5	0	35	0.05	9	0	57	5	0	36	0.039
Tea	150	13	500	80	0	400	<.001	146	14	540	74	0	367	<.001
Sweet beverage	0	0	12	0	0	0	0.015	0	0	12	0	0	0	0.015

P25 = 25th percentile, P75 = 75th percentile; ex = exchange; 1 exchange of whole grain and refined grain = 70 kcal, 1 exchange of vegetables is equivalent to 100g, 1 exchange of fruits = 60 kcal, 1 exchange of nuts =45 kcal, 1 exchange of dairy = 8g protein, 1 exchange of meat, fish, egg, soy = 7g protein.

Table 4-5. Comparison of food intakes between non-vegetarian and vegetarian pre-menopausal women

	Crude intake							Standardized to 2000kcal						
	Nonvegetarians (n=592)			Vegetarians (n=376)			P	Nonvegetarians (n=592)			Vegetarians (n=376)			P
	Median	P25	P75	Median	P25	P75		Median	P25	P75	Median	P25	P75	
Whole grain	1.4	0.4	3.0	2.1	0.9	4.3	<.001	1.7	0.6	3.9	2.7	1.2	4.9	<.001
Refined grain	5.9	3.7	8.8	6.6	4.1	9.8	0.0071	7.8	5.5	10.9	8.4	5.7	11.0	0.49
Vegetables	3.8	2.5	5.7	4.3	2.8	6.4	0.002	5.2	3.2	7.5	5.2	3.7	7.6	0.28
Fruits	1.0	0.5	2.0	1.0	0.5	2.0	0.45	1.4	0.6	2.4	1.2	0.6	2.3	0.40
Nuts	0.1	0.0	0.3	0.3	0.1	0.9	<.001	0.1	0.0	0.4	0.3	0.1	1.0	<.001
Dairy	0.2	0.0	0.7	0.2	0.0	0.5	0.48	0.3	0.0	0.9	0.2	0.0	0.6	0.24
Soy	1.0	0.5	1.7	1.5	0.9	2.5	<.001	1.4	0.8	2.1	1.9	1.3	2.8	<.001
Meat	0.4	0.1	1.0	0	0	0	-	0.6	0.2	1.3	0	0	0	-
Fish	0.2	0.1	0.6	0	0	0	-	0.3	0.1	0.8	0	0	0	-
Egg	0.4	0.2	0.6	0.3	0.1	0.6	<.001	0.5	0.3	0.8	0.4	0.1	0.7	<.001
Coffee	23	0	133	13	0	120	0.20	30	0	171	18	0	145	0.09
Tea	97	10	350	33	0	267	<.001	126	12	468	44	0	324	<.001
Sweet beverage	0	0	10	0	0	0	0.015	0	0	11	0	0	0	0.013

P25 = 25th percentile, P75 = 75th percentile; ex = exchange; 1 exchange of whole grain and refined grain = 70 kcal, 1 exchange of vegetables is equivalent to 100g, 1 exchange of fruits = 60 kcal, 1 exchange of nuts =45 kcal, 1 exchange of dairy = 8g protein, 1 exchange of meat, fish, egg, soy = 7g protein.

Table 4-6. Comparison of food intakes between non-vegetarian and vegetarian post-menopausal women

	Crude intake							Standardized to 2000kcal						
	Nonvegetarians (n=964)			Vegetarians (n=865)			P	Nonvegetarians (n=964)			Vegetarians (n=865)			P
	Median	P25	P75	Median	P25	P75		Median	P25	P75	Median	P25	P75	
Whole grain	2.0	0.8	4.1	2.5	1.1	5.2	<.001	2.9	1.2	5.9	3.3	1.4	6.9	0.002
Refined grain	5.5	3.1	8.6	6.5	3.5	9.8	<.001	8.4	5.1	11.2	8.9	5.0	12.0	0.045
Vegetables	4.0	2.4	5.8	4.4	2.9	6.6	<.001	5.6	3.6	8.1	5.7	3.8	8.2	0.22
Fruits	1.0	0.5	2.0	1.0	0.6	2.0	0.65	1.6	0.9	2.7	1.4	0.8	2.5	0.004
Nuts	0.1	0.0	0.5	0.3	0.1	0.9	<.001	0.2	0.0	0.7	0.3	0.1	1.0	<.001
Dairy	0.22	0.02	0.72	0.18	0.02	0.63	0.044	0.3	0.0	1.0	0.2	0.0	0.8	0.002
Soy	0.9	0.5	1.6	1.3	0.7	2.2	<.001	1.3	0.7	2.1	1.7	1.1	2.7	<.001
Meat	0.2	0.1	0.6	0.0	0.0	0.0	-	0.3	0.1	0.9	0.0	0.0	0.0	-
Fish	0.3	0.1	0.7	0.0	0.0	0.0	-	0.4	0.1	1.0	0.0	0.0	0.0	-
Egg	0.29	0.10	0.43	0.29	0.07	0.43	<.001	0.34	0.15	0.63	0.29	0.08	0.52	<.001
Coffee	0	0	47	0	0	23	0.004	0	0	67	0	0	30	0.001
Tea	10	0	200	0	0	70	<.001	14	0	248	0	0	99	<.001
Sweet beverage	0	0	0	0	0	0	0.22	0	0	0	0	0	0	0.21

P25 = 25th percentile, P75 = 75th percentile; ex = exchange; 1 exchange of whole grain and refined grain = 70 kcal, 1 exchange of vegetables is equivalent to 100g, 1 exchange of fruits = 60 kcal, 1 exchange of nuts =45 kcal, 1 exchange of dairy = 8g protein, 1 exchange of meat, fish, eggs.

Protein intake per kg body weight is shown in **Figure 4 – 1**. Men tend to consume more protein than women. Greater than 30% of men and 40% of women had protein intake less than 0.80g/kg body weight.

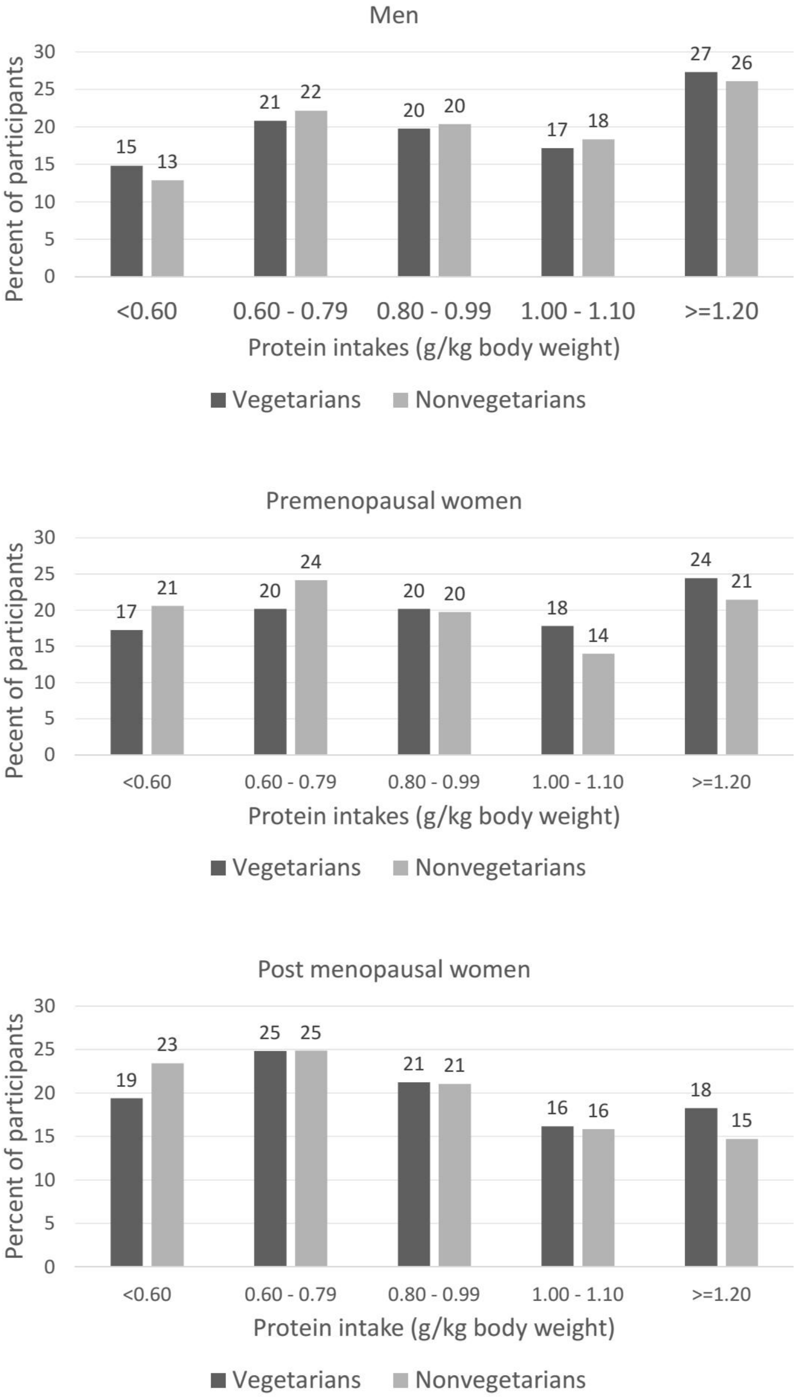

Figure 4 – 1. Protein intake per kg body weight.

In addition, we compared the dietary intake of vegetarians and nonvegetarians against the Taiwanese DRIs for men (**Figure 4 – 2**), premenopausal women (**Figure 4 – 3**), and post-menopausal women (**Figure 4 – 4**). Most participants consumed enough vitamin A and vitamin C to meet the recommendation. However, a substantial proportion of participants may not be consuming adequate amount of vitamin D, vitamin B6, vitamin B12 (especially for vegetarians), calcium, magnesium, and zinc.

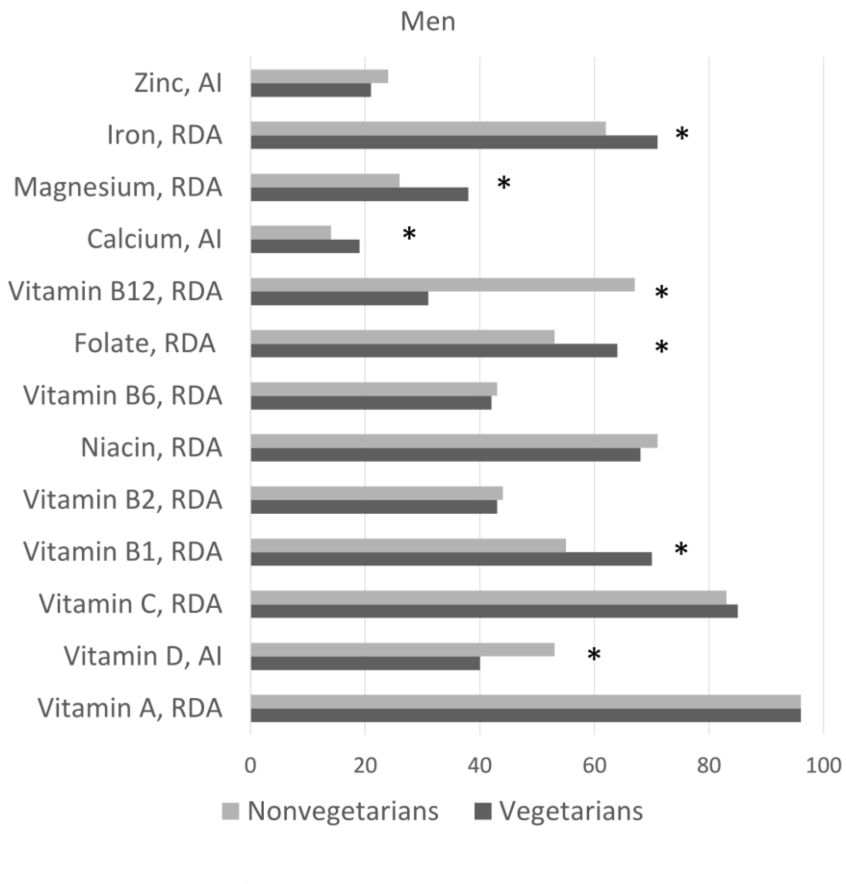

Figure 4 – 2. Percent of men meeting the Taiwanese dietary recommended intakes (DRIs) for nutrients. * indicates $p<0.05$ for chi-square test. RDA = recommended dietary allowance, AI = adequate intakes.

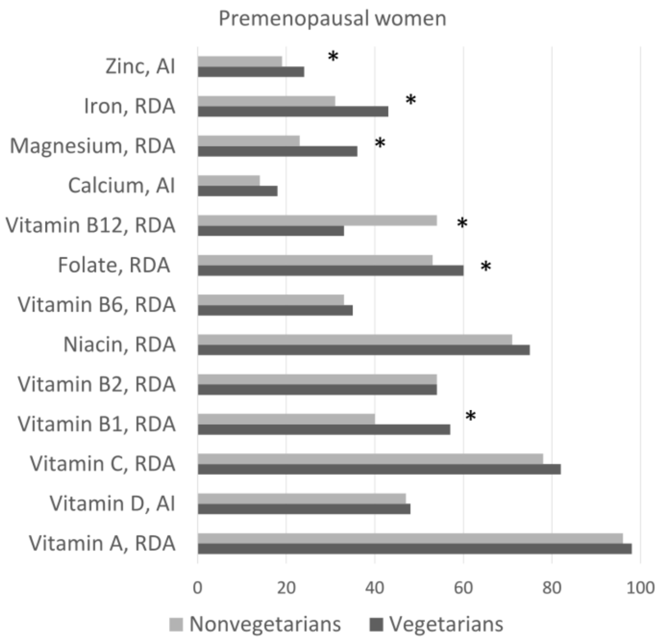

Figure 4 – 3. Percent of premenopausal women meeting the Taiwanese dietary recommended intakes (DRIs) for nutrients. * indicates p<0.05 for chi-square test. RDA = recommended dietary allowance, AI = adequate intakes.

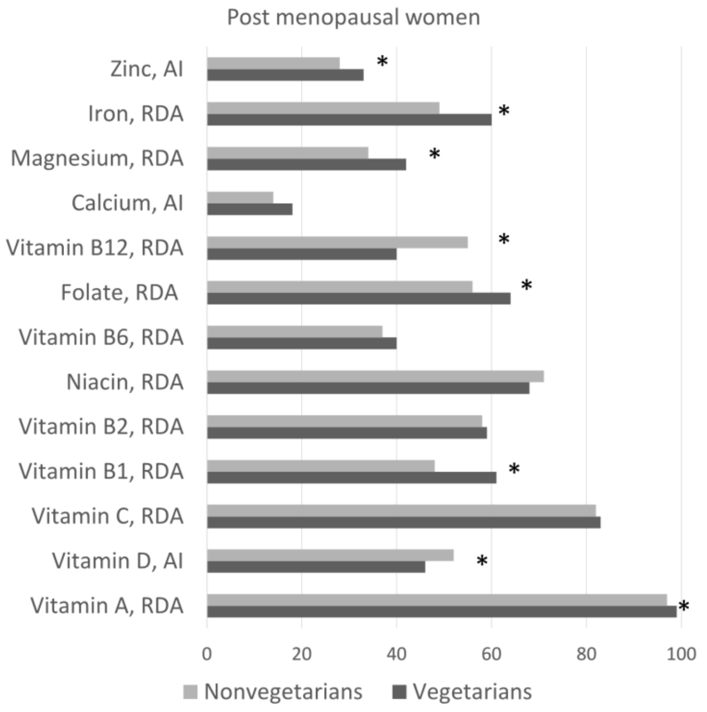

Figure 4 – 4. Percent of post-menopausal women meeting the Taiwanese dietary recommended intakes (DRIs) for nutrients. * indicates p<0.05 for chi-square test. RDA = recommended dietary allowance, AI = adequate intakes.

4.2 Metabolic syndrome

Table 4 – 7 shows the demographics, lifestyle, and cardiometabolic risk factors between vegetarians and nonvegetarians. Compared with nonvegetarians, vegetarians had lower BMI, waist circumferences, all types of cholesterol, and glucose. Vegetarian men and premenopausal women tend to have similar TG as their nonvegetarian counterparts, but post-menopausal female vegetarian had higher TG than nonvegetarians (the difference is insignificant when compared using 150 mg/dL as the cut off point for hypertriglyceridemia). The proportion of low HDL-C is higher among vegetarians (30 – 40%) than nonvegetarians (20 – 30%). No significant difference was found in history of smoking and alcohol drinking.

Table 4 – 8 shows the association between vegetarian diet and two definitions of metabolic syndrome. Vegetarian diet is associated with 16% (OR: 0.84, 95% CI: 0.70 – 1.00, p=0.047) and 38% (OR: 0.62, 95% CI: 0.49 – 0.77, p<0.001) reduction in metabolic syndrome by ATP III and IDF definitions, respectively. Subgroup analysis in men, premenopausal women, and post-menopausal women showed similar magnitude of protection in all groups, though protective association were statistical insignificance due to smaller sample size. Agreement between ATP and IDF diagnosis were better for nonvegetarians (kappa=0.77) than for vegetarians (kappa=0.66).

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Table 4 – 7. Demographics and cardiometabolic characteristics between vegetarians and nonvegetarians

	Men			**Premenopausal women**			**Post menopausal women**		
	Nonvegetarians (N=1111)	**Vegetarians (n=380)**	**P**	**Nonvegetarians (n=595)**	**Vegetarians (n=382)**	**P**	**Nonvegetarians (n=924)**	**Vegetarians (n=805)**	**P**
Age	54±10	55±9	0.29	44±6	45±5	0.008	58±7	58±17	0.41
SBP	129±15	127±16	0.11	120±16	119±15	0.19	129±18	127±17	0.04
DBP	78±10	77±10	0.23	70±11	69±10	0.2	74±10	73±10	0.09
BMI	24.3±3.1	23.4±3.0	<.001	23.1±3.4	22.5±3.0	0.003	23.8±3.3	23.0±3.0	<.001
Waist	83±8	81±8	<.001	74±8	72±7	<.001	76±8	75±8	0.002
Total cholesterol	191±36	173±35	<.001	188±35	170±31	<.001	206±34	190±32	<.001
HDL-C-c	49±13	45±11	<.001	58±14	55±14	0.003	59±15	55±14	<.001
LDL-C-c	128±32	114±29	<.001	120±32	107±28	<.001	135±32	123±29	<.001
Fasting glucose	95±18	94±16	0.15	91±18	89±11	0.034	97±24	93±16	<.001
TG*	123±86	124±89	0.74	91±46	91±53	0.65	110±67	117±73	0.022
Education									
Elementary	17	17	0.39	9	10	0.64	39	42	0.42
Secondary	48	52		65	67		46	44	
College	35	31		26	23		15	14	
LTPA									
<30min	29	34	0.07	50	52	0.37	28	33	0.05
30-180min	32	33		33	29		36	33	
>180min	39	32		17	19		36	33	

Table 4 – 7. Continues

	Men			Premenopausal women			Post menopausal women		
	Nonvegetarians (N=1111)	Vegetarians (n=380)	P	Nonvegetarians (n=595)	Vegetarians (n=382)	P	Nonvegetarians (n=924)	Vegetarians (n=805)	P
Smoking									
Past	33	31	0.33	2	2	0.93	1	1	0.35
Never	67	69		98	98		99	99	
Alcohol drinking									
Past	24	29	0.06	1	1	0.96	1		0.73
Never	76	71		99	99		99		
Elevated TG	24	25	0.75	9	11	0.42	18	20	0.45
Elevated BP	50	44	0.032	26	20	0.046	48	46	0.52
Elevated glucose	24	17	0.006	12	7	0.009	28	18	<.001
Large waist	17	13	0.07	18	13	0.042	25	20	0.024
Low HDL-C-c	22	32	<.001	29	38	0.005	29	40	<.001
MS-ATP	18	15	0.25	11	9	0.5	21	19	0.25
MS-IDF	10	7	0.033	8	6	0.13	15	11	0.003

Data are mean ± standard deviation or percentage. *P-value calculated using log transformed data. SBP = systolic blood pressure, DBP= diastolic blood pressure, BMI= body mass index, Waist = waist circumference, TG = triglyceride, Elevated TG = triglyceride ≧ 150mg/dL, LTPA = leisure time physical activities, Elevated BP = systolic blood pressure ≧130 mmHg or diastolic blood pressure ≧85mmHg or use of anti-hypertensive medication. Elevated glucose = fasting glucose ≧100mg/dL, large waist = waist circumference ≧90 cm for men or ≧80 cm for women, low HDL-C = high density lipoprotein cholesterol <40 mg/dL for men or <50 mg/dL for women. MS-ATP = metabolic syndrome by Adult Treatment Panel III of the National Cholesterol Education Program. MS-IDF = metabolic syndrome by International Federation of Diabetes.

Table 4 – 8. Vegetarian diet and metabolic syndrome. Odds ratios (95% confidence interval) of metabolic syndrome according to Adult Treatment Panel III (ATP-III) definition and International Federation of Diabetes (IDF).

	ATP-III				IDF			
	OR	95%CI		P	OR	95%CI		P
All	0.84	0.70	1.00	0.047	0.62	0.49	0.77	<.0001
Men	0.82	0.59	1.13	0.23	0.60	0.38	0.95	0.029
Premenopausal women	0.80	0.52	1.25	0.33	0.62	0.36	1.05	0.08
Post menopausal women	0.83	0.65	1.05	0.13	0.60	0.45	0.80	0.001

Model adjusted for age, gender, education, leisure time physical activities, history of smoking, history of alcohol, and history of alcohol drinking

4.3 Impaired glucose metabolism

Table 4 – 9 compares the demographics and health characteristics between vegetarians and nonvegetarians included in the cross-sectional analysis of impaired glucose metabolism. **Table 4 – 10** compares the demographics and health characteristics among participants with different stages of impaired glucose metabolism: normal, IFG, and diabetes. Diabetic participants were the oldest, had the highest BMI, waist circumference, family history of diabetes, lowest education, and were more likely to participate in LTPA.

Polytomous logistic regression analysis comparing the association between diet and stages of impaired glucose metabolism showed that vegetarian diet is associated lower chance of having IFG and diabetes for all of men, pre-menopausal women, and post-menopausal women (**Table 4 – 11**).

Table 4 – 9. Demographics characteristics and health characteristics (for impaired glucose metabolism analysis)

	Pre-menopausal women			**Menopausal women**			**Men**		
	Veg	**Nonveg**	**P**	**Veg**	**Nonveg**	**P**	**Veg**	**Nonveg**	**P**
N	**343**	**614**		**792**	**997**		**349**	**1289**	
Impaired glucose metabolism									
Diabetes	0.6%	2.3%	<0.001*	2.8%	10%	<0.001	4.3%	8.1%	0.001
Impaired fasting glucose	5.8%	9.0%		14%	18%		12%	17%	
Age (years)	46±5	45±6	0.007	59±8	58±7	0.25	55±9	55±10	0.14
BMI (kg/m^2)	22.6±2.9	23.1±3.4	0.023	23±3	24±3	<0.001	23±3	24±3	<0.001
Waist (cm)	72±7	73±8	0.008	75±8	76±8	<0.001	81±8	84±8	<0.001
Body fat (%)	28±5	30±7	<0.001	28±6	31±6	<0.001	19±5	22±5	<0.001
Education									
Elementary or lower	10%	10%	0.90	44%	41%	0.35	19%	17%	0.65
Secondary	67%	65%		42%	45%		50%	49%	
College or higher	24%	25%		14%	14%		31%	34%	
Family history of diabetes	34%	36%	0.50	27%	33%	0.009	28%	27%	0.85
Smoking									
Current	0%	0.5%	0.043*	0%	0%	0.09*	0%	5%	<0.001*
Past	2%	1.5%		1%	1%		31%	33%	
Never	98%	98%		99%	99%		69%	62%	
Alcohol									
Current	1%	2%	0.012*	1%	1%	0.025*	1%	10%	<0.001*
Past	1%	1%		1%	1%		26%	22%	
Never	98%	97%		98%	98%		72%	68%	
LTPA per week									
0-30min	51%	49%	0.65	33%	28%	0.057	32%	29%	0.037
31-180min	31%	33%		32%	35%		35%	31%	
>180min	19%	17%		34%	37%		33%	40%	

Data are presented as either mean ± standard deviation or percent. Veg = vegetarians. Nonveg= nonvegetarians. BMI = body mass index. LTPA = leisure time physical activity. *Fisher's exact test

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Table 4 – 10. Characteristics of participants with different stages of impaired glucose metabolism.

	Pre-menopausal women				**Menopausal women**				**Men**			
	Normal	**IFG**	**Diabetes**	**P**	**Normal**	**IFG**	**Diabetes**	**P**	**Normal**	**IFG**	**Diabetes**	**P**
N	**866**	**75**	**16**		**1382**	**285**	**122**		**1253**	**266**	**119**	
Age (years)	45±6	47±5	48±4	<0.001	58±7	60±7	62±8	<0.001	54±10	58±9	59±8	<0.001
BMI (kg/m^2)	23±3	24±4	27±4	<0.001	23±3	25±3	25±4	<0.001	24±3	25±3	25±3	<0.001
Waist (cm)	72±7	77±8	83±9	<0.0001	74±7	79±9	80±8	<0.001	82±8	86±9	87±9	<0.001
DM family history	35%	33%	63%	0.07	28%	28%	63%	<0.001	24%	27%	58%	<0.001
Education												
Elementary or lower	9%	12%	44%	<0.001*	39%	50%	58%	<0.001	17%	23%	16%	0.009
Secondary	65%	77%	50%		46%	40%	29%		48%	50%	59%	
College or higher	26%	11%	6%		15%	10%	13%		35%	27%	25%	
Smoking												
Current	0%	0%	0%	0.15*	0%	0%	0%	0.013*	4%	3%	5%	0.56
Past	2%	0%	0%		1%	1%	0%		33%	29%	36%	
Never	98%	100%	100%		99%	98%	100%		63%	67%	59%	
Alcohol												
Current	1%	4%	0%	0.004*	1%	0%	0%	0.004*	8%	10%	8%	0.69
Past	1%	0%	6%		1%	1%	1%		23%	23%	24%	
Never	97%	96%	94%		98%	99%	99%		70%	67%	68%	
LTPA per week												
0-30 minutes	49%	55%	50%	<0.001*	31%	33%	22%	0.023	29%	29%	29%	0.33
31 - 180 minutes	33%	31%	31%		34%	32%	28%		33%	28%	28%	
>180 minutes	18%	15%	19%		35%	35%	50%		37%	42%	43%	
Diet												
Vegetarian	37%	27%	13%	<0.001*	48%	39%	18%	<0.001	23%	16%	13%	0.001
Nonvegetarian	63%	73%	88%		52%	61%	82%		77%	84%	87%	

Data are presented as either mean ± standard deviation or percent. IFG = impaired fasting glucose BMI = body mass index. LTPA = leisure time physical activity. *Fisher's exact test.

Table 4 – 11. Polytomous logistic regression analysis of the association between Taiwanese vegetarian diet and impaired glucose metabolism

	IFG			**Diabetes**		
	OR	**95% CI**		**OR**	**95% CI**	
Men	0.66	0.46	0.95	0.49	0.28	0.89
Premenopausal women	0.60	0.35	1.04	0.26	0.06	1.21
Post menopausal women	0.73	0.56	0.95	0.25	0.15	0.42

IFG = impaired fasting glucose. OR = odds ratio. Model adjusted for age, BMI, family history of diabetes, education, leisure time physical activities, smoking (current vs never), alcohol drinking (current vs never).

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4.4 Nonalcoholic fatty liver

Table 4 – 12 compares the demographics and health characteristics of nonvegetarians and vegetarians. Vegetarians were older and less likely to have a history of smoking or alcohol drinking, had higher proportions as female, and less educated. Vegetarians had lower liver enzymes (GGT, ALT, AST), glucose, waist circumference, all types of cholesterol, blood pressures, and lower prevalence of diabetes while there was no significant difference in TG and metabolic syndrome. Although vegetarians have lower HDL-C, their total cholesterol to HDL-C ratio were actually lower.

The associations between fatty liver and demographic, lifestyle, and metabolic characteristics are presented in **Table 4 – 13**. Fatty liver was associated with lower education, history of smoking, history of alcohol drinking, metabolic syndrome and all of its components, as well as diabetes. The prevalence of fatty liver is greater than 80% among those with metabolic syndrome, high waist circumference, diabetes, or elevated TG.

Logistic regression analysis on the association between vegetarian diet and fatty liver is shown in **Table 4 – 14**. Vegetarian diet is associated with lower risk of fatty liver (OR=0.79, 95% CI: 0.68, 0.91) in Model 1 (adjusted for age, gender, education, history of smoking, history of alcohol drinking). But this protective association attenuated after further adjustment for BMI in Model 2. Similar trends were observed in the subgroup analyses by gender, history of drinking or smoking, and presence of diabetes or metabolic syndrome. Stratification by BMI

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also fully accounted for the protective association of a vegetarian diet (for BMI <24 kg/m^2: OR: 0.91, 95% CI: 0.75, 1.11; for BMI ≧24 kg/m^2: OR: 1.10, 95% CI: 0.83, 1.45). In our sensitivity analyses, vegetarian diets were inversely associated with fatty liver among participants with hepatitis B (n = 718; model 1: OR = 0.68, 95% CI = 0.49, 0.91; model 2: OR = 0.86, 95% CI = 0.61, 0.1.23), but not those with hepatitis C (n = 203; model 1: OR = 1.08, 95% CI = 0.59, 1.99; model 2: OR = 1.21, 95% CI = 0.63, 2.32).

Among 1911 participants with fatty liver, only 1 vegetarian and 14 nonvegetarians had NAFLD Fibrosis Score greater than 0.676 (advance fibrosis). Vegetarians had lower mean scores than nonvegetarians (-4.168 vs -3.914) and were less likely to have advanced fibrosis (**Figure 4 – 5**).

Table 4 – 12. Demographics and health characteristics of vegetarians and nonvegetarians (for nonalcoholic fatty liver analysis)

	Nonvegetarians (n=2127)		**Vegetarians (n=1273)**		
	Mean or %	**SD**	**Mean or %**	**SD**	**P**
Age, y	54	10	55	9	<.001
BMI, kg/m^2	23.9	3.2	22.9	3	<.001
WC, cm	78.4	8.9	75.4	8.2	<.001
TG, mg/dL	115	75	116	75	0.57*
GGT, units/L	28	24	21	17	<.001*
AST, units/L	24	11	23	7	<.001*
ALT, units/L	25	17	20	11	<.001*
Fasting glucose, mg/dL	95	20	93	16	<.001
SBP, mmHg	127	17	126	17	0.006
DBP, mmHg	75	11	73	10	<.001
Total cholesterol, mg/dL	198	36	184	33	<.001
HDL-C, mg/dL	55	15	53	14	<.001
LDL-C, mg/dL	130	33	119	29	<.001

Table 4 – 12. Continues.

	Nonvegetarians (n=2127)		Vegetarians (n=1273)		
	Mean or %	**SD**	**Mean or %**	**SD**	**P**
Total-C / HDL-C ratio	3.86	1.18	3.67	1.09	<.001
Female, %	59		78		<.001
MS, %	19		17		0.15
Elevated TG, %	21		21		0.89
Low HDL-C, %	26		37		<.001
High WC, %	20		16		0.003
High fasting glucose, %	24		16		<.001
Elevated BP, %	44		41		0.07
Education					
Elementary, %	23		29		<.001
Secondary, %	52		50		
College, %	25		20		
LTPA					
<30min, %	33		37		0.021
30 - 180 min, %	33		33		
>180min, %	34		30		
Diabetes†, %	8		4		<.001
Smoking					
Past, %	15		7		<.001
Never, %	85		93		
Alcohol drinking					
Past, %	11		7		0.001
Never, %	89		93		
Fatty liver, %	59		52		<.001

BMI, body mass index; WC, waist circumference; TG, triglyceride; GGT, gamma-glutamyl-transferase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high density lipoprotein cholesterol; LDL-C, low densit lipoprotein cholesterol; MS, metabolic syndrome as defined by ATP III criteria; LTPA, leisure time physical activities. Elevated TG: ≧ 150 mg/dL, low HDL-C: < 40 mg/dL for men and < 50 mg/dL for women, high WC: ≧ 90 cm for men and ≧ 80 cm for women, elevated fasting glucose: ≧ 100 mg/dL, elevated blood pressures: SBP ≧ 130 mmHg or DBP ≧ 85 mmHg or on antihypertensive medication. *P-value calculated based on $\log_e$ transformed values. †Data available for 2119 nonvegetarians and all vegetarians (8 nonvegetarians with glucose >126 mg/dL but no other data to confirm diabetes status were omitted).

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Table 4 – 13. Risk of nonalcoholic fatty liver by demographics, lifestyle, and metabolic characteristics

		Model 1	**Model 2**
	Cases / n (%)	**OR (95% CI)**	**OR (95% CI)**
Age, per 1 year increase		1.02 (1.01, 1.03)	1.02 (1.01, 1.03)
Gender			
Female	1209 / 2244 (54)	1	1
Male	702 / 1156 (60)	1.12 (0.95, 1.33)	0.74 (0.61, 0.91)
Education			
College	412 / 783 (53)	1	1
Secondary	970 / 1745 (56)	1.12 (0.94, 1.33)	1.01 (0.82, 1.23)
Elementary	529 / 872 (61)	1.22 (0.98, 1.52)	0.81 (0.63, 1.04)
LTPA			
>180min	657 / 1101 (60)	1	1
30 - 180 min	627 / 1116 (56)	0.95 (0.80, 1.13)	1.09 (0.89, 1.33)
< 30 min	627 / 1183 (53)	0.87 (0.73, 1.03)	0.88 (0.72, 1.08)
Smoking			
Never	1630 / 2991 (54)	1	1
Past	281 / 409 (69)	1.61 (1.23, 2.11)	1.42 (1.04, 1.95)
Alcohol drinking			
Never	1701 / 3082 (55)	1	1
Past	210 / 318 (66)	1.14 (0.85, 1.52)	1.06 (0.75, 1.48)
TG			
Normal	1323 / 2691 (49)	1	1
Elevated	588 / 709 (83)	4.85 (3.92, 5.99)	3.36 (2.67, 4.23)
HDL-C-c			
Normal	1150 / 2363 (49)	1	1
Low	761 / 1037 (73)	3.04 (2.59, 3.58)	2.11 (1.75, 2.53)
Fasting glucose			
Normal	1387 / 2694 (51)	1	1
Elevated	524 / 706 (74)	2.50 (2.07, 3.02)	1.88 (1.51, 2.34)
Waist circumference			
Normal	1386 / 2774 (50)	1	1
Elevated	525 / 626 (84)	5.10 (4.06, 6.04)	1.25 (0.95, 1.64)

Table 4 – 13. Continues

	Cases / n (%)	Model 1 OR (95% CI)	Model 2 OR (95% CI)
Blood pressures			
Normal	919 / 1934 (48)	1	1
Elevated	992 / 1466 (68)	2.17 (1.86, 2.52)	1.39 (1.17, 1.66)
Metabolic syndrome			
No	1368 / 2779 (49)	1	1
Yes	543 / 621 (87)	6.81 (5.30, 8.76)	3.04 (2.30, 4.01)
Diabetes			
No	1728 / 3174 (54)	1	1
Yes	177 / 218 (81)	3.23 (2.28, 4.59)	2.53 (1.70, 3.77)
BMI			
<24	652 / 1822 (38)	1	
≧24	1259 / 1578 (80)	7.07 (6.03, 8.30)	
Per 1 kg/m^2	-	1.62 (1.56, 1.68)	

OR, odds ratio; 95% CI, 95% confidence interval; BMI, body mass index; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LTPA, leisure time physical activities. Model 1: adjusted for age, gender, education, history of smoking, and history of alcohol drinking. Model 2: additional adjustment of BMI. Elevated TG: ≧ 150 mg/dL, low HDL-C: < 40 mg/dL for men and < 50 mg/dL for women, high WC: ≧ 90 cm for men and ≧ 80 cm for women, elevated fasting glucose: ≧ 100 mg/dL, elevated blood pressures: SBP ≧ 130 mmHg or DBP ≧ 85 mmHg or on antihypertensive medication. Metabolic syndrome is defined by ATP III criteria.

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Table 4 – 14. Risk of nonalcoholic fatty liver in vegetarians versus nonvegetarians

	Model 1	**Model 2**
	OR (95% CI)	**OR (95% CI)**
All	0.79 (0.68, 0.91)	1.05 (0.89, 1.25)
Subgroup analyses		
Men	0.74 (0.56, 0.97)	0.97 (0.70, 1.35)
Women	0.80 (0.67, 0.95)	1.08 (0.89, 1.31)
No diabetes	0.82 (0.71, 0.95)	1.08 (0.91, 1.28)
With diabetes	0.61 (0.29, 1.31)	1.10 (0.48, 2.65)
Never drinkers	0.78 (0.67, 0.91)	1.05 (0.88, 1.26)
Past drinkers	0.83 (0.49, 1.39)	1.04 (0.57, 1.90)
Never smokers	0.78 (0.67, 0.91)	1.04 (0.87, 1.24)
Past smokers	0.78 (0.48, 1.28)	1.16 (0.62, 2.16)
BMI < 24	0.91 (0.75, 1.11)	0.98 (0.80, 1.21)
BMI ≧ 24	1.10 (0.83, 1.45)	1.20 (0.90, 1.59)
No MS	0.81 (0.69, 0.95)	0.98 (0.82, 1.18)
with MS	0.77 (0.47, 1.26)	1.32 (0.77, 2.29)

OR, odds ratio; 95% CI, 95% confidence interval; BMI, body mass index; MS, metabolic syndrome defined by ATP III criteria. Model 1, adjusted for age, gender, education, history of smoking, history of alcohol drinking, and history of smoking. Model 2, additional adjustment for BMI.

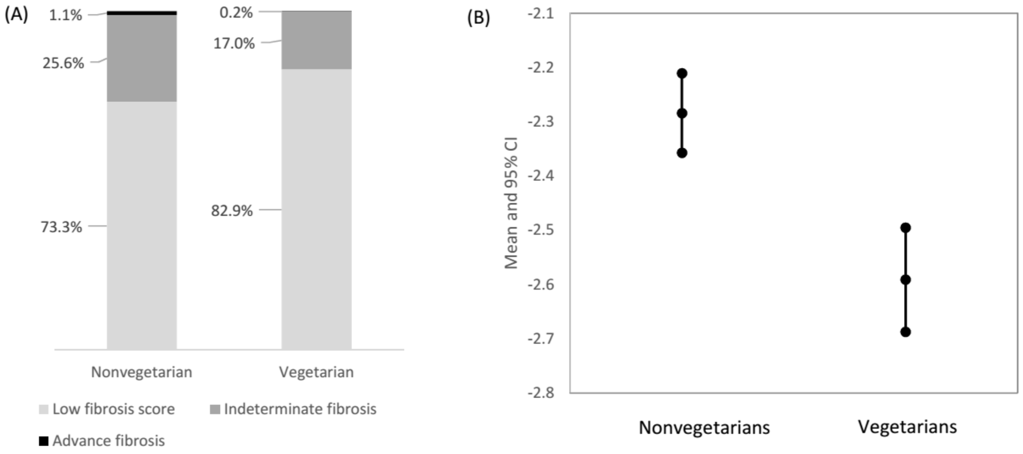

Figure 4 – 5. Nonalcoholic Fatty Liver Disease (NAFLD) Fibrosis Scores. Comparison of NAFLD Fibrosis scores between nonvegetarians and vegetarians among 1911 participants with nonalcoholic fatty liver. (A) Proportion of participants with different stages of liver fibrosis scores. Low fibrosis score: <-1.455, indeterminate fibrosis: -1.455 to 0.676, advanced fibrosis: >0.676. (B) Mean and 95% confidence interval of NAFLD Fibrosis Score (B).

The association between food groups and fatty liver in isocaloric conditions is presented in **Table 4-15**. Fatty liver is associated with higher intake of meat (OR = 1.09, 95% CI = 1.01, 1.18), fish (OR = 1.09, 95% CI = 1.00, 1.20), and fruits/fruit juice (OR = 1.07, 95% CI = 1.01, 1.13). Other animal protein foods such as dairy and eggs were associated with non-significant increases in risk. Whole grains appeared to be protective (OR = 0.96, 95% CI = 0.94, 0.98), while soy was associated with a non-significant protection, though the magnitude of protection is comparable to whole grains. Substituting soy with meat or fish, or substituting whole grains with refined grains or fruits/fruit juice were associated with increased risk for fatty liver (**Figure 4 – 6**).

Table 4 – 15. Association between selected food groups and nonalcoholic fatty liver

	Model 1 **OR (95% CI)**	**Model 2** **OR (95% CI)**
Meat	1.09 (1.01, 1.18)	1.04 (0.95, 1.14)
Fish	1.09 (1.00, 1.20)	1.01 (0.91, 1.12)
Dairy	1.07 (0.98, 1.18)	1.02 (0.92, 1.14)
Eggs	1.05 (0.90, 1.23)	0.99 (0.82, 1.19)
Soy	0.96 (0.91, 1.03)	0.95 (0.88, 1.02)
Whole grains	0.96 (0.94, 0.98)	0.99 (0.96, 1.01)
Refined grains	1.00 (0.98, 1.02)	1.01 (0.99, 1.03)
Vegetables	1.01 (0.99, 1.04)	1.01 (0.98, 1.04)
Fruits / fruit juice	1.07 (1.01, 1.13)	1.02 (0.96, 1.08)

OR, odds ratio; 95% CI, 95% confidence interval. Excluding 121 participants with extreme energy intake (men: energy intake < 800 kcal or >4000 kcal, women: energy intake < 500 kcal or >3500 kcal). Model 1: adjusted for age, gender, education, history of smoking, history of alcohol drinking, total energy intake, and vegetarian diet. Model 2: additional adjustment for BMI.

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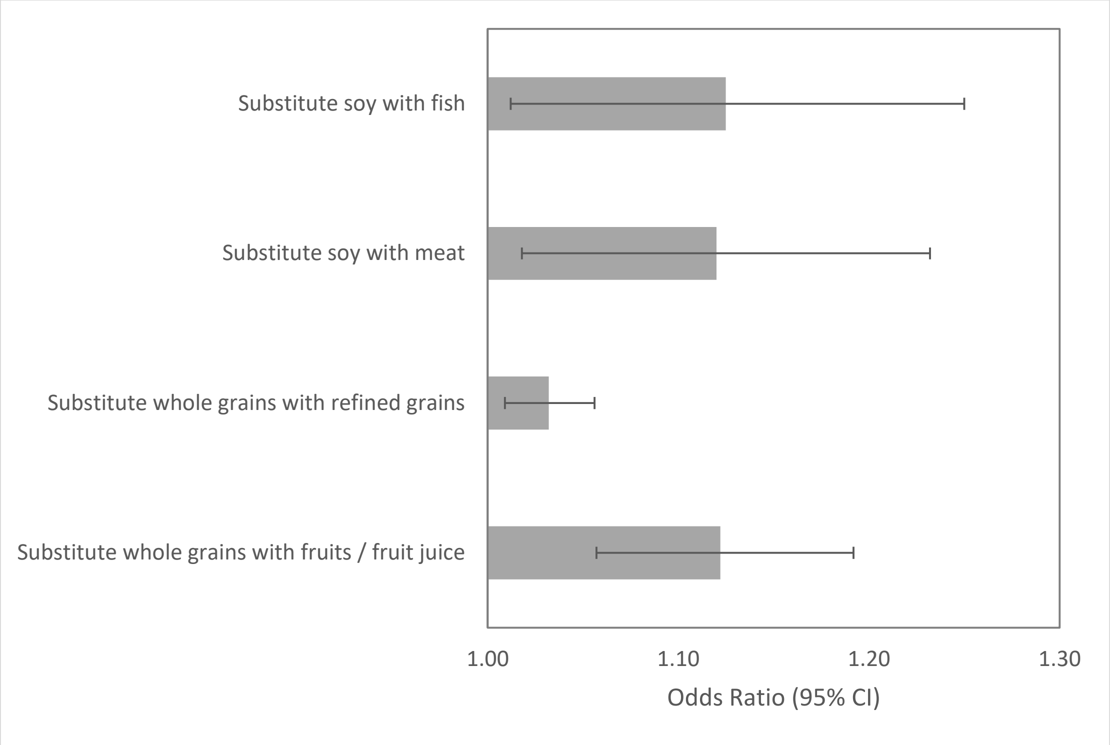

Figure 4 – 6. Food substitution and nonalcoholic fatty liver. Odds ratios and 95% confidence intervals of food substitution associated with nonalcoholic fatty liver. Excluding 121 participants with extreme energy intake (men: energy intake < 800 kcal or >4000 kcal, women: energy intake < 500 kcal or >3500 kcal). Model adjusted for age, gender, education, history of smoking, history of alcohol drinking, total energy intake, and vegetarian diet.

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4.5 Changes in weight and BMI

Analyses in this section includes only those with follow-up weight measurements. **Table 4 – 16** shows the baseline characteristics of participants with different dietary patterns, stratified by sex. In women, baseline vegetarians were slightly older, with lower BMI, weight, and waist circumference. In men, vegetarians had the lowest weight, while no significant differences were observed for other variables.

Figure 4 – 7 shows the average changes in weight per year by sex and dietary patterns. In women, both vegetarians and nonvegetarians gained weight though the difference in weight change is insignificant between the groups. The converted gained less weight than consistent vegetarians (P=0.001). In men, nonvegetarians and the reverted gained weight, while no significant weight change was seen in vegetarian or the converted.

Figure 4 - 8 shows the BMI patterns at baseline and follow-up five years later. About 7% of vegetarian and 16% of nonvegetarians are considered obese by Taiwanese standard, with BMI $\geqq 27$ kg/m^2. Obesity prevalence increased slightly for most diet groups. There appears to be a two fold increase in obesity among vegetarian men who reverted to nonvegetarian diet. However, the sample size is very small (n=17), and is likely influenced by random variation.

Table 4 – 16. Baseline characteristics by dietary patterns and sex (for weight change analysis).

	Vegetarian	Reverted	Converted	Nonvegetarian	P-value
Women (n)	**741**	**82**	**493**	**486**	
Age, y	54 (8)	54 (8)	52(8)	53(9)	0.014
BMI, kg/m^2	22.7 (2.8)	22.9 (3.1)	23.2(3.1)	23.7(3.3)	<.001
Waist circumference, cm	73.4 (7.1)	73.9 (8.4)	74.1(7.3)	75(7.9)	0.004
Weight, kg	55.2 (7.3)	55.5 (8.1)	56.9(8.2)	57.9(8.5)	<.001
Height, cm	156 (5)	156 (5)	157(6)	156(6)	0.29
Education, %					
Elementary or lower	30	30	25	29	0.29
Secondary	54	59	56	55	
College or higher	16	11	19	16	
LTPA per week, %					
<30 min	37	46	39	37	0.72
30 - 180 min	33	28	34	35	
>180 min	29	26	27	27	
Men (n)	**138**	**17**	**132**	**286**	
Age, y	55 (9)	55 (9)	55(9)	55(10)	0.97
BMI, kg/m^2	23.2 (2.8)	24.3 (2.8)	23.4(2.5)	23.9(3)	0.07
Waist circumference, cm	81 (7.3)	82 (6.6)	80.7(7.1)	81.9(8.2)	0.43
Weight, kg	64.1 (8.7)	66.3 (8.1)	65.1(8.4)	66.8(10)	0.034
Height, cm	166 (5)	165 (5)	167(6)	167(6)	0.30
Education, %					
Elementary or lower	20	24	17	17	0.93
Secondary	48	53	50	48	
College or higher	32	24	33	35	
LTPA per week, %					
<30 min	34	41	31	29	0.38
30 - 180 min	30	35	35	28	
>180 min	36	24	34	43	

Reverted, diet changed from vegetarian to nonvegetarian; converted, diet changed from nonvegetarian to vegetarian. BMI, body mass index; LTPA, leisure time physical activities.

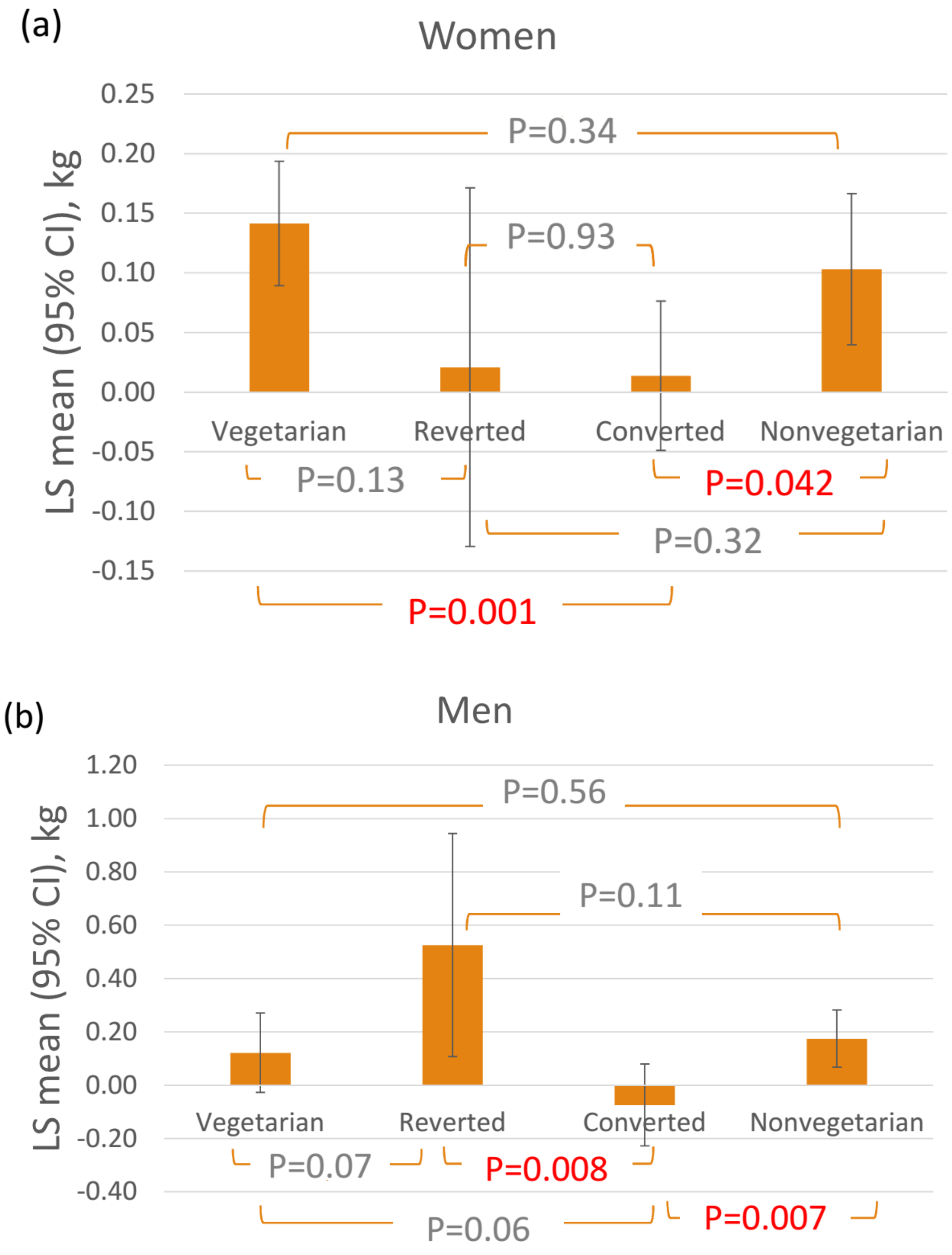

Figure 4 – 7. Average weight change per year, in women (a) and men (b). Estimations adjusted for baseline age, education, leisure time physical activities, and followed months using general linear model. LS mean = lease square mean estimated by general linear model.

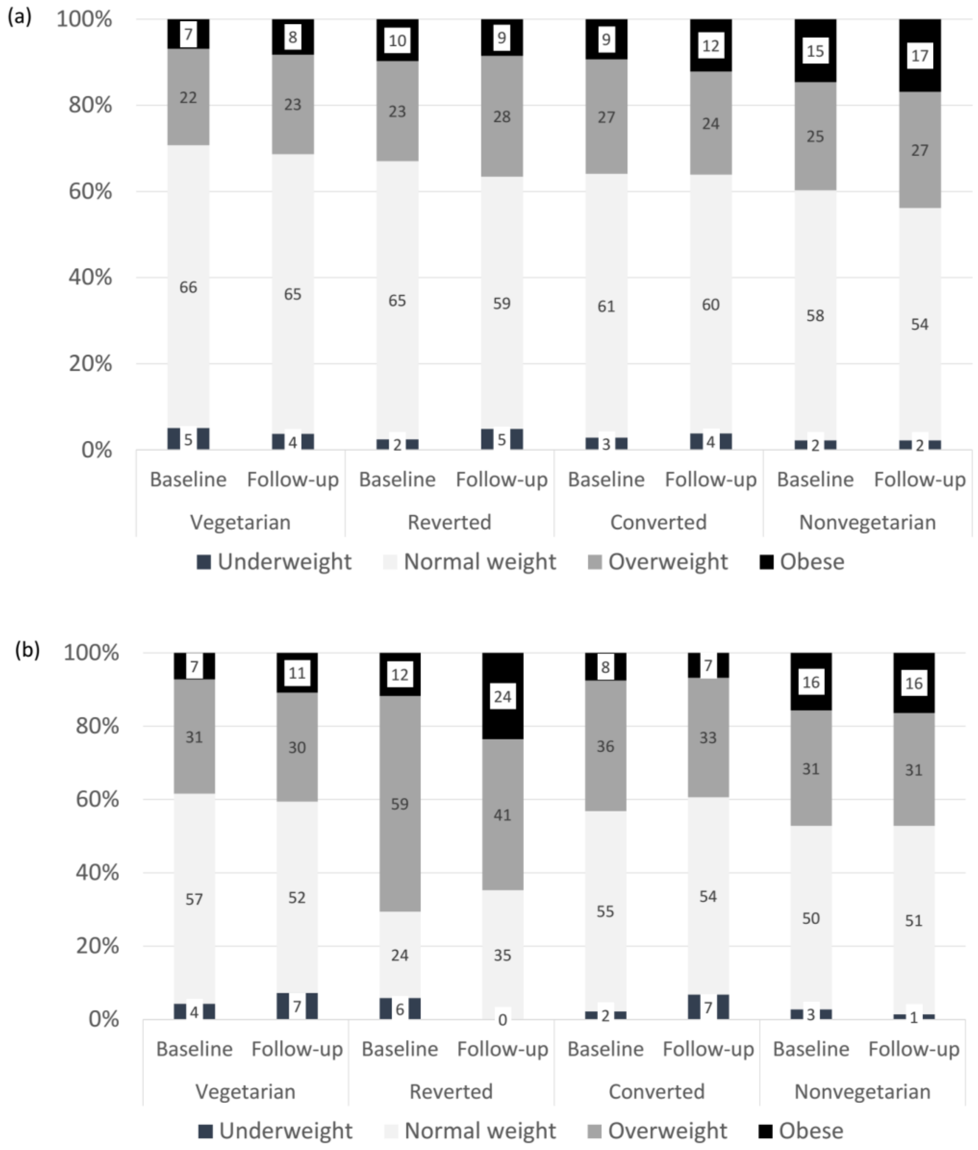

Figure 4 – 8. Change in BMI pattern over 5 years, in women (a) and men (b). Underweight: BMI < 18.5 kg/m^2. Normal weight: BMI=18.5 – 23.9 kg/m^2. Overweight: BMI=24.0 – 26.9 kg/m^2. Obese: BMI≧27 kg/m^2.

4.6 Diabetes incidences

Table 4 – 17 shows the baseline characteristics of different dietary patterns. Nonvegetarians tend to have higher BMI and waist circumference (among female), and fasting blood glucose. Female were more likely to consume vegetarian diet at baseline or switch to a vegetarian diet later. The converted had the lowest proportion with metabolic syndrome. **Figure 4 – 9** shows the baseline food intakes (median) of different diet groups.

Of the 183 cases of diabetes identified, 102 (56%) were newly identified through health examination, while 81 (44%) self-reported diabetes in the follow-up questionnaire. The effect of dietary patterns on risk of diabetes is shown in **Table 4 – 18**. Consistent vegetarians and the converted tend to show about 40 – 60% reduction in risk of diabetes, compared with nonvegetarians. This pattern appears to be consistent across most of the subgroups. However, in the subgroup analysis by baseline fatty liver status, the protective effect of vegetarian diet appears to be mainly in those with fatty liver, though the test of interaction between dietary pattern and fatty liver is not significant (p=0.50 for Model 1, p=0.60 for Model 2). The effect of the reverting from vegetarian diet to nonvegetarian diet were all statically insignificant due to small sample size. The converted seems to experience greater protection than vegetarians in some subgroups (those with BMI < 24, and those without family history of diabetes) but the difference did not reach statistical significances (P>0.05 for in all models).

Similar trends were found for our sensitivity analyses: (1) When unconfirmed diabetes

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were counted as diabetes cases, protective effect was seen in both consistent vegetarians (Model 1: HR = 0.53, 95% CI = 0.39 – 0.73; Model 2: HR = 0.64, 95% CI = 0.46 – 0.89) and the converted (Model 1: HR = 0.43, 95% CI = 0.29 – 0.64; Model 2: HR = 0.45, 95% CI = 0.30 – 0.68). (2) When counting only the self-reported diabetes as cases, similar trends were found (Model 1: HR = 0.56, 95% CI = 0.35 – 0.88; Model 2: HR = 0.69, HR = 0.43 – 1.10), and the converted (Model 1: HR = 0.49, 95% CI = 0.28 – 0.87; Model 2: HR = 0.50, 95% CI = 0.28 – 0.88). (3) Addition of metabolic syndrome to Model 2 showed similar a trend for vegetarians (HR: 0.61, 95% CI: 0.43 – 0.86) and the converted (HR: 0.48, 95% 0.31 – 0.73). (4). When change in BMI or change in weight were separately added to Model 2, no substantial changes was observed, and diabetes risk was not associated with per kg weight change (HR = 1.00, 95% CI = 0.95 – 1.05) or per kg/m^2 BMI increase (HR = 1.00, 95% CI = 0.88 – 1.12).

Table 4 -19 shows the association between food groups and diabetes among consistent vegetarians and nonvegetarians. Fish intake is associated with marginal increased risk, while meat and eggs are associated with a nonsignificant increase in risk of diabetes. The association between diabetes and fish or eggs appear to be similar regardless of whether BMI is adjusted or not. Most food groups are not significantly associated with diabetes.

Of all the 3185 to be included for analysis (after exclusion criteria applied), 210 (6.6%) were lost to follow-up, while 2394(75.2%) and 581(18.3%) were followed through health examination and questionnaire, respectively. Of those who were followed through health

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examination, 1902 returned for first follow-up (2010 to 2012), 1739 returned for second follow-up (2013 – mid-2016), and 1247 returned for both. The baseline characteristics by follow-up status and methods were compared at **Table 4 – 20**. Male participants were less likely to be followed (either through health examination or mailed questionnaire), while female with lower education were more likely to return for health examination. There was no significant difference in BMI, waist circumference, impaired fasting glucose, family history of diabetes, LTPA, metabolic syndrome, fatty liver, or diet among those lost to follow-up, those who returned for health examination, and those who responded to the follow-up questionnaire.

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Table 4 – 17. Baseline characteristics by dietary patterns (for diabetes incidence analysis)

	Vegetarian	Reverted	Converted	Nonvegetarian	P
n	1053	124	697	1044	
Age, y	54.1 (9)	53.6 (8.5)	52.6 (8.7)	52.7 (9.8)	0.001
BMI, kg/m2	22.8 (2.8)	23.2 (3.4)	23.3 (3.1)	23.8 (3.3)	<.001
Waist (all), cm	74.6 (7.8)	75.7 (9.2)	75.5 (8)	77.4 (8.8)	<.001
Female*	73.5 (7.3)	74.6 (9.4)	74.1 (7.6)	74.8 (7.8)	0.011
Male**	80.7 (7.3)	81.3 (6.2)	80.6 (7.2)	82 (8.4)	0.16
Weight (all), kg	56.6 (8.3)	57.6 (9.2)	58.7 (9.1)	61.2 (10.4)	<.001
Female*	55.1 (7.4)	55.9 (8.8)	56.9 (8.3)	57.6 (8.4)	<.001
Male**	64.1 (8.6)	65.9 (6)	65.6 (8.4)	67.5 (10.5)	0.002
Height (all), cm	158 (6)	157 (7)	159 (7)	160 (8)	<.001
Female*	156 (5)	156 (5)	157 (6)	156 (6)	0.09
Male**	166 (5)	167 (6)	167 (6)	167 (6)	0.26
Fasting glucose, mg/dL	90 (8)	92 (8)	91 (9)	92 (9)	<.001
Female, %	84	83	79	63	<.001
Education, %					
Elementary	28	27	22	23	0.003
Secondary	52	56	55	51	
College	20	17	24	26	
Education, (female*) %					
Elementary	30	29	24	26	0.22
Secondary	53	55	56	55	
College	17	16	20	19	
Education, (male**) %					
Elementary	19	19	14	17	0.79
Secondary	46	57	50	45	
College	36	24	35	38	
Family history of diabetes, %	27	26	29	31	0.18
Follow-up methods					
Health examination	84	79	89	75	<.001
Questionnaire only	16	21	11	25	

Table 4 – 17. Continues

	Vegetarian	**Reverted**	**Converted**	**Nonvegetarian**	**P**
n	**1053**	**124**	**697**	**1044**	
LTPA, min/week					
<30	38	45	36	35	0.09
30 - 180	33	30	35	33	
>180	29	25	28	33	
LTPA (female*), min/week					
<30	39	48	38	38	0.62
30 - 180	33	28	35	35	
>180	28	24	27	28	
LTPA (male**), min/week					
<30	35	33	30	29	0.25
30 - 180	31	38	37	29	
>180	34	29	33	42	
BMI categories					
<18.5	5	4	3	2	<.001
18.5 - 23.9	65	58	60	55	
24.0 - 26.9	23	27	28	27	
>=27.0	7	10	9	15	
Metabolic syndrome, %	14	17	10	15	0.035
Fatty liver, %	49	53	50	56	0.008
Impaired fasting glucose, %	11	15	14	17	0.001
Elevated TG, %	17	20	13	17	0.026
Low HDL-C, %	38	29	26	24	<.001

P-values are from ANOVA and X^2 test. Reverted, diet changed from vegetarian to nonvegetarian; converted, diet changed from nonvegetarian to vegetarian. BMI, body mass index; LTPA, leisure time physical activities. **Women : 886 vegetarians, 103 reverted, 550 converted, 660 nonvegetarians. **Men: 167 vegetarians, 21 reverted, 147 converted, 384 nonvegetarians.

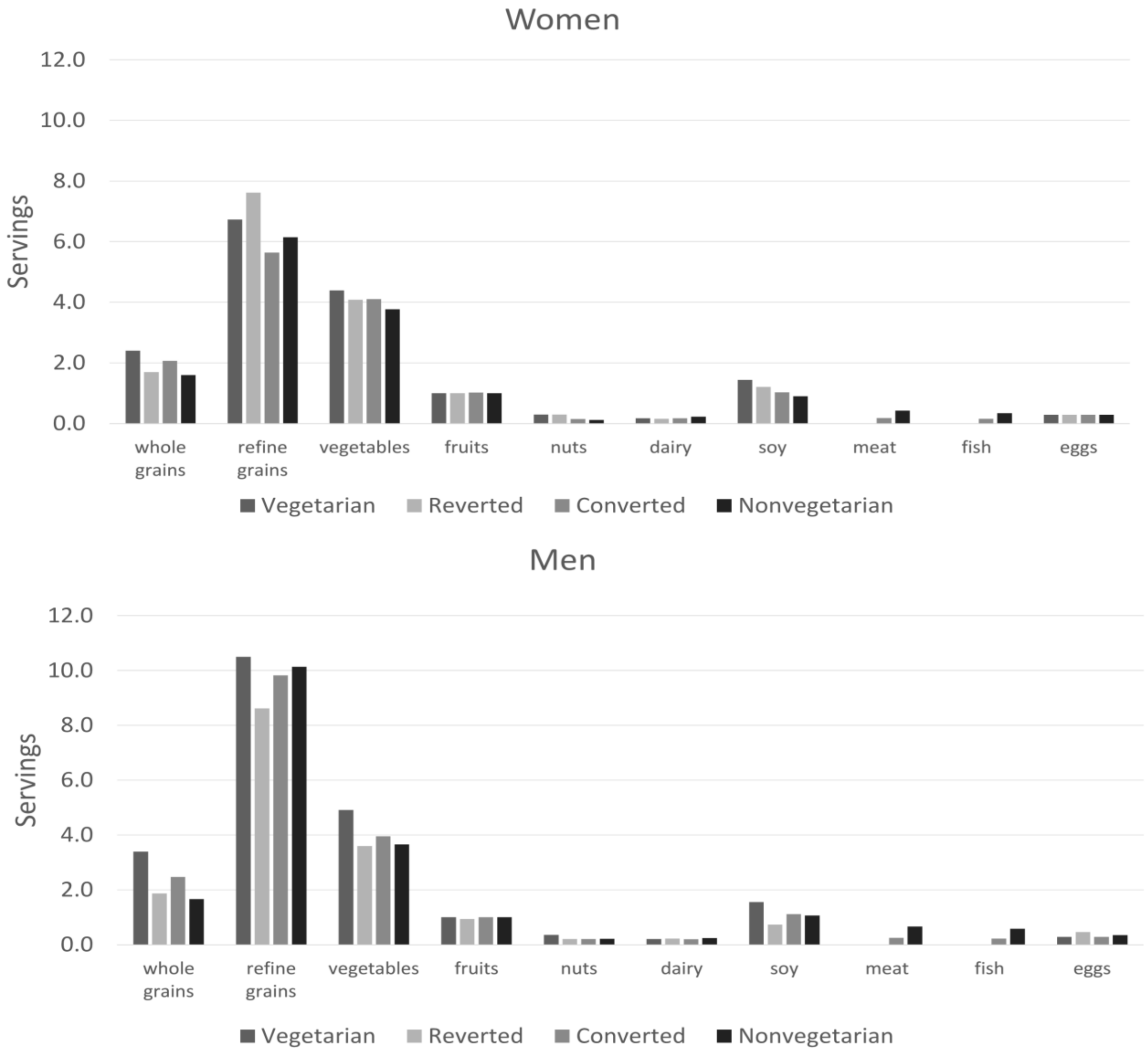

Figure 4 – 9. Baseline food intakes (per day, median) of different diet groups, assessed by food frequency questionnaire; including (A) 2199 women (vegetarian: 886, reverted: 103, converted: 550, nonvegetarian: 660) and (B) 719 men (vegetarian: 167, reverted: 21, converted: 147, nonvegetarian: 384). Serving size defined as Taiwanese food exchange list: one serving of whole grains and refined grains = 70 kcal, one serving of vegetables = 100g, one serving of fruit = 60 kcal, one serving of nuts = 45 kcal, one serving of dairy = 8g protein, one serving of soy, meat, fish, egg, = 7g protein

Table 4 – 18. Dietary patterns and diabetes risk. Hazard Ratio (95% confidence interval) of incident diabetes.

	Vegetarian	Reverted	Converted	Nonvegetarian
All				
Cases/Person-year	55 / 5431	6 / 583	29 / 3496	93 / 5456
Model 1	0.52 (0.37, 0.73)	0.58 (0.25, 1.32)	0.43 (0.28, 0.66)	1 (Ref)
Model 2	0.63 (0.45, 0.89)	0.62 (0.27, 1.42)	0.45 (0.29, 0.69)	1 (Ref)
Female				
Cases/Person-year	48 / 4551	4 / 488	22 / 2749	61 / 3463
Model 1	0.53 (0.36, 0.78)	0.44 (0.16, 1.22)	0.39 (0.24, 0.63)	1 (Ref)
Model 2	0.65 (0.44, 0.95)	0.49 (0.18, 1.36)	0.40 (0.24, 0.65)	1 (Ref)
Male				
Cases/Person-year	7 / 881	2 / 95	7 / 748	32 / 1993
Model 1	0.44 (0.19, 1.02)	1.90 (0.44, 8.26)	0.65 (0.28, 1.49)	1 (Ref)
Model 2	0.55 (0.24, 1.29)	1.97 (0.45, 8.56)	0.73 (0.31, 1.69)	1 (Ref)
No MS				
Cases/Person-year	33 / 4733	3 / 482	15 / 3160	51 / 4742
Model 1	0.58 (0.37, 0.91)	0.57 (0.18, 1.84)	0.39 (0.21, 0.69)	1 (Ref)
Model 2	0.63 (0.40, 1.00)	0.59 (0.18, 1.90)	0.39 (0.22, 0.69)	1 (Ref)
With MS				
Cases/Person-year	22 / 699	3 / 101	14 / 337	42 / 714
Model 1	0.52 (0.37, 0.74)	0.55 (0.24, 1.27)	0.43 (0.28, 0.66)	1 (Ref)
Model 2	0.64 (0.45, 0.90)	0.62 (0.27, 1.44)	0.44 (0.28, 0.67)	1 (Ref)
No fatty liver				
Cases/Person-year	15 / 2793	0 / 269	5 / 1789	14 / 2475
Model 1	0.92 (0.43, 1.97)	NA	0.55 (0.19, 1.57)	1 (Ref)
Model 2	1.06 (0.49, 2.29)	NA	0.58 (0.20, 1.64)	1 (Ref)
With fatty liver				
Cases/Person-year	38 / 2555	6 / 297	24 / 1652	78 / 2910
Model 1	0.48 (0.32, 0.71)	0.69 (0.30, 1.60)	0.47 (0.30, 0.75)	1 (Ref)
Model 2	0.53 (0.35, 0.79)	0.73 (0.31, 1.70)	0.47 (0.29, 0.75)	1 (Ref)
BMI < 24				
Cases/Person-year	24 / 3867	3 / 367	6 / 2268	31 / 3229
Model 1	0.55 (0.32, 0.95)	0.72 (0.22, 2.41)	0.23 (0.1, 0.56)	1 (Ref)
Model 2	0.59 (0.34, 1.01)	0.81 (0.24, 2.69)	0.24 (0.1, 0.58)	1 (Ref)
BMI >=24				
Cases/Person-year	31 / 1564	3 / 216	23 / 1229	62 / 2226
Model 1	0.58 (0.37, 0.91)	0.46 (0.14, 1.46)	0.61 (0.37, 0.99)	1 (Ref)
Model 2	0.64 (0.41, 1.01)	0.47 (0.15, 1.50)	0.61 (0.38, 1.00)	1 (Ref)

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Table 4 – 18. Continues

	Vegetarian	Reverted	Converted	Nonvegetarian
Normal glucose				
Cases/Person-year	33 / 4861	2 / 485	14 / 3045	37 / 4653
Model 1	0.71 (0.44, 1.16)	0.48 (0.11, 1.99)	0.49 (0.26, 0.92)	1 (Ref)
Model 2	0.80 (0.49, 1.30)	0.48 (0.11, 2.00)	0.47 (0.25, 0.89)	1 (Ref)
IFG				
Cases/Person-year	22 / 571	4 / 98	15 / 451	56 / 803
Model 1	0.51 (0.30, 0.84)	0.59 (0.21, 1.66)	0.44 (0.25, 0.79)	1 (Ref)
Model 2	0.63 (0.37, 1.07)	0.65 (0.23, 1.87)	0.48 (0.27, 0.86)	1 (Ref)
TG < 150 mg/dL				
Cases/Person-year	34 / 4533	2 / 469	16 / 3073	65 / 4585
Model 1	0.47 (0.31, 0.72)	0.30 (0.07, 1.21)	0.32 (0.18, 0.56)	1 (Ref)
Model 2	0.56 (0.36, 0.87)	0.32 (0.08, 1.33)	0.31 (0.18, 0.54)	1 (Ref)
TG >=150 mg/dL				
Cases/Person-year	21 / 898	4 / 114	13 / 424	28 / 871
Model 1	0.58 (0.32, 1.05)	0.92 (0.31, 2.69)	0.80 (0.40, 1.61)	1 (Ref)
Model 2	0.69 (0.37, 1.28)	0.94 (0.32, 2.76)	0.88 (0.43, 1.78)	1 (Ref)
Normal HDL-C				
Cases/Person-year	23 / 3453	2 / 427	16 / 2598	54 / 4218
Model 1	0.46 (0.28, 0.76)	0.35 (0.09, 1.45)	0.41 (0.23, 0.73)	1 (Ref)
Model 2	0.58 (0.35, 0.96)	0.38 (0.09, 1.60)	0.42 (0.24, 0.74)	1 (Ref)
Low HDL-C				
Cases/Person-year	32 / 1978	4 / 156	13 / 899	39 / 1238
Model 1	0.47 (0.29, 0.77)	0.72 (0.26, 2.05)	0.45 (0.24, 0.84)	1 (Ref)
Model 2	0.58 (0.35, 0.95)	0.82 (0.29, 2.34)	0.49 (0.26, 0.94)	1 (Ref)
No family history				
Cases/Person-year	31 / 3941	5 / 441	11 / 2510	55 / 3737
Model 1	0.47 (0.30, 0.74)	0.78 (0.31, 1.97)	0.26 (0.14, 0.51)	1 (Ref)
Model 2	0.56 (0.35, 0.88)	0.83 (0.33, 2.09)	0.29 (0.15, 0.55)	1 (Ref)
With family history				
Cases/Person-year	24 / 1491	1 / 143	18 / 986	38 / 1719
Model 1	0.60 (0.36, 1.02)	0.24 (0.03, 1.79)	0.71 (0.4, 1.26)	1 (Ref)
Model 2	0.77 (0.45, 1.32)	0.25 (0.03, 1.82)	0.75 (0.42, 1.35)	1 (Ref)

Reverted, diet changed from vegetarian to nonvegetarian; converted, diet changed from nonvegetarian to vegetarian. MS = metabolic syndrome defined by ATP III definition. IFG = impaired fasting glucose. TG = triglyceride. HDL-C = high density lipoprotein cholesterol. Model 1 adjusted for age gender, education, leisure time physical activities, family history of diabetes, follow-up methods (health examination or questionnaire only), Model

2 additionally adjusted for BMI.

Table 4 – 19. Food groups and diabetes risk. Hazard Ratio (95% confidence interval).

	Model 1			Model 2		
	HR	95% CI		HR	95% CI	
Meat	1.15	0.90	1.46	1.05	0.81	1.35
Soy	1.02	0.84	1.24	1.02	0.84	1.24
Fish	1.17	1.00	1.37	1.17	0.99	1.38
Eggs	1.46	0.83	2.55	1.56	0.87	2.78
Dairy	1.02	0.74	1.41	1.01	0.73	1.40
Whole grains	0.97	0.89	1.07	1.00	0.91	1.10
Refined grains	0.97	0.88	1.07	0.97	0.88	1.08
Vegetables	1.02	0.95	1.10	1.01	0.94	1.09
Fruits	0.94	0.79	1.11	0.95	0.80	1.13

Data excluded participants with censored age less than 50 years. Model 1 adjusted for age, gender, education, leisure time physical activities, family history of diabetes, follow-up methods (health examination or questionnaire only), calories, and all the food groups listed in the table. Model 2 additionally adjusted for BMI. All food groups were adjusted for energy using residual method.

Table 4 – 20. Baseline characteristics of participants by follow-up status and methods.

	Lost to follow-up 210	Health examination 2394	Questionnaire only 581	P-value
Age	52.4 (13.2)	53.7 (8.8)	51.6 (11)	<.001
BMI	23 (3.2)	23.2 (3)	23.3 (3.4)	0.44
Weight (all)	23 (3.2)	23.2 (3)	23.3 (3.4)	0.51
Female	22.6 (2.9)	23.1 (3.1)	23.1 (3.3)	0.16
Male	23.7 (3.6)	23.6 (2.9)	23.9 (3.4)	0.51
Height	160.3 (8.1)	158.7 (7.1)	159.1 (7.9)	0.009
Female	156.5 (5.6)	156.2 (5.4)	155.9 (5.7)	0.48
Male	167.7 (7.2)	166.8 (5.8)	168.2 (6)	0.031
Waist (all)	75.9 (8.7)	75.8 (8.2)	76.2 (9.1)	0.51
Female	55.4 (7.6)	56.4 (8)	56.1 (8.5)	0.28
Male	66.6 (10.2)	65.8 (9.3)	67.7 (10.6)	0.09
Fasting glucose	91.3 (8.5)	91 (8.7)	91.1 (9)	0.86
Female sex	66	76	74	0.007
Impaired fasting glucose	14	14	15	0.96

Table 4-20. Continues

	Lost to follow-up 210	Health examination 2394	Questionnaire only 581	P-value
LTPA (all), weekly				
<30min	34	36	38	0.55
30 - 180 min	31	33	33	
>180min	35	30	29	
LTPA (female), weekly				
<30min	33	38	41	0.26
30 - 180 min	32	34	32	
>180min	35	28	26	
LTPA (male), weekly				
<30min	35	31	29	0.75
30 - 180 min	30	31	35	
>180min	35	38	36	
Family history of diabetes	26	29	31	0.25
Metabolic syndrome	12	14	13	0.86
Fatty liver	47	53	49	0.06
Elevated TG	21	16	15	0.12
Low HDL-C	25	30	27	0.13
Vegetarians	35	41	37	0.08
Female	42	46	42	0.37
Male	21	27	24	0.45
Education (all)				
Elementary	25	26	20	<.001
Secondary	44	53	50	
College	31	21	30	
Education (female)				
Elementary	30	28	22	<.001
Secondary	45	55	52	
College	26	17	25	
Education (male)				
Elementary	17	18	13	0.13
Secondary	42	48	42	
College	41	34	44	

LTPA = leisure time physical activities

CHAPTER 5. DISCUSSION

5.1 Dietary intake and nutritional implications

Overall nutrient and food intake

Compared with nonvegetarians, vegetarians tend to have higher proportion of energy from carbohydrates and lower from fat and protein, higher intake of dietary fiber, calcium, magnesium, total iron, thiamin, folate, vitamin A, and lower intake of cholesterol, saturated fat, heme iron, vitamin D, and vitamin B12. Overall, a substantial proportion of participants may not be meeting the recommendation for protein, vitamin D, vitamin B6, calcium, magnesium, and vitamin B12 (especially for vegetarians).

In terms of food consumptions, vegetarians consumed more vegetables, whole grains, nuts and seeds, and soy. These foods may improve cardiometabolic risk profile, and protect against obesity, insulin resistance, and type 2 diabetes.

Macronutrients distribution

Vegetarians in our study had higher carbohydrates and lower fat and protein compared with nonvegetarians. Similar trends were observed in Western vegetarians(3,4,26). About 30 – 40 % of participants (both vegetarians and nonvegetarians) may have inadequate intake for protein, with daily intake less than 0.8g per kg body weight, as assessed by FFQ. Although our FFQ was not designed to assess exact nutrient intake, our result raises the possibility that some vegetarians may have inadequate protein intake, and should be encouraged to increase consumption of plant

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protein. Among US nurses and health professionals, animal protein is associated with mortality while plant protein is associated with protection (130). Besides soy, vegetarians should include more beans as main dishes and snacks. Achieving adequate protein does not seem to be a problem for about 50% of our vegetarian population.

Vitamin B12

Vitamin B12 is produced by bacteria, and consumed mainly from animal based foods. Vegetarians may obtain vitamin B12 from some laver, algae, fermented and fortified foods(131). Previous studies have repeatedly shown that inadequate vitamin B12 may be a problem among vegetarians in countries with limited fortified foods and when vegetarians do not consume supplements(27). In our study, vegetarians have much lower intake of vitamin B12 than nonvegetarians. Currently, there is limited foods fortified with vitamin B12 in Taiwanese markets, and vegetarians may not be aware of the need to include these foods on a daily basis. Subclinical deficiency may be asymptomatic, and the high folate intake may mask vitamin B12 deficiency in vegetarians(132). Subclinical vitamin B12 status may lead to neurodegenerative diseases and elevated homocysteine(133). More efforts should be put into designing food items that contain reliable sources of vitamin B12 (such as through fermentation or fortification) and educating vegetarians to consume these foods.

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Vitamin D

Vitamin D is an important nutrient that may be associated with reduced risk of diabetes(113), and have been reported to be low in vegetarians(134), due to limited food sources (mainly in some fish and fortified foods). Mushroom exposed to sunlight or UV light may produce large amount of vitamin D2 (ergocalciferol)(135). However, the level could range widely and the current agriculture practice in Taiwan typically plant mushrooms indoor. Plant sources of vitamin D3 include microalgae and leaves of several plant from the *Solanaceae* family(136). In our study, vegetarian men and postmenopausal women had lower intakes of vitamin D than nonvegetarians. Although our population could potentially synthesize enough vitamin D from sunlight exposure in the latitude of Taiwan, the vitamin D nutritional status of Taiwanese vegetarians is currently unknown and warrants further studies. Vegetarian status is associated with lower 25(OH)D levels, in the EPIC-Oxford(134), but not in AHS-2(137).

Calcium

Calcium appears to be another nutrient of concern. Although vegetarians had higher calcium intakes than nonvegetarians in our study, their intakes are much lower than the recommended 1000 mg. The overall low calcium intake in both vegetarians and nonvegetarians is likely due to the low dairy intakes. Although tofu, sesame seeds, and some leafy green vegetables are excellent sources of calcium, our population does not seem to consume enough of these foods to meet the calcium recommendations. Compared with Western countries, there are relatively fewer calcium fortified products. Although calcium fortified soy milk is available from a major brand, most Taiwanese probably are unware of their potential inadequate intake. Future work is needed to educate vegetarians on choosing high calcium foods on a daily basis.

Zinc

In our study, zinc consumption in vegetarian is higher (women) or similar (men) to nonvegetarians. Zinc nutritional status has been reported to be lower in vegetarians than nonvegetarians, possibly due to lower bioavailability from plant sources (138). Zinc rich plant foods include seeds and nuts, soy, and whole grains. The bioavailability of zinc from plants improves substantially when whole grains are soaked in water, as the soaking process reduces the binding of zinc by phytic acid(139). Taiwanese vegetarians should be encouraged to consume more whole grains, seeds and nuts in place of refined grains.

Magnesium

Replacing refined grains with whole grains may substantially increase magnesium intake(140). Magnesium comes mainly from whole grains and vegetables, and has been shown to be protective toward diabetes in Taiwanese(141). Vegetarians consume higher magnesium than nonvegetarians in our study, and in Western populations(3,4). A meta-analysis of prospective

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cohorts found that magnesium intake is associated with lower risk of diabetes in a dose-dependent manner (per 100 mg/d increment of magnesium was associated with 14% reduction in risk) and the effect appears to be most pronounced in overweight individuals(142).

Intakes of selected nutrients of vegetarians in our study and in several Western studies are presented in **Table 5 – 1.** Direct comparison is not possible as each study used different food frequency questionnaires, and one study used 3-day dietary records. Adventists vegetarian appear to have the highest intake for most nutrients, possibly due to the length of the questionnaire, and availability of fortified foods in North America. Future calibration study will be needed to more accurately assess the nutrient intakes in our vegetarian population.

Other important nutrients to study in vegetarians include n-3 fatty acids and iodine(25). We did not include these in our analysis as the Taiwanese nutrient database has many missing values for these nutrients. In addition, fatty acids profile and iodine status can be better studied through biomarkers such as erythrocyte fatty acids, and urinary iodine. Our FFQ cannot capture fatty acid profile accurately.

Overall, some vegetarians may have suboptimal intakes of selected nutrients, such as vitamin B12, vitamin D, and calcium. Development of fortified foods and nutrition education for vegetarians may be needed to improve nutritional status.

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Table 5 – 1. Intake of selected nutrients in TCHS and Western Vegetarians[3,4,26].

Populations	**TCHS vegetarians**		**AHS-2 vegetarians**		**AHS-2 vegans**		**EPIC-Oxford vegetarians**		**EPIC-Oxford vegans**		**Finnish vegans**
Assessment methods	**64-item FFQ**		**204-item FFQ**		**204-item FFQ**		**130-item FFQ**		**130-item FFQ**		**3-day DR**
Sex	**Combined**		**Combined**		**Combined**		**Male**	**Female**	**Male**	**Female**	**Combined**
Nutrients	**Median**	**Mean**	**Median**	**Mean**	**Median**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**
Energy, kcal	1682	1781	1803	1896	1791	1894	2098	1816	1914	1666	2151
Carbohydrates, %	65	64	57	54	62	58	51	53	55	56	49
Protein, %	12	12	14	14	14	14	13	14	13	14	14
Fat, %	25	25	33	32	29	28	31	30	28	28	37
K, mg	2195	2385	3667	3745	4120	4234	3867	3656	4029	3817	
Ca, mg	622	725	1145	1332	933	1156	1087	1012	610	582	1001
Mg, mg	294	316	514	567	591	652	396	352	440	391	
Fe, mg	12	16	22.1	34.1	22.2	31.6	14	13	15	14	21
Zn, mg	9	12	11.5	17.9	11.3	16.3	8.4	7.7	8.0	7.2	12
Thiamin, mg	1.6	2.6					1.9	1.8	2.3	2.1	1.7
Riboflavin, mg	1.1	1.8					2.2	2.1	2.3	2.1	1.5
Niacin, mg	20	24					21	18	24	21	27
Vitamin B6, mg	1.2	2.0	3.3	13.6	3.2	14.4	2.0	1.9	2.2	2.1	
Folate, μg	491	568	729	889	723	888	367	350	431	412	586
Vitamin B12, μg	1.3	19.6	8	24.2	6.3	23.3	2.6	2.5	0.4	0.5	0.9
Vitamin C, mg	168	199	271	497	293	531	123	147	155	169	181
Vitamin D, μg	4	96	4.6	8.6	2.4	6.3	1.56	1.5	0.88	0.9	5

TCHS = Tzu Chi Health Study (the current study). AHS-2 = Adventist Health Study 2. FFQ = food frequency questionnaire. 3-day DR = three day dietary records.

5.2 Vegetarian diet and cardiometabolic risk factors

In our study, vegetarians had a more favorable cardiometabolic profile, characterized by lower BMI and abdominal obesity, lower fasting blood glucose, total and LDL-C-cholesterol, and metabolic syndrome by both ATP III and IDF definition. These may translate into lower risk for diabetes and cardiovascular diseases.

Impaired glucose metabolism

Vegetarians have lower fasting glucose levels in our study despite higher carbohydrates intake. This may be due to higher insulin sensitivity, which has been consistently demonstrated in cross-sectional studies(46,47,48) and a randomized controlled trial(74). The better glucose metabolism appears to be independent of BMI in our analyses. Replacing meat with soy has been associated with better insulin resistance in randomized controlled trials(83,84). In addition, vegetarians consume more magnesium. Low magnesium diets have been shown to adversely affect both insulin sensitivity and insulin action in rats(87).

HDL-C and triglyceride

Vegetarians in our study scored better on most cardiometabolic risk factors except HDL-C and TG. These findings are consistent with meta-analyses of randomized controlled trials using vegetarian diets(143,144,145,146,147). Male and premenopausal female vegetarians in our study had a

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similar TG as nonvegetarians, while post-menopausal female had slightly higher TG than their nonvegetarian counterparts, despite lower BMI. When controlling for BMI, vegetarian diet tend to be associated with higher TG(50). About 30 – 40% of vegetarians in our study have low HDL-C, and this is higher than in nonvegetarians (20 – 30%). High TG and low HDL-C may be induced by high carbohydrate diets(148). **Figure 5 – 1** and **Figure 5 – 2** show the association between carbohydrate intake and fasting TG and HDL-C, respectively, in our study.

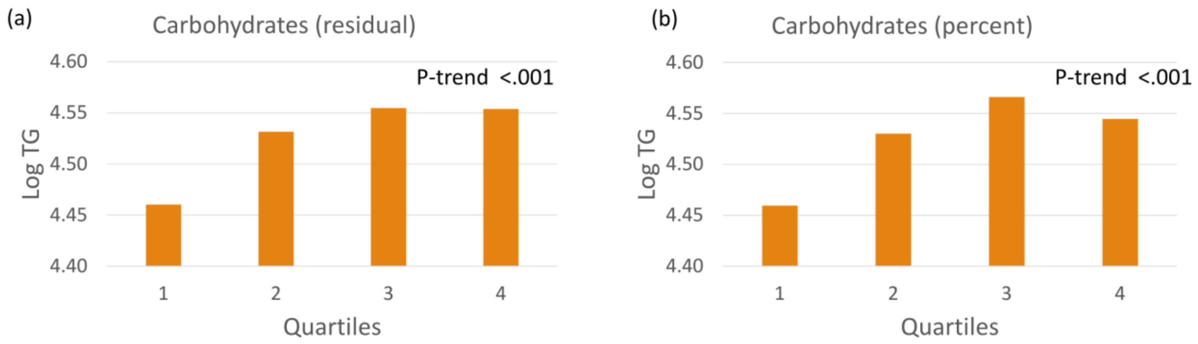

Figure 5 – 1. Association between logarithm transformed fasting triglyceride and (a) energy adjusted carbohydrates (using residual method), (b) carbohydrates as percent of energy, among participants without diabetes, self-reported history of cancer, hypertension, hyperlipidemia, cardiovascular diseases, stroke, gout, and chronic kidney diseases, chronic use of medications.

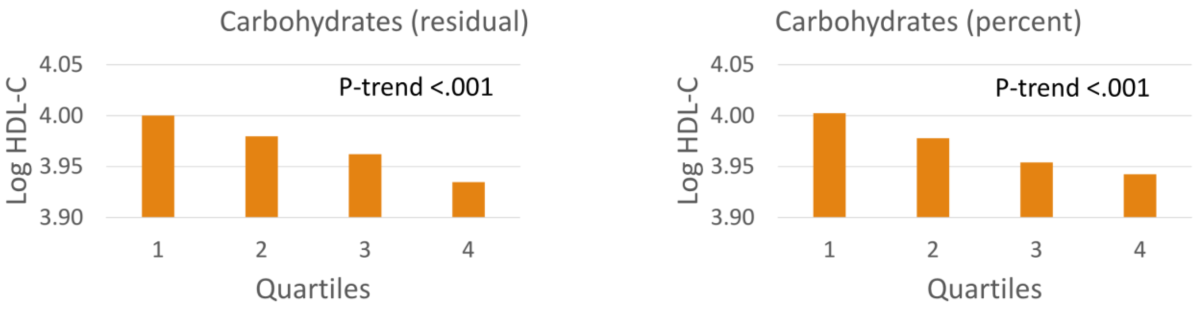

Figure 5 – 2. Association between logarithm transformed fasting high density lipoprotein cholesterol (HDL-C) and (a) energy adjusted carbohydrates (using residual method), (b) carbohydrates as percent of energy, among participants without diabetes, self-reported history of cancer, hypertension, hyperlipidemia, cardiovascular diseases, stroke, gout, and chronic kidney diseases, chronic use of medications.

Low HDL-C and high TG are common combinations of dyslipidemia resulted from insulin resistance(149). Insulin resistance stimulates hepatic TG-rich VLDL-C production and increase cholesteryl ester transport protein-mediated TG exchange between VLDL-C and HDL-C; which increases TG content in HDL-C, making them more susceptible to catabolism by hepatic lipase(149). Previous Taiwanese studies showed that despite lower HDL-C, vegetarians actually had better insulin sensitivity than nonvegetarians(47,48,150), and a clinical trial found vegetarian diet to be more effective in improving insulin sensitivity than conventional diabetes diet in an isocaloric condition(74). In the Framingham Heart Study, incident coronary heart disease risk associated with plasma HDL-C and TG was significantly increased only in the presence of insulin resistance(151). Insulin resistance typically enhance hepatic production of glucose and triglyceride, but vegetarians in our study have lower fasting glucose and fatty liver, suggesting the low HDL-C and high triglyceride may have a different biological meaning than typically found in insulin resistant individuals.

It is uncertain at this point whether the lower HDL-C in vegetarian, associated with higher carbohydrates consumption would increase future cardiovascular risk in the absence of insulin resistance since the total cholesterol to HDL-C ratio is also lower in vegetarians. Nevertheless, elevated TG and low HDL-C are associated with increased risk for diabetes among vegetarians in our study (**Table 5 – 2**). Therefore, vegetarians should also watch out for these potential risk factors.

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Table 5 – 2. Effect of abnormal TG and HDL-C on diabetes risk among consistent vegetarians

	Model 1			**Model 2**		
	HR	**95% CI**		**HR**	**95% CI**	
Elevated TG vs normal TG	2.62	1.50	4.61	2.07	1.17	3.67
Low HDL-C vs normal HDL-C	2.50	1.43	4.35	1.95	1.10	3.44

Elevated TG defined as TG >= 150 mg/dL. Low HDL-C defined as < 50mg/dL for women and <40mg/dL for men. Model 1 adjusted for age, sex, education, family history of diabetes, leisure time physical activities, follow-up methods. Model 2 additionally adjusted for BMI.

Metabolic syndrome

Our finding that vegetarian diet is associated with lower likelihood for metabolic syndrome, is consistent with the AHS-2(152), but in contrast with Huang et al's report on elderly Taiwanese from the NAHSIT(153), which found no difference between vegetarians and nonvegetarians. One reason is the difference in definition of vegetarian: Huang et al included part-time vegetarians who consume one meatless meal a day as vegetarians, where as we defined vegetarians as those who completely avoid any animal flesh. The lower metabolic syndrome in vegetarian is mainly driven by lower fasting glucose and waist circumference. Despite lower HDL-C and slightly higher TG, vegetarians were less likely to have metabolic syndrome.

The current definitions of metabolic syndrome were derived using nonvegetarian populations. The agreement between ATP III and IDF is also better in nonvegetarians (kappa = 0.77) than vegetarians (kappa=0.66). Future studies among vegetarians are needed to understand this discrepancy. In our population, both ATP III and IDF definitions of metabolic syndrome are associated with greater future diabetes risk in nonvegetarians than in vegetarians (**Table 5 – 3**).

Table 5 – 3. Effect of metabolic syndrome on diabetes risk among consistent vegetarians and nonvegetarians.

	Model 1			**Model 2**		
	HR	**95% CI**		**HR**	**95% CI**	
Vegetarians						
MS-IDF	2.50	1.21	5.14	1.27	0.57	2.80
MS-ATP	3.77	2.15	6.61	2.72	1.50	4.94
Nonvegetarians						
MS-IDF	4.29	2.73	6.74	2.27	1.30	3.97
MS-ATP	5.57	3.67	8.45	3.74	2.27	6.15

Model 1 adjusted for age sex, education, family history of diabetes, leisure time physical activities, follow-up methods. Model 2 additionally adjusted for BMI. MS-IDF = metabolic syndrome defined by the International Diabetes Federation. MS-ATP = metabolic syndrome defined by Adult Treatment Plan III of the National Cholesterol Education Program.

5.3 Vegetarian diet and nonalcoholic fatty liver

We found that vegetarian diets were inversely associated with fatty liver due to lower BMI. This result was consistent across gender, history of smoking and alcohol drinking, and status of diabetes, metabolic syndrome or hepatitis B. Substituting meat or fish with soy, or substituting refined sugar with whole grains may be protective, independent of the vegetarian dietary pattern. In addition, we found that the prevalence of fatty liver was very high (greater than 80%) among participants with diabetes, metabolic syndrome, elevated triglyceride, or high waist circumference. Vegetarians tend to have lower NAFLD Fibrosis Scores than nonvegetarians.

Mediation through BMI

BMI appeared to be an important mediator for the protective association between vegetarian diets and fatty liver in our study. Controlling for BMI attenuated the protective association in both our study (through model adjustment and stratification) and in Choi et al's study (through matching for BMI and metabolic syndrome in research design)(115). The effect of vegetarian diets on BMI reduction has been confirmed in meta-analyses of randomized controlled trials(143,147). This effect may be independent of caloric intake, as a 6-week randomized controlled feeding trial comparing an isocaloric vegetarian diet with a conventional diabetic diet found that the vegetarian diet was more effective in reducing body weight, BMI, and waist circumference(74). Plant based foods such as whole grains, fruits, vegetables, and nuts are rich in fiber, and were found to have 10 – 20 % lower metabolizable energy than calculated from Atwater factors typically used in food composition tables(154,155,156). The lower caloric availability may therefore contribute to lower BMI in vegetarians when total energy consumption appears to be similar to nonvegetarians.

Vegetarian diet and fatty liver severity

Our results also indicate that vegetarian diets may be associated with a less significant liver fibrosis, suggesting lower severity for NAFLD and NASH. Vegetarian diets have consistently been shown to reduce cholesterol levels(144), and cholesterol crystal formation in liver fat droplets may drive the progression of simple steatosis to NASH(107). In addition, oxidative

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stress, insulin resistance, and inflammation are important determinants of NAFLD progression(65). Iron from plant based foods is less bioavailable than from meat(157), and vegetarians tend to have lower iron stores than nonvegetarians(158). Iron may increase oxidative stress and insulin resistance(159,160), and iron overload may augment the risk for NASH(161). On the other hand, polyphenols from plant based foods may reduce oxidative stress, inflammation, and insulin resistance, thereby reducing NAFLD progression(92,114). The lower NAFLD Fibrosis Score in vegetarians found in our study may imply future reduction in mortality, particularly cardiovascular mortality(162).

Fatty liver and different protein-rich foods

Typical Taiwanese dietary patterns are centered on rice, with many side dishes of stewed or stir-fried vegetables, fish, and meat. Vegetarians usually have a similar pattern, except replacing meat or fish with soy. Our substitution analysis shows that replacing a serving of soy with a serving of meat or fish is associated with increased risk for fatty liver. Meat consumption is associated with NAFLD in an Israeli population independent of BMI(105). A dietary pattern characterized by animal foods is also associated with NAFLD in a middle age Chinese population(163). Meat and other animal foods are major sources of cholesterol and saturated fat, which may contribute to hepatic lipotoxicity(164,165). A 7-week clinical trial found that overfeeding saturated fat compared with polyunsaturated fat causes fat accumulation in liver(166).

Dietary fat and cholesterol have also been shown to interact synergistically to induce NASH(167). On the other hand, soy may reduce hepatic lipogenesis and isoflavone from soy may increase hepatic fat oxidation(168).

Fatty liver and different types of grains

Randomized controlled trials have demonstrated that diets low in carbohydrates reduce liver fat more effectively than high carbohydrate diets(108,109). However, these trials were not designed to distinguish between the types of carbohydrates. While refined grains were associated with NAFLD, whole grains may be associated with lower likelihood of NASH, possibly mediated through lowering of abdominal obesity and inflammation(169). Whole grains are rich in fiber, which stimulates gut microbiota production of short chain fatty acids such as butyrate, which may lower inflammation and hepatic lipid synthesis(170,171,172). The inverse association between whole grains and fatty liver in our study further suggests that whole grains may be protective and should be consumed instead of refined grains as part of a healthy diet.

Fatty liver and fruits and fruit juice

The positive association between fruits/fruit juice and fatty liver in our study is inconsistent with another cross-sectional study in Hong Kong, which showed inverse association between fruits and NAFLD(173). The effect of fruits on related metabolic diseases, such as diabetes, has

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also been inconsistent and inconclusive(174,175,176,177). One limitation of our study is that fruits and fruit juices were combined into the same FFQ item, and this hampered our ability to separate the effect of fruits from fruit juice. Fruits and fruit juice are rich in fructose, and excess fructose may stimulate lipogenesis and suppress mitochondrial fatty acid oxidation(178). However, clinical trials examining the effect of fructose on fatty liver tend to be confounded by excess energy intake, and unable to conclude on the isocaloric effect of fructose(179). To make sound recommendations on fruits for fatty liver prevention and management, more studies are needed to (1) distinguish the lipogenic effects between different fruits and fruit juices, and (2) find out the threshold for fructose tolerance for individuals at risk of fatty liver.

Fatty liver in Asians

Despite lower BMI, the prevalence of nonalcoholic fatty liver in our population (56%) is higher than previously reported in the general US population (34%, as assessed in the 1988 – 1994 National Health and Nutrition Examination Survey, which also assessed fatty liver by ultrasounds)(162). While this may be due to difference in age (15 years older in our population), Asians are also more susceptible to metabolic obesity(180). In working with Asian ethnicity, health professionals and public health educators should be aware of potential NAFLD disguised under normal BMI; and early dietary intervention focusing on wholesome plant based foods may be initiated at signs of weight gain, possibly even prior to the onset of metabolic syndrome,

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triglyceride elevation, and diabetes.

5.4 Diet and weight change over time

Over 5 years, we observed a small weight gain of 0.4 – 0.7 kg in both vegetarians and nonvegetarians while the converted experienced weight maintenance. This observation is consistent with the EPIC-Oxford that found the least weight gain for those converting in the direction from meat eaters → fish eaters → vegetarians → vegans(31). The smaller weight gain in our study than in the EPIC-Oxford (0.1 vs 0.4 kg per year) may be influenced by several reasons: (1) older age in our population, as weight gain tend to occur more rapidly at younger ages (181,182); (2) smaller frame size (therefore per kg weight gain translates into a larger percentage of body weight); and (3) very low meat consumption in our nonvegetarians, who may have further reduced meat intake after baseline assessment.

The prevalence of obesity in our cohort (vegetarian: 7%, nonvegetarians: 15%) is much lower than in the 2005 – 2008 national nutrition survey (21%) for similar age group (age 46 – 65)(183). This could be related to a healthier overall dietary pattern. Our cohort participants appear to consume more leafy vegetables, less sugar-sweeten beverage, process meat, and red meat than reported in the 2005 – 2008 NAHSIT(184), though this comparison may not be accurate due to use of different diet assessment methods. Sugar-sweetened beverages, red meats, and processed meat have been associated with long term weight gain in prospective studies(95).

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Another potential mechanism that warrants future investigation is the effect of antibiotics on weight gain. Antibiotics is widely used to promote weight gain in livestock farming likely through affecting intestinal microbiota (185). A 7-week randomized controlled trial in healthy young American men showed that antibiotics increases weights compared with placebo(186). Anitibiotics residues are detected in meat (187), that a short term vegetarian diet has been found to reduce urinary antibiotics, and positive correlations were found between urinary antibiotics concentration and intake level of various animal products, including beef, chicken, pork and dairy in a Korean study (6).

5.5 Vegetarian diet and diabetes risk

In our prospective analysis, both consuming a vegetarian diet and switching to a vegetarian diet are associated with substantial reduction in risk of diabetes. This trend is consistent across sex, baseline BMI categories, metabolic syndrome, impaired fasting glucose, and HDL-C statuses. To the best of our knowledge, this is the first prospective study that examines the impact of consuming a vegetarian diet and switching to a vegetarian diet on diabetes risk.

Plant based dietary patterns and diabetes

The magnitude of protective effect of a vegetarian diet in our study is comparable to the Adventist Health Study – 2 (39), and consistent with those reported in US nurses and health

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professionals (104). All these studies showed dose-dependent protective effect with increasing degree of plant based diet in conjunction with decreasing animal based foods, independent of BMI. Vegetarians in our cohort consumed more whole grains and vegetables than nonvegetarians, and these may protect against diabetes through higher fiber and magnesium (142). In addition, soy is a major source of protein for Taiwanese vegetarians, and soy has been shown to improve insulin resistance when replacing meat in randomized controlled trials (83,84). Increase in soy and legume consumption is inversely associated with risk of diabetes in a Chinese cohort (102). A vegetables-fruits-soy dietary pattern is also inversely associated with diabetes incidence in Singaporean Chinese (101).

Meat and diabetes risk

Although the protective effect is likely caused by various plant components, it may also be influenced by the simultaneous elimination of meat. Meat is high in saturated fats, and saturated fat have been shown to trigger human β-cell apoptosis (18). Fatty acids from meat have also been adversely associated with insulin secretion, and Disposition Index (β cell function accounting for insulin sensitivity) (89). In our study, meat consumption is associated with a nonsignificant increase in diabetes risk (per 30g serving of meat: HR = 1.15, 95% CI: 0.90 – 1.46). The statistical insignificance may be related to small sample size.

Red meat and processed meat appear to be the most diabetogenic(188,189), whereas the role of

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other types of meat is less clear. Heme iron found in red meat and nitrites from processed meat may exacerbate insulin resistance and damage β-cell(90,91,159,160).

However, the effect of meat on diabetes is equivocal among Asian women: meat was not associated with diabetes risk in Japanese women (190), and was associated with protection among normal weight Chinese women in Shanghai (191). None of these studies actually included a diet range of complete meat avoidance, and it is possible that even the lowest quantile in these cohorts did not consume low enough meat (and high enough healthy plant foods) to observe maximum protection. **Figure 5 – 3** demonstrates a potential non-linear association between meat intake and diabetes risk. There may be a threshold of risk (triangle) above which, risk of diabetes increases (range of meat intake of Western populations). On the other end of spectrum, there may be a turning point of accelerated protection (star), below which risk drastically reduces (a range of meat intake our study, TCHS). Many Asian populations may have diet range in-between the threshold of risk and the turning point, and thus unable to detect the meat – diabetes association.

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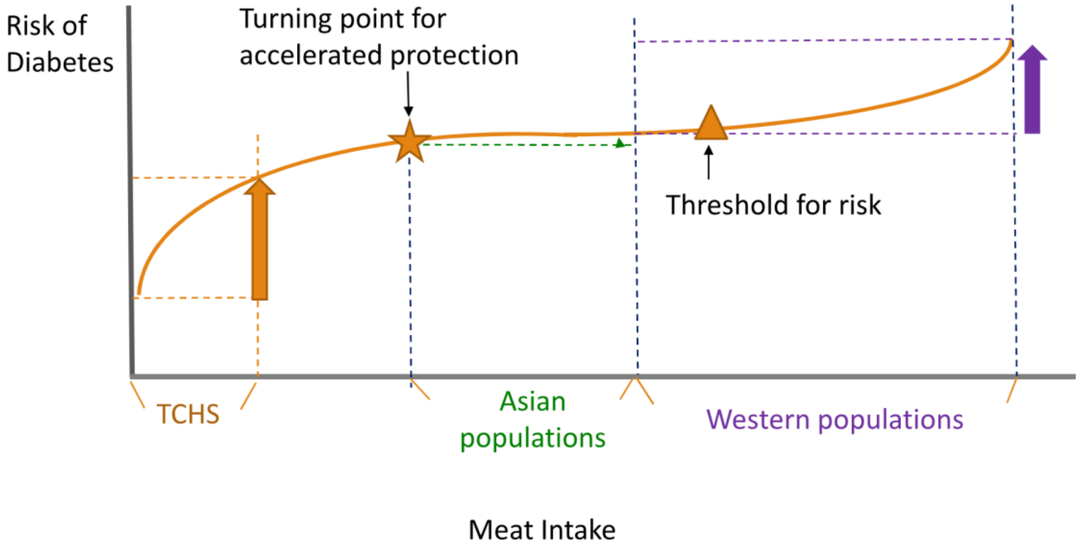

Figure 5 – 3. Potential nonlinear relationship between meat consumption and diabetes risk. TCHS = Tzu Chi Health Study (current study).

The inverse association between meat intake and diabetes in the Shanghai Women's Health Study may be confounded by unmeasured social economic factor and possibly early life food insecurity. Those in the lowest quintile differ greatly from the highest quintiles in education (37% vs 10% with no eduction), income (21.5% vs 13.7% with income <10000), occupation (63% vs 37% retired or housewife), and were on average 5 years older(191), suggesting they may have come from different social economic classes and from different birth cohorts, possibly implying different degree of exposure to famine in early life. Early life undernutrition could trigger epigenetic changes to induce diabetes risk (192).

Interaction between meat and metabolic risk factors

In the Shangahi Women's Health Study (191) and in Japanese Americans within the

Multiethnic Cohort [190], effect of meat or meat-fat dietary pattern appeared to be modified by BMI status, where meat is associated with diabetes risk among those with higher BMI, but not those with normal BMI. In our study, vegetarian diet is protective across statuses of BMI, metabolic syndrome, HDL-C, and impaired fasting glucose. However, when stratified by fatty liver status, the protective effect of vegetarian diet appears to be more protective among those with fatty liver at baseline. It is possible that the insulin sensitizing effect of a vegetarian diet helps ameliorate insulin resistance associated with fatty liver, thereby lowering risk of diabetes. Although our cohort may be too small to detect significant interaction, it is possible that the effect of vegetarian diet is not due solely to either the minimization of animal product or the higher functional plant ingredient, but the combined effect of both (more discussion later).

Fish and diabetes

Fish and sea food intake has been shown to increase risk for diabetes in American populations, but decrease risk for some Asian populations in previous meta-analyses of cohort studies[193,194]. The Singapore Chinese Health Study found that it is the plant omega-3 (ALA), not the marine omega-3 (which corresponds to fish intake), that exert the protective effect for diabetes[195]. A Japanese cohort found the protective effect of fish only in men, not women[196]. In our study, fish consumption was associated with marginal increase in diabetes risk (per 30g increase in fish intake: HR: 1.17, 95% CI: 1.00 – 1.37) among those who did not change dietary

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patterns (excluded the reverted and the converted).

Fish is known to be contaminated with mercury and other contaminants in Taiwan and abroad(197,198), and vegetarians living in contaminated area in Taiwan have been found to have lower blood level of dioxin compared with their nonvegetarian counterparts(5). The lower exposures to these environmental toxins may reduce insulin resistance and lessen the damage to β-cell function and thereby protect against diabetes(199,200). In addition, a trial showed that while plant polyphenol improves glucose metabolism, fish omega-3 decreases insulin secretion and postrandial GLP-1 (92).

Eggs and diabetes

We observed a non-significant association between eggs and risk of diabetes. Egg consumption was associated with increased risk of diabetes in Physician's Health Study I and Women's Health Study(201), but not in the Cardiovascular Health Study that enrolled those ≧65 years old(202). Egg is rich in cholesterol and choline. Egg yolk-enriched high cholesterol diet has been shown to increase in plasma glucose in rats(203). Choline may be metabolized to produce trimethylamine N-oxide (TMAO) via intestinal microbes and liver(204), and higher TMAO has been associated diabetes(205). More research is needed in this topic.

Conversion to vegetarian diet

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Our finding that the converted experienced a strong protection also suggests that diabetes risk or protection may be influenced by recent diets. In US nurses and health professionals, increase in red meat consumption over 4 years has been associated with diabetes risk, independent of baseline red meat intake and BMI (188). Trials using vegetarian diet had also observed improvement in glycemic control in weeks (145). Switching to a complete plant based diet can increase intestinal microbes that ferment fiber to produce butyrate in a matter of days (72). Butyrate may induce incretin secretion, contributing to β-cell proliferation (70). Microbiome screening showed F. *prausnitizii* (a butyrate producing bacteria) to be low in diabetes (206,207) and high in vegetarians (208), suggesting a potential diet-microbiome-disease link.

5.6 Integrated effects of multiple dietary components on overall metabolic health

Although vegetarianism is defined by avoidance of meat, fish, and possibly other animal products, such as eggs and dairy (for vegans), the beneficial effect of a vegetarian dietary pattern on diabetes appear to go beyond just the avoidance of animal products. In our study, the effect of food groups on diabetes risk appears to be small and mostly insignificant, while the effect of vegetarian pattern is large and robust. It is most likely the combination of low harmful components from animal products and the healthful plant components that act additively to improve metabolic health.

Figure 5 – 4 proposes how a healthful vegetarian diet may act through various metabolic

pathways to influence the twin cycles of diabetes. Vegetarian diet may decrease liver fat via lower body weights due to lower metabolizable energy in some plant foods(154,155,156), and potential change in microbiome(70,72,209). The lower iron store(158,159) and higher magnesium and soy intake may all contribute to lower insulin resistance(83,84,87,159). Due to higher carbohydrate intake, TG may not necessarily be reduced. However, vegetarians may minimize β-cell dysfunction by lowering consumption of saturated fat(18) and environmental contaminants(200). In addition, the lower iron store(158,159) will likely reduce oxidative stress to β-cell(19). Finally, plant polyphenol and microbial fermentation of fiber to short chain fatty acid may stimulate GLP-1 secretion, improve glucose control, and enhance β-cell function(70,93).

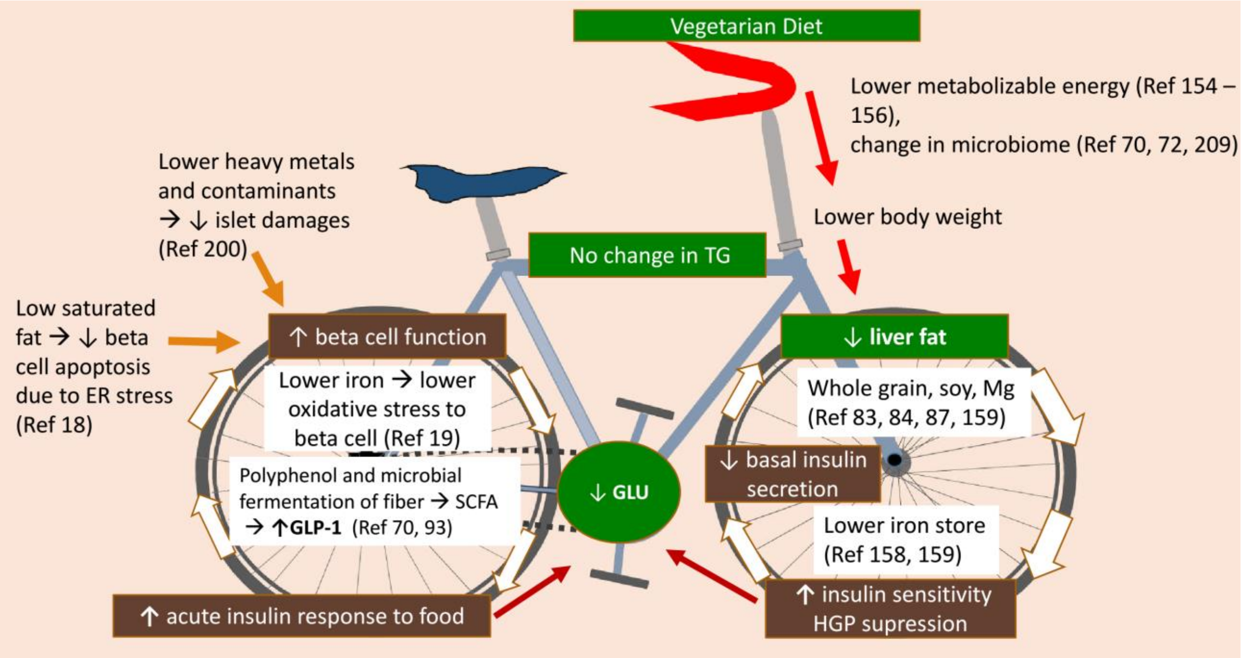

Figure 5 – 4. Potential mechanisms on how a vegetarian diet affects metabolic health in the context of the twin cycle for diabetes. TG = triglyceride, GLU = glucose, SCFA = short chain fatty acids, GLP-1 = glucagon-like-peptide-1, ER = endoplasmic reticulum, Mg = magnesium. Modified from Taylor's twin cycle model(66).

Vegetarian diet appear to benefit metabolic health via different pathways. However, in our study, vegetarians tend to consume a high carbohydrate, low protein, low fat diet. This may offset the decreased TG that is expected with lower body weight. Vegetarians may benefit from replacing some carbohydrates (particularly refined carbohydrates and simple sugar) with plant protein, as this may improve TG and HDL-C profile, leading to further protection for diabetes.

5.7 Study strength and limitations

The large sample size and detailed health examination enable us to study the effect of vegetarian diet on diabetes risk in the context of cardiometabolic risk factors, including metabolic syndrome and fatty liver. The homogenous population of non-smokers and non-alcohol drinkers from the same religious community may reduce unmeasured confounding and strengthen internal validity, although the generalizability to other population will require further confirmation from other studies. To date, there are only a handful of cohorts with sufficient number of vegetarians to prospectively investigate the impact of vegetarian diets on health, and most of these studies are from Western countries(210), and based only on questionnaire without health examination data.

The prospective design with high follow-up rate (93%) of our study reduces recall and selection biases. The majority (75%) of participants have their diabetes status confirmed by HbA1C or two fasting blood glucose, or use of diabetes medication (through medical records).

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This practice has reduced misclassification of disease outcome.

Baseline diet was assessed by a validated FFQ, and interviewed by trained research assistants. The FFQ had been shown to have good relative validity in ranking nutrient intakes, but is not accurate for exact nutrient assessment, and our estimation of food and nutrient intake may be subjected to systematic error. Future calibration study is needed to better estimate nutrient and food intake. The FFQ was interviewed instead of self-administered, and this prevents missing data on dietary intakes. Unfortunately, follow-up dietary assessment was made through a simple questionnaire. The lack of detail diet prevented us from analyzing detail dietary changes, except that meat and fish intake changed from small to zero for the converted. Nevertheless, we captured dietary changes pertinent to our study aim (vegetarian vs nonvegetarian dietary patterns), providing more insights than most cohorts that rely only on one baseline dietary assessment.

The use of ultrasound could determine presence of fatty liver but could not distinguish severity of fatty liver. However, a meta-analysis concluded that ultrasonography has good reliability and accuracy for detecting moderate to severe fatty liver, compared against biopsy(211), which is invasive and impractical in epidemiological settings. We attempted to assess fatty liver severity by calculating the NAFLD Fibrosis Score. Although this is not a direct assessment, it has good validity for determining liver fibrosis (126) and predicts mortality(162).

CHPATER 6. CONCLUSION

Vegetarian diet is associated with better metabolic profile, lower prevalence of fatty liver, and reduced risk of diabetes among Taiwanese. The inverse association between vegetarian diet and diabetes is independent of BMI, while the association with fatty liver is BMI-dependent. Although it is difficult to separate the effect of animal components from plant components when examining a vegetarian dietary pattern as a whole, it is likely that the lack of harmful animal components and healthful plant components together drive the protective effect of a vegetarian diet.

There is, however, room for improvement in the current vegetarian dietary practice in Taiwan. About 70% of vegetarians did not meet the recommendation for vitamin B12. In addition, intakes of protein, calcium, magnesium, and zinc may be suboptimal among some vegetarians. Dietary planning should aim to increase more plant protein, whole grains, nuts and seeds, as well as vitamin B12 supplements or fortified foods, to improve the nutritional status of Taiwanese vegetarians.

The negative association between vegetarian diet and nonalcoholic fatty is mainly related to BMI. Besides limiting caloric intake, substituting meat or fish with soy, or substituting refined sugar with whole grains may help prevent fatty liver.

Plant-based diets with minimal animal products serve as a frame for diabetes prevention, but more researches on how plant functional components target the diabetes pathophysiology

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(such as impaired insulin secretion and function) will be needed to disclose etiology for diabetes prevention.

Our consistent finding with Western populations has a far-reaching public health and environmental implication. The large and consistent protective effect of plant based diets and the over-consumption of meat with inadequate consumption of fruits, vegetables and whole grains by the majority today suggest enormous population-attributable protection potential of vegetarian diets. At the same time, shifting toward plant based diets is estimated to reduce food-related greenhouse gas emissions by 29 – 70%(212). Vegetarian diet may be a stunning dietary solution to the diet-environment-health trilemma that our globe urgently need to tackle, for the welfare, if not the survival, of many who are deeply threatened by climate change and noncommunicable chronic diseases such as diabetes.

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APPENDIX

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APPENDIX A

大林慈濟醫院

飲食型態、慢性疾病與癌症—世代追蹤研究

問卷調查表

素食 □　非素食□

doi:10.6342/NTU201700574

親愛的師兄師姐您好:

很榮幸有機會邀請您加入本院研究計畫。國人的健康一向是本院關心的健康議題，因此本院特別從事飲食方面的研究。懇請師兄師姐（葷素食者皆可）一同參加本研究。有關本研究之一切資料，本院會嚴加保密，敬請師兄師姐詳閱下列各項資料並鼎力協助。如蒙同意加入，敬請於同意書簽名處簽名。

倘若您對本研究進行的方法及步驟仍有疑慮，本研究計畫人員，願意提供進一步解釋，以期您能充分了解。

計畫主持人 林俊龍 院長 及 王英偉 主任 合十感恩

(本問卷請您事先填寫，並於健檢當天一同帶來醫院）

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財團法人佛教慈濟綜合醫院大林分院
臨床試驗計畫受試者同意書

計畫編號：TCRD-I9605-02

計畫名稱：飲食型態、慢性疾病與癌症–世代追蹤研究(跨院區研究)

執行單位：　大林慈濟醫院　　電話：05-2648000 轉 3324

主 持 人：　林俊龍 院長 / 王英偉 主任

受試者姓名：　　　　　　性別：□男　□女　　　年齡：

病歷號碼：□□□□□□□□□□

通訊地址：

聯絡電話：

緊急聯絡人：　　　　　　電話：

通訊住址：

一、. 試驗目的

本計畫主要探討飲食型態與慢性疾病及癌症的關係

二、試驗方法及相關配合檢驗

我們將會以問卷的方式，詢問您的飲食型態(素食或葷食)、飲食內容、生活型態(運動習慣、吸煙、喝酒等)，再配合您在健檢時所得到的健檢結果，期望在長期追蹤下，能了解飲食型態與疾病的關係。

此外，將由專人進行脈衝波速的檢測，以做為動脈粥狀硬化的早期預測指標。

三、可能產生之副作用、危險、處理方法

不會有副作用或其他危險性

四、其他可能之治療方式及說明

無

五、試驗預期效果

期望能瞭解飲食型態與疾病的相關性

六、試驗進行中之禁忌或限制活動

本研究不涉及任何醫療性的治療，您在住院健檢期間的健康檢查，不會受到影響，亦沒有任何禁忌與限制活動。

七、機密性

您所填寫的問卷資料均會受到完全的保密，除了學術發表外，不會用於其他用途，論文發表時您的身分也將保密。

八、賠償

本研究不涉及治療，所以不會對您造成傷害，若對於本研究期間有因本研究引起之損害，我們會依法為您做合適合理的處理。

九、研究結束後檢體處理方法：無檢體

□ 願意繼續提供財團法人佛教慈濟綜合醫院大林分院從事其他基因方面研究（屆時將再請您另簽一份同意書，且該份同意書和研究計畫必須先通過財團法人佛教慈濟綜合醫院大林分院研究倫理委員會的審查）

□ 由財團法人佛教慈濟綜合醫院大林分院銷毀

□ 歸還（鑒於剩餘檢體可能為病灶組織，其保存及攜帶亦可能具有感染之危險性，建議如無特殊需求及保存設備，由財團法人佛教慈濟綜合醫院大林分院代為銷毀）

十、權利

(1) 參加本試驗皆不須繳交額外費用。

(2) 研究過程中有關的任何重大發現都將提供給您。

(3) 如果您在研究過程中對研究工作性質產生疑問，對身為患者之權利有意見或確信因參與研究而受害時，應該隨時與試驗執行人 林名男 醫師聯絡，其聯絡電話為05-2648000 ext.3324。
24小時緊急連絡電話為[redacted](手機)。

(4) 為進行研究工作，您必須接受林名男醫師的照顧。如果您現在或於研究期間任何問題或狀況，請不必客氣，可與林名男醫師聯絡。

(5) 林名男醫師已將同意書副本交給我，並已完整向我說明本研究之性質與目的。林名男醫師已回答我有關研究的問題，並已解釋我有權隨時退出研究工作，且不會引起任何不愉快或影響其日後對我的醫療照顧。

(6) 對個人權益有疑慮，可和本院研究倫理委員會聯絡，電話：05-2648000 分機 5908、傳真：05-2648000 分機 5916、E-mail：irb_DL@tzuchi.com.tw 或郵寄地址：622 嘉義縣大林鎮民生路 2 號 大林慈濟綜合醫院 研究倫理委員會收。

(7) 本計畫結束後，後續藥物提供方式為：無

受試者簽署：______________日期____年____月____日
試驗主持人簽署：______________日期____年____月____日

口頭同意之見證

茲證明研究人員已完整地向受試者解釋本研究內容。
見證人簽署：__________________日期____年____月____日
茲證明本人已完全了解前述所有要點，且已口頭同意參與本研究，同意書副本已收妥無誤。
試驗主持人簽署：______________日期____年____月____日

基本資料：

填寫日期：____年____月____日

姓名：________________ 性別：□1.男 □2.女

身分證字號：□□□□□□□□□□

資料填寫者： □1.本人 □2.家屬 □3.朋友 □4.其它______

電話：________________ 手機：________________

主要居住地：□1.國內：__________縣/市 __________鄉/鎮/市/區 □2.國外：________(請填國名)

出生日期：民國 ________年________月________日

現在職業：□有：________________，工作至今有__________年

□無：□1.退休 □2.家管 □3.學生

以前職業：1.______________________，工作__________年

2.______________________，工作__________年

教育程度：□1.不識字 □2.小學 □3.初中 □4.高中 □5.專科 □6.大學 □7.研究所以上

婚姻狀況：□1.未婚 □2.已婚(_____歲時) □3.再婚(____歲時) □4.分居 □5.離婚 □6.鰥寡

過敏史：藥物過敏：□1.無 □2.有，藥名：__________________

食物過敏：□1.無 □2.有，食物：__________________

其他過敏：□1.無 □2.有，請列出：________________

生活型態及疾病危險因子：

吸菸：

□1.沒有吸菸習慣

□2.有吸菸習慣，已吸了______年，每天平均約吸________包

□3.曾經有吸菸習慣，但已戒，曾吸過_______年，每天平均約吸________包，

已停止吸菸________年

喝酒：

□1.沒有喝酒習慣

□2.有喝酒習慣，已喝了______年，每週約喝_______天，一次約喝________杯/罐 (請圈選單位)

(請勾選種類：□啤酒 □紅酒 □紹興酒 □米酒 □威士忌 □白蘭地

□高粱酒 □補藥酒 □其他____________)

□3.以前有喝酒習慣，現在不喝，曾經喝過______年，已停喝了________年

檳榔：

□1.沒有嚼檳榔的習慣

□2.有嚼檳榔的習慣，已經嚼了______年，每天平均嚼______顆

□3.以前嚼，現在不嚼，曾經嚼過______年，每天平均嚼______顆，已停嚼了_______年

運動習慣：

□1.沒有運動習慣

□2.有（可複選）

□2.1.快走，爬樓梯

(1)平均每天運動時間：_______分鐘 (2)平均每週運動天數：_______天

□2.2.伸展運動（如：瑜珈，柔軟操，太極拳）

(1)平均每天運動時間：_______分鐘 (2)平均每週運動天數：_______天

□2.3.有氧運動（如：慢跑，騎腳踏車，游泳，有氧舞蹈，土風舞，爬山）

(1)平均每天運動時間：_______分鐘 (2)平均每週運動天數：_______天

□2.4.球類運動（如：桌球，高爾夫球，羽球，網球，籃球）

(1)平均每天運動時間：_______分鐘 (2)平均每週運動天數：_______天

□2.5.肌肉運動（如：仰臥起坐，伏地挺身）

(1)平均每天運動時間：_______分鐘 (2)平均每週運動天數：_______天

□2.6.其它：__________

(1)平均每天運動時間：_______分鐘 (2)平均每週運動天數：_______天

家族疾病史：

乳癌家族史: □1.無
□2.有, (請圈選) 母親、姊妹、姑姑、阿姨、祖母、外祖母
□3.不清楚

結腸直腸癌家族史: □1.無
□2.有, (請圈選) 祖父母、外祖父母、父母、兄弟姐妹、子女
□3.不清楚

其他癌症家族史: □1.無
□2.有, 請列出癌症名稱___________________
□3.不清楚

其他家族史: 您的父母、祖父母、外祖父母、兄弟姐妹有以下的疾病嗎?
□1.無
□2.有, (可複選)
□(1)高血壓　□(2)糖尿病　□(3)高脂血症　□(4)腦中風
□(5)冠狀動脈心臟病 (包含: 心絞痛, 心肌梗塞)
□(6)痛風　□(7)其他, 請詳列____________________
□3.不清楚

個人疾病史：

癌症病史：
□1.無
□2.有，___年前，請勾選疾病：
□(1)肝癌　□(2)肺癌　□(3)結腸直腸癌　□(4)子宮頸癌　□(5)乳癌
□(6)口腔癌　□(7)攝護腺癌　□(8)胃癌　□(9)其他,請詳列_______________

病毒性肝炎病史：
B 型肝炎：□1.無　□2.有,已___年　□3.不清楚
C 型肝炎：□1.無　□2.有,已___年　□3.不清楚

長期用藥史：□1.無　□2.有

其他病史：
□1.無
□2.有, 請勾選疾病：
□2.1.高血壓____________年,藥物治療：□(1)無　□(2)不規則服藥　□(3)規則服藥
□2.2.糖尿病____________年,藥物治療：□(1)無　□(2)不規則服藥　□(3)規則服藥
□2.3.高脂血症__________年,藥物治療：□(1)無　□(2)不規則服藥　□(3)規則服藥
□2.4.冠狀動脈心臟病____年,藥物治療：□(1)無　□(2)不規則服藥　□(3)規則服藥
□2.5.腦中風____________年,藥物治療：□(1)無　□(2)不規則服藥　□(3)規則服藥
□2.6.痛風(高尿酸)______年,藥物治療：□(1)無　□(2)不規則服藥　□(3)規則服藥
□2.7.慢性腎衰竭________年,藥物治療：□(1)無　□(2)不規則服藥　□(3)規則服藥
□2.8.其他：__________
□2.9.手術：
□(1)心臟：□a.冠狀動脈氣球擴張術(含放支架)，在_______歲時
□b.冠狀動脈繞道手術，在_______歲時　□c.心瓣膜置換術，在_______歲時
□(2)乳房手術(□良性, □惡性)，在______歲時　□(3)子宮切除(□良性, □惡性)，在_____歲時
□(4)卵巢切除(□雙側, □單側)，在_____歲時　□(5)甲狀腺手術(□良性, □惡性)，在_____歲時
□(6)人工膝關節手術，在______歲時　□(7)人工髖關節手術，在______歲時
□(8)脊椎手術，在______ 歲時　□(9)白內障手術，在_______歲時
□(10)膽囊切除，在________ 歲時　□(11)其它：_____________，在______歲時

女性填寫：

初經______歲，生產_______胎，流產_______胎,

是否曾經哺育母乳： □1.否

□2.是,哺育_____胎

是否曾使用口服避孕藥：□1.否

□2.是，使用期間 從____歲 至_____歲

是否停經：□1.未停經,

□2.已停經, ____歲停經;

2.1.曾經補充女性荷爾蒙嗎? □(1)無 □(2)有,補充多久?____年

飲食習慣：

1.外食情況

□1.1.無

□1.2.有，平均一個月外食_____天，一天外食____餐

2.您這個月所吃的食物是否與您平日所吃的類似?

□2.1.是

□2.2.否，不一樣的原因是為什麼________________________________

3.您目前的飲食習慣為何？

□3.1.非素食 **(→ 請跳答下一頁)**

□3.2.不完全素食**(沒有每天 3 餐吃素)**

(1)平均一個月吃素______天

(2)在吃素的日子，平均一天吃素______餐

□3.3.完全素食 **(每天 3 餐都吃素)**

3.3.1.素食型態：

□(1)純素 (完全不食用動物性食品如:肉、魚、奶、蛋)

□(2)奶蛋素

□(3)奶素

□(4)蛋素

3.3.2.您這種素食習慣已持續多久? ______年 (_____年_____月開始吃素)

5.您素食的動機? (可複選)

□5.1.宗教相關因素 (例如：佛教戒律, 加入慈濟, 發願, 因緣, 不忍殺生)

□5.2.因為生病才改吃素, 請勾選 (□(1)癌症 □(2)中風 □(3)冠心病 □(4)糖尿病

□(5)高血壓 □(6)高血脂 □(7)痛風 □(8)其他，請列舉__________)

□5.3.為了促進健康

□5.4.受家人、朋友的影響

□5.5.其他____

(→請繼續往下一頁回答，感恩!)

飲食頻率與營養補充劑問卷

1.本問卷請您事先填寫，**並於健檢當天一同帶來醫院**，現場交予研究助理 施珮淇 或 吳玉茹 小姐，當天會為您做更進一步的飲食定量紀錄，將需要佔用您一點寶貴時間，謝謝您的參與及配合，感恩。

2.請根據**最近一個月內**您的飲食狀況回答下列問題，**選擇最接近的次數** (請✔選)

食物名稱	攝取頻率													
	沒吃 或 每月 <1 次	每月			每週						每天			
		1 次	2 次	3 次	1 次	2 次	3 次	4 次	5 次	6 次	1 次	2 次	3 次	>3 次
範例：														
1.最近這一個月都沒有吃新鮮魚類	✔													
2.每週吃 4 次蛋類								✔						
3.這個月喝了 2 次全脂奶			✔											
4.每天三餐都有吃深綠色蔬菜													✔	
(請從以下開始作答)：														
1.新鮮魚類(如：淡水魚、海魚…等)														
2.螺貝類(如：牡蠣、蛤、鳳螺…等)														
3.其他海鮮類(如:蝦、花枝、章魚、海蔘、螃蟹…等)														
4.帶骨小魚乾(如:丁香魚、吻仔魚、小魚乾…等)														
5.加工水產品(如：魚罐頭、黑輪、魚丸、魚鬆、甜不辣…等)														
6.家禽類(如：雞、鴨、鵝…等)														
7.家畜瘦肉類(如：豬、牛、羊…等)														
8.半肥肉類(如：蹄膀、五花肉、絞肉、牛腩…等)														
9.肉製品(如：香腸、火腿、熱狗、肉鬆、貢丸、蛋餃、燕餃…等)														
10.內臟類(如：豬、牛、雞、鴨、鵝的心臟、腰子、大腸、小腸、肝、魚卵…等)														
11.煙燻燒烤肉類(如：燻雞、燻肉、燻香腸、燻臘肉…等)														
12.您吃清蒸或水煮的葷食的頻率														
13.您吃油煎或油炒的葷食的頻率														
14.您吃油炸葷食的頻率														
15.您吃滷的或紅燒的葷食的頻率														

食物名稱	攝取頻率													
	沒吃或每月<1 次	每月			每週						每天			
		1次	2次	3次	1次	2次	3次	4次	5次	6次	1次	2次	3次	>3次
16.蛋類(如：雞蛋、鴨蛋、鳥蛋...等)														
17.加工蛋(如：皮蛋、鹹鴨蛋…等)														
18.全脂奶(含牛、羊之鮮奶、奶粉)														
19.低脂奶(含牛、羊之鮮奶、奶粉)														
20.脫脂奶(含牛、羊之鮮奶、奶粉)														
21.調味乳(如：果汁牛奶、蘋果牛奶、巧克力牛奶…等)														
22.發酵乳類(如：養樂多、優酪乳、優格…等)														
23.其他乳製品(如：乳酪、起士..等)														
24.黃豆														
25.豆漿(含黑豆漿、黃豆漿)														
26.豆製品類(如：豆腐、豆干、干絲、豆雞、豆包、豆腸、百頁、豆花...等)														
27.油炸豆製品類(如：豆皮、豆節、炸豆包、油豆腐、豆支簽、素魚翅、藍花干、臭豆腐…等)														
28.麵筋製品(生麵腸、麵丸、麵肚…等)														
29.油炸麵筋製品(如：麵筋泡、麵輪、皮絲..等)														
30.濃縮大豆蛋白(如：素肉絲、素肉角、素肉片、素肉末…等)														
31.大豆加工類(如：素火腿、素香腸、素八寶捲、素肉排、素鱈魚、素鮭魚、素黃金鴨….等)														
32.納豆														
33.豆腐乳														
34.蒟蒻類(如：素腰花、素白花枝、素紅魷魚、蒟蒻塊…等)														
35.您吃清蒸或水煮的豆製品的頻率														
36.您吃油煎或油炒的豆製品的頻率														
37.您吃油炸豆製品的頻率														
38.您吃滷的或紅燒的豆製品的頻率														

食物名稱	攝取頻率													
	沒吃 或 每月 <1 次	每月			每週						每天			
		1 次	2 次	3 次	1 次	2 次	3 次	4 次	5 次	6 次	1 次	2 次	3 次	>3 次
39.深綠色蔬菜類(如：菠菜、青江菜、莧菜、韭菜、芥蘭菜、甘藷葉、空心菜、綠花菜、龍鬚菜、茼蒿、A 菜、油菜…等)														
40.淺色蔬菜類(如：小白菜、大白菜、白花椰菜、高麗菜、菜心、芹菜…等)														
41.筍類(如：筊白筍、蘆筍、竹筍…等)														
42.豆類蔬菜(如：四季豆[敏豆]、菜豆、豌豆片[花蓮豆]、甜豌豆..等)														
43.根莖類蔬菜(如：紅蘿蔔、白蘿蔔、洋蔥、牛蒡、大頭菜…等)														
44.瓜類蔬菜(如：冬瓜、小黃瓜、胡瓜[刺瓜仔]、絲瓜、苦瓜、瓢瓜[蒲瓜]..等)														
45.果類蔬菜(如：蕃茄、茄子、青椒(大同仔)、彩椒、秋葵(胃豆)…等)														
46.菇蕈類(如：香菇、草菇、金針菇、蘑菇[洋菇]、木耳…等)														
47.海產類植物(如：海帶、昆布、紫菜..等)														
48.芽菜類(如：黃豆芽、綠豆芽、苜蓿芽、小豆苗…等)														
49.罐頭蔬菜(如：玉米粒罐、草菇罐、、金針菇罐、玉米筍罐…等)														
50.冷凍蔬菜(如：青豆仁、白花菜、綠花菜、胡蘿蔔、毛豆莢、毛豆仁、三色豆、敏豆...等)														
51.醃漬蔬菜(如：蔭瓜、脆瓜、樹子、蔭鳳梨、醬瓜、雪裡紅、蘿蔔乾、酸筍、泡菜…等)														
52.生吃蔬菜的頻率														
53.您吃清燙或水煮的蔬菜的頻率														
54.您吃油煎或油炒的蔬菜的頻率														
55.您吃油炸蔬菜的頻率 (如：油炸蔬菜、薯條、洋芋片)														
56.您吃滷的或紅燒的蔬菜的頻率														

食物名稱	攝取頻率													
	沒吃 或 每月 <1 次	每月			每週						每天			
		1 次	2 次	3 次	1 次	2 次	3 次	4 次	5 次	6 次	1 次	2 次	3 次	>3 次
57.新鮮水果及果汁														
58.罐頭水果(如：鳳梨罐頭、水蜜桃罐頭…等)														
59.脫水水果、蜜餞(如：龍眼乾、芒果乾、梅子、葡萄乾…等)														
60.堅果類及其製品(如：芝麻、花生、杏仁、腰果、核果…等)														
61.白米飯														
62.胚芽米飯、糙米飯、五穀飯….等														
63.麵類 (如：麵條、米粉、冬粉、粿仔條、米苔目、油麵、麵線…等)														
64.油炸麵類(如：速食麵、泡麵、鍋燒意麵…等)														
65.燕麥、米麩、薏仁、五穀粉														
66.其它主食類(如：馬鈴薯、山藥、南瓜、蕃薯、芋頭、玉米、皇帝豆、紅豆、綠豆…等)														
67.燒餅、油條、煎包、鍋貼														
68.白麵包、白吐司、白饅頭														
69.全穀類製品(如：麩皮麵包、雜糧饅頭、全麥土司…等)														
70.其他烘焙產品 (如：甜鹹土司、甜鹹麵包、蛋糕、餅乾、鳳梨酥、喜餅…等)														
71.咖啡														
72.茶類(如：綠茶、花茶、烏龍茶….等)														
73.含糖飲料 (如：汽水、可樂、奶茶、沙士、運動飲料、盒裝或罐裝果汁…等)														
食物名稱	攝取頻率													

	沒吃或每月<1次	每月			每週						每天			
		1次	2次	3次	1次	2次	3次	4次	5次	6次	1次	2次	3次	>3次
74.烹調食物用飽和脂肪油(如：豬油、牛油、奶油、椰子油、棕櫚油、清香油、寶素齋、素清香…等)														
75.烹調食物用多不飽和脂肪油(如：沙拉油[大豆油]、玉米油、花生油、葵花油、葡萄籽油…等)														
76.烹調食物用單不飽和脂肪油 (如：橄欖油、苦茶油、茶油、芥花油、菜籽油..等)														
77.奶精、乳瑪琳、沙拉醬使用頻率														

個人飲食嗜好：

1.您吃蛋時，會吃蛋黃嗎？

□(1)通常會　□(2)偶爾會　□(3)不會

2.您吃魚、家禽或家畜時，會連皮一起吃嗎？

□(1)通常會　□(2)偶爾會　□(3)不會

3.您吃魚、蝦時，會連頭部內的腦髓一起吃嗎？

□(1)通常會　□(2)偶爾會　□(3)不會

4.您喝飲料時，會習慣加糖嗎?(例如：點飲料、泡咖啡、泡茶、泡牛奶…..等)

□(1)通常會　□(2)偶爾會　□(3)不會

5.您吃東西的時候，是否會加調味料？

□(1)否

□(2)是，您會加何種調味料？(可複選)

(1)辣椒醬：使用頻率為何？□(1)常常　□(2)偶爾
(2)沙茶醬：使用頻率為何？□(1)常常　□(2)偶爾
(3)醬油：　使用頻率為何？□(1)常常　□(2)偶爾
(4)烏醋：　使用頻率為何？□(1)常常　□(2)偶爾
(5)豆瓣醬：使用頻率為何？□(1)常常　□(2)偶爾
(6)味噌：　使用頻率為何？□(1)常常　□(2)偶爾
(7)胡椒鹽：使用頻率為何？□(1)常常　□(2)偶爾
(8)蕃茄醬：使用頻率為何？□(1)常常　□(2)偶爾

營養補充劑使用情況

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1.最近一個月來，您是否有食用營養補充劑？

□(1)否

□(2)是；相當規律 (固定時間吃且持續吃)

□(3)是；但不規律 (想吃就吃，或剛開始規律吃但沒有持續)

2.您使用哪些營養補充劑？食用量如何？

維生素補充劑種類及品牌	食用頻率		每次用量
	頻率單位	次數	(粒、瓶、包、c.c.、其他)
a.善存綜合維它命	□(1)每天 □(2)每星期 □(3)每月 □(4)每月＜1		
b.銀寶綜合善存維它命	□(1)每天 □(2)每星期 □(3)每月 □(4)每月＜1		
c.維它命 B 群 請寫出品牌名稱____________ 或來源__________(如：醫師開立)	□(1)每天 □(2)每星期 □(3)每月 □(4)每月＜1		
d.維它命 B12 請寫出品牌名稱：____________ 或來源__________(如：醫師開立)	□(1)每天 □(2)每星期 □(3)每月 □(4)每月＜1		
e. 其他 品牌：________________ 名稱：________________ (例如：[品牌：三多　名稱：維他命 B 群]、綠藻、螺旋藻、紅毛台、啤酒酵母、三寶粉…等)	□(1)每天 □(2)每星期 □(3)每月 □(4)每月＜1		

問卷結束　　　　　　　　　　　　　　　　　　**感恩**

Grouping of FFQ items into food groups:

Food groups	FFQ items
Meat	#6 家禽類, #7 家畜瘦肉類, #8 半肥肉類, #9 肉製品, #10 內臟類, #11 煙燻烤肉類。若為葷食者，加上#67 煎包、鍋貼之含肉量。
Fish	#1 新鮮魚類, #2 螺貝類, #3 其他海鮮, #4 帶骨小魚乾, #5 加工水產品。
Eggs	#16 蛋類, #17 加工蛋類。
Soy	#24 黃豆, #25 豆漿, #26 豆製品, #27 油炸豆製品, #30 濃縮大豆蛋白, #31 大豆加工類, #32 納豆, #33 豆腐乳。
Dairy	#18 全脂奶, #19 低脂奶, #20 脫脂奶, #21 調味乳, #22 發酵乳, #23 其他乳製品。
Vegetables	#39 深綠色蔬菜類, #40 淺色蔬菜類, #41 筍類, #42 豆類蔬菜, #43 根莖類蔬菜, #44 瓜類蔬菜, #45 果類蔬菜, #46 菇類, #47 海產類植物, #48 芽菜類, #49 罐頭蔬菜, #50 冷凍蔬菜, #51 醃漬蔬菜。若為素食者，加上#67 煎包、鍋貼之含蔬菜量。
Fruits	#57 新鮮水果及果汁, #58 罐頭水果, #59 脫水水果。
Refined grains	#61 白飯, #63 麵類, #64 油炸麵類, #67 燒餅、油條、煎包、鍋貼, #68 白麵包、白吐司、白饅頭, #70 其他烘培產品。
Whole grains	#62 胚芽米飯、糙米飯、五穀飯, #65 燕麥、米麩、薏仁、五穀粉, #66 其他主食。
Nuts	#60 堅果及其製品。

資料貼紙
黏貼處

佛教慈濟醫療財團法人大林慈濟醫院

健康狀況調查表

為使我們能對您的健康狀況有詳細的了解，以便能作適當的指導，請勾選或填寫以下資料

壹、基本資料

目前職業：	______工作迄今共 ____年 □退休 □家管 □學生
以前職業：	1.______工作 ____ 年 2.______工作 ____ 年
教育程度：	□不識字 □小學 □國中 □高中/高職 □專科 □大學 □碩士 / 博士
婚姻狀況：	□未婚 □已婚(____歲時) □離婚 □鰥寡
經醫師診斷的慢性病：	□高血壓 □糖尿病 □心臟病 □氣喘 □攝護腺肥大 □___型肝炎 □腎臟病 □關節炎 □青光眼 □高血脂 □胃或十二指腸潰瘍 □慢性阻塞性肺病 □甲狀腺或副甲狀腺疾病 □其他：______
曾接受過外科手術：	□無 □骨折，骨折部位 ______ □有，原因 ______ 部位 ______ 手術：民國 ____ 年，或 ____年前，醫院名稱 ______
過敏病史：	□無 □其他 ______ □有，藥名 ______ □有，食物 ______
供女性填寫：	初經 ____歲，停經時 ____歲，已停經 ____年 生產 ____胎，自然流產____胎，人工流產____胎

貳、生活型態

是否每天都吃早餐？	□ 是 □ 否
是否素食者？	□否 □早齋 □初一、十五 □不固定 □是，____年 □全素 □蛋奶素 □蛋素 □奶素
是否有喝咖啡？	□是 □偶爾 □經常 □否
是否有喝茶？	□是 □偶爾 □經常 □否
是否服用或補充？	□牛奶 □鈣片 □維他命D □女性賀爾蒙 □皮質類固醇 □骨質疏鬆症治療藥物
目前吸菸情況：	□不吸菸 □吸菸，吸過____年，每天約____根/包 □已戒掉，停吸____年，曾吸過____年
目前喝酒情況：	□不喝 □喝，已喝____年，每天約____杯 □以前喝，已停喝____年 □應酬時喝
目前嚼檳榔情況：	□不吃 □偶爾會吃 □吃，已吃____年 □以前吃，但已停吃____年
過去兩週有沒有做運動？	□每天 □每週約三次以上 □偶爾 □沒有運動

病歷管理委員會 103/02/17 通過

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叁、活動量簡易自我評量

	是	否
1. 醫師是否告訴過您，您的心臟有些問題，只能做醫師建議的運動？	□	□
2. 當您活動時是否會有胸痛的感覺？	□	□
3. 過去幾個月以來，您是否有在未活動的情況下出現胸痛的情況？	□	□
4. 您是否因暈眩而失去平衡或意識的狀況？	□	□
5. 您是否有骨骼或關節問題，且可能因活動而更惡化？	□	□
6. 您是否有因高血壓或心臟疾病而需服藥(醫師處方)？	□	□
7. 您是否知道您有任何不適合活動的原因？	□	□

肆、家族病史

你的親屬中(祖父母，父母，兄弟姐妹，子女及其它血親)是否曾有被醫師診斷下列慢性病

□高血壓	□胃或十二指腸潰瘍	□糖尿病	□心臟病(動脈硬化症、心絞痛、心肌梗塞)			
□肺結核	□類風濕性關節炎	□腎臟病	□腦血管障礙(腦出血、腦栓塞、半身不遂)			
□大腸癌	□肝癌	□肺癌	□乳癌	□子宮頸癌	□口腔癌	□其他癌症______
□失智症	□氣喘	□骨折	□憂鬱症	□精神分裂症		□其他________

健康體能評估（此部分由醫師填寫）

項目	數據	結果		
		無異常	尚可	需加強
腰臀比		□	□	□
體質指數		□	□	□
握力		□	□	□

伍、同意檢查項目包含有愛滋病、梅毒之檢驗，簽名 ：

____

陸、受檢者本人了解貴院為教學醫院，為了提升住院醫師或實習醫學生的臨床診察能力，以提供更優質的醫療服務，在不影響受檢者隱私與顧及受檢者安全的情況下，

□同意　□不同意　由貴院主治醫師、住院醫師及實習醫學生共同組成之醫療服務團隊，進行各項診療服務及相關之教學活動。

立同意書人：______________　與受檢者的關係：受檢者之 ______________

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APPENDIX D

佛教大林慈濟醫院
Buddhist Dalin Tzu Chi Hospital.

敬愛的＿＿＿＿＿＿＿＿＿＿師兄姐您好：

感恩您於 2007 年至 2009 在大林慈濟醫院健康檢查時，參加了林名男副院長主持之素食研究計畫：「癌症與營養、飲食及生活型態之相關性研究」。目前我們正在追蹤師兄姊的後續飲食改變及健康狀況，**您的回覆對研究結果非常重要，能夠幫助醫學界了解素食對健康的影響!**

請您撥冗填寫此問卷，並於 2 週內用回郵信封寄回大林慈濟醫院；如有任何疑問可致電: (05)-2648000 轉 5891 家醫科 研究助理 黃宜萱。

感恩您

林名男 敬啟

1. **您最近一年飲食習慣:**

□ 葷食 (有吃魚或肉類，含僅早齋、初一十五吃素者)

□ 素食 (不吃任何魚、肉類及其製品)

是否有吃蛋: □有 □無

是否有吃乳製品，像牛奶、優酪乳、起司、乳酪: □有 □無

什麼時候開始吃素? ＿＿＿ 年 ＿＿＿ 月

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2. 過去這 9 年來是否有被醫師診斷下列之慢性病：

慢性病	有	診斷時間(年)	無	不確定
舉例：白內障	✔	2010		
糖尿病				
高血壓				
高膽固醇				
心臟病				
脂肪肝				
慢性腎臟病				
其他疾病(及診斷時間):				

非常感謝您撥冗填寫，祝您健康！

簽名：________________________　聯絡電話：______________________

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國人膳食營養素參考攝取量修訂第七版(Dietary Reference Intakes，DRIs)

行政院衛生署

中華民國100年修訂

營養素	身高	體重	熱量(2)(3)	蛋白質(4)	維生素A(6)	AI 維生素D(7)	AI 維生素E(8)	AI 維生素K	維生素C	維生素B$_1$	維生素B$_2$	菸鹼素(9)	維生素B$_6$	維生素B$_{12}$	葉酸	AI 膽素	AI 生物素	AI 泛酸	AI 鈣	AI 磷	鎂	鐵(5)	AI 鋅	碘	硒	AI 氟
單位 年齡(1)	公分 (cm)	公斤 (kg)	大卡 (kcal)	公克 (g)	微克 (μg RE)	微克 (μg)	毫克 (mg a-TE)	微克 (μg)	毫克 (mg)	毫克 (mg)	毫克 (mg)	毫克 (mg NE)	毫克 (mg)	微克 (μg)	微克 (μg)	毫克 (mg)	微克 (μg)	毫克 (mg)	毫克 (mg)	毫克 (mg)	毫克 (mg)	毫克 (mg)	毫克 (mg)	微克 (μg)	微克 (μg)	毫克 (mg)
0 - 6月	男 女 61 60	男 女 6 6	100/公斤	2.3/公斤	AI=400	10	3	2.0	AI=40	AI=0.3	AI=0.3	AI=2	AI=0.1	AI=0.4	AI=70	140	5.0	1.7	300	200	AI=25	7	5	AI=110	AI=15	0.1
7 - 12月	72 70	9 8	90/公斤	2.1/公斤	AI=400	10	4	2.5	AI=50	AI=0.3	AI=0.4	AI=4	AI=0.3	AI=0.6	AI=85	160	6.5	1.8	400	300	AI=70	10	5	AI=130	AI=20	0.4
1 - 3歲	92 91	13 13	男 女	20	400	5	5	30	40	0.6	0.7	9	0.5	0.9	170	180	9.0	2.0	500	400	80	10	5	65	20	0.7
(稍低)			1150 1150																							
(適度)			1350 1350																							
4 - 6歲	113 112	20 19		30	400	5	6	55	50	男 女 0.9 0.8	男 女 1 0.9	男 女 12 11	0.6	1.2	200	220	12.0	2.5	600	500	120	10	5	90	25	1.0
(稍低)			1550 1400																							
(適度)			1800 1650																							
7 - 9歲	130 130	28 27		40	400	5	8	55	60	1.0 0.9	1.2 1.0	14 12	0.8	1.5	250	280	16.0	3.0	800	600	170	10	8	100	30	1.5
(稍低)			1800 1650																							
(適度)			2100 1900																							
10 - 12歲	147 148	38 39		55 50	男 女 500 500	5	10	60	80	1.1 1.1	1.3 1.2	15 15	1.3	男 女 2.0 2.2	300	350 350	20.0	4.0	1000	800	男 女 230 230	15	10	110	40	2.0
(稍低)			2050 1950																							
(適度)			2350 2250																							
13 - 15歲	168 158	55 49		70 60	600 500	5	12	75	100	1.3 1.1	1.5 1.3	18 15	男 女 1.4 1.3	2.4	400	男 女 460 380	25.0	4.5	1200	1000	350 320	15	男 女 15 12	120	50	3.0
(稍低)			2400 2050																							
(適度)			2800 2350																							
16 - 18歲	172 160	62 51		75 55	700 500	5	13	75	100	1.4 1.1	1.6 1.2	18 15	1.5 1.3	2.4	400	500 370	27.0	5.0	1200	1000	390 330	15	15 12	130	55	3.0
(低)			2150 1650																							
(稍低)			2500 1900																							
(適度)			2900 2250																							
(高)			3350 2550																							
19 - 30歲	171 159	64 52		60 50	600 500	5	12	男 女 120 90	100	1.2 0.9	1.3 1.0	16 14	1.5 1.5	2.4	400	450 390	30.0	5.0	1000	800	380 320	男 女 10 15	15 12	140	55	3.0
(低)			1850 1450																							
(稍低)			2150 1650																							
(適度)			2400 1900																							
(高)			2700 2100																							
31 - 50歲	170 157	64 54		60 50	600 500	5	12	120 90	100	1.2 0.9	1.3 1.0	16 14	1.5 1.5	2.4	400	450 390	30.0	5.0	1000	800	380 320	10 15	15 12	140	55	3.0
(低)			1800 1450																							
(稍低)			2100 1650																							
(適度)			2400 1900																							
(高)			2650 2100																							
51 - 70歲	165 153	60 52		55 50	600 500	10	12	120 90	100	1.2 0.9	1.3 1.0	16 14	1.6 1.6	2.4	400	450 390	30.0	5.0	1000	800	360 310	10	15 12	140	55	3.0
(低)			1700 1400																							
(稍低)			1950 1600																							
(適度)			2250 1800																							
(高)			2500 2000																							
71歲 -	163 150	58 50		60 50	600 500	10	12	120 90	100	1.2 0.9	1.3 1.0	16 14	1.6 1.6	2.4	400	450 390	30.0	5.0	1000	800	350 300	10	15 12	140	55	3.0
(低)			1650 1300																							
(稍低)			1900 1500																							
(適度)			2150 1700																							
懷孕 第一期			+0	+10	+0	+5	+2	+0	+10	+0	+0	+0	+0.4	+0.2	+200	+20	+0	+1.0	+0	+0	+35	+0	+3	+60	+5	+0
懷孕 第二期			+300	+10	+0	+5	+2	+0	+10	+0.2	+0.2	+2	+0.4	+0.2	+200	+20	+0	+1.0	+0	+0	+35	+0	+3	+60	+5	+0
懷孕 第三期			+300	+10	+100	+5	+2	+0	+10	+0.2	+0.2	+2	+0.4	+0.2	+200	+20	+0	+1.0	+0	+0	+35	+30	+3	+60	+5	+0
哺乳期			+500	+15	+400	+5	+3	+0	+40	+0.3	+0.4	+4	+0.4	+0.4	+100	+140	+5.0	+2.0	+0	+0	+0	+30	+3	+110	+15	+0

*表中未標明AI(足夠攝取量Adequate Intakes)值者，即爲RDA(建議量Recommended Dietary allowance)值

(註) (1) 年齡係以足歲計算。

(2) 1大卡(Cal；kcal)=4.184仟焦耳 (kj)

(3)「低、稍低、適度、高」表示生活活動強度之程度。

(4) 動物性蛋白在總蛋白質中的比例，1歲以下的嬰兒以佔2/3以上爲宜。

(5) 日常國人膳食中之鐵質攝取量，不足以彌補婦女懷孕、分娩失血及泌乳時之損失，建議自懷孕第三期至分娩後兩個月內每日另以鐵鹽供給30毫克之鐵質。

*表中未標明AI(足夠攝取量Adequate Intakes)值者，即爲RDA(建議量Recommended Dietary allowance)值

(註) (6) R.E.(Retinol Equivalent)即視網醇當量。
1μg R.E.=1μg視網醇(Retinol)=6μg β-胡蘿蔔素(β-Carotene)

(7) 維生素D係以維生素D$_3$(Cholecalciferol)爲計量標準。
1μg=40 I.U.維生素D$_3$

(8) α-T.E.(α-Tocopherol Equivalent)即α-生育醇當量。
1mg α-T.E.=1mg α-Tocopherol

(9) N.E.(Niacin Equivalent)即菸鹼素當量。菸鹼素包括菸鹼酸及菸鹼醯胺，以菸鹼素當量表示之。

上限攝取量(Tolerable Upper Intake Levels，UL)

修訂第七版

營養素 單位 年齡	維生素A 微克 (µg RE)	維生素D 微克 (µg)	維生素E 毫克 (mg a-TE)	維生素C 毫克 (mg)	維生素B_6 毫克 (mg)	菸鹼素 毫克 (mg NE)	葉酸 微克 (µg)	膽素 毫克 (mg)	鈣 毫克 (mg)	磷 毫克 (mg)	鎂 毫克 (mg)	‡ 鐵 毫克 (mg)	鋅 毫克 (mg)	碘 微克 (µg)	硒 微克 (µg)	氟 毫克 (mg)
0 - 6 月	600	25										30	7		40	0.7
7 - 12 月													7		60	0.9
1 - 3 歲	600	50	200	400	30	10	300	1000	2500	3000	145	30	9	200	90	1.3
4 - 6 歲	900		300	650	40	15	400	1000			230		11	300	135	2
7 - 9 歲						20	500	1000			275		15	400	185	3
10 - 12 歲	1700		600	1200	60	25	700	2000		4000	580		22	600	280	10
13 - 15 歲	2800		800	1800		30	800	2000			700	40	29	800	400	
16 - 18 歲					80		900	3000					35	1000	400	
19 - 30 歲	3000		1000	2000		35	1000	3500								
31 - 50 歲																
51 - 70 歲																
71 歲 -										3000						
懷孕 第一期 第二期 第三期	3000	50	1000	2000	80	35	1000	3500	2500	3500	700	40	35	1000	400	10
哺 乳 期	3000	50	1000	2000	80	35	1000	3500	2500	4000	700	40	35	1000	400	10

‡ 此量不包括非強化飲食之含鐵量，只適用於強化食品與補充劑等之總鐵量

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