School of Pharmacy

Glycaemic effects of betel nut chewing in Type 2 Diabetes Mellitus

Stella Tilu Tulo

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DECLARATION

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgement has been made. This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

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Abstract

Background: The prevalence of Type 2 diabetes mellitus (T2DM) is increasing globally and Papua New Guinea (PNG) is no exception. T2DM and the hyperglycaemia associated with it can virtually affect all systems of the human body. Preventive measures are therefore important in curtailing this epidemic. For those already diagnosed with the disease, optimal glycaemic control to slow the progression of complications improves quality of life and reduces premature death. One of the challenges of achieving optimal control is modifying lifestyle behaviours. Betel nut, a stimulant, and a social habit common in PNG, has been linked to hyperglycaemia and T2DM. Determining the glycaemic effects of this habit in T2DM patients is important because they already have defects in glucose homeostasis. If betel nut chewing contributes to poor glycaemic control in T2DM, patients must be educated on this complication.

Aim: This research project aimed to identify any relationship between betel nut chewing and glycaemic control as measured by oral glucose tolerance (OGT), capillary blood glucose (CBG) and/or glycated haemoglobin (HbA1c) in T2DM.

Methods: To identify any long term association of betel nut chewing with glycaemic control in T2DM (Phase 1), a questionnaire was developed based on the World Health Organization STEPS survey and was used to conduct face-to-face interviews with patients diagnosed with the disease. Participants were recruited from the Port Moresby General Hospital (PMGH) Diabetes Clinic. Information collected included demographics, lifestyle behaviours, and physical and biochemical measurements. Questions on diabetes management were included in the questionnaire and information on diabetes management was confirmed from patients' clinical cards when available. All responses were entered on the questionnaire forms used. A total of 392 participants were recruited. Because those with T2DM already have impaired blood glucose control, the study also included a cohort without T2DM (non-T2DM cohort) to identify any long term association of betel nut chewing with glycaemic control (Phase 3). Data for the non-T2DM cohort (N=972) were extracted from the PNG STEPS survey which was conducted 2-3 years prior to the present study. Data for this were obtained from HOPE worldwide PNG in an Excel format.

Data for the two cross-sectional studies were entered into an Excel® data sheet and transferred into SPSS® versions 20/21 statistical software for statistical analysis.

To determine the acute glycaemic effects of betel nut chewing in T2DM, betel nut chewers from Phase 1 who gave consent to participate, were enrolled into a clinical study (Phase 2). On Day 1 (betel nut chewing day), CBG was measured before and 5-10 minutes after each chewing episode and hourly in between chewing episodes. On Day 2 (no betel nut day), measurements were made hourly. Diet was standardised for both study days. Measurements were entered onto a data collection sheet developed for the study. Statistical analysis of the data used SAS® version 9.0.

Results: A total of 392 T2DM participants were recruited from a total pool of 2,572 diabetes patients registered at the PMGH Diabetes Clinic for Phase 1 but 385 were included in the study. The prevalence of betel nut chewing among this cohort was 55.1% (N = 212). Data for a total of 922 participants from the STEPS survey were included in Phase 3. The prevalence of betel nut chewing among that cohort (non-T2DM participants) was 80.8% (N=745). Fasting CBG (FCBG) was not affected by betel nut chewing in both cohorts. Betel nut chewing had a significant positive relationship with BMI, HbA1c/OGT and physical activity. That is, betel nut chewers were leaner, were more physically active and had better glycaemic control than non-chewers. This was observed in both T2DM and non-T2DM participants. Betel nut chewing was also strongly associated with alcohol consumption and smoking among those with and without T2DM.

For the study aimed at determining the acute glycaemic effects of betel nut chewing (Phase 2), 148 (69.8%) of the 385 T2DM participants, were eligible. Of these, 70 (47.3%) gave consent to participate, 57 (38.5%) refused, and a further 21(14.2%) were excluded because they were not contactable by phone, or were hospitalised or deceased. Thirty eight participants were included in this phase of the study. Results from this study showed that betel nut chewing did not have an acute glycaemic effect on those with T2DM. Variable non-significant glucose changes (increase, decrease, no change) were observed.

Conclusions: It was observed that betel nut chewing had a long term beneficial effect on HbA1c but not FCBG in T2DM. This is supported by similar observations in the non-T2DM cohort which showed that betel nut had a beneficial effect on glucose tolerance but not FCBG. However, this beneficial effect was more likely from lower doses of the betel nut compared to higher doses. The acute glycaemic effect of betel nut chewing in T2DM from the clinical study was non-significant. Although this study provides evidence for a beneficial effect of betel nut on glycaemic control, the mechanism of action cannot be confirmed from this study. Further studies are required to confirm this relationship.

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Publications related to the thesis

Research paper:

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List of Abbreviations

AAPDs	Atypical Antipsychotic Drugs
ACE	Angiotensin Converting Enzyme
AChE	Acetylcholinesterase
AMPK	Adenosine 5'-monophosphate-activated protein kinase
ANG ll	Angiotensin ll
ATP	Adenosine triphosphate
AUC	Area under the curve
BMI	Body mass index
BP	Blood pressure
CAR	Constitutive Androstane Receptor
CBG	Capillary blood glucose
CNS	Central Nervous System
CRP	C-reactive Protein
DBP	Diastolic blood pressure
EEG	Electroencephalographic
FCBG	Fasting Capillary Blood Glucose
Fox01	Forkhead box 01 protein
G6Pase	Glucose-6-Phosphatase
GABA	gamma-aminobutyric acid
$GABA_AR$	Gamma-aminobutyric acid A Receptor
GCG	Glucagon gene
GLP-1	Glucagon-like Peptide-1
GLUT 4	Glucose transporter type 4
GNβ3	β-Polypeptide 3 Gene
HbA1c	Glycated Haemoglobin
HDL	High density lipoprotein
HMG-CoA	3-hydroxy-3-methyl-glutaryl-CoA
IARC	International Agency for Research on Cancer
IDF	International Diabetes Federation
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
LDL	Low density lipoprotein
LXRβ	Liver X Receptor-β
MIA	Moderate-intensity activity
MISFRA	Moderate-intensity sports, fitness and recreational activity
mRNA	messenger ribonucleic acid
NCD	National Capital District

NGI	New Guinea Islands
OGT	Oral Glucose Tolerance
OGTT	Oral glucose tolerance test
PBI	*Piper betle* Inflorescence
PBL	*Piper betle* Leaf
Pdk2	Pyruvate Dehydrogenase Kinase Isoenzyme
PEPCK	Phosphoenolpyruvate carboxykinase
PICs	Pacific Island Countries
PMGH	Port Moresby General Hospital
PNG	Papua New Guinea
$PPAR_{\gamma}2$	Peroxisome proliferators activated receptor gamma 2
PXR	Pregnane X Receptor
RAAS	Renin-angiotensin-aldosterone system
RAS	Renin-angiotensin System
SBP	Systolic blood pressure
SNS	Sympathetic Nervous System
STZ	Streptozotocin
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
TNF	Tumor necrosis factor
VIA	Vigorous-intensity activity
VISFRA	Vigorous-intensity sports, fitness and recreational activity
WHO	World Health Organization

Chapter I: Introduction

1.1 Introduction

There is no country in the world that has been spared from the incidence of Type 2 Diabetes Mellitus (T2DM), and Papua New Guinea (PNG) is no exception. Furthermore, the prevalence of T2DM is increasing in developing countries such as PNG. PNG has a population of about 7 million people and the prevalence of T2DM in PNG has recently been reported to be 14.4%.[1] There are many known factors which have been associated with T2DM. Some of these factors are social habits, such as excessive alcohol consumption [2, 3] and tobacco smoking[4-6]. Betel nut is a social habit which has been linked with T2DM and risk factors for the disease.[7-12] Two epidemiological studies linking betel nut chewing to hyperglycaemia were conducted in PNG; one in a cohort without diabetes [13] and another in a cohort with the disease.[14] The two studies [13, 14] have reported that betel nut chewing is associated with hyperglycaemia. An earlier study in PNG showed that about 60% of PNG patients with T2DM had poor glycaemic control.[15] Whet:

her betel nut is contributing to poor glycaemic control in those with T2DM requires further investigation because those with the disease already have underlying problems with optimal glycaemic control. With a high prevalence of betel nut chewing and an increasing prevalence of T2DM in PNG, this study investigated the effects of betel nut chewing on the blood glucose levels of PNG patients with T2DM.

1.2 Background

Diabetes mellitus is a group of metabolic diseases resulting from defects in insulin secretion, insulin action or both; all of which lead to hyperglycaemia.[16] It is capable of affecting virtually all the body systems. There are two main types of diabetes mellitus: type 1 (T1DM) and type 2 (T2DM). Understanding the pathogenesis of hyperglycaemia is very important when distinguishing between these two main categories. The diagnosis of either T1DM or T2DM depends on the clinical presentation, and differentiating between these two main types and other types of diabetes mellitus requires understanding of the pathogenesis. Understanding the

pathogenesis is also important because it determines how a particular type of diabetes can be treated effectively.[16] T1DM accounts for ≤10% of all diabetes mellitus cases worldwide.[16]

1.2.1 Type 1 diabetes mellitus

This type of diabetes was previously known as insulin-dependent diabetes, or juvenile-onset diabetes. T1DM results from β-cell destruction, which usually leads to absolute insulin deficiency.[16]

The majority of patients with T1DM have the immune-mediated form while a minority have the idiopathic form with no known aetiology. Immune-mediated T1DM results from destruction of the β-cells of the pancreas by the immune system and, therefore, markers of this destruction are usually detected in these patients. These markers include islet cell autoantibodies, autoantibodies to insulin, autoantibodies to glutamic acid decarboxylase and autoantibodies to the tyrosine phosphatases.[17]

T1DM also has multiple genetic predispositions and may be related to environmental factors as well. The clinical presentation depends on the rate of β-cell destruction; rapid destruction is usually seen in infants and children while a slower rate of destruction is seen mainly in adults. Ketoacidosis may present as the first manifestation of the disease. In those where β-cell destruction is slow, they may not present with ketoacidosis for many years, perhaps not until there is absolute insulin deficiency that will require insulin replacement.[16]

Compared to immune-related T1DM, patients with idiopathic T1DM usually have varying degrees of insulin deficiency and, therefore, suffer from episodic ketoacidosis. Idiopathic T1DM is strongly inherited and is mostly seen in those of Asian and African descent.[18] Patients who have T1DM are usually lean, but this is not a diagnostic indicator. Symptoms include excessive excretion of urine (polyuria), thirst (polydipsia), constant hunger, weight loss, vision changes and fatigue. Those with T1DM require lifelong exogenous insulin replacement therapy in order to survive.

1.2.2 Type 2 diabetes mellitus

This type of diabetes was previously known as non-insulin-dependent diabetes or adult/maturity-onset diabetes. Compared to T1DM, those with T2DM have only relative (rather than total) insulin deficiency and the majority may not need insulin replacement at all throughout their lifetime.[16]

The two underlying problems in T2DM are impaired insulin secretion (β-cell failure) and function (insulin resistance). There are several mechanisms which may explain the pathogenesis of T2DM and these include glucotoxicity, lipotoxicity, oxidative stress, endoplasmic reticulum stress and amyloid deposition.[19] All these mechanisms have a role in both insulin resistance and islet β-cell death, except amyloid deposition, which is thought to have a role in β-cell failure. Furthermore, all these mechanisms are said to contribute to tissue inflammation and inflammation has been reported to be a contributory factor to development of T2DM.[19]

In an insulin-resistant individual, insulin secretion may be normal or elevated but, because of higher blood glucose levels, those with the disease may need even higher insulin levels to compensate for insulin resistance. Insulin secretion becomes defective as well, over time, as the F-cells fail. Insulin resistance is associated with obesity but not all obese insulin-resistant people actually develop T2DM.

T2DM may go undiagnosed for many years without the person knowing s/he has the disease. This is because the hyperglycaemia associated with the condition develops gradually and, in the initial stages, the classic symptoms of diabetes may go unnoticed. Patients with the disease may present with non-specific signs and symptoms such as polyuria, fatigue and repeated infections like vaginal thrush in women.[20] By the time T2DM is diagnosed, complications may already have occurred. Complications such as cardiovascular disease, amputations, neuropathy, renal failure and cerebrovascular disease are major causes of premature morbidity and mortality.[21-24] These complications are caused by poorly controlled hyperglycaemia. Infections also have been identified as an important contributory cause of the high morbidity and mortality in patients with diabetes.[25, 26]

Complications associated with T2DM lead to a poor quality of life and increased health care costs. Health care costs are incurred from hospitalisations and

associated expenses, and the use of medications.[27] The high cost of managing T2DM and its complications can be a significant economic burden to countries with a high prevalence of the disease.

Although the specific aetiology for T2DM is unknown, there are factors which are known to contribute to the development of the disease. One of the most important risk factors for T2DM is obesity. Not only is obesity associated with insulin resistance but it is also associated with inflammation.[28, 29] Other known risk factors are dyslipidaemia, lifestyle behaviours (for example, diet or physical activity) and genetics. There is also increasing evidence of the role of the gut microbiota (independent of environmental factors) in T2DM.[30] Drugs or chemicals also can induce or precipitate T2DM.[31, 32]

T2DM can be prevented and, once diagnosed, proper management can retard the development of complications or premature mortality and morbidity. Lifestyle modifications, coupled with diabetes education, are important interventions in the fight to reduce the prevalence of T2DM and impede the development of complications associated with the disease. Prevention of T2DM should focus on lifestyle factors which may contribute to the development of the disease. To delay the development of complications of T2DM and prevent premature deaths, a combination of lifestyle modifications, glucose monitoring and proper medication management is important.

1.3 Significance

This study is relevant in PNG because betel nut chewing is highly prevalent and also because of the high prevalence of T2DM in the country. Two cross-sectional studies[13, 14] conducted in PNG reported an association of betel nut chewing with poor glycaemic control. Other cross-sectional studies [7-12] in other betel nut chewing countries have also linked betel nut chewing with risk factors for T2DM such as obesity. There has not been any research done to investigate the acute glycaemic effect of betel nut chewing. Investigating the acute glycaemic effect of betel nut may confirm the glycaemic effect of betel nut chewing and provide some understanding of any long term association of betel nut chewing with T2DM.

If betel nut chewing is contributing to poor glycaemic control, T2DM patients must be educated in regard to this issue. Betel nut chewing is a social habit that may have to be modified to prevent T2DM, especially in those at risk of developing the disease.

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Chapter II: Literature review

2.1 Introduction

Type 2 diabetes mellitus (T2DM) has the tendency to affect the working-age population as well as seniors. The disease leads to premature mortality and increased morbidity, and an increased economic burden.[1-5] Increased morbidity continues to contribute to poor quality of life for those diagnosed with the disease. Reduced quality of life, itself, can lead to increased costs and premature deaths. Apart from being an economic burden as a result of its impact on productivity, the costs associated with the disease are a burden not only to the individuals who are affected by the disease but also to their families who provide support and care. Furthermore, the economic impact of T2DM is burdensome for countries with a high prevalence of the disease.

For those diagnosed with T2DM, emphasis on diabetes care and management focuses on optimal blood glucose control to prevent or retard micro- and/or macro-vascular complications. Complications or consequences of uncontrolled hyperglycaemia, such as cardiovascular disease, amputations, neuropathy, renal failure and cerebrovascular disease, are major causes of premature morbidity and mortality.[1-4, 6-8] These complications further contribute to the economic burden associated with T2DM. Health care costs are incurred from hospitalisations and associated expenses, including medications and other consumables such as syringes for insulin administration when necessary.[5]

T2DM used to be a disease which affected those who were more than 30 years of age. However, there is now evidence that the disease is affecting the much younger population.[9, 10] This should be a concern to countries with a high prevalence of the disease because T2DM and the complications associated with it have the tendency to strike at the many productive members of society.

An understanding of the pathogenesis, pathophysiology and, therefore, factors contributing to the development of diabetes is important in dealing with the T2DM epidemic. Understanding all these factors helps in identifying preventive measures

and, also, establishing appropriate glucose control for those already diagnosed with the disease.

Normal glucose regulation is complex, requiring a balance between release and action of insulin and the counter-regulatory responses. Insulin is released in response to blood glucose increases above normal physiological levels, while counter-regulatory responses are stimulated by falls in glucose levels below normal physiological levels. Normal glucose homeostasis can be affected by other metabolic effects. These metabolic effects can result from the environment and lifestyle factors interacting with inherent and acquired characteristics of an individual. Pharmacotherapeutic and habitual drugs such as ethanol (alcohol) can also affect normal glucose homeostasis.[11]

Research has shown that several chemical constituents of betel nut, a commonly used stimulant in Papua New Guinea (PNG), may affect glucose homeostasis. Most of the studies conducted have used individual chemical constituents, such as arecoline, rather than the whole betel nut chew (betel nut chewed with other components). Investigating the effect of betel nut alone on glucose homeostasis may not provide the same result as using the whole betel nut chew because betel nut is generally chewed with other components; the two most common additives being lime (calcium hydroxide or calcium oxide) and *Piper betle* leaf (PBL) or *Piper betle* inflorescence (PBI). These additives add further to the number of chemicals which may affect glucose homeostasis or affect the absorption of its chemical components in a betel nut chewer.

2.1.1 Examples of drugs which affect glucose homeostasis

Drugs affecting glucose homeostasis may result in either hypoglycaemia or hyperglycaemia.[11-13] Furthermore, some drugs may also have a synergistic effect upon each other to cause either hypoglycaemia or hyperglycaemia[11] and some may induce or increase the risk of obesity, which is an important contributing factor in the development or worsening of T2DM[14]. Drugs may also impair glucose homeostasis where there is concurrent diminished organ function, such as in liver disease.[15]

2.1.1.1 Drugs associated with hyperglycaemia or T2DM and their mechanisms of action

Drugs which have been reported to have a potential for inducing hyperglycaemia include cardiovascular drugs [(β-blockers[11-13, 16], thiazide diuretics[12, 13], statins[12, 13, 17-21], corticosteroids[11-13, 22, 23], atypical antipsychotic drugs[12, 13, 24-26], calcineurin inhibitors[27-29] and pregnane X receptor (PXR) agonists.[30-32] Although the mechanisms by which these drugs cause hyperglycaemia are mostly unknown, potential mechanisms have been proposed.

Corticosteroids are well known for causing hyperglycaemia. The use of corticosteroids, therefore, is not only a risk for development of T2DM but also for the worsening of glycaemic control in those already suffering T2DM. They are most commonly used in clinical practice as anti-inflammatories, immunosuppressants and chemotherapeutic agents, as well as in replacement therapy. There are several mechanisms by which corticosteroids affect glucose homeostasis. They blunt the action of insulin and promote hepatic gluconeogenesis.[33] Studies[34, 35] using mice, have demonstrated that the effect of corticosteroids on hepatic gluconeogenesis is through activation of liver x receptor-β (LXRβ) involving phosphoenolpyruvate carboxykinase (PEPCK) gene transcription. Activation of LXRβ involving PEPCK increases hepatic gluconeogenesis, causing hyperglycaemia.[34, 35] Recent studies using mice and cell-based assays have demonstrated that osteoblasts play a central role within systemic fuel metabolism;[36-38] a role affected by corticosteroids[39]. As demonstrated by these studies, a factor(s) originating from osteoblasts is(are) modified by glucocorticoid signalling in these cells, causing adverse glucose homeostasis. Osteoblasts secrete osteocalcin, a hormone involved in regulating glucose homeostasis.[40] Osteocalcin is an insulin secretagogue and influences blood insulin levels, glucose tolerance and insulin sensitivity. It also directly stimulates expression of the insulin genes.[40] Furthermore, osteocalcin influences fat mass, proliferation of β-cells and energy expenditure.[40] Glucocorticoids cause a marked decrease in serum osteocalcin levels.[39] Ferron et al [38] demonstrated that increased osteocalcin activity through insulin signalling in osteoblasts is necessary for whole body glucose homeostasis. Osteocalcin causes β-cells in the pancreas to release more insulin while, at the same time, directing adipose cells to release adiponectin that increases sensitivity to insulin. Lee et al[36] showed that lack of

osteocalcin leads to decreased β-cell proliferation, glucose intolerance and insulin resistance, all of which are important predisposing factors for T2DM.

β-blockers are used for the treatment of hypertension. Studies linking β-blockers and hyperglycaemia or T2DM have been conflicting. One possible reason for these conflicting reports may be their differences in terms of their mechanisms of action and physiological effects and, therefore, β-blockers should not be considered as a homogenous class of drugs when investigating their glycaemic effects.[16] Non-vasodilating β-blockers (for example, atenolol and metoprolol) have been reported to have negative effects on glucose and on lipid metabolism.[41] Studies investigating the glycaemic effect of this group of β-blockers also have been conflicting, but it has been suggested that conflicting results may arise from the type of glucose parameter measured.[16] Fonseca[16] suggests that glucose levels at a particular point in time (e.g. fasting glucose) may not reflect long term changes in glucose metabolism, as is reflected by glycated haemoglobin (HbA1c). Evidence provided for this argument is the finding, in a randomised double-blind crossover study, that metoprolol did not affect fasting plasma glucose but increased HbA1c.[16, 42] Proposed mechanisms of non-vasodilating β-blockers on glucose metabolism include unopposed α_1-adrenergic receptor activity resulting from the blocking of β_1-adrenergic or β_1- and β_2-adrenergic receptors. This may result in vasoconstriction causing reduction in blood flow to muscles and insulin-stimulated glucose uptake in the periphery (insulin resistance).[43] Insulin resistance is associated with increased activation of the renin-angiotensin-aldosterone system (RAAS), which results in stimulation of angiotensin receptors, thereby impairing insulin signalling at the vascular and skeletal muscle tissues.[41, 44] Other potential mechanisms include interference with insulin secretion from pancreatic β-cells[45] and reduction of the first phase of insulin release.[41, 45] Non-vasodilating β-blockers also have been associated with worsening hyperglycaemia in those with abdominal obesity.[14]

Thiazide diuretics not only have been reported to cause hyperglycaemia but also the development of T2DM.[14, 46-49] There is evidence that new onset diabetes may be more prevalent in obese patients taking hydrochlorothiazide than in those who are not obese.[14, 50] The exact mechanism of action of thiazides on glucose homeostasis that results in hyperglycaemia is unknown. They appear to exert their effects on

glucose homeostasis through many complex and interacting mechanisms.[51] Several postulated mechanisms resulting in hyperglycaemia include worsening of insulin resistance, inhibition of glucose uptake, reduction of insulin release, induction of hypokalaemia and down-regulation of peroxisome proliferator-activated receptor gamma.[51-55] The latter not only activates the RAAS but also decreases insulin release. By activating the RAAS, angiotensin II (ANG II) and aldosterone are elevated, with consequent hyperglycaemia. The hyperglycaemia results as a consequence of induced insulin resistance via increased oxidative stress and altered insulin signalling that lead to decreased glucose transport.[56] ANG II also increases the risk of hyperglycaemia by contributing to oxidative stress, inflammation and apoptosis in pancreatic β-cells.[56] It also has been reported that genetics may play a role in the development of diabetes in those who are taking thiazides.[57, 58] Bozkurt et al[57] reported a reduction in the risk of diabetes in patients with polymorphisms in the guanine nucleotide binding protein β-polypeptide 3 gene (GNβ3) who were taking thiazides. That study [57] showed that those with polymorphisms in the angiotensin converting enzyme (ACE), who also were taking thiazides, showed an increased risk.

Statins (HMG-CoA reductase inhibitors) inhibit cholesterol biosynthesis and are therefore used to treat hyperlipidaemia. They are commonly used among those with T2DM because obesity is a usual presentation in those with the disease. Reports of hyperglycaemia or new-onset diabetes in patients receiving statins have been a concern, as statins have been reported to benefit T2DM patients with hyperlipidaemia in preventing or reducing premature adverse cardiovascular outcomes such as myocardial infarction, stroke or cardiovascular death.[59-61] The hyperglycaemic effects of statins may not be a class action but may apply more in certain statins than others.[18, 20, 62-64] Furthermore, this effect may be dose-dependent[17-19, 64-66], more pronounced in older patients[17] and influenced by the pharmacology of individual statins.[62, 64, 65] The exact mechanism remains unknown but several conflicting mechanisms have been postulated. These include perturbations of the metabolic pathway such as the ATP-dependent potassium channel,[21] depolarisation and calcium influx,[21, 65] and glucokinase.[67] Statins also may worsen glycaemic control and increase insulin resistance by affecting the cholesterol synthetic pathways, especially by affecting metabolites such as

isoprenoids and ubiquinone.[66, 68-70] Effects of statins on glucose homeostasis also may be genetically influenced.[71]

Cyclosporin and tarcrolimus are examples of calcineurin inhibitors which have been implicated in elevated glucose levels. These drugs are usually employed in transplant therapy to avoid allograft rejection. Heit et al[72] used knockout mice to demonstrate calcineurin function in glucose homeostasis. They deleted the calcineurin phosphatase regulatory unit, calcineurin 1, and observed that the mice developed age-dependent diabetes resulting from decreased β-cell proliferation and mass, reduced pancreatic insulin content and hypoinsulinaemia. These findings indicate that inhibition of calcineurin contributes to the development of diabetes. Again, several mechanisms have been postulated. Administration of cyclosporin and tacrolimus to rats for up to two weeks resulted in hyperglycaemia[73, 74], reduction in serum and pancreatic insulin levels[73-76], glucose intolerance[75, 76] and a decreased insulin transcription which was time-dependent.[76] In a recent study by Goodyer et al[77], it was observed that inactivation of calcineurin in mouse islets impaired biogenesis of dense core granules, and reduced both insulin secretion and cell proliferation and mass. The study used islets of knockout mice similar to those used by Heit et al.[72] Interestingly, recent animal studies[78] have demonstrated that long-term activation of calcineurin by transgenic overexpression of active calcineurin induces impaired glucose tolerance by altering β-cell mass. The findings of these studies suggest that chronic activation of calcineurin affects β-cell proliferation and survival. Another mechanism by which calcineurin inhibitors cause hyperglycaemia may involve inhibition of calcineurin-dependent glucose sensing in pancreatic β-cells.[79]

Atypical antipsychotic drugs (AAPDs) such as risperidone, olanzapine and clozapine are commonly used in the treatment of schizophrenia and bipolar disorder. Schizophrenia itself has long been associated with diabetes mellitus[80] and has also been reported to be associated with a higher prevalence of metabolic syndrome, compared to the general population.[81-83] Use of AAPDs has been reported to affect glucose homeostasis resulting in hyperglycaemia, which increases the risk of T2DM or can worsen hyperglycaemia in those already affected by the disease.[84-87] Apart from AAPDs being associated with hyperglycaemia resulting from long term use,

acute hyperglycaemia also has been reported after short term use.[88] It is thought that hyperglycaemia is most likely due to the weight gain promoted by these agents. Some of the likely mechanisms by which weight gain is promoted are through antagonism at serotonin and central histamine H_1 receptors, development of insulin resistance by affecting cellular glucose transport, impaired insulin secretion and alterations in leptin levels.[85-90] However, human studies[88] investigating the acute hyperglycaemic effects of AAPDs, as well as animal studies,[91-93] have demonstrated that AAPDs have direct effects on blood glucose levels that are independent of obesity and, therefore, T2DM can develop in the absence of obesity. Although the exact mechanism by which AAPDs affect glucose homeostasis is unknown, many complex mechanisms have been proposed. In an animal study[89] using mice, it was reported that a mechanism by which this group of drugs causes hyperglycaemia may be activation of the sympathetic nervous system (SNS). Although Ikegami et al,[94] in another study using mice, demonstrated that olanzapine causes hyperglycaemia by increasing hepatic glucose production via the SNS and does so by activating hypothalamic adenosine 5'-monophosphate-activated protein kinase (AMPK). In the study, systemic administration of olanzapine increased blood glucose in both fasted and unfasted mice, but more so in unfasted mice. Central administration of the drug, however, only increased blood glucose levels in the unfasted mice. Further tests were performed to investigate the effect of olanzapine on the mRNA levels of gluconeogenic or glycolytic enzymes in mouse liver, the results of which showed an increase in the mRNA level of Glucose-6-Phosphatase (G6Pase) but no effect on other enzymes. The authors suggested that olanzapine activated AMPK in the hypothalamus, which stimulated the SNS, thereby increasing hepatic G6Pase via the β-adrenergic receptors and, consequently, resulting in hyperglycaemia. Activation of the hypothalamic AMPK increased endogenous glucose production.[95] Using an animal model, Hahn et al[93] also centrally administered olanzapine and demonstrated that the drug reduced insulin secretion in response to glucose challenge. An earlier study[96] used the same model but administered olanzapine and clozapine peripherally (subcutaneous injection) and found that these drugs increased hepatic glucose production, decreased peripheral glucose utilisation and impaired β-cell function (reflected by the decrease in insulin secretion). The two aforementioned studies[93, 96] demonstrate that centrally administering AAPDs such as olanzapine, perhaps, has no effect on insulin

sensitivity. Other mechanisms by which hyperglycaemia is induced via the SNS include impairment of cholinergic-stimulated insulin secretion by blocking muscarinic M_3 receptors,[97] and activation of hypothalamic AMPK by antagonising histamine H_1 receptors, dopamine D_2 receptors, serotonergic $5HT_{2A}$ receptors and α_1-adrenoceptors[91, 98]. Mechanisms such as increase in hepatic phosphorylase activity, increased expression of the level of G6Pase, mitochondrial damage and inflammation also have been proposed.[92, 99] In terms of inflammation and its association with T2DM, research has shown that microbiota resident in the human gut play an important role in the development of diabetes. Gut microbiota modulate intestinal permeability, which increases metabolic endotoxin secretion leading to chronic low-level inflammation and consequent T2DM.[100] Recently reported animal studies[101] suggest that olanzapine causes metabolic adverse effects by changing the gut flora. When an antibiotic cocktail was administered to olanzapine-treated rats, a shift in gut flora attenuated the adverse metabolic effects of the drug.

PXR activators have been reported to cause hypoglycaemia but the majority of evidence supports a stronger link with hyperglycaemia or T2DM. PXR has been found to be species-specific.[31] Two known potent human PXR activators reported to induce hyperglycaemia are rifampicin and rifaximin (a rifampicin analogue). [30-32] PXR is mainly expressed in the liver and in the small intestine.[32] Rifaximin has been reported to be a gut-specific human PXR activator. [102] There are several pathways by which PXR activation is suggested to affect metabolic homeostasis. Most of the data suggests that hyperglycaemia results from interference with transcription factors or co-factors involved in transcriptional regulation of gluconeogenic enzymes such as G6Pase and PEPCK. These interferences result in repression of gluconeogenesis, glucose transport and glycogen storage. PXR regulates not only the expression of enzymes and transporters involved in drug metabolism but also the genes involved in the metabolism and excretion of endobiotics.[103, 104] Furthermore, PXR affects energy metabolism through direct gene regulation, or through crosstalk with other transcriptional regulators, and orchestrates immune responses to protect against stresses caused by exposures to xenobiotics.[103, 105, Recent animal studies[31, 106] have shown down-regulation of the hepatic glucose transporter 2 (Glut 2), pyruvate dehydrogenase kinase isoenzyme 2 (Pdk2) and glucokinase by PXR activation. Hyperglycaemia can also result from disruption of

lipid formation and catabolism provoked by PXR activation.[104] Activation provokes reduction of β-oxidation related gene expression, increased fatty acid uptake in the liver resulting in hepatic steatosis, and increased hepatic expression of transcription factors and enzymes which are involved in lipogenesis.[107, 108]

2.1.1.2 Drugs associated with hypoglycaemia and their mechanisms of action

Apart from known hypoglycaemic effects of agents clinically used to lower blood glucose, alcohol[109], aspirin (salicylates)[109] and some cardiovascular drugs [β-blockers[109, 110], Renin-angiotensin system (RAS) blockers (ACE inhibitors and angiotensin receptor blockers)][111, 112] and constitutive androstane receptor (CAR) agonists [(example; phenobarbital)[113, 114]] may induce hypoglycaemia. Some of these drugs may act synergistically with hypoglycaemic agents used for diabetes treatment to cause or worsen hypoglycaemia. Hypoglycaemia is, therefore, more common in those with diabetes mellitus compared to those without the disease.

Vasodilating β-blockers, also known as non-selective β-blockers have been reported to be associated with hypoglycaemia. Non-selective β-blockers are more likely to cause hypoglycaemia, compared to selective agents. Similarly, selective β-blockers (non-vasodilating β-blockers) are less likely to be associated with hypoglycaemia compared to those which are non-selective.[115, 116] Two mechanisms have been proposed for this hypoglycaemic effect in non-selective β-blockers. The first of these is the blunting of the signs and symptoms of hypoglycaemia.[115] This may worsen a hypoglycaemic episode or delay recovery from a hypoglycaemic attack.[116] The second mechanism involves these β-blockers directly potentiating the effects of insulin, which results in a heightened insulin effect.[109] The consequences of a heightened insulin effect are increased glucose utilisation in the periphery and inhibition of lipolysis. Further, use of β-blockers may cause a reduction in glycogenolysis and gluconeogenesis resulting from a diminished physiologic response to hypoglycaemia.[115, 117]

ACE inhibitors and angiotensin receptor blockers block the RAS. These drugs are thought to cause hypoglycaemia through haemodynamic or direct effects resulting from the inhibition of the RAS. Haemodynamic effects increase insulin release from the pancreas and improve delivery of glucose to peripheral tissues.[111-113, 118] ANG II

has a direct inhibitory effect on insulin signalling and glucose transport. Therefore, inhibition of the RAS prevents this inhibitory effect, resulting in improved insulin sensitivity, improved delivery of glucose to insulin-sensitive tissues and reduced glucose levels.[119-126] Other possible mechanisms by which the blocking of RAS causes hypoglycaemia are improvement of insulin sensitivity through greater differentiation of adipocytes from pre-adipocytes as a result of increased adiponectin levels, retention of potassium or protection of pancreatic islets from glucotoxicity and oxidative stress.[127]

Aspirin, a salicylate drug, is a common non-steroidal analgesic. The exact mechanism by which it causes hypoglycaemia is not known but there are several which have been postulated. These include reduction of hepatic gluconeogenesis, increased insulin secretion, reduced insulin clearance and enhanced plasma insulin response.[128, 129] Gao et al[130] also demonstrated that aspirin prevented insulin-induced glucose uptake in 3T3-L1 adipocytes pre-treated with TNF-α and they concluded that aspirin probably protects insulin receptor substrate proteins from serine phosphorylation catalysed by multiple kinases. In protecting these proteins, aspirin may enhance insulin sensitivity, causing hypoglycaemia.[130] Paracetamol, another analgesic, has been said to cause symptomatic hypoglycaemia as a result of hepatic necrosis following an overdose and, at therapeutic levels, causes hypoglycaemia, especially in children.[131, 132]

The association of hypoglycaemia with alcohol intake is well-established, especially in those with T2DM and more so in patients who are on insulin or sulphonylureas.[133, 134] Alcohol causes hypoglycaemia by inhibiting gluconeogenesis.[109, 135] It is also thought that alcohol may increase endogenous insulin secretion, thus causing hypoglycaemia.[116] In a fasting state, T2DM patients who consume alcohol, and who are receiving hypoglycaemic agents, can experience severe hypoglycaemia. This is because, during the fasting state, the body relies on other sources of glucose but, if alcohol is inhibiting gluconeogenesis and hypoglycaemic agents such as insulin are reducing glucose, severe hypoglycaemia is experienced and the person can end up in a hypoglycaemic coma. Hartling et al[134] in their study involving 10 normal-weight non-diabetic participants demonstrated that the return of blood glucose toward fasting level was delayed by ethanol. In their study, they used glipizide, a

sulphonylurea. The study evaluated □-cell secretory activity by measuring concentrations of insulin and C-peptide; concentrations of which were unchanged by ethanol. Hartling et al[134] therefore argued that ethanol can prolong, but does not augment, hypoglycaemia. Alcohol-associated hypoglycaemia also has been reported in those without T2DM.[136]

The CARs are closely related to the PXRs and they both suppress gluconeogenesis but CARs appear to have a beneficial effect on blood glucose, compared to PXRs. Phenobarbital is a CAR agonist which has been reported to decrease blood glucose levels and improve insulin sensitivity in T2DM.[113, 114] Animal and cell culture studies have demonstrated that, similar to PXRs, phenobarbital represses gluconeogenesis by suppressing the expression of PEPCK and G6Pase.[137, 138] However, unlike PXRs, CAR activation appears to offer a beneficial effect on glucose homeostasis. This perhaps suggests that other factors, or other metabolic pathways, interact with CARs to achieve this beneficial effect. Activation of CARs also may improve glucose control by improving lipid profiles as they have been demonstrated to inhibit lipogenesis.[139] Improving lipid profiles improves insulin sensitivity. In mice, the nuclear receptor has been reported to significantly suppress or reverse adiposity induced by a high fat diet.[139]

Betel nut is said to be one of the most commonly used drugs in the world, after tobacco, alcohol and caffeine. It has been estimated that approximately 600 million people consume betel nut worldwide.[140] The nut is said to be indigenous to India, Sri Lanka, the Maldives, Bangladesh, Myanmar, Taiwan and many islands in the South Pacific, including PNG.[140] It contains chemicals which may contribute to the development of hyper- or hypo-glycaemia. Some mechanisms by which betel nut affects glucose homeostasis already have been postulated but evidence supporting the glycaemic effects of betel nut and its chewing components, so far, are conflicting. It is, therefore, important that research continues to investigate not only the glucose homeostatic effects of the chemical components of betel nut itself, but also the effect of betel nut and its additives during and after mastication. Furthermore, it is important to investigate the glycaemic effect of betel nut chewing in T2DM patients as they already have impaired glucose homeostasis. Any findings from such research will assist efforts to improve glycaemic control in these patients

and thereby reduce morbidity, premature mortality and the economic burden of the disease, especially in those countries where the habit of betel nut chewing is endemic.

2.2 Global perspectives of T2DM

Over the last decade and a half, there have been several estimates of the worldwide prevalence of diabetes. These estimates, based on available data from different countries, all project an increase in the prevalence of diabetes worldwide. Different methodologies are used to calculate estimates and new data are incorporated into the analysis as they become available. However, estimates may generally under- or over-estimate the prevalence of diabetes and, therefore, country-level reporting using standardised formats may improve estimates, especially when based on the reporting of new incidences of diabetes. There may also be a need to develop systematic ways of assessing which studies to incorporate when calculating estimates for the prevalence of diabetes.[141] However, the estimates reported by different organisations are very close to each other, suggesting that there is indeed an increase in the prevalence of diabetes.

The most recent estimates from the International Diabetes Federation (IDF) suggest that the number of people with diabetes, worldwide, was 366 million in 2011 and 382 million in 2013, more than 90% of whom had T2DM.[142, 143] Increases in the prevalence of T2DM have been seen in many population groups and mostly in populations with a genetic susceptibility to the development of T2DM. It is estimated that 8.3% of those aged 20-79 years live with diabetes and this is projected to increase to 9.9% in 2030.[142, 143] The estimated worldwide prevalence of diabetes is expected to increase to 592 million by 2035. [142, 143]

Most of the increase in T2DM is reported to be occurring in developing countries and within disadvantaged minority groups in developed countries. Regions estimated to have the highest prevalence of diabetes among adults aged 20-79 years in both 2011 and 2030 are the Middle East and North Africa, North America and the Caribbean, South East Asia and the Western Pacific.[142, 143] The top 10 countries for diabetes prevalence in 2011 and 2030 were, and will be, in the Middle East and North Africa and the Western Pacific regions.[142, 143]

2.3 T2DM in the Pacific Island Countries

The region with the highest estimated number of people with diabetes (138 million) is the Western Pacific region,[142, 143] which includes the Pacific Island countries (PICs). The PICs are divided into three regions: Melanesia comprising of PNG, the Solomon Islands, Vanuatu, Fiji and New Caledonia; Polynesia comprising of Tonga, the Cook Islands, Niue, American and Western Samoa, Tahiti, Wallis and Futuna, and Tokelau; and Micronesia comprising of Kiribati, Nauru, the Federated States of Micronesia, the Marshall Islands, the Northern Mariana Islands and Guam. Of the top 10 countries/territories for comparative prevalence of diabetes among 20-79 year olds in 2013 [142], seven of these were PICs, which is alarming.

In early 2000, the World Health Organization (WHO) initiated collaborative country surveys within PICs, aiming to identify risk factors for non-communicable diseases such as diabetes in the region. These surveys were conducted with a step-wise approach commencing with behavioural risk factors, followed by physical measurements and then biochemical measurements, hence the name 'STEPS' survey. Several reports of these surveys have been released. Results of these surveys have shown that, among the PICs, Polynesian[144-147] countries have the highest prevalence of T2DM based on fasting capillary blood glucose (FCBG), with American Samoa[147] having one of the highest rates (47.3%) in the world. The prevalence rates range from 13.5% to 47.3% in Polynesia [144-147], 14.4% to 21.2% in Melanesia [148-151] and 19.6% to 28.1% in Micronesia [152-154]. Some of these country reports calculated prevalence rates for age groups 15-64 years while others did so for age groups 25-64 years. The prevalence rates may therefore be higher for those countries that calculated prevalence rates based on the age group 25-64 years compared to those that based calculations on the ages 15-64 years, considering that T2DM now affects young adults in their twenties. Most of these countries used values of FCBG ≥6.1mmol/L to indicate fasting hyperglycaemia while a few used FCBG ≥7.0 mmol/L which may lead to under- or over-estimation of fasting hyperglycaemia when comparing rates between these countries.

Earlier studies in Melanesian populations showed a low prevalence of T2DM which led to the suggestion that this group of Pacific Islanders had genes which protected them from impaired glucose tolerance.[155] However, as indicated by the recent

STEPS surveys in Melanesian countries, the prevalence of diabetes is certainly increasing [148-151], mostly in those populations that have been westernised and are living in urban or periurban areas.[156-162] These findings question the protective gene theory. Thus far no gene has been isolated. It is thought that, as communities become more westernised, their finely tuned metabolic systems break down.[163]

2.4 T2DM in Papua New Guinea

PNG has a population of about 7 million people. It is estimated[142] that over 200,000 people in PNG have T2DM, and only about 45% of these know that they have it. In 2013, the national prevalence of diabetes, estimated using extrapolated data from similar countries, was 5.4%.[142] However, a preliminary report from the STEPS survey conducted in PNG from 2007 to 2008 has reported a diabetes prevalence rate of 14.4%.[151] The preliminary national prevalence rate for diabetes is the first to be reported from a national survey in PNG and confirms the high prevalence of diabetes in the country.

Several small surveys carried out within certain populations in PNG from 1962 to 1983 also have demonstrated this increase in the number of people with T2DM.[156-158, 161, 164-167] These surveys were not performed using a standardised methodology and only involved small samples of a few populations, yet they do indicate an increase in the number of people with T2DM within the populations studied. The increase in the prevalence of T2DM in PNG has been attributed to several factors. These factors include westernisation and urbanisation.[168-171] Westernisation and urbanisation have led to changes in diet, physical activity and social habits.[168-172] Before westernisation and urbanisation, people worked in their gardens to grow their own food and were physically active. Urbanisation has led to land development and, therefore, loss of garden land. As a result of westernisation and urbanisation, people are now consuming refined foods and living more sedentary lifestyles. Those in urbanised areas are at higher risk because of their more sedentary lifestyles, increased mechanisation of manual tasks and changes in diet. Although the diet of rural villagers also is changing, these villagers are mostly subsistence farmers and, therefore, are more physically active. Studies have shown that the prevalence of T2DM is higher in urban populations compared to rural populations.

[157, 158, 160, 161] Western civilisation was only introduced to the highlands of PNG in the 1930s and studies carried out in some populations in this region of the country have shown a low prevalence of T2DM.[159, 160] A study comparing a highlands population with a coastal population showed no T2DM in the highland population of 257 studied and a 4% prevalence of diabetes in the coastal population of 273.[159] The same study[159] showed a 1.9% prevalence of impaired glucose tolerance in the highlands population. This indicates the increasing risk of T2DM for this ethnic group as westernisation and urbanisation progress.

Studies in PNG have shown that a significantly high percentage of T2DM patients exhibit poor glycaemic control,[7, 173, 174] although no recent studies have been conducted or published to validate this finding. A study by Savige et al. also showed that diabetes in PNG has a high case fatality rate with a median survival of 4 to 5 years.[175] Important contributory causes of the high mortality and morbidity in patients with diabetes in PNG, as reported in the late 1980s, were diabetic coma and infections.[7, 175]

Despite the high morbidity and mortality associated with T2DM in PNG, resources allocated to manage the disease are very much limited. Not all the hospitals in the country have specialist diabetes clinics. The capacity to detect new cases of the disease, and to monitor complications, also is limited.[176] In a country with economic constraints and limited resources, it is even more critical to reduce the prevalence of T2DM.

2.5 Betel nut chewing

Betel nut, scientifically known as *Areca* nut, is obtained from the *Areca catechu* palm tree. The palm tree is widely distributed throughout East Africa, South Asia and the Pacific Islands.[177] It is in these countries where chewing of betel nut is common among certain populations. Betel nut chewing is also popular in migrant communities from countries where the habit is common, as observed among the PNG community living in Perth. Different components chewed with betel nut vary in different parts of the world where the habit is practised.

Before chewing, betel nut may be prepared in different ways; it may be used fresh, or dried and cured, before chewing. The nut can be boiled, baked or roasted.[178] In

Asian countries, a fresh or dried seed of betel nut is chewed with a fresh PBL, a dab of slaked lime (calcium hydroxide), and various flavourings such as cardamom and tobacco. The mixture of ingredients wrapped in PBL is termed the betel quid. The betel quid is prepared by smearing a betel leaf with slaked lime. Pieces of betel nut, as well as other flavouring agents, are added to the PBL smeared with slaked lime. The ingredients are then enfolded by the PBL and chewed.[140, 178] In mainly Chinese chewers in Taiwan, a piece of the PBI and red lime paste are sandwiched between two unripe halves of betel nut.[179]

Adding known carcinogens such as tobacco to the betel nut quid is a practice reported in Asian countries. In a study[180] investigating betel quid dependence, it was reported that chewers in Taiwan, Malaysia, Sri Lanka, Indonesia and Nepal added tobacco to the quid, with the prevalence of tobacco-added quid varying among these countries. The study indicated that the prevalence of tobacco-added quid was the highest in Nepal, with 100% of chewers adding tobacco, while 100% of Chinese chewers in mainland China did not add tobacco. The next highest prevalence of tobacco-added quid was seen among Indonesian chewers and this was followed by Malaysia and Sri Lanka, with Taiwan having the lowest prevalence. Interestingly, the study reported that 100% of the mainland Chinese users chewed the husk of betel nut rather than the seed.

In Melanesian PICs, such as PNG, the fresh nut (ripe or unripe) is chewed with PBI or rolled PBL dipped in powdered lime, with the use of PBI being more common than PBL. All different components of the betel nut chew in PNG (Figure 2.1) are added individually into the mouth (making up the betel nut chew), starting with the betel nut itself. PBI is dipped in lime before adding it to the mashed nut in the mouth and this is done until the chew turns red. The excessive saliva and/or betel nut juice is either swallowed or spat out. Whether juice is swallowed or spat out mostly depends on the bitterness of the betel nut. Most chewers swallow the betel nut chew once it is red or the amount of saliva produced during mastication is reduced. In PNG, betel nut is consumed at different stages of maturity according to individual chewers' preferences. The outer shell of the palm nut is removed before the seed is chewed. Lime is usually prepared by heating sea shells or corals until a powdered form is obtained.

Betel nut chewing is more common along the coastal areas of PNG but it has been introduced to those in the highlands of PNG where the source palm tree does not grow. The habit is socially acceptable and, therefore, common in social gatherings such as peace ceremonies, weddings and other cultural ceremonies. It also is used by traditional healers as part of healing rituals, or may be used to cast out evil spirits.

Betel nut and PBI PBI Lime PBI dipped in lime

Figure 2.1 Components of the PNG betel nut chew (Source: Martina Burain, 2014)

2.6 Chemical composition of betel nut and additives

The elemental composition of betel nut has been investigated and common elements found include sodium, aluminium, chloride, calcium, potassium, bromide, manganese and copper. Other elements also have been detected. [181-183]

Betel nut contains alkaloids, proteins (peroxidase), carbohydrates, lipids, fibre and polyphenols (flavonoids, tannins, syringic acid).[184-189] Flavonoids include catechin and epicatechin.[188] The main alkaloids are arecoline, arecaidine, guvacine and guvacoline.[184, 185, 187] Of all these alkaloids, arecoline is reported to be the most abundant.[185] However, the main alkaloid found in a mixture of betel nut quid and blood of chewers is arecaidine.[186, 190] Arecaidine is a by-product of betel nut when chewed with lime. Variations in total alkaloid content of betel nut also have been observed and are thought to be due to seasonal factors and/or geographical location.[184]

The chemical constituents increase as more components are added to the betel nut quid. It is also thought that betel nut contains many other chemicals which are yet to be discovered. These yet-to-be-identified chemicals may be responsible for pathological effects with unknown mechanisms.

The PBL also has been found to contain elements such as manganese, zinc, potassium, chloride, arsenic and rubidium.[182] Other minerals found are calcium, iron, iodine and phosphorus. The leaf has been reported to contain proteins, carbohydrates, minerals, fat, fibre, essential oil, tannin and an alkaloid, arakene. Additionally, vitamins B1, B2, B3, A and C have been reported.[191] PBI also contains phenolic compounds such as safrole and hydroxychavicol.[192]

Chewing betel nut, therefore, exposes the chewer not only to chemicals contained in the betel nut but also to chemicals contained in the other components chewed with the nut.

2.7 Consequences of betel nut chewing

Diverse consequences of betel nut have been reported by studies using betel nut and/or PBI/PBL extracts, or the pure chemical constituents of betel nut.[192-210] The types of studies investigating such consequences include cell, animal, human and epidemiological studies. Results of many studies have been conflicting and there is continuing research on betel nut chewing and its components. Claims or experiences reported by betel nut chewers have led to more investigations to determine evidence, if any, to support such claims.

2.7.1 Traditional benefits

Traditionally, betel nut has been used in some societies for treatment of indigestion, constipation and halitosis. Betel nut chewers have reported increased well-being and stamina, heightened alertness, prevention of hunger, increased capacity to work, sweating and a warm sensation, soothing effects on digestion (carminative), protection of the mouth and gums, and some euphoria.[193, 194]

2.7.1.1 Mechanisms of actions for traditional benefits of betel nut chewing

The major alkaloid in betel nut, arecoline, mainly acts on the central and the autonomic nervous systems. Arecoline possesses parasympathomimetic properties that lead to stimulation of both muscarinic and nicotinic receptors.[194]

A number of studies have been conducted by Chu to investigate claims of the effects of betel nut chewing by chewers. These investigations have included cardiovascular responses,[195] effects on performance reaction time[196], electroencephalographic (EEG) activity[197], skin temperature[198] and sympathetic skin responses[199].

In one of Chu's studies, cardiovascular responses were compared between habitual, occasional and fresh (novice) chewers.[195] It showed a decrease in heart rate, which was related to the duration of betel nut exposure. As the duration of exposure was increased, the mean heart rate decreased. That is, the highest increase in heart rate was seen in fresh chewers, followed by occasional chewers; the least increase was seen in habitual chewers. This also is consistent with findings by Lin et al.[200] Blood pressure, however, was significantly increased only for those who were fresh chewers.[200]

To investigate claims of heightened alertness, Chu investigated the effect of betel nut chewing on performance reaction time.[196] The study investigated both simple and choice reaction times in habitual users, with chewing gum and practice groups being the control groups. The study demonstrated no differences in simple reaction time among the three groups but a significant shortening of choice reaction time in the betel nut chewing group. The finding that there was no difference in the simple reaction time is different to that found by an earlier study. The study by Stricherz et al[201] found that reaction time latencies were significantly lengthened in those who chewed all three components of the quid compared to those who did not chew betel nut and those who only chewed betel nut and PBL. Further, Stricherz et al[201] observed that simple reaction time was lengthened only during the first 20 reaction time trials, a finding they attributed to practice or "inhibition of familiarity". However, the timing of the onset of the reaction time tests during betel nut chewing may have

contributed to the finding. The study allowed only 60 seconds to elapse after chewing before introduction of the reaction time stimulus, which may have been too early for any effect of betel nut chewing to make any difference. The longer onset of the effects of betel nut chewing is supported by the finding of Chu that the onset of cardiovascular effects of betel nut chewing begins within 2 minutes with a maximal effect within 4-6 minutes.[195] EEG activity measurements using spectral analysis and topographic mapping, both before and during betel nut chewing, showed that betel nut chewing was associated with a state of arousal and a state of relaxation (to a lesser extent).[197]

The immediate effects of betel quid chewing include palpitations, sweating and facial flushing, with a feeling of skin warmth.[198, 200] In the Chu study[198], the measurement of body temperature was conducted to investigate claims that betel nut chewing produces sweating, facial flushing and a warm sensation in the body. This was conducted by recording skin temperature before and during betel nut chewing among habitual chewers. The study showed that the skin temperature of betel nut chewers was increased by 0.5 to 2.0°C, an effect which was abolished by atropine and partially inhibited by propranolol. Lin et al, in their study,[200] reported that betel nut chewing enhanced blood flow in the external carotid artery (main supplying artery to the face and scalp). These studies support reports that betel nut chewing produces sweating, facial flushing and a sensation of warmth in the body.

Gilani et al[202] investigated the claim that betel nut is used as a digestive aid, a laxative and a carminative in an animal study using mice. The study showed that betel nut extract had gastrointestinal stimulant activities and produced wet faeces (laxative). The effects of the extract in the study were similar to that of physostigmine, a standard acetylcholinesterase (AChE) inhibitor. The authors therefore concluded that these effects may be due to some unknown constituent(s) of betel nut because arecoline and other known constituents of betel nut did not exhibit AChE inhibitory activity in the study.

There are also reports that betel nut causes heightened alertness and increased capacity to work. Psychological well-being and dependence caused by betel nut chewing are said to result from stimulation of the central and autonomic nervous

systems.[194] The stimulation of the central nervous system may also be a result of AChE inhibition by betel nut.[202]

The finding that betel nut relieves constipation is supported by a study conducted by Li et al[203] which demonstrated that arecoline stimulates distal colonic contraction in rats. Constipation is consequently relieved by stimulating muscle contraction.[203]

2.7.2 Possible health benefits

There are claims of potential health benefits of betel nut and other components chewed with it.

Hannan et al[204] investigated the antioxidant activities of different betel nut extracts (obtained using different solvents) by determining their reducing powers and hydrogen peroxide scavenging abilities using spectrophotometry. The antioxidant activities of these extracts were compared with ascorbic acid as a standard. That study also quantified tannins and determined phenolic contents of the different betel nut extracts. The betel nuts used in the study were found to contain high tannin and total phenolic content and the latter was related to their antioxidant properties. Three types of betel nut extracts (methanol, methanol-water, water) showed high reducing power and significantly higher hydrogen peroxide scavenging power than ascorbic acid. The results from this study were consistent with the findings of Zhang et al.[188] that betel nut has a high phenolic content and antioxidant properties. Possessing antioxidant properties suggests that betel nut may be useful in oxidative stress-related diseases. However, the study investigated betel nut only, and whether or not these antioxidant properties remain when betel nut is chewed with other additives needs to be investigated.

Studies have also examined the antioxidant properties of PBL/PBI. Lei et al.[192] conducted *in vitro* studies to investigate the antioxidative effects of aqueous extracts of PBI. The study used xanthine and xanthine oxidase to produce superoxide radicals which were inhibited by the extract in a dose-dependent manner. The extract also scavenged hydroxyl radicals produced by hydrogen peroxide and ferrous chloride. These findings are consistent with findings by Choudhary and Kale[205], and Rathee et al[206]. Choudhary and Kale[205] also included an *in vivo* study,

supplemental to the *in vitro* study. The *in vivo* study used albino Swiss mice that were administered the PBL extract orally for two weeks. The hepatic oxidant status of each mouse was assessed. Results of the study showed that PBL has antioxidant activity and has potential to elevate the antioxidant status. In that study, the presence of the leaf extract during irradiation of rat liver microsomes inhibited the oxidative damage. The most recent study by Hasan et al further supports these findings that PBL has antioxidant activity.[207] The study by Hasan confirmed that PBL activated the nuclear factor-erythroid 2 p45 factor 2 and induced the antioxidant response element.

Other potential benefits of betel nut and its additives that have been reported are anti-migraine effects[208], hepatoprotective effects[209, 210], antimicrobial properties[211, 212], vasorelaxation[213] and inhibition of platelet aggregation[192, 214]. The hepatoprotective effects have been shown to be due to PBL in a study[210] using male albino Wistar rats. This finding is supported by Young et al[209] who induced liver damage in rats using carbon tetrachloride. Levels of liver enzymes, elevated in the presence of injury, were inhibited by the PBL extract. Furthermore, histological examinations showed that the PBL extract had a protective effect on the liver from damage induced by carbon tetrachloride.

More studies are required to ascertain any such health benefits of betel nut in humans.

2.7.3 Pathological consequences

Betel nut chewing has been associated with various health problems. The most common problem associated with betel nut chewing is oral cancer. Betel nut is listed as a carcinogen by the International Agency for Research on Cancer (IARC).[178] There are numerous epidemiological studies linking betel nut chewing with different oral and oropharyngeal cancers.[215-219] There are also many studies, including many animal studies which have investigated the possible mechanisms for development of oral cancer associated with betel nut chewing.

Additionally, betel nut chewing has been shown to affect the gastrointestinal system. Gastrointestinal adverse effects include peptic ulceration[220, 221], abnormal liver

function tests in rodents[222] and stimulation of pancreatic lipase secretion in rats.[223] The latter is said to be caused by PBL.[214] However, PBL/PBI has been reported to have hepatoprotective properties.[209, 210]

Betel nut has been linked to inflammation. [224] This is of concern because there is increasing evidence of the association of inflammation with T2DM.[225, 226] The finding that betel nut causes inflammation is different to the findings that the betel nut chew additive PBI/PBL has anti-inflammatory properties.[212, 227, 228] There are many pathways involved in the inflammatory process, and pathways by which betel nut causes inflammation are being investigated. A study[224] comparing betel nut chewers in Karachi, Pakistan, reported that betel nut chewers had significantly higher odds of an elevated C-reactive protein (CRP) compared to controls who were non-betel nut chewers. This study suggests that systemic inflammation may be a pathway by which betel nut increases the risk of systemic diseases such as T2DM.

With some evidence that PBI/PBL has anti-inflammatory properties, it would be useful to investigate whether PBI/PBL in the betel nut chew offers protection from inflammation associated with T2DM.

2.8 Metabolic consequences of betel nut chewing

Metabolic consequences include effects on blood pressure, HDL cholesterol, triacylglycerols (triglycerides), glucose and BMI or waist circumference. A number of epidemiological studies have reported the association of betel nut chewing with the metabolic syndrome, as a whole, or with individual components of the syndrome. Results of studies investigating the metabolic effects of betel nut chewing have been conflicting. Furthermore, most of the studies have been conducted in Taiwan.[229-234] Such studies in other countries where betel nut chewing is endemic are lacking.

2.8.1 Studies linking betel nut chewing to the metabolic syndrome

Yen et al[229] investigated the association of betel nut chewing and the metabolic syndrome in men in a large population-based study in Taiwan. That study excluded women because the prevalence of betel nut chewing was less than 1.0% among women. The prevalence of betel nut chewing in the study population was 15%. Higher risks for the metabolic syndrome were found with age and a family history of

diabetes or hypertension. The study reported a high age-adjusted prevalence rate of metabolic syndrome in betel nut chewers compared to non-chewers. Duration of betel nut exposure also was associated with metabolic syndrome. Those who had chewed for more than 20 years or chewed more than 20 chews per day were more likely to have the metabolic syndrome compared to those who did not. Interestingly, quitting the habit had an effect on risk of metabolic syndrome with the risks among chewers decreasing over time after they had quit.

In another smaller Taiwanese study[230] including both males and females aged 20-64 years old, the daily rate of betel nut use significantly and independently increased the odds of incidence of the metabolic syndrome.

The finding by Yen et al[229] is consistent with that of Shafique et al[235] in Pakistan. The cross-sectional study by Shafique et al was similar but had a smaller study sample (N=1070) than the former (N=19,839). The prevalence of betel nut chewing in that study sample was 32.5% and included both males and females aged 16-75 years old. Females were slightly more likely to chew betel nut than males in that cohort and had a slightly higher prevalence of metabolic syndrome than the males. The study also included those who chewed betel nut with tobacco and reported that the subgroup had a stronger association with metabolic syndrome than those who chewed without tobacco. In contrast to the study by Yen et al[229], that study did not include other well known risk factors such as diet, family history of metabolic disorders and physical activity. The study [235] adjusted for age, gender and social class only.

2.8.2 Studies linking betel nut chewing to blood pressure

Reports of the influence of betel nut on blood pressure have been inconsistent. Heck et al[236] reported an association of betel nut chewing with blood pressure among Bangladeshi adults aged 18-75 years. Their study reported that betel nut chewers who chewed the nut without tobacco had higher systolic blood pressure (SBP), diastolic blood pressure (DBP) and arterial pressure compared to those who had never used betel nut. A stronger association between high blood pressure and betel nut chewing was observed in females, compared to males. After controlling for other factors, the association with SBP remained. Higher SBP was not associated

with the level of betel nut exposure (frequency and duration). The finding that higher blood pressure was associated with betel nut chewing is consistent with findings by Guh et al.[230] A recent finding by Lin et al[231] that betel nut chewing is associated with higher SBP further supports both Heck et al[236] and Guh et al[230]. The former study[231], however, included those aged 50 years and older. It is known that, as age increases, the risk of SBP also increases.[237, 238]

Lin et al[200] studied the cerebral haemodynamic effects of betel nut chewing in 30 healthy participants who were divided into three groups of 10; 1) chronic chewers, 2) occasional chewers and 3) new chewers (never chewed or tried only a few times before). After baseline measurements of blood pressure, the participants firstly chewed fruit flavoured gum for 10 minutes, rested for 10 minutes and then were asked to chew betel nut, slaked lime and PBL. The study showed that SBP tended to increase, especially in new chewers, but this was not statistically significant. Interestingly, betel nut chewing reduced DBP.[200]

Studies also have shown that betel nut chewing has rapid effects on the cardiovascular system, for example heart rate.[195, 200] Chu[195] demonstrated that the onset of increased heart rate was within 2 minutes after chewing, the peak effect was reached within 4-6 minutes and the effect lasted for an average of 16.8 minutes.[195] The study by Lin et al[200] showed that the increase in heart rate was more significant in new and occasional chewers when compared to chronic chewers, probably suggesting that tolerance develops in habitual chewers.

2.8.3 Studies linking betel nut chewing to obesity and lipids

2.8.3.1 Epidemiological studies

Chang et al[232] reported an association between betel nut chewing and obesity among non-aboriginal Taiwanese male adults aged 20-59 years of age. Females were excluded from the study because of the low prevalence of betel nut chewing among this group. The study reported that betel nut chewing was associated with obesity and that betel nut chewers were more likely to be obese compared to non-chewers. The study also reported that betel nut chewers were more likely to have

more helpings of rice per day compared to their counterparts who were non-chewers or who had quit the habit.

This finding, that betel nut chewing is associated with obesity, is consistent with other studies [229, 230, 233-235, 239], although not all studies have found this association.[236] The study by Heck et al[236] found that weight and BMI were highest among those who had never chewed betel nut. All Taiwanese studies which investigated the associations of betel nut chewing consistently showed that betel chewers were more likely to be obese. This is contradictory to the Bangladeshi[236] and Pakistani[224, 235] studies that did not show such an association. An exception to this was one of the Pakistani[235] studies, which showed that betel nut chewers who chewed the nut with tobacco were more likely to have a higher waist circumference compared to both those who chewed the nut without tobacco and non-chewers. The Pakistani study (235) accounted for age, gender and social class (based on employment type) but did not account for confounding factors for obesity such as physical activity, alcohol and dietary intake. The Bangladeshi study only accounted for socioeconomic factors such as education, occupation and television ownership.

There are also studies which have shown an association between betel nut chewing and lipid levels.[229, 230, 233, 234] All of these were Taiwanese studies and they showed that betel nut chewers were more likely to have hypertriglyceridaemia (high levels of triglycerides). However, the Pakistani study,[235] which also included lipid levels as a variable, reported no difference in cholesterol levels between betel nut chewers and non-chewers. The study by Guh et al[230] showed that betel nut chewers were more likely to have hypertriglyceridaemia but there was no association with HDL-cholesterol. One of the strengths of the Taiwanese studies is that they had large sample sizes ranging from 1049 to 56, 116. However, the Bangladeshi study had a larger sample size (n=19,934) than some of the Taiwanese studies.

2.8.3.2 Animal studies

Animal studies reporting the effects of betel nut on cholesterol or obesity also have been inconsistent. A number of animal studies [240-243] have found a favourable effect of betel nut or arecoline on lipids. Zhou et al[240] found that a low dose of areca oil plus arecoline significantly reduced total cholesterol and increased the level of HDL.

They concluded that areca oil plus arecoline may play a synergistic role in enhancing hypolipidaemia in rats. Chiang et al[241] used two-week old hamsters, which were fed with betel nut for 18 months, and observed decreasing body weight in these animals. Ling et al[243] reported increased mRNA PXR and CAR levels, a reduced lipid measurement and improved insulin sensitivity in diabetes-induced rats. Iqbal et al, in a rat model,[242] reported no association of betel nut with hypertriglyceridaemia but a dose-related effect on total cholesterol, with a low dose causing a significant increase and a high dose having no effect. That study also reported no body weight gain from betel nut. In contrast, an earlier study by Boucher et al,[244] using young adult CD1 mice fed with betel nut that was mixed with standard feed, for 2-6 days, reported the mice developing central obesity. Betel nut extract also has been demonstrated to inhibit activity on cholesterol absorption in high cholesterol diets, resulting in reduced plasma lipid concentrations.[245, 246]

2.8.4 Studies linking betel nut chewing to glycaemic control

2.8.4.1 Epidemiological studies

Tung et al[247], in a large population-based cross-sectional survey including Taiwanese men (N=14,816), reported an association of betel but chewing with hyperglycaemia. Using fasting plasma glucose levels of ≥6.1 mmol/L to indicate hyperglycaemia, the study reported that the unadjusted prevalence rate for hyperglycaemia was 9.3% in chewers and 10.7% in non-chewers but, when participants were categorised according to age groups, chewers aged 50-69 were significantly more likely to have hyperglycaemia compared to non-chewers in the same age group. After adjusting for age and other confounders, results indicated that betel nut chewers were more likely to have hyperglycaemia or T2DM. The significant association of betel nut chewing with hyperglycaemia or T2DM was in the manner of a dose-response (duration of chewing and quantity of nuts chewed), with those chewing betel nut for more than 20 years and those chewing more than 20 pieces of betel nut per day being more likely to be affected when compared to non-chewers.

Tseng[248] compared ever-chewers (current and those who had quit) with non-chewers in a study investigating betel nut chewing and the incidence of newly

diagnosed T2DM in Taiwanese men. This study included those with known T2DM. The authors combined those who had quit chewing with current chewers because the number of those who had quit the habit was too small. Results of the study reported a link between betel nut chewing and the development of T2DM. Furthermore, there was an age-specific incidence of newly diagnosed T2DM that increased with age, reaching a peak in the age group of 60-69 years in ever-chewers but increasing beyond that age in those who were never-chewers. Betel nut chewers in this study were younger, with those aged 60-69 years having the lowest prevalence. It is well established that, as age increases, the risk of T2DM also increases. If betel nut has a link with hyperglycaemia or T2DM, the results of this study indicate that betel nut may not have an immediate but, rather, a long term effect on glycaemic control, if there is any effect at all. The study did not include important confounding factors such as physical activity and diet.

Yen et al, in their study[229] investigating any association between betel nut chewing and the metabolic syndrome reported that the association between betel nut chewing and hyperglycaemia was smaller than that for hypertriglyceridaemia . That study [229] also included dietary data, which Tung et al[247] and Tseng[248] did not include. Another Taiwanese study by Guh et al[230] did not find any association between betel nut and hyperglycaemia. Shafique et al[235] found that Pakistanis who chewed betel nut with tobacco were more likely to have hyperglycaemia when compared to non-chewers and those who chewed the nut without tobacco.

Two smaller cross-sectional epidemiological studies in PNG also reported an association of betel nut chewing with fasting hyperglycaemia.[249, 250] One study was conducted among non-T2DM participants and the other among those with T2DM. Both studies were conducted in the National Capital District in Port Moresby. The non-T2DM study had a sample number (N=769) less than that used by Tung et al[247] and other Taiwanese population-based studies. Using FCBG ≥7.0 mmol/L to indicate hyperglycaemia, the study[249] reported that betel nut chewing was significantly associated with T2DM but did not adjust for confounding factors such as diet, physical activity and alcohol consumption. That study had a small number of betel nut chewers (102/769) because 78% of the participants were from the religious group, Seventh Day Adventist, which discourages betel nut chewing among its

followers. As with other studies, the prevalence of hyperglycaemia increased with increasing age.

2.8.4.2 *In vivo* / *in vitro* studies

Boucher et al[244] demonstrated, in their study, that feeding betel nut to young adult mice can cause glucose intolerance. Other studies, however, have shown either no effect[242] or a beneficial effect[243, 251] of betel nut or arecoline on glucose levels. Ling et al[243] recently demonstrated a reduction in fasting blood glucose in T2DM rats treated with different doses of arecoline. Beneficial effects of betel nut extract on glucose control also have been demonstrated in Alloxan-induced diabetic rats.[252]

Chempakan, in a small study, showed that subcutaneously administered injections of arecoline induced hypoglycaemia.[251] However, routes of administration other than orally or through the buccal mucosa may not appropriately reflect the effect of betel nut chewing.

Glycaemic effects of betel nut chewing also have been investigated using PBL. In a study by Arambewela et al, different doses of hot water and cold ethanol extracts of PBL were orally administered to rats to investigate their antidiabetic activities.[253] Effects on fasting blood glucose levels were determined after fasting the rats for 16 hours. Effects of PBL extracts on the oral glucose tolerance of normoglycaemic rats and the blood glucose levels of streptozotocin (STZ)-induced diabetic rats also were determined. The hypoglycaemic potential of the two types of PBL extract were compared to that of tolbutamide, a known hypoglycaemic drug, which was used as the reference. Interestingly, all doses of hot water extract significantly reduced fasting blood glucose levels for up to four hours, except for the lowest dose, which impaired the blood glucose only for the first two hours. In contrast, the cold ethanol extract impaired blood glucose levels for up to four hours. The study reported a marked dose-dependent impairment of blood glucose levels using both extracts. In regard to the effects of the extracts on glucose tolerance, a significant improvement was observed for up to three hours; an observation which was comparable to the effect of tolbutamide. In diabetes-induced rats, the 200 mg/kg dose (the only dose used) of hot water extract significantly reduced hyperglycaemia induced by STZ.

2.9 Mechanisms of betel nut and additives on glycaemic control

Several mechanisms have been linked to the pathological consequences of betel nut chewing. Of importance to this current research is (are) the mechanism(s) by which betel nut chewing may cause or increase the risk of developing T2DM.

Many of the mechanisms postulated from human studies are mostly based on experiences of betel nut chewers and biochemical measurements of blood glucose and lipids. There also have been a number of animal studies conducted to investigate the glycaemic effects of betel nut alkaloids.

2.9.1 GABA inhibition

Arecal alkaloids, by inhibiting GABA, probably block the inhibitory effects of GABA on glucagon and somatrophin secretion, thereby increasing their release. [193, 254] A rise in glucagon leads to insulin release with subsequent hypoglycaemia. As hyperglucagonaemia becomes chronic a person could develop diabetes. [193]

It has been suggested that arecaidine and guvacine contribute to the psychic effects observed in betel nut chewers and that the mechanism of action of these effects is through inhibition of GABA uptake.[255] Inhibition of GABA uptake increases the extracellular concentrations of the neurotransmitter. Although GABA is largely a central nervous system (CNS) neurotransmitter, it has been reported to exist in places other than the CNS. Outside of the CNS, GABA is found in the pancreatic islets.[256] The concentration of GABA in the pancreatic islets is reported to be the highest outside the CNS.[257, 258]

However, Lodge et al[259], in their study using the CNS of cats, reported that it is unlikely that the behavioural effect of betel nut is due to the reduction of GABA inactivation. The study further suggests that some components of the betel nut chew may be influencing GABA either directly or indirectly. One of the mechanisms suggested by this study is that some components in the betel nut chew may be modifying the blood-brain barrier or arecaidine metabolism. Constituents of betel nut may, therefore, affect glucose homeostasis by direct or indirect action on GABA in the pancreas.

An *in vitro* study[260] using isolated mouse islets in the presence of 0.5 mmol/L glucose showed that GABA inhibited the release of glucagon to a similar extent as in the presence of 10 mmol/L of glucose. Another *in vitro* study[261] using rat insulinoma INS-1 cells suggested that GABA activates the $GABA_AR$ (GABA A receptor) by depolarising the β-cells in the pancreas to enhance insulin secretion. The study[261] further suggests that insulin down-regulates GABA-$GABA_AR$ signalling in a feedback mechanism to fine-tune β-cell secretion.

2.9.2 Catecholamine stimulation

The catecholamines, adrenaline and noradrenaline, are involved in glucose homeostasis. These catecholamines inhibit insulin release from β-cells and stimulate glucagon release from α-cells in the pancreas, thereby increasing plasma glucose.

Animal studies investigating the effect of betel nut on catecholamines have reported release or elevation of catecholamine levels.[262, 263] Using bovine adrenal chromaffin cells, Wang et al[262] investigated the effect of betel nut chewing juice mixtures and found that these mixtures and their additives stimulated basal catecholamines. This finding is an indication that betel nut and its additives have an influence on adrenal function and may, therefore, have a role to play in glycaemic control. Furthermore, the chewing juices inhibited carbachol-induced catecholamine secretion, perhaps indicating competitive receptor binding or some other mechanism. Possible mechanisms for the inhibition were further investigated by Wang et al and they found that catecholamine release evoked by K^+ was inhibited by chewing juices, possibly indicating that catecholamine release was not by depolarisation.[262] The authors suggest that the inhibition of catecholamine release by K^+ and carbachol may have been mediated by calcium influx through voltage-sensitive channels or the steps of secretion after calcium entry. The results of that study indicate that particular chemicals in betel nut and its additives also activate the SNS whereas the major alkaloid in betel nut, arecoline, has been reported to affect the parasympathetic nervous system. Betel nut and PBI contain different chemicals and, when betel nut is chewed with lime, by-products such as arecaidine and guvacaidine are formed.

2.9.3 Modulation of metabolic signals.

Two randomised, placebo-controlled, double-blind studies by Strickland et al[264] showed that arecoline appears to modulate metabolic signals regulating human appetite for food in both the fed and fasted states. The studies were divided into two, with Study 1 consisting of fasted individuals and Study 2 consisting of fed individuals. In study 1, participants were randomly assigned to receive a predetermined and unique sequence of treatments over the four hour runs so as to minimise possible effects of dose order. Bioadhesive gel formulations delivered 0, 5, 10 or 20 mg arecoline to the buccal mucosa. After an overnight fast, those in the fasted group were given different doses of arecoline, including the placebo after measurement of the basal metabolic rate (BMR). In study 2, after an overnight fast, participants were fed after measurement of BMR and 10-15 minutes after the standard meal, these participants only had the placebo or 10 mg arecoline. Participants were randomly allocated to receive two alternate gel sequences with a minimum 5-day wash out period allowed between measurements. The protocol was identical for both studies after administration of the gel. Measurements included calorimetry and blood samples at 15, 155 and 365 minutes after dosing for assays of plasma arecoline, urea and insulin, and to determine glucose at 365 minutes. Plasma arecoline, insulin and glucose levels, energy expenditure, delta energy expenditure and substrate utilisation rates (urinalysis) were measured or calculated at predetermined time points. Twenty minutes before starting the final hour's measurement, participants in both groups were instructed to chew and swallow any remaining gel. Hunger (appetite) was a subjective measurement (feelings of hunger, thoughts of food, urges to eat, fullness of stomach). In the fasted state, plasma arecoline was dose-dependent, with a final surge in levels at 365 minutes (end of study) probably resulting from chewing and swallowing the remainder of the gel. No participant showed evidence of fasting hyperinsulinaemia. The dose of arecoline affected hunger, which was lowest after 10 mg and highest after 20 mg. Arecoline increased carbohydrate utilisation transiently in a dose-dependent manner but glucose status was not affected. In the fed state, marginally increased rates of carbohydrate disposal, reduced blood glucose and reduced fat utilisation were observed following arecoline. In both groups, arecoline affected hunger, but in a non-linear dose-dependent manner. Betel nut both lowered hunger ratings at given

levels of delta energy expenditure and altered the nature of this relationship. Arecoline also appeared to disrupt the correlation between delta carbohydrate utilisation and hunger in the post prandial state. Furthermore, arecoline appeared to influence hunger independently of delta carbohydrate utilisation in both studies. The finding in this study, that hunger following placebo was higher than after betel nut, is different to the epidemiological study by Chang et al[232], where betel nut chewers were more likely to have more servings of noodles compared to the non-chewers. Both studies share the limitation that hunger is entirely subjective.

2.9.4 Other possible mechanisms for glycaemic effects

Arambewela et al determined the possible mode of hypoglycaemic activity of PBL using a 200 mg/kg dose of hot water extract.[253] Their investigations included effects on the liver and skeletal muscle glycogen and glucose absorption from the intestine. Findings from these investigations indicated that the extract did not significantly inhibit glucose absorption from the lumen of the intestine but stimulated and increased accumulation of glycogen in the liver and the skeletal muscle. Increased weight of the spleen was observed, which the authors suggest may have been due to lymphoproliferative activity.

Ling et al[243] reported an increase in both PXRs and CARs and a significant decrease in levels of fasting blood glucose, lipids, insulin and mRNA G6Pase, PEPCK, IL-6 and TNF-α. Reduction of PEPCK and G6Pase are associated with reduced fasting blood glucose levels resulting from repression of hepatic gluconeogenesis. An increase in p-AKT and GLUT 4 protein expression also were observed. Further, hepatic insulin resistance was improved. Increased expression of GLUT 4 by arecoline is supported by the findings of a study by Prabhakar and Doble.[265] PXR activation has been reported to adversely affect blood glucose while CARs have a beneficial effect.[32, 105, 107] Inhibition of AKT disrupts glucose transport and inhibits enzymes involved in glycolysis, while activation results in the accumulation of Fox01 which stimulates expression of PEPCK and G6Pase, and suppresses glucokinase in liver cells.[107]

In the study by Ling et al[243], they used fructose-induced diabetic rats. Diabetes induced by a fructose diet results in loss of normal insulin function or in insulin

resistance that is due to the diminished ability of insulin to suppress hepatic output, rather than by decreasing the glucose uptake of muscle. [266, 267] So, the resultant reduced fasting glucose levels via arecoline may have resulted from suppression of hepatic output of glucose. PXRs and CARs are known to repress gluconeogenesis. There are different complex metabolic pathways that could have been affected by feeding the diabetic rats with arecoline. It is likely that CAR activity may have dominated, resulting in reduced plasma glucose and improved insulin sensitivity because phenobarbital, an activator of this nuclear receptor, is known to decrease plasma glucose levels and improve insulin sensitivity in diabetic patients.[113] There is also a possibility that PXR may have been involved via an unknown mechanism. There are other chemicals in betel nut, such as procyanidins, which have been reported to suppress fasting glucose by reducing hepatic gluconeogenesis. [268]

2.10 Mechanisms of betel nut constituents and additives on major risk factors for T2DM

2.10.1 Obesity and Adiposity

Obesity is one of the most important modifiable risk factors for the development of T2DM. The exact mechanism(s) by which obesity leads to T2DM is(are) not well established. Increased amounts of non-esterified fatty acids, glycerol, hormones and pro-inflammatory cytokines are released from adipose tissue in an obese individual.[269, 270] These factors have been shown to be involved in the development of insulin resistance. The exact mechanism linking betel nut chewing and obesity is unknown. It is, however, speculated that betel nut increases appetite for food, which increases the risk of obesity.[232]

In an *in vitro* study by Hsu et al[271] it was shown that arecoline affects adipogenesis, lipolysis and glucose uptake of adipocytes. The study, using 3T3-L1 preadipocytes from mouse embryos exposed to different concentrations of arecoline, reported that betel nut modulates adipose cell metabolism. This could explain the association of betel nut chewing with obesity as shown in a number of epidemiological studies. Results of that study[271] concluded that betel nut may modulate adipose cell metabolism by inhibiting the adipogenic differentiation of preadipocytes, inducing lipolysis in adipocytes through an adenylyl cyclase-dependent pathway and

attenuating insulin-induced glucose uptake by adipocytes. Although the study used cells from mouse embryos, which may not be comparable to fat cells from different tissues or organs, this study demonstrates a possible mechanism by which betel nut may be diabetogenic or worsen glycaemic control in people with T2DM. It would also be important, as suggested by the authors, to determine how the arecoline concentrations used in this study were comparable to internal concentrations of arecoline in those who chew betel nut, especially when all components of the betel nut chew are masticated together. A small study[190] comprising of 15 participants attempted to determine a correlation between betel nut chewing and arecoline concentrations. The study[190] reported that there are different chemical constituents, additional to arecoline, in betel nut and these may have different effects on glucose homeostasis.

Another similar study[272] using both betel nut extract and arecoline, rather than laboratory grade arecoline only, found that both the extract and arecoline block insulin signalling and lipid storage in 3T3-L1 adipocytes. That study reported the same finding: that arecoline reduced lipid droplet accumulation in adipocytes. This study and the previous study,[271] however, disagreed on the cause of the reduced lipid droplet formation. The former study suggested that the reduction in droplets was due to a reduced number of differentiated adipocytes, while the latter suggested otherwise because their research used differentiated adipocytes. Unlike the previous study[271], this study[272] used both betel nut extract (betel nut and PBL) and pure arecoline. The betel nut extract, despite having an estimated amount of arecoline less than that of the laboratory grade arecoline used, had a better effect in reducing cellular lipids. This suggests that there may be other constituents of betel nut extract that inhibit the accumulation of lipids in adipocytes, not only from betel nut but also *Piper betle*.

There is emerging evidence that arecoline increases mRNA levels of CARs and PXRs and, therefore, it may be an agonist for both nuclear receptors.[243] Activation of PXRs may partly explain the in vitro findings by the two studies[271, 272] previously described. Activation of PXRs stimulates lipogenesis and inhibits lipid oxidation, gluconeogenesis, glycogen storage and glucose transport.[32, 103, 107] There are also findings that rats orally fed with betel nut extract have lowered absorption of

cholesterol[245] or triglycerides[246] and, therefore, reduced plasma lipid concentrations. The study by Ling et al[243], which showed activation of CARs and PXRs by arecoline, reported a reduction in lipids and improved hepatic insulin resistance in fructose-induced diabetic rats. All these studies reflect inconsistencies and some of these may be due to the types of study (*in vitro* versus *in vivo*) and interspecies differences in metabolic pathways. It is important to consider that the gut microbiome plays an important role in energy metabolism that may partly lead to the differences seen in the *in vitro* and *in vivo* studies.

Apart from the type of diet affecting weight gain as a consequence of energy content, alterations in gut microbiota may also affect weight gain.[273] There are substantial changes in composition and metabolic function of gut microbiota under obesity, indicating an influence of gut microbes on energy metabolism.[273] This may be due to interactions between diet, gut microbiota and host metabolism.[273-275] Hormones such as glucagon-like peptide-1 (GLP-1) and ghrelin are involved in glucose and energy homeostasis and these may be affected by alterations in gut microbiota.[276]

2.10.2 Blood pressure

Regulation of blood pressure is complex and involves different mechanisms, such as neural mechanisms (sympathetic nervous system), renal endocrine-hormonal mechanisms, local endothelium-derived factors and other hormones.

Betel nut and its constituents may also have a central sympathetic effect that results in increased heart rate.[200] It has been reported by Lin et al that betel nut chewing reduces DBP, which shows that betel and/or its additives may have a peripheral cholinergic effect.[200]

Betel nut may also affect blood pressure through an effect on catecholamine release. In the Gilani study, using rabbit jejunum, the crude betel nut extract showed a dose-dependent spasmodic effect in the spontaneously contracting jejunum; an effect similar to that produced by physostigmine.[202] This means that betel nut, like physostigmine, probably increases plasma adrenaline. In a human study by Kennedy et al[277], it was shown that high doses of physostigmine

significantly increased heart rate and systolic and diastolic blood pressure but a low dose, despite increasing adrenaline levels, did not alter plasma adrenaline or increase heart rate or systolic or diastolic blood pressure.

Gilani et al,[278] in an earlier study, investigated the presence of cholinomimetic and calcium antagonist constituents in PBL. The researchers used PBL extracts on isolated guinea pig ileum and rabbit jejunum for their investigations. To determine possible calcium channel antagonist activity, the rabbit jejunum was selected. After depolarising the preparation with K^+ to cause spontaneous contractions, the crude plant extract was added cumulatively. Results showed a dose-dependent relaxant effect caused by the PBL crude extract, indicating spasmolytic activity. The ethyl extract of PBL, however, was more potent (10 times) than the crude extract. The authors suggest that the PBL crude extract's inhibition of K^+-induced contractions may be a result of blocking the calcium channels. It was further observed that the ethyl extract inhibited Ca^{2+} contractions, followed by the displacement of high Ca^{2+} concentrations, which the authors conclude supports the presence of calcium channel inhibitory agent(s) in the ethyl fraction.[278] The finding that PBL may contain calcium channel antagonist(s) adds to the evidence of effects of multiple chemical constituents of the betel nut chew. Furthermore, this finding may assist in understanding the variable effects of betel nut chewing on blood pressure and, more specifically, its hypotensive effect.

2.10.3 Systemic inflammation

It is known that chronic inflammation is a risk factor for T2DM.[279]. Betel nut has been linked to inflammation, thereby increasing the risk of T2DM in betel nut chewers. Epidemiological studies have shown increased levels of inflammatory markers in betel nut chewers when compared to non-chewers. Chung et al[280] reported increased plasma TNF-α in men who were betel nut chewers. Shafique et al[224] found increased levels of CRP in betel nut chewers. Therefore, inflammation associated with betel nut chewing predisposes the chewer to T2DM.

2.11 Summary of findings from the literature

Most of the studies investigating the metabolic consequences of betel nut chewing are epidemiological. These studies contribute important findings of the associations between betel nut and metabolic derangements. However, a few studies have reported contradictory findings. As with epidemiological findings, a causal relationship between betel nut use and metabolic derangements cannot be established. Attempts to establish mechanisms of action have been pursued using *in vitro* or *in vivo* animal studies. These studies may assist in clarifying the links between betel nut and metabolic derangements. However, as seen from the studies, betel nut and its additives (PBL/PBI) contain many chemicals which may exert their effects in many ways. The metabolic homeostasis is a complex process. Animal studies may not appropriately reflect what happens in a human body. Furthermore, there are other factors, such as ethnicity, genetics, socioeconomic status or development, environment and lifestyle, which may affect metabolic homeostasis.

Similarly, there may be differences in the chemical contents of betel nut, with some studies showing differences in the arecoline content of betel nut from different countries including PNG, and also differences according to betel nut maturity. Also, it is possible that the methods of chewing may influence the chemical constituents in the chew.

Of importance to this research is the association between betel nut chewing and hyperglycaemia or T2DM. Studies linking betel nut chewing with hyperglycaemia or T2DM used fasting glucose levels only. Fasting glucose levels are a reflection of hepatic glucose output during fasting states, rather than post prandial glucose levels, and may not reflect any direct immediate effect of betel nut chewing on glucose levels. It is therefore important to establish the glycaemic effect of betel nut during mastication to establish any immediate effect of betel nut chewing on glycaemic control.

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Chapter III: Hypothesis and Aim

3.1 Null Hypothesis

H_0: Betel nut chewing has no significant glycaemic effect in type 2 diabetes mellitus (T2DM)

3.2 Alternative hypothesis

H_1: Betel nut chewing significantly increases blood glucose levels in T2DM.

3.3 Main aim of the study

The main aim of the study is to identify if any relationship occurs between betel nut chewing and glycaemic control [as measured by oral glucose tolerance, capillary blood glucose and/or glycated haemoglobin in T2DM patients

Chapter IV: Glycaemic effects of betel nut chewing and its associated factors in patients with T2DM

4.1 Objectives

The main objectives of this part of the research, involving a cohort of type 2 diabetes mellitus (T2DM) patients, were to:

1 Identify their characteristics, with a focus on their demographics, lifestyle behaviours, diabetes management, and physical and biochemical measurements
2 Estimate prevalence of betel nut use
3 Identify demographic, lifestyle and physical factors associated with betel nut chewing
4 Determine the effects of factors associated with betel nut chewing on glucose control [as measured by glycated haemoglobin (HbA1C)]
5 Determine whether betel nut chewing is associated with poor glycaemic control and whether the association, if any, is independent of other confounding factors included in this research.

4.2 Methodology

4.2.1 Study setting

The study was conducted at the Port Moresby General Hospital (PMGH) Diabetes Clinic in Papua New Guinea (PNG). This is the largest hospital in PNG, and, as it is a referral hospital, it also has the largest Diabetes Clinic in terms of patient numbers.

4.2.2 Study design

This research was a cross-sectional study.

4.2.3 Study participants

All ethnic Papua New Guineans who were diagnosed with T2DM and were registered at the PMGH Diabetes Clinic were considered for inclusion. Patients included in the study were those who had been diagnosed with T2DM at least three months prior to recruitment. This ensured that recently diagnosed patients were excluded from study, as one of the main items of interest concerned glucose control over the three months leading up to enrolment in the study. These patients were identified from the Diabetes Clinic appointment book. Patients diagnosed with HIV/AIDS, pregnant women and those using a wheelchair were excluded from the study. These patients were excluded because their physical measurements were either difficult to obtain (wheelchair bound), or confounded (HIV/AIDS or pregnant). Patients who lacked understanding of the study and what was required of them also were excluded. This group included those who could not understand either of the two languages (Pidgin and English) used during the interview.

4.2.4 Participant recruitment

A verbal announcement was made about the study by the diabetes nurse each morning of the Diabetes Clinic. On the first day of the study, participant information sheets [(PIS) Appendix 6] were handed to all the possible eligible participants. From the second day until the end of the study, a list of participants already recruited was given to the clinic clerk. The clinic clerk only handed the PIS to those who had not been already recruited during previous clinics. The recruitment process is shown in Figure 4.1.

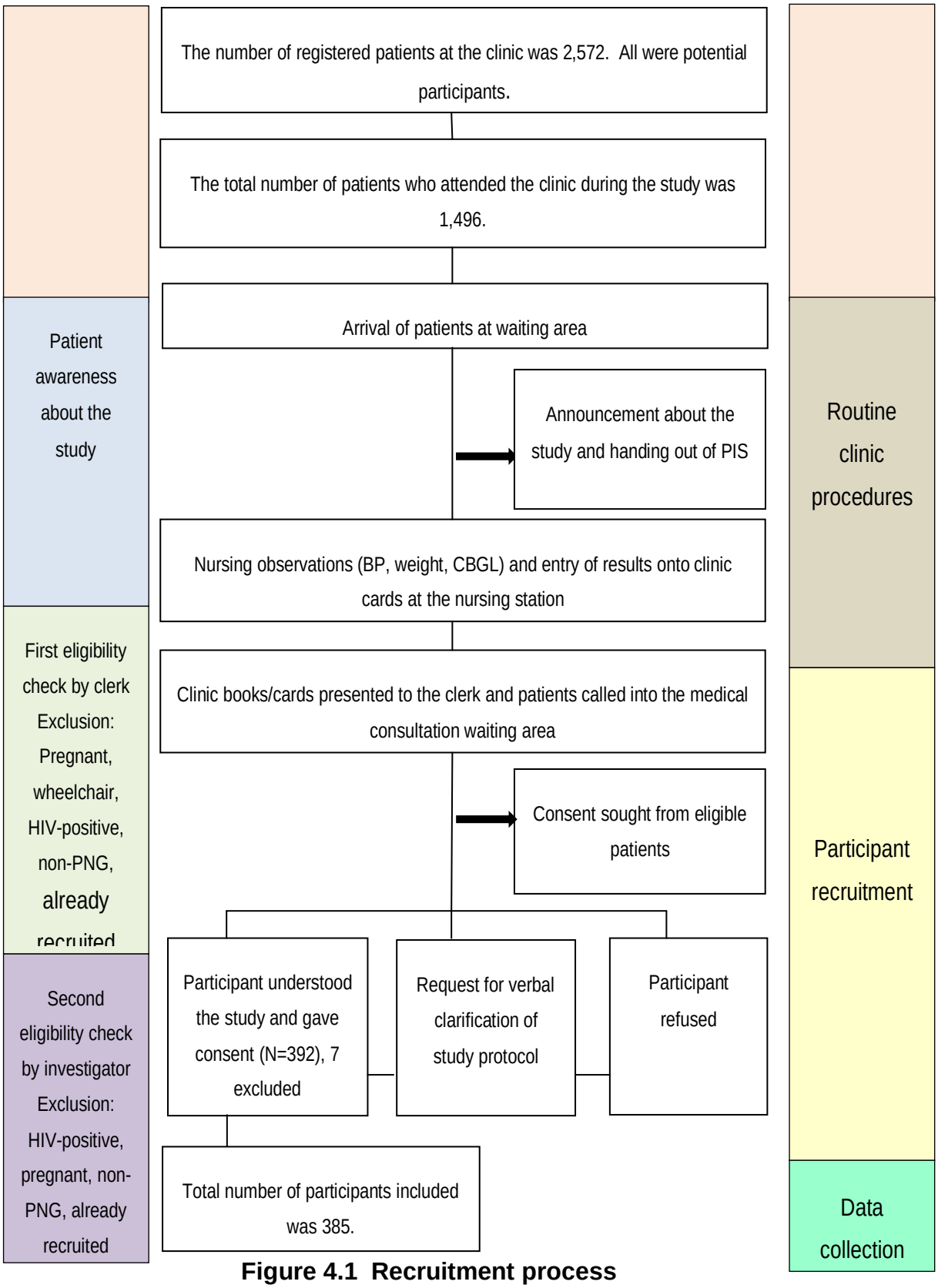

Figure 4.1 Recruitment process

4.2.5 Data collection

4.2.5.1 Pilot questionnaire

The study questionnaire (Appendix 8) was constructed using the World Health Organization (WHO) STEPwise approach to surveillance of non-communicable diseases (STEPS). [1] The STEPS questionnaire was chosen based on prior knowledge because it was used to collect data in PNG two years prior to the current study. Data collected from participants with T2DM (current study) was to be compared with data from the non-T2DM participants of the STEPS study to meet the objectives of the study as a whole. Questions on betel nut use within the STEPS questionnaire were expanded and questions on medication and some biochemical measurements were added into the instrument. Some questions on social behaviour were modified to achieve the aims of the study. For example, the STEPS survey asked participants how many times they used betel nut daily while the current study asked participants how many betel nuts they chewed per day. This question was modified based on prior knowledge that some betel nut chewers chew more than one nut each time they chew betel nut. Data collected included demographic information, behavioural measurements (betel nut chewing, vegetable and fruit consumption, physical activity, smoking and alcohol consumption), physical measurements (height, weight, waist and hip circumferences and blood pressure), biochemical measurements (fasting/random blood glucose, HbA1c, lipid profile, urea, creatinine, and urine protein and glucose) and diabetes management. Certain items in STEPS, such as Oral Glucose Tolerance tests and questions on oral health were not included in the questionnaire. The questionnaire was pretested at the PMGH Diabetes Clinic.

4.2.5.2 Final questionnaire

The pretesting of the questionnaire did not result in any changes in the questionnaire.

4.2.5.3 Interviews

Data were collected using face-to-face interviews. All responses were entered onto the questionnaire used. Show cards used in the STEPS (Appendix 9) survey also

were used to clearly explain terms such as servings of fruits and vegetables, and quantities of alcohol. During the pretesting of the questionnaire, it was found that participants were not able to understand the term “serving” and when this was equated to a cup, they could not visualise a cup. In PNG, the usage of the word “cup” is not specific to cup as a measure and it commonly includes a mug as well. To visualize a cup as a measure, a measuring cup was used to guide the participants in estimating the quantity of vegetable and fruit they consumed. The number of cups was entered onto the questionnaire and was later converted to number of servings before data entry using the STEPS show card.

4.2.5.4 Clinic Cards

Participants’ clinic cards were used to validate some of the responses and information required, such as names of medications, their doses, date of birth, suburb of residence, pathology tests, and year of diagnosis and/or registration at the Diabetes Clinic.

4.2.5.5 Measurement of HbA1c

HbA1c was measured using the Point-of-Care Siemens/Bayer DCA 2000 Vantage™ analyser (Siemens Medical Solutions USA Inc, Palvern, PA, USA). This machine was only able to measure HbA1c to 14.0%, so any reading more than 14.0% was given as >14.0% with no specific reading. During data entry, this was entered as 15.0% to indicate a reading in excess of 14.0%.

4.2.6 Sample size and sampling

The objectives of the study were to estimate the prevalence of betel nut chewing and to develop regression models to identify factors associated with betel nut chewing and glycaemic control. A sample size of N=385 should lead to an estimate of prevalence with a 95% confidence interval of no more than +/-5%. The confidence interval would be widest if the prevalence estimate was near 50%, and it would be narrower when it is either lower or higher than this. For the regression model, a sample of this size would be adequate to identify any independent

variables exhibiting a small to moderate effect size.[2] Hence, the study aimed to recruit N=385 participants. The method of sampling was convenience sampling.

4.2.7 Ethics

Patients were provided with a PIS (Appendix 6) to read before they were asked if they wanted to participate. The PIS was written in English or orally translated into Pidgin English to those who requested it. Patients also were asked whether they wanted the interview in English or Pidgin English before the interview commenced. Only those eligible patients who consented were recruited for the study. Consent forms were signed by both the interviewer and the participant before the interview began.

Approval for the study was granted by the Curtin University Human Research Ethics Committee [(HR 38/2011) Appendices 1,3)], The University of PNG School of Medicine and Health Sciences Research and Ethics Committee (Appendix 4) and the Medical Research Advisory Committee of the National Department of Health of PNG (Appendix 5). Permission to undertake the study at the Diabetes Clinic at the PMGH was granted by the Chief Executive Officer of the hospital.

4.2.8 Statistical analysis

Data were entered into an Excel dataset and transferred into SPSS versions 20/21 statistical software for analysis. Simple descriptive statistics (frequencies and percentages or means and standard deviations, or medians and ranges, as appropriate) were used to summarise demographic and lifestyle factors, physical measurements, diabetes management and biochemical measurement variables.

4.2.8.1 Univariate analyses

The statistical significance of differences in betel nut chewing habits according to demographic factors including age, gender, suburb of residence, region of origin, level of education, employment status and lifestyle factors were assessed using the Chi-square statistics. Similarly, univariate differences in glycaemic control between demographic variables, as well as lifestyle factors, physical activity, diabetes management and physical measurements such as body mass index (BMI) and

blood pressure, also were assessed using these tests. Univariate logistic regression models were used to investigate the direction of the associations for different categories of each variable.

4.2.8.2 Multivariate analyses

Multiple Logistic Regression models were developed to identify which (if any) of the:

i) demographic and lifestyle variables were independently associated with the prevalence of betel nut chewing; and

ii) demographic, lifestyle, biochemical, physical measurement and diabetes management variables were independently associated with poor glycaemic control (HbA1c>7.0%).

The results of regression analysis were presented as Odds Ratios, along with their 95% confidence intervals and p-values. Following convention, a p-value of <0.05 was taken to indicate a statistically significant association in all tests.

4.3 Results

4.3.1 Study setting

Apart from provincial divisions, PNG also is divided into four regions. These regions are Southern, New Guinea Islands (NGI), Momase and Highlands as shown in Figure 4.2. Port Moresby, the national capital of PNG is situated in the Southern region. Port Moresby is not only the national capital of PNG but is also the capital of the Central Province. The Central Province has its headquarters in Port Moresby but the administration is responsible for affairs of the Central Province only. The administrative unit of the city of Port Moresby is the National Capital District (NCD) and the administrative authority of the city is the NCD Commission. Although not a province as such, NCD is classified as the equivalent of a province.

Each province in PNG has a provincial hospital, except for the two newly established provinces of Jiwaka and Hela. The largest hospital in the country is the PMGH. This hospital not only serves those who live in the city but also those who live in the rural areas of the Central Province. Furthermore, this is the country's

referral hospital, where all medical or surgical cases which cannot be dealt with in other provincial hospitals are managed.

Not all provincial hospitals have specialist diabetes clinics. When that is the case, patients with diabetes are usually cared for in general internal medicine clinics. There are five diabetes clinics in PNG, of which four are in Port Moresby. Of all these clinics, PMGH Diabetes Clinic is the largest. The clinic not only cares for patients who live in Port Moresby but also those from other provinces in the country who have registered at the clinic.

During the time of the study, the PMGH diabetes clinic was run once a week for three hours on Tuesday mornings. The consultation rooms are shared with other internal medicine specialties and paediatrics and, therefore, clinics for these specialties are usually rostered to run on a weekly basis.

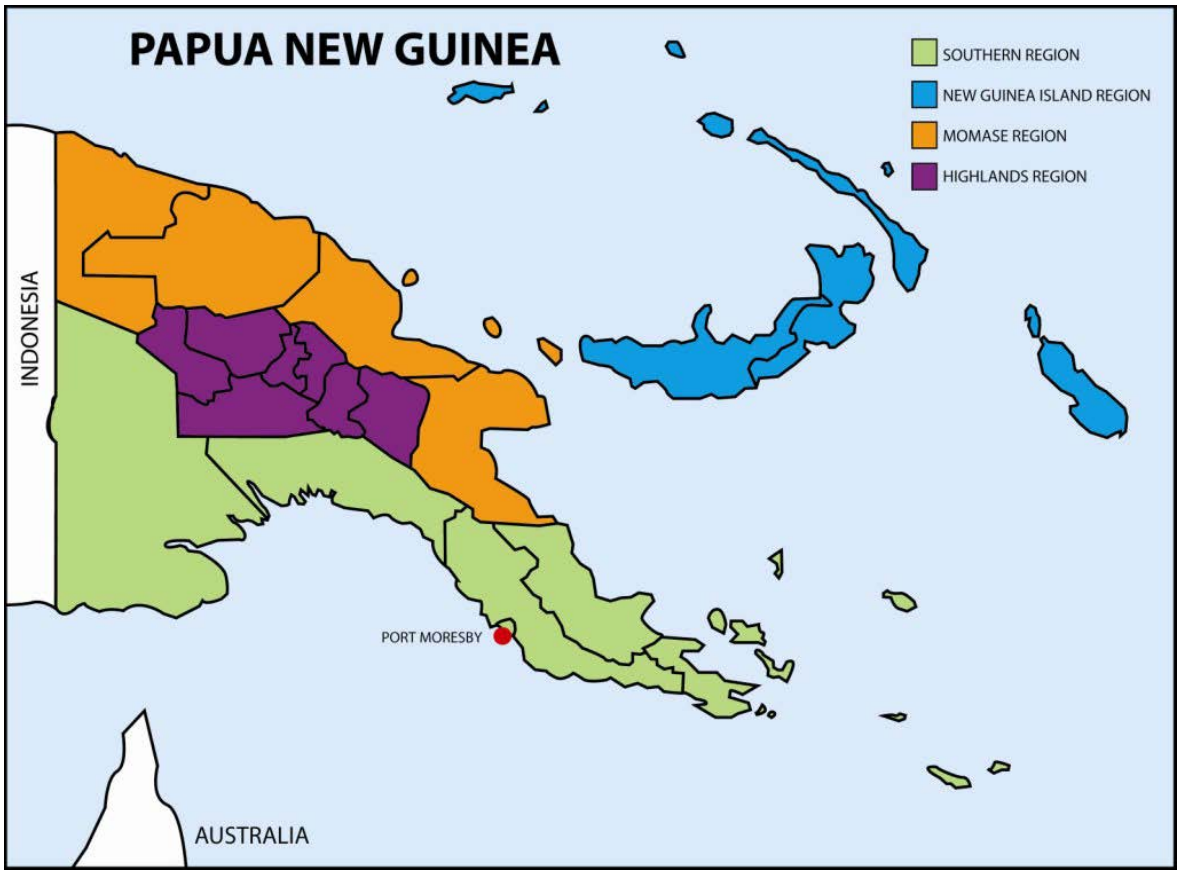

Figure 4.2 Regions of Papua New Guinea (Source: Andrew Tulo, 2014)

4.3.2 Study participant recruitment

Data were collected from 5th July to 25th October 2011 and then from 13th March 2012 to 12th June 2012. Data collection ceased in October 2011 because, in November of that year, the clinic was only attending to patients who were unstable in terms of cardiovascular morbidities (e.g. high blood pressure and blood glucose levels). In December 2011 and January 2012, data could not be collected because of the annual closure of the clinic during these two months.

Data were collected once weekly over 32 weeks (on Tuesdays) excluding the annual closure of the clinic in December and January. This length of time was sufficient to recruit any patient who had previously refused to participate, if they changed their minds. Of these 32 days, there were five days when the clinic was closed for a variety of reasons (shortage of staff, examinations for undergraduate and postgraduate medical students, or civil and political unrest).

A total of 2,572 diabetes patients were registered at the Diabetes clinic during the time of this study. During the study, a total of 1,496 patients attended the clinic. A total of 392 participants were recruited but seven were later excluded. Of those seven excluded, six were not Papua New Guineans and one was pregnant. A final total of 385 participants were recruited into the study, with an average of 15 patients recruited into the study each clinic day.

4.3.3 Demographic characteristics

Of the 385 participants, 241 (62.6%) were females and 294 (76.4%) participants were from the Southern region of PNG where Port Moresby is situated (Table 4.1). The mean age for participants was 54.4±10.5 years (range 14 to 85 years). Three hundred and sixty five (94.8%) participants knew their date of birth while 20 (5.2%) did not. This affected any data which required age for calculation of other variables, for example, calculation of the age when a participant started smoking or chewing betel nut. The highest numbers of participants were in the age group 50-59 years.

As shown in Table 4.1, the majority of participants resided in the many individual suburbs of Port Moresby; while 20% were from rural villages, 20% from urban

villages or settlements surrounding Port Moresby and about 4% were from other provinces. The suburbs or residential places were reclassified into areas of residence, namely: urban, peri-urban, rural and other province (Figure 4.3). Urban dwellers were those who were living in urbanised suburbs within the city, peri-urban were those living in partly urbanised villages or settlements between the city's suburbs and the rural villages within the outskirts of the city, rural dwellers were those living in rural villages in the Central Province and dwellers in "other province" were those who lived outside of the NCD and Central Province. The peri-urban areas were administratively under the NCD. More than 50% of the participants lived in urban residences. Forty one percent of the participants had lived in Port Moresby for more than 10 years, and 20.5% were born in Port Moresby and had spent their entire lifetime there. Ninety seven (25.2%) of the participants were not residing in Port Moresby; these participants were residing either in the rural or other province areas.

Participants were asked about the highest level of education they had achieved where a certificate of completion was awarded. Of the 385 participants, 88 (22.9%) either had no formal education or did not complete basic primary education (Grades 6). Eighty six (22.3%) participants attained a secondary school certificate by completing Grades 10 or 12. Vocational training in PNG was previously after completion of Grade 6 but is currently after completion of Grade 8. Vocational training, however, may also be undertaken after completion of Grades 10 and 12. For those participants who indicated that they completed vocational training, it was not known whether they did the training after completion of basic primary education or secondary education.

One hundred and ninety five (50.6%) participants were either in unpaid employment (volunteers, homemakers, Christian missionaries, students) or were unemployed. Twenty one percent of the participants were in regularly paid employment, both in the government and non-government sectors, while 39 (10.1%) were self-employed. Seventy (18.2%) participants were retired. Table 4.1 shows the demographic characteristics of the participants.

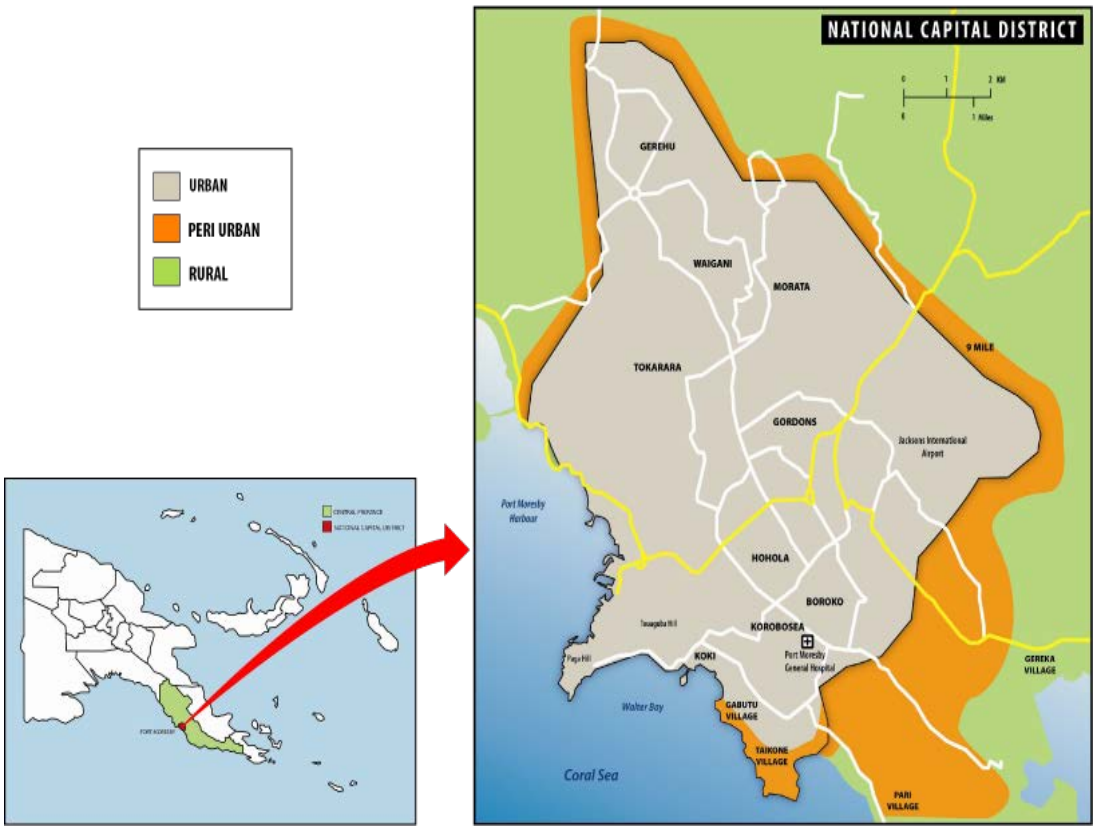

Figure 4.3 Areas of residence of participants (Source: Andrew Tulo, 2014)

Table 4.1 Demographic characteristics of study participants (N=385)

Characteristic	n*	Percentage
Gender		
Male	144	37.4
Female	241	62.6
Age category (years)		
<40	24	6.2
40–49	89	23.1
50–59	145	37.7
60–69	86	22.3
≥70	21	5.5
Region of origin		
Southern	294	76.4
Momase	26	6.8
Highlands	29	7.5
New Guinea Islands	36	9.4
Level of education		
No formal education	39	10.1
Less than Grade 6	49	12.7
Grade 6	71	18.4
Grade 8	40	10.4
Grade 10	74	19.2
Grade 12	12	3.1
Vocational training	29	7.5
Tertiary education	70	18.2
Area of residence		
Urban	212	55.1
Peri-urban	77	20.0
Rural village	80	20.8
Other province	15	3.9
Employment status		
Homemaker	125	32.5
Retired	70	18.2
Unpaid	8	2.1
Self-employed	39	10.1
Unemployed, able to work	34	8.8
Unemployed, unable to work	25	6.5
Government worker	47	12.2
Non-Government worker	34	8.8
Student	3	0.8
Number of years of in Port Moresby		
0[#]	97	25.2
1-2	11	2.9
3-5	5	1.3
6-10	12	3.1
>10	159	41.3
Lifetime	79	20.5

* Number may not always add up to total because of missing values for some items;
[#]Participant does not reside in Port Moresby

4.3.4 Lifestyle characteristics

Lifestyle characteristics included in the study were alcohol consumption, smoking, betel nut chewing, physical activity, and fruit and vegetable consumption.

4.3.4.1 Alcohol consumption

The Chi-square statistic was used to test for any associations between alcohol consumption and the demographic factors (categorical variables). Those variables which were found to show some association ($p<0.05$) were entered into a univariate logistic regression model to investigate the direction of the associations for different categories of each variable.

Only a small number of 38 (9.9%) participants reported consuming alcohol in the preceding three months before the study (Table 4.2). Of those who consumed alcohol in the preceding three months, 63.9% reported consuming 10 drinks or less on a single occasion, while 36.1% consumed more. For this subgroup, the mean number of days that male participants had consumed five or more standard drinks in a single day within the preceding three months was 5.27±4.48 days (n=15). In comparison, the mean number of days that female participants had consumed four or more standard drinks in a single day was 1.29±0.76 days (n=7). The most common sources of alcohol were friends and relatives. More than 60% of the participants who consumed alcohol, had ≤10 alcoholic drinks as their largest number of drinks on a single occasion. Although drinking at a party was not listed on the questionnaire as an option, it was one of the sources of alcohol reported by two participants who consumed alcohol but could not identify an appropriate alcohol source within the list of the questionnaire. These parties were work-related and, therefore, alcohol was supplied by the employers of these two participants.

Table 4.2 Alcohol consumption amongst participants

Variables	Frequency [n/N(%)]
Alcohol consumed in the previous three months	
No	347/385 (91.9)
Yes	38/385 (9.9)
Frequency of having at least one drink in the previous 3 months	
1-7 days/week	7/38 (18.4)
1-3 days/month	14/38 (37.8)
Less than once a month	16/38 (43.2)
Alcohol consumed in the previous 30 days	
No	7/38 (18.4)
Yes	31/38 (81.6)
Average number of alcoholic drinks at any one time in a day	
≤5	20/38 (52.6)
6-10	11/38 (28.9)
>10	7/38 (18.4)
Alcohol consumed in the previous seven days	
No	25/38 (65.8)
Yes	13/38 (34.2)
Largest number of drinks on a single occasion in the previous three months	
1-10	23/38 (63.9)
11-20	10/38 (27.8)
>20	3/38 (8.3)
Source of alcohol*	
Bought by self	18/38 (47.4)
Friends	25/38 (65.8)
Relatives	25/38 (65.8)
Parties	2/38 (5.3)

*****Numbers add to more than the total number of those who consumed alcohol because participants gave more than one source of alcohol supply.

Age, gender and employment status had a statistically significant association with alcohol consumption in the preceding three months. As age increased, the number of participants who consumed alcohol decreased (Table 4.3). Those aged <50 years were more likely to consume alcohol compared to those aged 50 years or older. Male participants appeared to consume more alcohol than their female counterparts. Of all the 38 participants who consumed alcohol, 24 (63.2%) of these were males. Those who did not complete basic education and those who completed primary education only were less likely to consume alcohol compared to their

counterparts in other categories of education. Employment status also had an important influence on alcohol consumption, with those in paid employment and those who were self-employed more likely to consume alcohol than the other participants.

Table 4.3 Associations of demographic factors with alcohol consumption

Variable	Alcohol consumed in the previous three months		p-value*
	No	Yes	
Gender			0.001
Female	227 (94.2)	14 (5.8)	
Male	120 (83.3)	24 (16.8)	
Age category (years)			<0.001
<50	90 (79.6)	23 (20.4)	
50-59	134 (92.4)	11 (7.6)	
≥60	103 (96.3)	4 (3.7)	
Level of Education			0.003
Did not complete basic education	87 (98.9)	1 (1.1)	
Primary basic education	103 (92.8)	8 (7.2)	
Secondary education	74 (86.0)	12 (14.0)	
Vocational training	24 (82.8)	5 (17.2)	
Tertiary education	58 (82.9)	12 (17.1)	
Employment status			<0.001
Paid	66 (81.5)	15 (18.5)	
Unpaid/unemployed	185 (94.9)	10 (5.1)	
Retired	66 (94.3)	4 (5.7)	
Self-employed	30 (76.9)	9 (23.1)	
Area of residence			0.798
Urban	193 (91.0)	19 (9.0)	
Peri-urban	69 (89.6)	8 (10.4)	
Rural village	70 (87.5)	10 (12.5)	
Other Province	14 (93.3)	1 (6.7)	
Region of origin			0.395
Southern region	266 (90.5)	28 (9.5)	
New Guinea Islands	30 (83.3)	6 (16.7)	
Momase	25 (96.2)	1 (3.8)	
Highlands	26 (89.7)	3 (10.3)	
Years of residence in Port Moresby			0.143
0[#]	85 (87.6)	12 (12.4)	
1-10	25 (89.3)	3 (10.7)	
>10	150 (94.3)	9 (5.7)	
Lifetime	68 (86.1)	11 (13.9)	

[#]The p-values were obtained from the Chi-square statistic, and assess the strength of association; [#]Participant does not reside in Port Moresby

Using a reply of “Yes” to the question of whether alcohol was consumed as the dependent variable, multivariate logistic regression analysis indicated that age, gender and years of residence in Port Moresby were independently associated with alcohol consumption. Participants aged <50 years were 10 times more likely to be consuming alcohol compared to their counterparts aged 60 years and older. Female participants had lower odds of consuming alcohol compared to their male counterparts. Those who were not born in Port Moresby were less likely to consume alcohol and this was significant for those who had moved to and lived in Port Moresby for more than 10 years. Those who completed vocational training had a positive risk of consuming alcohol. However, this did not reach statistical significance. All other demographic variables did not appear to be associated with alcohol consumption. The results of the multivariate logistic regression analysis are shown in Table 4.4.

Although employment status had an influence on alcohol consumption, as shown in Table 4.3, backward elimination (logistic regression) dropped this variable and this may have been due to its correlation with age. Retired participants are included in the age group 60 years and older.

Table 4.4 Multivariate logistic regression analysis of demographic risk factors for alcohol consumption (N=38)

Variable	n(%)*	Adjusted OR	95% CI	p-value
Age category (years)				<0.001
<50	23 (20.4)	10.76	3.06-37.92	<0.001
50-59	11(7.6)	2.37	0.64-8.80	0.198
≥60	4 (3.7)	1 (reference)		
Gender				0.002
Female	14 (5.8)	0.26	0.12-0.61	
Male	24 (16.8)	1 (reference)		
Years of residence in Port Moresby				0.037
0[#]	12 (12.4)	0.90	0.32-2.51	0.837
1-10	3 (10.7)	0.24	0.04-1.48	0.124
>10	9 (5.7)	0.19	0.06-0.67	0.009
Lifetime	11 (13.9)	1 (reference)		

*The column showing 'n/N (%)' shows the number of people (and percentage) of alcohol consumers within each variable. The dependent variable was "Yes" to alcohol consumed in the previous three months; [#]Participant does not reside in Port Moresby

4.3.4.2 Tobacco smoking

Tobacco smokers were further categorised according to their tobacco smoking status (current, never and quit), and as to whether they were ever (both current and those who had quit) or never smokers. The number of years of smoking also was calculated and participants were categorised according to these numbers of years. Age at onset and cessation of smoking, and the number of years of smoking, were not normally distributed and therefore are reported as median and range where appropriate.

Like the consumption of alcohol, the number of participants who smoked tobacco was small, with only 24 (6.2%) of the participants reporting that they were current smokers (Table 4.5). Of these 24 smokers, 19 (79.2%) were daily smokers. Two hundred and seventy two (70.6%) participants had never smoked tobacco, while 113 (29.4%) were “ever” (current and quit) smokers. Of these, 89 (78.8%) participants had quit the habit.

For those classified as smokers, the median age at which participants had started smoking was 18 but this ranged over 44 years (range: 12-56 years). The median number of years of daily smoking for current smokers was 28.5 but this ranged over 38 years (range: 3-41 years).

For participants who had quit smoking, the median age at which these participants had quit the habit was 43 but this ranged over 54years (range: 15-69 years). The median number of years that this group of participants had been smoking before they quit was 13, with a range of 43.5 years (range: 0.5-44 years)

Thirteen (54.2%) participants who were smokers had been smoking for more than 20 years. Of the 24 participants who were smokers, 6 (25.0%) could not remember when they had started smoking and, therefore, the number of years these participants had smoked could not be calculated and were reported as missing data.

Manufactured cigarettes were the most common type of tobacco product used by smokers. Of the 24 smokers, 14 (58.3%) smoked manufactured cigarettes while eight (33.3%) smoked hand-rolled cigars. Two participants did not indicate the type of tobacco product they smoked, while none of those who smoked used pipes of tobacco. Of the fourteen who smoked manufactured cigars, 85.8% smoked 20 cigars or less per day, while all those who smoked hand-rolled cigars smoked less than 10 per day (Table 4.5).

Table 4.5 Frequency of tobacco smoking and the characteristics of participants

Variables	Frequency* [n/N (%)]
Current smoker	
No	361/385 (93.8)
Yes	24/385 (6.2)
Age (years) at onset of smoking for current smokers [median (range)]	18 (12-56)
Age (years) when quit smoking [median (range)]	43 (15-69)
Number of years of smoking for current smokers [median (range)]	28.5 (3-41)
No. of years of smoking for those who quit [median (range)]	13 (0.5-44)
Smoker status	
Never	272/385 (70.6)
Quit	89/385 (23.1)
Current	24/385 (6.2)
Number of years of smoking	
≤ 10	1/24 (4.2)
11–20	4/24 (16.7)
21-30	7/24 (29.2)
>30	6/24 (25.0)
Number of manufactured cigars smoked/day	14/24 (58.3)
1-10	6/14 (42.9)
11-20	6/14 (42.9)
>20	2/14 (14.3)
Number of hand-rolled cigars smoked/day	8/24 (33.3)
1-10	8/8 (100)
11-20	0/8 (0)
>20	0/8 (0)

*May not add up to the total because of missing values

As age increased, the number of those smoking decreased. The younger aged participants were more likely to smoke, especially those who were younger than 50 years of age (Table 4.6).

Sample numbers were very small for the smoking categories because of the small number of participants who were classified as smokers and, therefore, no further analysis could be performed to draw any additional valid conclusions.

Table 4.6 Demographic factors associated with tobacco smoking (N=385)

Variable	Current tobacco smoker [n (%)]		p-value*
	No	Yes	
Age category (years)			0.009
<50	99 (87.6)	14 (12.4)	
50-59	138 (95.2)	7 (4.8)	
≥60	104 (97.2)	3 (2.8)	
Area of residence			0.068§
Urban	204 (96.2)	8 (3.8)	
Peri-urban	71 (92.2)	6 (7.8)	
Rural village	72 (90.0)	8 (10.0)	
Other Province	13 (86.7)	2 (13.3)	
Years of residence in Port Moresby			0.090§
0#	87 (89.7)	10 (10.3)	
1-10	28 (100.0)	0 (0.0)	
>10	153 (96.2)	6 (3.8)	
Lifetime	73 (92.4)	6 (7.6)	

*The p-values were obtained from the Chi-square statistic, and assess the strength of association; §Fisher's Exact Test; #Participant does not reside in Port Moresby

4.3.4.3 Fruit and vegetable consumption

Participants were requested to think of a typical week (in the preceding three months) when they had consumed vegetables or fruit, and recall the number of days and the number of cups of fruits or vegetables consumed during that week. The number of cups was converted to number of servings, based on the conversions in Appendix 9.

As shown in Table 4.7, vegetable and fruit consumption was poor. Ninety two percent of the participants reported consuming ≤3 servings of vegetables per day in a typical week. Despite eating less serves of vegetable in a day, 42.3% of the participants reported eating vegetables 6-7 days in a typical week. When compared with vegetable consumption, 70% of the participants consumed fruit on two days or less in a typical week, and 70% had ≤2 serves of fruit on a day when they had fruit.

Univariate logistic regression analysis indicated that the number of fruit servings was associated with gender and this relationship was statistically significant. Male

participants were almost twice as likely to consume <2 serves of fruit (Crude OR=1.872, 95% CI=1.20-2.93, p=0.006) compared to their female counterparts. There was no statistically significant relationship between fruit consumption and employment status, level of education, area of residence or age. Similarly, no demographic variable had a statistically significant impact on vegetable consumption.

Table 4.7 Frequencies of fruit and vegetable consumption characteristics (N=385)

Variables	Frequency*n (%)
Vegetable servings/day	
<3	355 (92.2)
≥3	28 (7.3)
Number of vegetable-eating days/week	
0-2	96 (24.9)
3-5	124 (32.2)
6-7	163 (42.3)
Fruit servings/day	
<2	271 (70.4)
≥2	112 (29.1)
Number of fruit-eating days/week	
0-2	272 (70.6)
3-5	70 (18.2)
6-7	41 (10.6)

*****May not add up to total because of missing values

4.3.4.4 Physical activity

Participants were asked about physical activity in a typical week within the preceding three months before the study. Physical activity included work-related physical activity, walking and cycling to get to and from places, and participation in sports, fitness and recreational activities. They were asked if they were involved in these activities for at least 10 minutes continuously on a single occasion. The response was 'no' if the physical activity took less than 10 minutes. None of the participants cycled to get to and from places. Work-related physical activity included paid or unpaid work such as study/training, household chores, planting, tending and harvesting food crops, fishing or hunting for food, marketing and seeking employment.

Work-related physical activity was classified according to moderate- and vigorous-intensity activities (MIA and VIA, respectively). Likewise, sports, fitness and recreational activities also were classified according to moderate- and vigorous-intensity activities (MISFRA and VISFRA, respectively). A show card (Appendix 12) was used to identify which physical activities were classified as moderate- or vigorous-intensity activities. The number of minutes each participant reported undertaking a particular activity was multiplied by the number of days in a week such activities were undertaken to calculate the total minutes of physical activity per week.

Participants were further categorised according to the amount of physical activity they performed in a week. These categories were: sufficient, insufficient and no physical activity. Participants were classified as doing sufficient physical activity (in minutes per week), if any of the types of physical activity they participated in met the WHO recommendations for the number of minutes per week for a particular intensity of physical activity. [3]

As shown in Table 4.8, results indicated that walking to get to and from places was the most common physical activity, with 76.9% (n=296) reporting that they had walked for at least 10 minutes continuously to get to and from places.

In comparison to walking as a type of physical activity, the numbers of participants participating in both work-related VIA and VISFRA were small. Only 53 (13.8%) and 34 (8.8%) of the study participants were involved in work-related VIA and VISFRA, respectively. In general, as the intensity of physical activity increased, the number of participants undertaking these activities decreased.

Two hundred and eighteen (56.6%) participants reported undertaking sufficient physical activity while the remainder either performed insufficient or no physical activity (Table 4.8).

Table 4.8 Frequencies of self-reported physical activity

Variables	Frequency* [(n/N)%]
Work-related VIA for at least 10 minutes	
No	332/385 (86.2)
Yes	53/385 (13.8)
Minutes of work-related VIA /week	
<75	17/53 (32.1)
≥75	35/53 (66.0)
Performs VISFRA for at least 10 minutes	
No	351/385 (91.2)
Yes	34/385 (8.8)
Minutes of VISFRA/week	
<75	14/34 (41.2)
≥75	20/34 (58.8)
Work-related MIA for at least 10 minutes	
No	225/385 (58.4)
Yes	160/385 (41.6)
Minutes of work-related MIA/week	
<150	56/160 (35.0)
≥150	102/160 (63.8)
Performs MISFRA for at least 10 minutes	
No	317/385 (82.3)
Yes	68/385 (17.7)
Minutes of MISFRA/week	
<150	51/68 (75.0)
≥150	17/68 (25.0)
Walks to get to and from places for at least 10 minutes	
No	89/385 (23.1)
Yes	296/385 (76.9)
Minutes walking /week	
<150	133/296 (44.9)
≥150	152/296 (51.4)
Amount of physical activity	
Insufficient	109/385 (28.3)
Sufficient	218/385 (56.6)
None	58/385 (15.1)

*May not add up to total because of missing values; VIA = vigorous-intensity activity; MIA = moderate-intensity activity; VISFRA = vigorous-intensity sports, fitness and recreational activity; MISFRA = moderate-intensity sports, fitness and recreational activity.

Using Chi-square statistics, the amount of physical activity, which summarises all types of physical activity, was further examined to determine if there was an association and, if so, the strength of any association with demographic factors. Furthermore, the Chi-square statistics also were used to determine if there was an

association between age and employment status, and different types of physical activities.

Chi-square analysis indicated that age and employment appeared to be associated with the amount of physical activity (Table 4.9). Those who were less than 50 years old were more likely to do sufficient physical activity. In reference to employment status, those who were self-employed were more likely to do sufficient physical activity, while those who were retired were more likely to lack sufficient physical activity. Participants who were rural village dwellers were more likely to do sufficient physical activity compared to their counterparts who lived in other residential areas, but this did not reach statistical significance.

Age influenced whether or not respondents participated in sports, fitness and recreational activities but it did not affect work-related physical activities. Those aged 50 years and older were less likely to participate in both MISFRA (χ^2, p=0.002) and VISFRA (χ^2, p<0.001). There was no significant association between age and different intensities of work-related physical activity.

The Chi-square statistics indicated that both work-related physical activity and participation in sports, fitness and recreational activities were influenced by employment status.

Participants who were self-employed were more likely to undertake work-related MIA and VIA at their workplaces compared to the other categories of employment status (χ^2, p=0.015, p<0.001 for each scale of intensity of physical activity, respectively). Those who were self-employed were also more likely to participate in MISFRA and VISFRA compared to the other categories of employment status (χ^2, p=0.008, p=0.019 for each scale of intensity of physical activity, respectively). Overall, retirees were the least active, while those who were self-employed were the most physically active in terms of both work-related physical activities, and sports, fitness and recreational activities.

Table 4.9 Demographic factors associated with amount of physical activity

Variable	Sufficient physical activity	Insufficient physical activity	Lack of physical activity	p-value*
Age category (years)				0.012
<50	78 (69.0)	19 (16.8)	16 (14.2)	
50-59	80 (55.2)	48 (33.1)	17 (11.7)	
≥60	65 (60.7)	21 (19.6)	21 (19.6)	
Employment status				0.016
Paid	49 (60.5)	22 (27.2)	10 (12.3)	
Unpaid/unemployed	115 (59.0)	53 (27.2)	27 (13.8)	
Retired	40 (57.1)	11 (15.7)	19 (27.1)	
Self-employed	30 (76.9)	7 (17.9)	2 (5.1)	
Years of residence in Port Moresby				0.079
0#	69 (71.1)	16 (16.5)	12 (12.4)	
1-10	16 (57.1)	5 (17.9)	6 (16.7)	
>10	96 (60.4)	39 (24.5)	3 (11.5)	
Lifetime	41 (51.9)	27 (34.2)	6 (20.7)	

*The p-values were obtained from the Chi-square statistic, and assess the strength of association; #Participant does not reside in Port Moresby

As shown in Table 4.8, walking as a type of physical activity was the most common, with more than 70% of the participants reporting that they walked to get to and from places.

Demographic factors shown in Table 4.1 were examined using univariate logistic regression to confirm any significant association between walking to get to and from places and the recommended number of minutes (≥150) of walking per week. Univariate logistic regression also was used to examine the direction of associations, in addition to the p-values.

As shown in Table 4.10, univariate logistic regression analysis indicated that the only demographic factor which had an impact on a participant walking to get to and from places was gender. Female participants were more likely to walk to get to and from places. Age, employment status, area of residence and region of origin of the participants had Odds Ratios of more than 1 (more likely to walk to get to and from

places), but these did not reach statistical significance. Multivariate logistic regression analysis indicated that gender was the only significant independent influence on the likelihood of walking to get to and from places. The adjusted odds for female participants walking to get to and from places was almost two (OR 1.709, 95% CI 1.031-2.831, p=0.038).

Table 4.10 Univariate logistic regression analysis of demographic factors affecting whether or not a participant walked to get to and from places

Variable	Crude OR	95% CI	p-value
Age category (years)			0.116
<50	1.36	0.75-2.47	0.315
50-59	1.87	1.04-3.36	0.038
≥60	1 (reference)		
Gender			0.030
Female	1.70	1.05-2.75	
Male	1 (reference)		
Level of Education			0.329
Did not complete basic education	1.44	0.67-3.12	0.350
Primary basic education	1.30	0.63-2.66	0.477
Secondary education	0.88	0.43-1.82	0.727
Vocational training	0.61	0.24-1.56	0.302
Tertiary education	1 (reference)		
Employment status			0.224
Paid	1.67	0.70-3.97	0.244
Unpaid/unemployed	1.78	0.83-3.82	0.141
Retired	1.04	0.44-2.43	0.933
Self-employed	1 (reference)		
Area of residence			0.897
Urban	1.15	0.35-3.76	0.820
Peri-urban	1.39	0.39-4.94	0.614
Rural village	1.35	0.38-4.77	0.644
Outside Province	1 (reference)		
Region of origin			0.889
Southern	1.29	0.55-3.05	0.560
New Guinea Islands	1.14	0.38-3.47	0.814
Momase	1.60	0.45-5.70	0.468
Highlands	1 (reference)		
Years of residence in Port Moresby			0.574
0[#]	1.30	0.63-2.67	0.475
1-10	0.67	0.26-1.72	0.404
>10	1.01	0.54-1.90	0.979
Lifetime	1 (reference)		

The dependent variable was "Yes", respondent walks to get to and from places.
[#]Participant does not reside in Port Moresby

Although female participants were more likely to walk to get to and from places, they were less likely to walk for ≥150 minutes per week (Table 4.11). Area of residence did not influence whether or not a participant walked to get to and from places (Table 4.10) but, when examining the number of minutes that participants walked in a week, area of residence had an influence (Table 4.11). Those living in rural areas and outside of Port Moresby were more likely to walk for ≥150 minutes per week compared to their urban and peri-urban counterparts.

Univariate logistic regression indicated that rural village dwellers were more likely to walk for ≥150 minutes or more per week to get to and from places compared to their study counterparts. Participants who had not lived in Port Moresby were three times more likely to walk for ≥150 minutes in a week, while those who had moved to live in Port Moresby were twice as likely to walk for ≥150 minutes compared to their counterparts who were born in Port Moresby (Table 4.11)

Table 4.11 Univariate analysis of demographic factors affecting the number of minutes a participant walked to get to and from places

Variable	Crude OR	95% CI	p-value
Age category (years)			0.067
<50	1 (reference)		
50-59	0.51	0.29-0.90	0.021
≥60	0.72	0.38-1.38	0.324
Gender			0.021
Female	0.55	0.34-0.91	
Male	1 (reference)		
Employment status			0.195
Paid	0.46	0.17-1.21	0.117
Unpaid/unemployed	0.43	0.18-1.06	0.066
Retired	0.69	0.25-1.92	0.479
Self-employed	1 (reference)		
Area of residence			0.036
Urban	1 (reference)		
Peri-urban	0.63	0.34-1.15	0.131
Rural village	1.87	1.01-3.48	0.048
Outside Province	1.37	0.37-5.05	0.636
Years of residence in Port Moresby			0.005
0[#]	3.68	1.79-7.54	<0.001
1-10	2.68	0.93-7.73	0.068
>10	2.36	1.23-4.51	0.010
Lifetime	1 (reference)		

The dependent variable was ≥ 150 minutes per week spent walking; [#]Participant does not reside in Port Moresby

4.3.5 Medical characteristics

Medical characteristics included the number of years since being diagnosed with diabetes, diabetes management, and biochemical and physical measurements. The number of years since a participant had been diagnosed with diabetes, capillary blood glucose (CBG) and HbA1c were not normally distributed and are reported as median and range, where appropriate. Waist circumference, BMI, fasting CBG and HbA1c were classified according to the PNG Diabetes Clinical Guidelines 2012. There were discrepancies in hip circumference measurements and, therefore, no further analysis was undertaken using this variable.

The median number of years since having been diagnosed with diabetes was 4.0, with a minimum and maximum of 0.5 and 30.0 years, respectively.

As shown in Table 4.12, the median and range values for HbA1c and fasting CBG, and for BMI, at time of enrolment were above the ideal values of ≤7.0% (HbA1c), ≤7 mmol/L (CBG) and <25 kg/m^2, respectively. Mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also above normal. The mean waist circumference was at the normal value for male participants (normal is ≤102 cm) but was higher than normal for female participants (normal is ≤88cm).

Diabetes management included lifestyle modifications, as well as pharmacological and other types of treatment employed by the participant, whether or not participants missed their prescribed doses of medications, and reasons for missing doses if they did, and pharmacological management of co-morbidities.

Table 4.12 Medical characteristics of participants at the time of enrolment (N=385)

Variable	n/N (%)*	Mean	SD
Weight (kg)	371 (96.4)	70.6	14.2
Waist circumference (cm)	384 (99.7)	101.3	11.7
Female	240/385 (62.3)	102.2	12.0
Male	144/385 (37.4)	99.8	11.2
Hip circumference (cm)	382 (99.2)	101.8	11.2
BMI (kg/m^2)	368 (95.6)	27.0	4.9
SBP (mmHg)	380 (98.7)	150.1	25.0
DBP (mmHg)	380 (98.7)	83.0	13.9
CBG (mmol/L)	380 (98.7)	10.4†	2.0 – 34.0§
Fasting	147/380 (38.7)	9.3†	2.0 – 23.9§
Random	150/380 (39.5)	12.3†	4.7 – 34.0§
Unknown	83/380 (21.8)	9.9†	3.1- 23.7§
HbA1c (%)	362 (94.0)	8.7†	4.8 - >14.0§
Number of years diagnosed with diabetes	384 (99.7)	4.0†	0.5 - 30.0§

*Percentages do not add up to 100% because of missing values; †Median; §Range; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; CBG = capillary blood glucose; HbA1c = glycated haemoglobin

4.3.5.1 Initial diabetes management when diagnosed

Participants were questioned about their initial management when they were first diagnosed with diabetes. Of the 385 participants, 336 (87.3%) were treated with hypoglycaemic medications while 48 (12.5%) were diet-controlled. Of those treated with hypoglycaemic medications, 45 (13.4%) were treated with insulin (as a single agent or with oral therapy) and 317 (94.3%) were treated with oral hypoglycaemic medications. Twenty five participants (7.4% of those on hypoglycaemic medications) were treated with both insulin and oral hypoglycaemic medications. None of the participants was on a prescribed diet, as such, but 99 (25.7%) were advised about their diet. Of these, 59 (59.6%) changed their diet in line with advice provided by their medical officers.

Apart from hypoglycaemic medications and diet management, participants employed other ways to manage their diabetes. Twenty three (6.0%) used herbal products, while 15 (3.9%) used traditional medicine.

4.3.5.2 Diabetes management in the three months preceding study recruitment

Three hundred and fifty six (92.5%) participants were prescribed hypoglycaemic medications in the preceding three months (Table 4.13). However, five of these 356 participants had ceased their medications for more than three months. These five participants continued to attend scheduled reviews but did not inform their medical officers that they had ceased taking their hypoglycaemic medications. These participants were, therefore, excluded from any statistical analysis on hypoglycaemic medication use. In the preceding three months, only 29 of the participants had diet-controlled diabetes.

4.3.5.3 Hypoglycaemic medications in the preceding three months

Glibenclamide, metformin and insulin were the only hypoglycaemic medications available through the public health care system during the time of this study. Glibenclamide was available in 5mg, and metformin in 500 mg, tablets. There was an inconsistent supply of insulin and insulin syringes during the period of the study. More than 50% of the participants were receiving only one hypoglycaemic medication. The least used hypoglycaemic medication was insulin, with only 19 (5.4%) using it, and the most commonly used medication was glibenclamide (76.9%). More than 80% of participants were on the mid- and highest dose ranges for both glibenclamide and metformin, as shown in Table 4.13.

Results indicated a change of diabetes management for 48 of the participants, from diet control to the use of pharmacological agents in the preceding three months, and a reduction in the number of participants treated with insulin since diagnosis with T2DM.

Table 4.13 Hypoglycaemic medication use and participants' self-reported adherence

Variable	Frequency* n/N (%)
Any hypoglycaemic medications prescribed in the previous three months	
No	29/385 (7.5)
Yes	356/385 (92.5)
Missed any hypoglycaemic doses in the previous three months	
No	143/351 (40.7)
Yes	208/351 (59.3)
Number of hypoglycaemic agents	
1	187/351 (53.3)
2 or 3	159/351 (45.3)
Hypoglycaemic used[†]	
Glibenclamide	270/351 (76.9)
Metformin	223/351 (63.5)
Insulin	19/351 (5.4)
Glibenclamide used[†]	
No	108/351 (30.8)
Yes	270/351 (76.9)
Glibenclamide dose/day	
≤5mg	44/270 (16.3)
7.5–15 mg	152/270 (56.3)
>15 mg	74/270 (27.4)
Glibenclamide dose missed	
No	112/270 (41.5)
Yes	158/270 (58.5)
Metformin used	
No	156/351 (40.5)
Yes	223/351 (57.9)
Metformin doses/day	
≤500mg	39/223 (17.5)
750–1,000 mg	112/223 (50.2)
>1,000 mg	71/223 (31.8)
Metformin dose missed	
No	99/223 (44.4)
Yes	123/223 (55.2)

* May not add up to total because of missing values; [†]Exceeds total because some participants took more than one medication

4.3.5.4 Hypoglycaemic medication use and duration of diabetes

The use of hypoglycaemic medication was significantly associated with duration of diabetes, as shown in Table 4.14. The daily dose of insulin was not included in the analysis because more than 80% of the 19 participants on insulin could not recall their doses of insulin. The daily doses of glibenclamide and metformin were higher for those who had been undergoing treatment for diabetes for >5 years, compared to their counterparts. Those taking two or three hypoglycaemic medications were more likely to be those who had been suffering with diabetes for more than five years. Participants diagnosed with diabetes for >5 years were also more likely to use insulin than their counterparts.

Table 4.14 Association of hypoglycaemic medication use with duration of diabetes

Variable	Duration of diabetes (years)		p-value*
	≤ 5	> 5	
Glibenclamide use			0.001
No	72 (66.7)	36 (33.3)	
≤5 mg/day	25 (56.8)	19 (43.3)	
7.5-15mg/day	86 (57.0)	65 (43.0)	
>15mg/day	27 (36.5)	47 (63.5)	
Metformin use			0.0015
No	92 (59.4)	63 (40.6)	
≤500 mg/day	26 (66.7)	13 (33.3)	
750-1,000mg/day	64 (57.7)	47 (42.3)	
>1,000mg/day	28 (39.4)	43 (60.6)	
Insulin use			0.002
No	208 (57.0)	157 (43.0)	
Yes	4 (21.1)	15 (78.9)	
No. of hypoglycaemic medications/day			<0.001
0#	22 (75.9)	7 (24.1)	
1	117 (62.6)	70 (37.4)	
2 or 3	71 (44.9)	87 (55.1)	

#* The p-values were obtained from the Chi-square statistic, and assess the strength of association

4.3.5.5 Adherence with hypoglycaemic medications

Of the 351 participants who were prescribed hypoglycaemic medications, 208 (59.3%) missed some of their doses while 143 (40.7%) reported that they did not miss any of their doses. Age had a statistically significant impact on adherence,

with those aged 60 years or more being more adherent than their younger counterparts (when adherence was defined both as missing any dose and missing 10% of doses) as shown in Table 4.15. The data shown in Table 4.15 are based upon non-adherence parameters.

Table 4.15 Results of Multivariate logistic regression with 'non-adherence' as the dependent variable

Variable	Non-adherence n/N (%)*	Odds Ratio	95% Confidence interval	p-value
100% adherence				
Age				
>60	51/105 (48.6)	1 (reference)		
≤60	157/246 (63.8)	1.87	1.18- 2.97	0.0081
95% adherence				
Age				
>60	27/104 (26.0)	1 (reference)		
≤60	77/241 (32.0)	1.34	0.80-2.24	0.2669
90% adherence				
Age				
>60	13/104 (12.5)	1 (reference)		
≤60	54/241 (22.4)	2.02	1.05-3.89	0.0353
80% adherence				
Age				
>60	9/104 (8.7)	1 (reference)		
≤60	38/241 (15.8)	1.98	0.92-4.25	0.0815

"Non-adherence' was the dependent variable; *The column showing 'n/N (%)' shows the number of people (and percentage) within each adherence level who were non-adherent

4.3.5.6 Association of hypoglycaemic daily doses with adherence

More than half of the participants (58.5%) prescribed glibenclamide missed some of their doses (Table 4.13). As shown in Table 4.16, of the 74 participants prescribed doses greater than 15mg daily, 53 (71.6%) missed some of their doses. The picture was much the same for metformin. Forty one participants, or 57.7% of the 71 participants prescribed the highest daily dose of 1,000mg or more, missed some of their doses. Those who were on the highest dose of metformin and glibenclamide appeared to be more non-adherent than those on lower doses, however, as shown

in Table 4.16, the association between missing any dose and daily doses of metformin and glibenclamide was not significant.

When comparing levels of adherence with the different categories of daily doses of glibenclamide and metformin, there was a significant association between doses of glibenclamide, but not with metformin, and 80% adherence. At this level of adherence, the proportion of those who were adherent increased as the dose of glibenclamide increased. Participants prescribed >15mg of glibenclamide were more likely to be more adherent, compared to those on lower doses (Table 4.16).

Those who missed their metformin and glibenclamide doses appeared to be more likely to be younger than 60 years. However, the differences in adherence rates between those younger than 60 and those 60 years or older was not statistically significant for metformin (χ^2, p=0.055) or glibenclamide (χ^2, p=0.081).

Table 4.16 Association of metformin and glibenclamide daily doses with medication adherence ≥80%

Variable	Level of adherence tested					
	100% adherence			80% adherence		
	Adherent n/N(%)	Non-adherent n/N(%)	p-value	Adherent n/N(%)	Non-adherent n/N(%)	p-value*
Glibenclamide (mg/day) [n=270]			0.080			0.032
≤5	19 (43.2)	25 (56.8)		32 (74.4)	11 (25.6)	
7.5–15	66 (43.4)	86 (56.6)		129 (86.6)	20 (13.4)	
>15	21 (28.4)	53 (71.6)		67 (91.8)	6 (8.2)	
Metformin (mg/day) [n=222]§			0.635			0.526
≤500	13 (33.3)	26 (66.7)		31 (81.6)	7 (18.4)	
750-1,000	42 (37.5)	70 (62.5)		97 (88.2)	13 (11.8)	
>1,000	30 (42.3)	41 (57.7)		62 (88.6)	8 (11.4)	

§Excludes one missing value; *The p-values were obtained from the Chi-square statistic, and assess the strength of association.

4.3.5.7 Self-reported factors contributing to non-adherence with hypoglycaemic medications

Two hundred and eight participants missed taking their medications (Table 4.13). Of these, 207 (99.5%) gave reasons for omitting doses of their hypoglycaemic medications. The most common factors cited by participants for omitting their hypoglycaemic medication doses were "patient-related" followed by "health care system" related factors (Table 4.17). The most common patient factor was forgetting to take doses. Seventy four (35.7%) participants forgot to take their doses. The next most common patient-related reason was not refilling prescriptions (32.4%). The most common factor related to the health care system was access to the diabetes clinic for repeat prescriptions. Problems with accessibility to the clinic were contributed to by the increasing number of patients registered, scheduling of appointments, number of clinic days and hours per week, cancellation/rescheduling of clinic times, shortage of staff and closure of clinic for 2 months every December and January. (Personal communication) Further, rural village dwellers found it difficult to travel to and from Port Moresby.

Table 4.17 Identified number of factors contributing to non-adherence (N=207).

Factors influencing adherence	Percentage* n (%)
Patient-related factors	
Forgot	74 (35.7%)
Had script but did not refill	67 (32.4%)
Refused to take hypoglycaemic medications	22 (10.6%)
Others	15 (7.2%)
(Travel, transport costs to and from remote villages to the city, alternative therapy, lack of psychosocial support)	
Medication-related factors	
Medication costs	15 (7.2%)
Perceived adverse effects	12 (5.8%)
Health care system-related factors	
Access to and from remote villages	5 (2.4%)
Inconsistent medical supplies in public hospitals	7 (3.4%)
Access to diabetes clinics for repeat scripts	33 (15.9%)
Prescriber factors	
Insufficient information about disease and medications	4 (1.9%)
Other reasons	
Theft of bag containing medications	2 (1.0%)

*Total percentage >100% because some participants gave more than one reason

4.3.5.8 Medications for co-morbidities in the three months preceding study recruitment

Data for diagnosed co-morbidities were not recorded but participants were questioned about other medications they were prescribed apart from their hypoglycaemic medications. Patient clinic cards also were used to verify the names of these co-medications and their doses.

Two hundred and twenty three participants (57.9%) were prescribed medications for co-morbidities (co-medications). Of these, 219 (98.2%) were participants who were prescribed hypoglycaemic medications and only four (1.8%) were participants whose diabetes was diet-controlled. Of the four who were not on hypoglycaemic medications, two ceased taking both their hypoglycaemic and antihypertensive medications without their doctor's advice for almost a year and therefore could not remember what medications they were on. The most common group of co-medications prescribed were those for hypertension. One hundred and ninety eight (88.8%) participants were prescribed enalapril, making enalapril the most prescribed co-medication. Table 4.18 shows the co-medication frequencies prescribed for co-morbidities.

Table 4.18 Co-medications use among participants (N=385)

Variable	Frequency* [n/N (%)]
Medications for co-morbidities	
No	164/385 (42.6)
Yes	221/385 (57.4)
Number of co-medications	
1	119/223 (53.4)
2	62/223 (27.8)
3 or 4	42/223 (18.8)
Co-medications prescribed†	
Antihypertensives	
Enalapril	198/223 (88.8)
Atenolol	41/223 (18.4)
Nifedipine	58/223 (26.0)
Methyldopa	17/223 (7.6)
Antiplatelet	
Aspirin	17/223 (7.6)
NSAID analgesics	9/223 (4.0)
Diuretics	
Frusemide	5/223 (2.2)
Lipid lowering agents	
Simvastatin	16/223 (7.2)
Others	11/223 (4.9)

*May not add up to total because of missing values; †Exceeds total because some participants took more than one medication; NSAID = non-steroidal anti-inflammatory drug

4.3.5.9 Non-pharmacological management

Participants were questioned about whether they were using any non-pharmacological type of management for their diabetes.

Many participants of this study also were using other forms of management for their diabetes, but 232 (60.3%) participants did not choose to use any non-pharmacological types of management for their diabetes. Of the 351 participants who were prescribed hypoglycaemic medications, 71 (20.2%) reported that they were doing exercise and 37 (10.5%) reported that they had modified their diet as part of their diabetes management. There was no participant on a specific prescribed diet. There were no Dietetics or Nutrition services during the time of the study.

A small number of participants were using herbal products and traditional medicines for their diabetes. Of the total participants, 37 (9.6%) were taking herbal products and 17 (4.4%) were using traditional medicines. Seven (1.8%) participants used other products like ionised/holy water, charcoal, honey and vinegar mixture, linseed and olive oil, and mushroom tea.

Using other forms of management for diabetes was influenced by whether or not a participant was taking a hypoglycaemic medication for diabetes. Those who were not taking any hypoglycaemic medications were five times more likely to use any other forms of management, such as herbal products, compared to those who were using hypoglycaemic medications (Crude OR = 5.946, 95% CI = 2.662-13.282, $p<0.001$). There were no statistically significant differences in the use of exercise as diabetes management between those who were on hypoglycaemic medications and those who used diet control.

4.3.6 Physical measurements

Physical measurements of participants included height, weight, SBP and DBP, and waist and hip circumferences. Height and weight measurements were used to calculate the body mass index (BMI) of participants. The categorical data on the number of years since diagnosis of diabetes was included with physical measurements (Table 4.19).

Table 4.19 Frequencies of physical characteristics of participants (N=385)

Variable	Frequency n (%)
SBP (mmHg)	
≤130	93 (24.2)
>130	287 (74.5)
DBP (mmHg)	
≤80	174 (45.2)
>80	206 (53.5)
BMI category	
Underweight	12 (3.1)
Normal weight	117 (30.4)
Overweight	143 (37.1)
Obese	96 (24.9)
Waist circumference	
Normal	114 (29.7)
Above normal	270 (70.1)
No. of years since diagnosis of diabetes	
≤5 years	212 (55.1)
>5 years	172 (44.7)

SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index; Normal waist circumference is ≤88cm (females) and ≤102cm (males)

4.3.6.1 Blood pressure

Blood pressure was categorised according to the PNG Diabetes Management Guidelines, where an SBP of >130 mmHg and a DBP of >80mmHg were classified as being high. About 50% of the participants had a high DBP while almost three

quarters (74.5%) of the participants had a higher than normal SBP (Table 4.19). As shown in Table 4.12, the mean SBP was 150±25 mmHg (Range: 95 mmHg to 235 mmHg) while the mean DBP was 83±14 mmHg (Range: 43 mmHg to 143 mmHg).

The likelihood of younger participants having an abnormally high SBP was lower, compared with those aged 60 years or older (Table 4.20). As age increased, the odds of an abnormally high SBP increased. Participants aged 60 years or older were five times more likely to have an abnormally high SBP compared to their younger counterparts. Employment status also had a statistically significant impact on SBP, with the odds of those in the unpaid/unemployed category and retirees having an abnormally high SBP being greater than for those who were in paid employment. BMI also had an impact on SBP. Participants with BMI ≥ 25 kg/m^2 had almost twice the likelihood of having an abnormally high SBP compared to their counterparts. Those who were underweight were more than 10 times less likely to have an abnormally high SBP.

Results indicated that smoker status was the most important factor (Table 4.21). Participants classified as non-smokers (including those who had quit) were three times more likely to have an abnormally high SBP compared to smokers. Another variable which appeared to influence SBP was the number of minutes of MISFRA in a week. Those who participated in MISFRA for ≥150 minutes in a week were less likely to have an SBP of >130 mmHg. Betel nut chewers who chewed betel nut only, or with PBI but not lime, were twice as likely to have an SBP of >130 mmHg but this did not reach statistical significance. Those who were not alcohol consumers were also more likely to have a higher than normal SBP, but this did not reach statistical significance either.

Table 4.20 Univariate logistic regression of demographic and medical factors associated with high SBP (>130 mmHg)

Variable	Crude OR	95% CI	p-value
Age category (years)			<0.001
<50	1 (reference)		
50-59	2.08	1.22-3.57	0.007
≥60	5.40	2.65-10.98	<0.001
Employment status			0.019
Paid	1 (reference)		
Unpaid/unemployed	2.07	1.17-3.67	0.012
Retired	3.11	1.41-6.85	0.005
Self-employed	1.48	0.64-3.40	0.360
Area of residence			0.138
Urban	1 (reference)		
Peri-urban	2.00	1.01-3.98	0.047
Rural	1.11	0.63-1.96	0.718
BMI (kg/m^2)			0.033
<25	1 (reference)		
≥25	1.76	1.05-2.95	
BMI			0.003
Underweight	0.09	0.02-0.32	<0.001
Normal weight	0.45	0.23-0.91	0.026
Overweight	0.51	0.26-1.00	0.051
Obese	1 (reference)		
Co-medications taken with hypoglycaemic medications			<0.001
No	0.21	0.13-0.35	
Yes	1 (reference)		
Waist circumference			0.118
Normal	1 (reference)		
Above normal	1.48	0.91-2.43	

The dependent variable was SBP > 130 mmHg; BMI = body mass index

Table 4.21 Univariate logistic regression of lifestyle factors associated with high SBP (>130 mmHg)

Variable	Crude OR	95% CI	p-value
Alcohol consumption in the previous three months			0.065
No	1.94	0.96-3.93	
Yes	1 (reference)		
Smoker status			0.016
Current	1 (reference)		
Never	3.34	1.43-7.80	0.005
Quit	3.58	1.39-9.24	0.008
Number of years of betel nut chewing			0.135
≤25	1 (reference)		
>25	1.96	0.81-4.76	
Betel nut chew composition			0.145
Bete nut, lime and PBI	1 (reference)		
Betel nut only or with PBI but no lime	2.12	0.77-5.80	
Performs MISFRA for at least 10 minutes			0.081
No	1.67	0.94-2.96	
Yes	1 (reference)		
Minutes of MISFRA/week			0.046
<150	1 (reference)		
≥150	0.31	0.10-0.98	
Minutes of work-related VIA/week			0.140
<75	1 (reference)		
≥75	0.291	0.06-1.50	
Performs VISFRA for at least 10 minutes			0.101
No	1.88	0.89-3.98	
Yes	1 (reference)		
Amount of physical activity/week			0.153
Sufficient	0.48	0.23-1.04	0.064
Insufficient	0.63	0.27-1.49	0.293
None	1 (reference)		

The dependent variable was SBP > 130 mmHg. MISFRA = moderate-intensity sports, fitness and recreational activities; VISFRA = Vigorous-intensity sports, fitness and recreational activities; VIA = vigorous-intensity activity; PBI = *Piper betle* inflorescence

As shown in Tables 4.20 and 4.22, age was an important factor influencing SBP. Participants aged 50 years and older were more likely to have an abnormally high SBP. Those aged 60 years and older had four times the likelihood of having an SBP that was >130 mmHg. Use of co-medications was the most important factor

independently influencing SBP. Those who were on co-medications were three times more likely to have an SBP that was >130 mmHg. Smoking was also an independent factor influencing SBP, with those who had never smoked and those who had quit being three and two times more likely to have an abnormally high SBP, respectively. Although participants with BMI > 25 kg/m^2 had higher odds of high SBP (Table 4.20), this did not reach statistical significance when demographic, medical and lifestyle factors were adjusted for each other (Table 4.22) and, therefore, BMI was not found to be an independent risk factor.

Table 4.22 Multivariate logistic regression of variables independently associated with high SBP (>130 mmHg)

Variable	n/N(%)*	Adjusted OR	95% CI	p-value
Age (years)				0.013
<50	66/111 (59.5)	1 (reference)		
50-59	107/142 (75.4)	1.58	0.84-2.97	0.160
≥60	95/107 (88.8)	3.24	1.48-7.09	0.003
Co-medications taken with hypoglycaemic medications				<0.001
No	89/151 (58.9)	1 (reference)		
Yes	193/221 (87.3)	3.39	2.13-6.76	
Smoker status				0.036
Current	12/24 (50.0)	1 (reference)		
Never	207/269 (77.0)	3.70	1.32-10.38	0.013
Quit	68/87 (78.2)	2.55	0.81-8.01	0.109

The dependent variable was SBP > 130 mmHg; *The column showing 'n/N (%)' shows the number of people (and percentage) within each variable with SBP > 130 mmHg; SBP=systolic blood pressure

Univariate logistic regression analysis indicated that employment status, gender, age and BMI had a statistically significant impact on DBP (Table 4.23). Participants who were retired, and those in the unpaid/unemployed category, tended to have

lower likelihood of an abnormally high DBP when compared with those who were in paid employment, but this only reached statistical significance when comparing retirees with those in paid employment. The odds of those who were self-employed having a DBP that was >80 mmHg appeared to be higher than those in paid employment but this did not reach statistical significance. Female participants, all those aged 50 years or older and those with BMI < 25kg/m^2 had a lower odds of having an abnormally high DBP. The only lifestyle factors associated with a high DBP were vegetable servings per day (χ^2, p=0.033) and work-related VIA (χ^2, p=0.002).

Table 4.23 Univariate logistic regression of factors having an impact on DBP

Variable	Crude OR	95% CI	p-value
Gender			0.044
Female	1 (reference)		
Male	1.54	1.01-2.35	
Age category (years)			0.011
<50	1 (reference)		
50-59	0.59	0.35-0.98	0.042
≥60	0.44	0.26-0.76	0.003
Employment status			0.019
Paid	1 (reference)		
Unpaid/unemployed	0.70	0.41-1.20	0.193
Retired	0.48	0.25-0.93	0.030
Self-employed	1.64	0.72-3.77	0.241
BMI (kg/m^2)			0.009
<25	1 (reference)		
≥25	1.86	1.170-2.97	

The dependent variable was DBP > 80 mmHg. BMI = Body mass index; DBP = diastolic blood pressure

Gender, age and BMI were the most important factors which influenced DBP. (Table 4.24) The odds of female participants having a DBP > 80 mmHg was lower, compared to their male counterparts. Older participants (≥50 years old) also had a lower odds of having a DBP > 80 mmHg, when compared with their younger counterparts, but this only reached significance when comparing those who were 60 years and older with those who were <50 years old. Participants with BMI ≥ 25kg/m^2 were twice as likely to have a DBP that was >80 mmHg, compared with their counterparts.

Table 4.24 Multivariate analysis of factors independently associated with abnormally high DBP (>80 mmHg)

Variable	n/N(%)*	Adjusted OR	95% CI	p-value
Gender				0.011
Female	119/237 (56.2)	0.54	0.33-0.87	
Male	87/143 (60.8)	1 (reference)		
Age category (years)				0.003
<50	72/111 (64.9)	1 (reference)		
50-59	74/142 (52.1)	0.60	0.35-1.04	0.070
≥60	48/107 (44.9)	0.36	0.20-0.65	0.001
BMI (kg/m^2)				0.003
<25	44/104 (42.3)	1 (reference)		
≥25	138/239 (57.7)	2.14	1.29-3.53	

*The column showing 'n/N (%)' shows the number of people (and percentage) within each variable with DBP > 80 mmHg. Note: The dependent variable was DBP > 80 mmHg. DBP = diastolic blood pressure; BMI = body mass index.

4.3.6.2 Body mass index

More than 50% of the participants were either overweight (37.1%) or obese (24.9%) and only 30.4% had normal weight (Table 4.19). Univariate logistic regression was used to determine any association between demographic variables and BMI, and the direction of any association. Those who were underweight were excluded from the analysis because the sample number was too small. Results indicated that the region from where the participants originated appeared to be associated with a BMI of ≥25 kg/m^2 (p = 0.041). A statistically significant association was observed between participants from the Highlands region and their BMI. Those from the Highlands region were three times more likely to have a BMI ≥ 25 kg/m^2 when compared with participants from the Southern region. There was no statistically significant difference in having an abnormally high BMI among those from the NGI, Momase and the Southern regions. (Table 4.25)

Using backward logistic regression (multivariate) analysis to determine which demographic factors (if any) were independently associated with BMI, there was an indication that the region of origin of participants appeared to independently influence BMI, but this did not reach statistical significance (p=0.061). The association was only significant when comparing those from the Highlands region with those from the Southern region, where those from the latter region had the lowest odds of having a BMI ≥ 25kg/m^2. Participants from the Highlands region were five times more likely to have a BMI ≥ 25kg/m^2 when compared with those from the Southern region (Adjusted OR = 5.148, 95% CI = 1.18 - 22.53, p=0.030).

Table 4.25 Univariate logistic regression of demographic factors significantly associated with BMI

Variable	Crude OR	95% CI	p-value
Gender			0.309
Female	1.28	0.80-2.05	
Male	1 (reference)		
Level of Education			0.094
Did not complete basic education	0.71	0.32-1.56	0.391
Primary basic education	0.49	0.24-1.03	0.060
Secondary education	0.42	0.20-0.90	0.025
Vocational training	1.11	0.35-3.52	0.854
Tertiary education	1 (reference)		
Region of origin			0.041
Southern	1 (reference)		
New Guinea Islands	2.27	0.90-5.71	0.082
Momase	2.22	0.73-6.81	0.161
Highlands	3.14	1.57-9.33	0.039

The dependent variable was BMI ≥ 25 kg/m^2; BMI = body mass index

Lifestyle factors other than physical activities were investigated for an association with BMI, and the direction of any association, using univariate logistic regression analysis. These lifestyle factors included betel nut chewing, smoking, alcohol consumption within the preceding three months, and fruit and vegetable consumption. Results indicated that betel nut exposure had an association with BMI. Results indicated that, of all the aforementioned factors, betel nut exposure was the only variable which influenced BMI (Table 4.26). Participants who had quit and those who chewed <5 nuts per day had lower odds of having a BMI that was ≥25 kg/m^2. The number of years of chewing did not have an association with BMI being ≥25 kg/m^2. Neither vegetable and fruit consumption nor smoking had an

association with BMI. Those who did not consume alcohol were less likely to have a BMI ≥ 25 kg/m^2 but this did not reach statistical significance.

Table 4.26 Univariate logistic regression of lifestyle factors significantly associated with BMI.

Variable	Crude OR	95% CI	p-value
Betel nut exposure			0.028
Never	0.56	0.25-1.25	0.154
Quit	0.32	0.14-0.71	0.005
≤5 nuts/day	0.39	0.18-0.84	0.016
>5 nuts/day	1 (reference)		
Alcohol consumed in the previous three months			0.080
No	0.44	0.18-1.10	
Yes	1 (reference)		

The dependent variable was BMI ≥ 25 kg/m^2; BMI = body mass index

Multivariate logistic regression analysis was performed on both lifestyle and demographic factors, where each variable was dropped one at a time until those independently associated with BMI remained (backward elimination). As there was very little difference in the odds ratios associated with BMI among participants from the NGI and Momase regions, these two categories were combined to increase sample numbers.

In the regression model, betel nut exposure was used as a variable. Results indicated that region of origin appeared to be the most important factor influencing BMI (Table 4.27). Participants from the Highlands region were more likely to have a BMI ≥ 25 kg/m^2 compared to their counterparts from other regions. The odds of participants from the Highlands region having a BMI ≥ 25 kg/m^2 was seven times that of those from the Southern region. The odds of those from the NGI/Momase regions having a BMI ≥ 25 kg/m^2 was twice that of those from the Southern region, but this did not reach statistical significance. Age and betel nut exposure also had an independent significant influence on BMI. The odds of participants younger than

50 years and with less or no exposure to betel nut having a BMI ≥ 25 kg/m^2 appeared to be significantly lower than those who chewed >5 betel nuts per day (Table 4.27).

Table 4.27 Multivariate logistic regression analysis of demographic and lifestyle factors associated with BMI

Variable	n/N (%)*#	Adjusted OR	95% CI	p-value
Gender				0.086
Female	154/215 (71.6)	1.60	0.94-2.74	
Male	85/128 (66.4)	1 (reference)		
Age category (years)				0.044
<50	67/101 (66.3)	0.55	0.31-0.98	
≥50	160/222 (72.1)	1 (reference)		
Alcohol consumption in the previous three months				0.114
No	210/308 (68.2)	0.44	0.16-1.22	
Yes	29/35 (82.9)	1 (reference)		
Betel nut exposure				0.047
Never	62/86 (72.1)	0.44	0.18-1.05	0.063
Quit	41/69 (59.4)	0.30	0.12-0.72	0.007
≤5 nuts/day	67/104 (64.4)	0.38	0.17-0.85	0.018
>5 nuts/day	51/62 (82.3)	1 (reference)		
Region of origin				0.011
Southern	172/262 (65.6)	1 (reference)		
NGI/Momase	43/53 (81.1)	2.20	0.99-4.88	0.052
Highlands	24/28 (85.7)	7.03	1.51-32.71	0.013

The dependent variable was BMI ≥ 25 kg/m^2 ; *The column showing 'n/N (%)' shows the number of people (and percentage) within each variable with BMI ≥ 25 kg/m^2; #The total may not add up because of missing data; BMI = body mass index; NGI = New Guinea Islands

4.3.6.3 Waist circumference

Waist circumference was categorised into normal and above normal. The normal waist circumference used for females and males was ≤88cm and ≤102cm, respectively, based on the PNG Diabetes Clinical Guidelines 2012.

Two hundred and seventy (70.1%) participants had a higher than normal waist circumference (Table 4.18).

Univariate logistic regression analysis was carried out to determine which (if any) factors were associated with an abnormally high waist circumference and, also, to examine the direction of any associations.

It was not possible to use univariate logistic regression analysis using participants' area of residence because one of the cells for this variable had a sample number which was less than five. To increase the sample number, those participants from other provinces were regrouped into either "urban" or "rural village" depending on their residential addresses in the provinces where they were living. Those who lived in urban towns (n=6) were included in the urban category and those in rural villages (n=9) were included with the original rural village category.

Univariate logistic regression analysis indicated that the most important demographic variable which influenced waist circumference was gender. Female participants were nine times more likely to have an abnormally high waist circumference compared to their male counterparts, as shown in Table 4.28.

Employment also had a statistically significant influence on waist circumference but this was only significant in those who were unpaid/unemployed. The odds of unpaid/unemployed participants having an abnormally high waist circumference were two-fold higher when compared with those in paid employment. The odds of retirees and participants who were self-employed having an abnormally high waist circumference also appeared to be higher, but these did not reach statistical significance. Although area of residence was not a significant influence on waist circumference, the odds of participants who lived in peri-urban areas having an

abnormally high waist circumference was almost two-fold higher and this appeared to be statistically significant (p=0.044), as shown on Table 4.28.

As shown in Table 4.29, none of the lifestyle variables (other than physical activity) had an influence on waist circumference. When participants were categorised according to betel nut exposure, the odds of an abnormally high waist circumference being associated with betel nut exposure did not reach statistical significance. However, the odds of those who never chewed betel nut having an abnormally high waist circumference was significantly lower than those who chewed >5 betel nuts per day. Those who had consumed alcohol in the preceding three months, and those who had vegetables on 0-5 days per week also appeared to have lower odds of having an abnormally high waist circumference, but these associations did not reach statistical significance. Participants who were current smokers and those who had never smoked tended to have higher odds of having an abnormally high waist circumference but this, again, was not statistically significant.

Table 4.28 Univariate analysis of demographic factors associated with waist circumference

Variable	Crude OR	95% CI	p-value
Age category (years)			0.124
<50	0.65	0.37-1.16	
50-59	1.12	0.63-1.97	
≥60	1 (reference)		
Gender			p<0.001
Female	9.17	5.56-15.15	
Male	1 (reference)		
Level of Education			0.089
Did not complete basic education	1.90	0.93-3.91	0.079
Primary basic education	1.31	0.68-2.50	0.423
Secondary education	0.75	0.39-1.45	0.390
Vocational training	1.09	0.43-2.76	0.860
Tertiary education	1 (reference)		
Employment status			0.007
Paid	1 (reference		
Unpaid/unemployed	2.56	1.47-4.46	0.001
Retired	1.36	0.70-2.63	0.368
Self-employed	1.45	0.65-3.22	0.365
Area of residence			0.119
Urban	1 (reference)		
Peri-urban	1.89	1.02-3.51	0.044
Rural village	1.29	0.75-2.21	0.358

The dependent variable was waist circumference above normal. Normal waist circumference is ≤88cm (females) and ≤102cm (males); NGI = New Guinea Islands.

Table 4.29 Univariate analysis of lifestyle factors associated with waist circumference

Variable	Crude OR	95% CI	p-value
Betel nut exposure			0.131
Never	0.43	0.21-0.88	0.021
Quit	0.59	0.27-1.26	0.171
≤5 nuts/day	0.51	0.25-1.02	0.057
>5 nuts/day	1 (reference)		
Smoker history			0.133
Current	1.86	0.67-5.13	0.234
Never	1.65	0.99-2.73	0.053
Quit	1 (reference)		
Alcohol consumed in the preceding three months			0.167
No	1 (reference)		
Yes	0.62	0.31-1.23	
Number of vegetable days/week			0.051
0-5	0.64	0.41-1.00	
6-7	1 (reference)		

Waist circumference above normal was the dependent variable; PBI = *Piper betle* inflorescence; Normal waist circumference is ≤102 cm (male) and ≤88cm (female)

Work-related moderate-intensity activities and walking to get to and from places appeared to have an influence on waist circumference (Table 4.30). Those who did work-related MIA were more likely, and those who did not walk were less likely, to have an abnormally high waist circumference. Those who did VIA for <75 minutes per week were twice as likely to have an abnormally high waist circumference compared to those who did ≥75 minutes per week, but this did not reach statistical significance. The impact of the amount of physical activity on waist circumference was only seen when comparing those who were insufficiently physically active with those who were not engaged in any physical activity. Surprisingly, the latter was less likely to have an abnormally high waist circumference compared to the former.

Multivariate logistic regression analysis was performed on both lifestyle and demographic factors, where each variable was dropped one at a time until those independently associated with BMI remained (backward elimination). Level of education was regrouped to increase sample numbers, so that the vocational and tertiary education categories were combined to form one category. Participants within these two categories are more likely to be employed than those with lower attainment levels.

As shown in Table 4.31, the logistic regression model indicated that the most important independent factor which influenced waist circumference was gender. Female participants were 13-fold more likely to have a waist circumference above normal, compared to their male counterparts. Although the association of age with waist circumference did not reach statistical significance, the odds of those aged <50 years having an abnormally high waist circumference appeared to be lower when compared with their counterparts who were 60 years and older. Level of education was associated with waist circumference. The odds of an abnormally high waist circumference were lower for participants who had completed basic primary and secondary education only. This association was statistically significant. The association of betel nut exposure and waist circumference was of borderline significance but those who chewed ≤5 nuts per day and those who never chewed betel nut had lower odds of an abnormally high waist circumference, and this was statistically significant (p=0.017 and p=0.012, respectively). None of the physical activity characteristics were independently associated with waist circumference.

Table 4.30 Univariate analysis of physical activity associated with waist circumference.

Variable	Crude OR	95% CI	p-value
Amount of physical activity			0.098
Sufficient	0.74	0.43-1.29	0.289
Lacking	0.46	0.22-0.94	0.032
Insufficient	1 (reference)		
Work-related VIA for at least 10 minutes			0.091
No	1 (reference)		
Yes	0.60	0.33-1.09	
Minutes of work-related VIA/week			0.265
<75	2.02	0.59-6.97	
≥75	1 (reference)		
Performs VISFRA for at least 10 minutes			0.722
No	1 (reference)		
Yes	0.87	0.41-1.85	
Minutes of VISFRA/week			0.261
<75	2.44	0.51-11.62	
≥75	1 (reference)		
Work-related MIA for at least 10 minutes			0.032
No	1 (reference)		
Yes	1.65	1.04-2.60	
Minutes of MIA at work/week			0.552
<150	0.80	0.38-1.69	
≥150	1 (reference)		
Performs MISFRA for at least 10 minutes			0.266
No	1 (reference)		
Yes	0.73	0.42-1.27	
Minutes of MISFRA/week			0.247
<150	0.48	0.14-1.67	
≥150	1 (reference)		
Walks to get to and from places for at least 10 minutes			0.037
No	0.59	0.36-0.97	
Yes	1 (reference)		
Minutes of walking/week			0.060
<150	1.68	0.98-2.88	
≥150	1 (reference)		

The dependent variable was waist circumference "above normal". Normal waist circumference is 88cm (females) and 102cm (males); VIA = vigorous-intensity activity; MIA = moderate-intensity activity; VISFRA = vigorous-intensity sports, fitness and recreational activity; MISFRA = moderate-intensity sports, fitness and recreational activity

Table 4.31 Multivariate logistic regression analysis of demographic and lifestyle factors associated with waist circumference.

Variable	n/N (%)*#	Adjusted OR	95% CI	p-value
Gender				<0.001
Female	209/241 (86.7)	1 (reference)		
Male	61/144 (42.4)	0.07	0.03-0.15	
Age category (years)				0.058
<50	72/113 (63.7)	0.49	0.24-1.03	
≥50	186/251 (74.1)	1 (reference)		
Level of Education				0.027
Did not complete basic education	70/88 (79.5)	1.08	0.37-3.16	0.889
Primary basic education	80/110 (72.7)	0.35	0.13-0.91	0.032
Secondary education	52/86 (60.5)	0.33	0.13-0.86	0.024
Tertiary/Vocational	67/99 (67.7)	1 (reference)		
Betel nut exposure				0.066
Never	60/95 (63.2)	0.26	0.09-0.78	0.017
Quit	54/54 (70.1)	0.36	0.11-1.17	0.089
≤5 nuts/day	79/118 (66.9)	0.25	0.09-0.73	0.012
>5 nuts/day	56/70 (80.0)	1 (reference)		

The analysis used betel nut exposure as a variable. The dependent variable was waist circumference above normal. Normal waist circumference is 88cm (females) and 102cm (males); *The column showing 'n/N (%)' shows the number of people (and percentage) within each variable with waist circumference above normal; #The total may not add up because of missing data.

4.3.7 Biochemical measurements

Biochemical measurements of participants included capillary blood glucose levels, total cholesterol, triglycerides, HbA1c, urine protein and glucose, and urea and creatinine levels.

Of all the biochemical measurements, CBG and HbA1c were measured on the day of the visit. Hospital outpatient toilet facilities were closed during the periods of data collection, so urine and protein measurements were not possible on the day of data collection. Thirty one patients (8.1%) agreed to collect urine the next morning and dropped off samples at the Diabetes Clinic for measurement of urine glucose and protein.

The most recent lipid profiles of nearly all participants were not available for data collection. Only a few records were found. Of all lipid profiles, no LDL measurements were found, whilst only one, 12 and 15 records of HDL, triglycerides and total cholesterol were included, respectively. Urea and creatinine measurements were only available for 20 and 19 participants, respectively (Table 4.32).

It is assumed that patients fasted before capillary blood testing on the day of their diabetes review, as per the protocol; however it was found that not all patients fasted before CBG testing. During the course of the study, a decision was made to also interview participants about whether their CBG was a random or fasting level after it was observed that many participants had very high CBG readings. Of all the participants, 147 (38.2%) had a fasting level and 150 (39%) had a random level (Table 4.30). The remaining 83 (21.6%) participants' CBG were categorised as unknown because this was the group of participants whose CBG was assumed to be fasting but may have also included those who did not fast. Records of CBG for five participants were missing and these were excluded in any analysis using CBG.

Table 4.32 Biochemical data of participants

Variable	Frequency; n/N (%)*
CBG	
Fasting	147/385 (38.1)
Random	150/385 (39.0)
Unknown	83/385 (21.5)
Glycated haemoglobin [HbA1c (%)]	
≤7.0	73/385 (19.0)
7.0-10.0	173/385 (44.9)
>10.0	116/385 (30.1)
Lipids	
Total cholesterol (data available)	15/385 (3.9)
≤5.0mmol/L	3/15 (20.0)
>5.0	12/15 (80.0)
Triglycerides (data available)	12/385 (3.1)
<2.0	3/12 (25.0)
≥2.0	9/12 (75.0)
LDL	0/385 (0)
HDL	1/385 (0.3)
Urea (mmol/L)	
≤7.1	12/20 (60.0)
>7.1	8/20 (40.0)
Creatinine (µmol/L)	
62-133	14/19 (73.7)
>133	5/19 (26.3)
Urine Glucose	
Negative	21/32 (65.6)
Trace	3/32 (9.4)
2+	4/32 (12.5)
3+	1/32 (3.1)
4+	2/32 (6.3)
Urine Protein	
Negative	2/32 (6.3)
Trace	9/32 (28.1)
1+	10/32 (31.3)
2+	3/32 (9.4)
3+	3/32 (9.4)
4+	5/32 (15.6)

LDL = low density lipoprotein; HDL = high density lipoprotein; CBG = capillary blood glucose;
*May not add up to total because of missing values

4.3.8 Betel nut chewing

Betel nut chewers, like tobacco smokers, were further categorised according to their betel nut chewing status (current, never and quit), as well as whether they were ever (both current and those who had quit) or never chewers. The number of years of chewing betel nut also was calculated and participants were categorised according to these numbers of years. The age of onset of chewing for both current chewers and those who had ceased chewing, and the number of years since cessation of betel nut chewing, were not normally distributed and are presented as median and range.

4.3.8.1 Prevalence of betel nut chewing

Of the 385 participants studied, 55% (212) reported that they were currently chewing betel nut. Ninety six (24.9%) participants had never chewed betel nut, while 77 (20.0%) had quit chewing betel nut. Overall, of all the participants studied, 289 (75.1%) had chewed betel nut at some time in their lives (Table 4.33).

As shown in Table 4.33, for those classified as current betel nut chewers, the median age for onset of chewing betel nut was 15 years (range: 4-59 years). The mean number of years of chewing betel nut was 37.2±13.0 years. The median quantity of betel nut chewed per day was 4.0 (range: 0.25-25.0).

For participants who had quit the habit, the median age for onset of chewing was 15.5 years (range: 3.0-52.0 years). The median number of years of cessation of betel nut chewing was 9.0 (range: 0.08-46.0).

The majority of participants in this study chewed betel nut with lime (calcium oxide) and *Piper betle* inflorescence (PBI). Of the 212 participants who reported chewing betel nut, 177(83.5%) chewed the nut with lime and with PBI. There were 22 (10.4%) who chewed the nut only and 12 (5.7%) who chewed the nut with PBI but without lime. Betel nut chewing variables are shown in Table 4.33.

Table 4.33 Frequencies of betel nut chewing characteristics

Variables	Frequency* n/N(%)
Betel nut chewer	
No	173/385 (44.9)
Yes	212/385 (55.1)
No. of betel nuts/day	
≤5	118/212 (55.7)
6-9	31/212 (14.6)
≥10	39/212 (18.4)
Betel nut chewing history	
Never	96/385 (24.9)
Quit	77/385 (20.0)
Current	212/385 (55.1)
Number of years of chewing betel nut	
≤25	25/212 (11.8)
26-49	119/212 (56.1)
≥50	25/212 (11.8)
Betel nut chewing components	
Betel nut only or + PBI with no lime	34/212 (16.0)
Betel nut + PBI + lime	177/212 (83.5)
Mean number of years of chewing ±SD	37.2±13.0
Age at onset of chewing for current betel nut chewers [median (range)]	15.0 (4.0-59.0)
Age at onset of chewing for those who quit betel nut chewing [median (range)]	15.5 (3.0-52.0)
No. of years since betel nut cessation for those who quit [median (range)]	9.0 (0.08-46.0)
No. of betel nuts chewed/day [median (range)]	4.0 (0.25-25.0)

*****May not add up to the total because of missing values; PBI = *Piper betle* inflorescence; SD = standard deviation

Age, the level of education and employment status were regrouped for logistic regression analysis because some of the categories had small sample numbers. Age was regrouped into three categories only. Level of education was categorised according to the former education structures in PNG, as the participants were too old with respect to the current education restructure. Employment status was regrouped to reflect financial income. Homemakers and students were reclassified as unpaid, and unpaid and unemployed were combined into one category. Government and non-government employees were combined under paid employment and categories of retirees and self-employed were retained. These categories were used when examining the relationships between the prevalence of betel nut chewing and these demographic factors.

The statistical process was chi-square testing, univariate logistic regression and then multivariate logistic regression.

4.3.8.2 Factors associated with betel nut chewing: Chi-Square testing

Chi-square statistical analysis was carried out to test for any associations between betel nut chewing and the demographic characteristics of participants such as gender, age, area of residence, level of education, region of origin, employment status and years of residence in Port Moresby.

According to the Chi-square statistic, the demographic factors influencing prevalence of betel nut chewing were the participant's area of residence, region of origin, years of residence in Port Moresby and level of education (Table 4.36). Age tended to be a factor but did not reach statistical significance. There were no differences in the prevalence of betel nut chewing between genders and different types of employment. Rural village and peri-urban dwellers were more likely to chew betel nut than those who resided in the urban suburbs, as well as those who were not residing in Port Moresby ($p<0.001$). Those who originated from the Southern region of PNG had a higher prevalence of betel nut chewing than those from the NGI, Momase and Highlands regions, as shown in Table 4.34.

Chi square analysis indicated that alcohol consumption, smoking, work-related MIA and amount of physical activity in a week were significantly associated with betel nut chewing, while the association of number of vegetable servings consumed, work-related VIA and walking to get to and from places with betel nut chewing was of borderline significance (Table 4.35). Smokers, alcohol consumers and those consuming <3 serves of vegetables in a day were more likely to be betel nut chewers. Betel nut chewers were more likely to perform work-related VIA and MIA, to walk to get to and from places and to undertake sufficient amount of physical activity in a week, compared to their counterparts.

Table 4.34 Association of demographic variables with betel nut chewing

Variable	Betel nut chewer		p-value*
	Yes (N [%])	No (N [%])	
Gender			0.123
Female	140 (58.1)	101 (41.9)	
Male	72 (50.0)	72 (50.0)	
Age category (years)			0.052
≤39	15 (62.5)	9 (37.5)	
40-49	56 (62.9)	33 (37.5)	
50-59	83 (56.8)	63 (43.2)	
60-69	44 (51.2)	42 (48.8)	
≥70	6 (28.6)	15 (71.4)	
Area of residence			<0.001
Urban	90 (42.5)	122 (57.5)	
Peri-urban	54 (70.1)	23 (29.9)	
Rural	60 (75.0)	20 (25.0)	
Other province	7 (46.7)	8 (53.3)	
Level of education			0.015
No formal education	11 (28.2)	28 (71.8)	
Less than Grade 6	25 (51.0)	24 (49.0)	
Grade 6	38 (53.5)	33 (46.5)	
Grade 8	28 (70.0)	12 (30.0)	
Grade 10	45 (60.8)	29 (39.2)	
Grade 12	6 (50.0)	6 (50.0)	
Vocational training	18 (62.1)	11 (37.9)	
Tertiary	41 (58.6)	29 (41.4)	
Employment status			0.822§
Unemployed - unable to work	14 (56.0)	11 (44.0)	
Unemployed - able to work	18 (52.9)	16 (47.1)	
Unpaid	5 (62.5)	3 (37.5)	
Homemaker	74 (59.2)	51 (40.8)	
Self-employed	23 (59.0)	16 (41.0)	
Government	26 (55.3)	21 (44.7)	
Non-government	19 (55.9)	15 (44.1)	
Retired	32 (45.7)	38 (54.3)	
Student	2 (66.7)	1 (33.3)	
Region of origin			<0.001
Southern	183 (62.2)	111 (37.8)	
Momase	7 (26.6)	19 (73.1)	
Highlands	6 (20.7)	23 (79.3)	
New Guinea islands	16 (44.4)	20 (55.6)	
Years of residence in Port Moresby			<0.001
0#	68 (70.1)	29 (29.9)	
1-10	9 (32.1)	19 (67.9)	
>10	68 (42.8)	91 (57.2)	
Lifetime	55 (69.6)	24 (30.4)	

*The p-values were obtained from the Chi-square statistic, and assess the strength of association; §Fisher's exact test

Table 4.35 Lifestyle factors associated with betel nut chewing

Variable	Betel nut chewer		p-value[#]
	Yes (N [%])	No (N [%])	
Alcohol consumed in the previous three months			<0.001
No	179 (51.6)	168 (48.4)	
Yes	33 (86.8)	5 (13.2)	
Current smoker			0.001
No	191 (52.9)	170 (47.1)	
Yes	21 (87.5)	3 (12.5)	
Vegetable servings/day			0.086
<3	199 (56.1)	156 (43.9)	
≥3	11 (39.3)	17 (60.7)	
Number of vegetable-eating days in a typical week			0.987
0-2	52 (54.2)	44 (45.8)	
3-5	68 (54.8)	56 (45.2)	
6-7	90 (55.2)	73 (44.8)	
Fruit servings/day			0.418
<2	145 (53.5)	126 (46.5)	
≥2	65 (58.0)	47 (42.0)	
Number of fruit-eating days in a typical week			0.414
0-2	144 (52.9)	128 (47.1)	
3-5	40 (57.1)	30 (42.9)	
6-7	26 (63.4)	15 (36.6)	
Work-related VIA for at least 10 minutes			0.084
No	177 (53.3)	155 (46.7)	
Yes	35 (66.0)	18 (34.0)	
Work-related MIA for at least 10 minutes			0.001
No	108 (48.0)	117 (52.0)	
Yes	104 (65.0)	56 (35.0)	
Performs MISFRA for at least 10 minutes			0.339
No	171 (53.9)	146 (46.1)	
Yes	41 (60.3)	27 (39.7)	
Walks to get to and from places for at least 10 minutes			0.089
No	42 (47.2	47 (52.8)	
Yes	170 (57.4)	126 (42.6)	
Amount of physical activity/week			0.011
Sufficient	141 (60.3)	93 (39.7)	
None/insufficient	71 (47.0)	80 (53.0)	

[#]The p-values were obtained from the Chi-square statistic, and assess the strength of association; VIA = vigorous-intensity activity; MIA = moderate-intensity activity; MISFRA = moderate-intensity sports, fitness and recreational activity; VISFRA = vigorous-intensity sports, fitness and recreational activity

4.3.8.3 Factors associated with betel nut chewing: univariate logistic regression analysis

The odds of betel nut chewing within each category defined by age group, area of residence, level of education and region of origin were compared using univariate logistic regression. Those variables which were found to show some association were entered into a (univariate) logistic regression model to investigate the direction of associations for different categories of demographic factors. Comparisons were performed for variables that had a statistically significant relationship using chi-square testing.

The odds of those living in rural villages and peri-urban areas chewing betel nut were four-fold and three-fold higher, compared to their urban counterparts, respectively. Participants from the Southern region were most likely to chew betel nut compared to those from the Highlands region. Participants from the Southern region and those from the NGI were six-fold and three-fold more likely, respectively, to chew betel nut when compared to their counterparts from the Highlands region. Although participants from the Momase region appeared to be more likely to chew betel nut when compared with those from the Highlands region, this did not reach statistical significance. There was no difference in prevalence of betel nut chewing between those who were not living in Port Moresby and those who had spent their lifetime there. Level of education and age were less important factors, although those less than 50 years of age were, significantly, almost twice as likely to consume betel nut when compared with those ≥60 years of age. With respect to level of education, participants who did not complete basic education were significantly less likely to chew betel nut compared to those who had completed tertiary education (Table 4.36).

As shown in Table 4.37, alcohol consumers and smokers were six times more likely to chew betel nut compared to those who did not; an association which was statistically significant. Betel nut chewers were almost two times more likely to consume <3 servings of vegetables compared to those who were not chewers, but this was of borderline significance.

Table 4.36 Univariate logistic regression analysis of demographic factors associated with betel nut chewing

Variable	Crude OR	95% CI	p-value
Age category (years)			0.052
<50	1.93	1.13-3.30	0.017
50-59	1.53	0.92-2.52	0.099
≥60	1 (reference)		
Area of residence			P<0.001
Urban	1 (reference)		
Peri-urban	3.18	1.82-5.57	P<0.001
Rural village	4.07	2.29-7.23	P<0.001
Other Province	1.19	0.42-3.39	0.750
Region of origin			P<0.001
Southern	6.32	2.50-16.00	P<0.001
New Guinea islands	3.07	1.01-9.34	0.049
Momase	1.41	0.41-4.92	0.588
Highlands	1 (reference)		
Level of education			0.053
Did not complete basic education	0.49	0.26-0.93	0.028
Primary basic education	1.04	0.57-1.91	0.906
Secondary education	1.03	0.54-1.96	0.926
Vocational training	1.16	0.48-2.81	0.747
Tertiary education	1 (reference)		
Years of residence in Port Moresby			P<0.001
0[#]	1.02	0.54-1.95	0.945
1-10	0.21	0.08-0.52	0.001
>10	0.33	0.18-0.58	P<0.001
Lifetime	1 (reference)		

The dependent variable was 'Yes' to being a betel nut chewer; [#]Participant does not reside in Port Moresby

Table 4.37 Univariate logistic regression analysis of lifestyle factors associated with betel nut chewing

Variable	Crude OR	95% CI	p-value
Alcohol consumed in the previous three months			<0.001
No	1 (reference)		
Yes	6.19	2.36 – 16.24	
Current smoker			0.003
No	1 (reference)		
Yes	6.23	1.83 – 21.26	
Vegetable servings/day			0.091
<3	1.97	0.90 – 4.33	
≥3	1 (reference)		
Work-related VIA for at least 10 minutes			0.086
No	1 (reference)		
Yes	1.70	0.93 – 3.13	
Work-related MIA for at least 10 minutes			0.001
No	1 (reference)		
Yes	2.01	1.33 – 3.05	
Walk to get to and from places for at least 10 minutes			0.090
No	1 (reference)		
Yes	1.51	0.94 – 2.43	
Amount of Physical activity/week			0.011
Sufficient	1.71	1.13 – 2.58	
None/insufficient	1 (reference)		

The dependent variable was 'Yes' to being a betel nut chewer; VIA = vigorous-intensity activity; MIA = moderate-intensity activity

4.3.8.4 Factors associated with betel nut chewing: multivariate logistic regression analysis

A logistic regression modelling procedure was applied to all the data for demographic characteristics. In each of these models, all the variables were initially included as covariates, and then dropped one at a time until all variables remaining in the model were associated with the prevalence of betel nut chewing (backward regression). The dependent variable was the "yes" response when the participants were asked whether or not they were betel nut chewers.

Results of logistic regression modelling (multivariate) indicated that the three major factors which were independently associated with the prevalence of betel nut chewing were age, area of residence and region of origin (Table 4.38).

The odds of participants younger than 60 years of age chewing betel nut was twice that of those who were 60 years or older. Those aged <50 years had almost three times the odds of chewing betel nut compared to their counterparts who were 60 years or older. The analysis also showed that participants from the Southern region were five times more likely to chew betel nut than those from the Highlands region. Betel nut chewing was significantly more prevalent in the rural village dwellers ($p<0.001$). Rural village dwellers and peri-urban dwellers were four and two times more likely to chew betel nut, respectively, than their counterparts in urban areas. Level of education also tended to have an independent significant influence on betel nut chewing, but this was a less important factor than age, area of residence and region of origin. The odds of participants who did not complete basic education chewing betel nut were significantly lower compared to those who had completed tertiary education and this association was statistically significant (Adjusted OR = 0.303, 95% CI=0.133-0.689, p=0.004).

In the univariate logistic regression, years of residence in Port Moresby was one of the most important factors which influenced betel nut chewing. This variable however, was not independently associated with betel nut chewing, possibly because of its correlation with area of residence and region of origin. Those who had resided for zero years in Port Moresby were those who were rural village and outer province dwellers, whilst those who had spent their lifetime in Port Moresby were from the Southern region.

Table 4.38 Multivariate logistic regression of factors independently associated with betel nut chewing.

Variable	"Yes" betel nut chewer n/N (%)*	Adjusted Odds Ratio	95% CI	p-value
Age category (years)				0.028
<50	71/113(62.8)	2.14	1.13-4.06	0.019
50-59	83/145 (57.2)	2.00	1.12-3.54	0.018
≥60	50/107 (46.7)	1 (reference)		
Area of residence				<0.001
Peri-urban	54/77 (70.1)	3.24	1.72-6.11	<0.001
Rural village	60/80 (75.0)	3.16	1.63-6.13	0.001
Other Province	7/15 (46.7)	1.65	0.50-5.50	0.415
Urban	90/212 (42.5)	1 (reference)		
Region of origin				0.001
Southern	183/294 (62.2)	6.32	2.07-19.26	0.001
New Guinea Islands	16/36 (44.4)	3.52	0.94-13.17	0.062
Momase	7/26 (26.9)	1.60	0.38 -6.72	0.525
Highlands	6/29 (20.7)	1 (reference)		
Alcohol consumed in the previous three months				0.001
No	179/347 (51.6)	1 (reference)		
Yes	33/38 (86.8)	6.36	2.11-19.14	
Current smoker				0.084
No	191/361 (52.9)	1 (reference)		
Yes	21/24 (87.5)	3.30	0.85-12.76	
Work-related MIA for at least 10 minutes				0.009
No	108/225 (48.0)	1 (reference)		
Yes	104/160 (65.0)	1.92	1.18– 3.12	

The dependent variable was "Yes" to being a betel nut chewer; *The column showing 'n/N (%)' shows the number (and percentage) of betel nut chewers within each variable; MIA = moderate-intensity activity

4.3.9 Factors influencing glycaemic control

Optimal glycaemic control was defined according to the PNG Diabetes Clinical Guidelines 2012; that is, HbA1c ≤ 7.0%. Consequently, poor glycaemic control was defined as HbA1c > 7.0. The Chi-square statistic was used to test for any association between optimal glycaemic control and the demographic, medical and lifestyle factors (categorical variables). Those variables which were found to show some association were entered into a (univariate) logistic regression model to investigate the direction of the associations for different categories of each variable. Variables which appeared to show even a weak association with glycaemic control on univariate analysis with $p<0.5$ were included in a multivariate logistic regression model to identify which (if any) of these variables were independently associated with glycaemic control. A backwards elimination strategy was used to find the most parsimonious model, whereby all independent variables were initially included in the model, and then the least significant was dropped, one at a time, until all variables remaining in the model were statistically significantly associated with optimal glycaemic control ($p<0.05$). Regrouping of categories of some variables was performed as required (if the numbers were too small in some categories). Variables which contained categories with very small sample numbers (< 5) and which could not be re-grouped, were excluded from logistic regression modelling. A final multivariate logistic regression analysis was performed (as described above) including variables from all of the three main groups of factors. The results of the final analysis showed all variables which appeared to be independently associated with glycaemic control [from all the demographic, medical (including physical measurements) and lifestyle factors taken together].

4.3.9.1 Univariate and multivariate analysis of demographic factors associated with poor glycaemic control

Demographic variables included in the analyses included gender, age, level of education, employment status, area of residency, region of origin and years of residency in Port Moresby.

The median HbA1c for all participants was 9.15% (Table 4.39). Results showed that the median HbA1c within each category of the demographic variables at the time of enrolment was higher than the recommended optimal target of ≤7.0% (Table 4.39).

Table 4.39 Median and range values of HbA1c at time of enrolment in the study

Variable	n/N* (%)	Median HbA1c (%)	HbA1c Range (%)
All participants	362/385 (94.0)	8.7	4.8 - >14.0
Gender			
Female	228/241 (94.6)	8.7	5.0 - >14.0
Male	134/144 (93.1)	8.5	4.8 - >14.0
Age category (years)			
<50	107/113 (94.7)	9.1	5.2 - >14.0
50-59	135/145 (93.1)	8.4	5.0 - >14.0
≥60	102/107 (95.3)	8.3	4.8 - 14.0
Level of education			
Did not complete basic education	81/88 (92.0)	8.5	4.9 - >14.0
Primary basic education	105/111 (94.6)	8.5	5.2 - >14.0
Secondary education	83/86 (96.5)	9.1	5.5 - >14.0
Vocational training	27/29 (93.1)	8.4	5.9 - 14.0
Tertiary education	65/70 (92.9)	8.7	4.8 - >14.0
Employment status			
Paid employment	76/81 (93.8)	9.4	5.9 - >14.0
Unpaid/unemployed	184/195 (94.4)	8.5	4.9 - >14.0
Retired	66/70 (94.3)	7.9	4.8 - >14.0
Self-employed	36/39 (92.3)	9.3	5.5 - 14.0
Area of residence			
Urban	199/212 (93.9)	8.5	4.8 - >14.0
Peri-urban	73/77 (94.8)	8.5	5.4 - >14.0
Rural	74/80 (92.5)	8.9	5.5 - 14.0
Other Province	15/15 (100.0)	7.3	5.2 - >14.0
Region of origin			
Southern	275/294 (93.5)	8.8	4.9 - >14.0
New Guinea Islands	35/36 (97.2)	9.0	4.8 - >14.0
Momase	24/26 (92.3)	7.9	6.0 - 12.6
Highlands	28/29 (96.6)	8.4	5.5 - 13.2
Years of residence in Port Moresby			
0[#]	92/97 (94.9)	8.9	5.2 - >14.0
1-10	26/28 (92.9)	8.4	4.8 - >14.0
>10	150/159 (94.3)	8.5	4.9 - >14.0
Lifetime	72/79 (91.1)	8.3	5.4 - >14.0

*The column n/N (%) represents the number of participants and % within each category whose HbA1c was measured at the time of enrolment; HbA1c = glycated haemoglobin; [#]Participant does not reside in Port Moresby

Results from Chi-square testing indicated that gender, age and employment status had a statistically significant association with glycaemic control (Table 4.40). Female participants appeared to have poor glycaemic control compared to their male counterparts. Younger participants (<50 years) and those who were self-employed also appeared to have poorer glycaemic control. Area of residence, region of origin, level of education and years of residence in Port Moresby did not have any statistically significant association with glycaemic control.

Table 4.40 Demographic factors associated with poor glycaemic control (HbA1c > 7.0%).

Variable	HbA1c categories		
	≤7.0 (N [%])	>7.0(N [%])	p-value*
Gender			0.03
Female	38 (16.7)	190 (83.3)	
Male	35 (26.1)	99 (73.9)	
Age category (years)			0.026
<50	13 (12.1)	94 (87.9)	
50-59	31 (23.0)	104 (77.0)	
≥60	27 (26.5)	75 (73.5)	
Level of education			0.348
Did not complete basic education	20 (24.7)	61 (75.3)	
Primary basic education	17 (16.2)	88 (83.8)	
Secondary education	13 (15.7)	70 (84.3)	
Vocational training	7 (25.9)	20 (74.1)	
Tertiary education	16 (24.6)	49 (75.4)	
Employment status			0.037
Paid	11 (14.5)	65 (85.5)	
Unpaid/unemployed	35 (19.0)	149 (81.0)	
Retired	22 (33.3)	44 (66.7)	
Self-employed	5 (13.9)	31 (86.1)	
Area of residence			0.218
Urban	41 (20.6)	158 (79.4)	
Peri-urban	14 (19.2)	59 (80.8)	
Rural village	12 (16.2)	62 (83.8)	
Other Province	6 (40.0)	9 (60.0)	
Region of Origin			0.248
Southern	56 (20.4)	219 (79.6)	
New Guinea Islands	5 (14.3)	30 (85.7)	
Momase	3 (12.5)	21 (87.5)	
Highlands	9 (32.1)	19 (67.9)	
Years of residence in Port Moresby			0.924
0#	18 (19.6)	74 (80.4)	
1-10	6 (23.1)	20 (76.9)	
>10	32 (21.3)	118 (78.7)	
Lifetime	13 (18.1)	59 (81.9)	

*The p-values were obtained from the Chi-square statistic, and assess the strength of association; #Participant does not reside in Port Moresby

Univariate logistic regression confirmed the significant association between optimal glycaemic control and age, gender and employment status (Table 4.41), while also providing the direction of associations. Younger participants (<50 years) were 2.6 times as likely to have poor glycaemic control compared to those aged 60 years and older. The odds ratio of female participants having poor glycaemic control was almost twice that of their male counterparts. Retirees were most likely to have better glycaemic control compared to those who were self-employed, and the difference in glycaemic control between these groups was statistically significant. However, there was no statistically significant difference in risk when comparing other categories (paid and unpaid/unemployed) with the self-employed.

Table 4.41 Univariate logistic regression analysis of demographic factors associated with poor glycaemic control (HbA1c>7.0%)

Variable	Crude OR	95% CI	p-value
Gender			
Female	1.77	1.05-2.97	0.032
Male	1 (reference)		
Age category (years)			0.03
<50	2.60	1.26-5.39	0.010
50-59	1.21	0.67-2.19	0.534
≥60	1 (reference)		
Employment status			0.026
Paid	0.95	0.31-2.98	0.934
Unpaid/unemployed	0.69	0.25-1.89	0.467
Retired	0.32	0.11-0.95	0.039
Self-employed	1 (reference)		

The dependent variable was HbA1c>7.0%. HbA1c = glycated haemoglobin

A multiple logistic regression analysis involving only the demographic variables indicated that employment status and gender were independently associated with glycaemic control (Table 4.42) and, therefore, other factors did not appear to make a significant contribution to the model after these two were taken into account.

Female participants had twice the risk of having poor glycaemic control, and retirees had a lower risk of having poor glycaemic control (more likely to have optimal control) than those who were self-employed. Although the odds of poor glycaemic control for those aged 49 years or younger appeared to be almost twice that for the older group, this did not reach statistical significance. This was almost certainly because of the correlation between age group and employment status (Table 4.42).

Table 4.42 Multivariate logistic regression analysis of demographic factors independently associated with poor glycaemic control (HbA1c > 7.0%)

Variable	n/N(%)*	Adjusted OR	95% CI	p-value
Gender				0.022
Female	190 (83.3)	2.04	1.05-2.97	
Male	99 (73.9)	1 (reference)		
Age category (years)				0.256
<50	94 (87.9)	1.80	0.80-4.02	0.154
50-59	104 (77.0)	1.00	0.53-1.87	0.991
≥60	75 (73.5)	1 (reference)		
Employment status				0.023
Paid	65 (85.5)	0.78	0.23-2.68	0.695
Unpaid/unemployed	149 (81.0)	0.39	0.12-1.26	0.117
Retired	44 (66.7)	0.26	0.08-0.83	0.023
Self-employed	31 (86.1)	1 (reference)		

The dependent variable was HbA1c > 7.0%; HbA1c = glycated haemoglobin; *The column showing 'n/N (%)' shows the number of people (and percentage) within each variable with poor glycaemic control (HbA1c > 7.0).

4.3.9.2 Univariate and multivariate analysis of lifestyle factors associated with poor glycaemic control

Lifestyle factors included betel nut chewing, vegetable and fruit consumption, smoking, alcohol consumption and physical activity.

Of these lifestyle factors, the only one which appeared to show an association with glycaemic control was smoking status (Table 4.43). A statistically significant association appeared between those who had ever smoked (both current smokers and those who had quit) and never smoked. A greater proportion of those who had never smoked appeared to have poor glycaemic control compared to their counterparts who had ever smoked. The number of vegetable-eating days in a typical week appeared to be associated with glycaemic control but this was of borderline significance.

Table 4.43 Association of alcohol, vegetable and fruit consumption, and tobacco smoking with poor glycaemic control (HbA1c > 7.0%)

Variable	HbA1c categories		p-value[#]
	≤7.0 (N [%])	>7.0 (N [%])	
Alcohol consumption in the previous three months			0.746
No	65 (19.9)	261 (80.1)	
Yes	8 (22.2)	28 (77.8)	
Vegetable servings/day			0.813
<3 serves	65 (19.6)	267 (80.4)	
≥3 serves	6 (21.4)	22 (78.6)	
Number of vegetable-eating days in a typical week			0.074
0-2	16 (17.6)	75 (82.4)	
3-5	16 (14.2)	97 (85.8)	
6-7	39 (25.0)	117 (75.0)	
Fruit servings/day			0.435
<2 serves	47 (18.7)	205 (81.3)	
≥2 serves	24 (22.2)	84 (77.8)	
Number of fruit-eating days in a typical week			0.307
0-2	55 (21.7)	198 (78.3)	
3-5	11 (16.2)	57 (83.8)	
6-7	5 (12.8)	34 (87.2)	
Current smoker			0.465
No	67 (19.8)	272 (80.2)	
Yes	6 (26.1)	17 (73.9)	
Smoker status			0.134
Current smoker	6 (26.1)	17 (73.9)	
Never a smoker	44 (17.4)	209 (82.6)	
Quit	23 (26.7)	63 (73.3)	
Smoker history			0.045
Ever	29 (26.6)	80 (73.4)	
Never	44 (17.4)	209 (82.6)	

[#]The p-values were obtained from the Chi-square statistic, and assess the strength of association

Betel nut chewing was assessed in different ways. Whether or not a participant was a betel nut chewer did not affect glycaemic control. As shown in Table 4.44, Chi-square testing indicated that betel nut chewing was significantly associated with glycaemic control only when participants were categorised according to their betel nut chewing history. A greater proportion of those who never chewed betel nut had poor glycaemic control compared to those who had ever done so (current chewers

and those who had quit). However, for those classified as betel nut chewers, the quantity of betel nuts chewed per day and number of years of chewing betel nut did not appear to be associated with glycaemic control. The accompaniments with which betel nut was chewed also did not influence glycaemic control.

Table 4.44 Association of betel nut chewing with poor glycaemic control (HbA1c > 7.0%).

Variable	HbA1c categories		
	≤7.0 (N [%])	>7.0 (N [%])	p-value[#]
Betel nut chewer			0.973
No	33 (20.2)	130 (79.8)	
Yes	40 (20.1)	159 (79.9)	
Betel nut chewing history			0.012
Current chewer	40 (20.1)	159 (79.9)	
Never a chewer	10 (11.5)	77 (88.5)	
Quit	23 (30.3)	53 (69.7)	
Betel nut chewing status			0.021
Never	10 (11.5)	77 (88.5)	
Ever	63 (22.9)	212 (77.1)	
Quantity of betel nuts chewed/day			0.297
≤ 5	25 (22.5)	86 (77.5)	
6-9	3 (10.0)	27 (90.0)	
≥10	8 (22.9)	27 (77.1)	
Number of years of betel nut chewing			0.550*
≤25	2 (9.1)	20 (90.9)	
26-49	21 (19.1)	89 (80.9)	
≥50	5 (20.0)	20 (80.0)	
Composition of betel nut chew			0.862
Betel nut + PBI + Lime	34 (20.0)	136 (80.0)	
Betel nut only, or with PBI (no lime)	6 (21.4)	22 (78.6)	

[#]The p-values were obtained from the Chi-square statistic, and assess the strength of association. *Fisher's Exact Test; HbA1c = glycated haemoglobin; PBI = *Piper betle* inflorescence

The number of participants who were involved in sports, fitness and recreational activities was small, as has been demonstrated earlier in Table 4.8. When these active participants were categorised according to whether or not they achieved optimal or poor glycaemic control, the number of those achieving optimal glycaemic control was small. Four of the measures of physical activity had small sample numbers (<5) in the group which achieved optimal glycaemic control. Of the 16 participants who performed MISFRA for ≥150 minutes per week, only one (6.3%) participant achieved optimal glycaemic control, while the remaining 15 (93.8%) had poor glycaemic control. Participants who did not participate in MISFRA appeared to have better control than their counterparts who did, but this did not reach statistical significance (Table 4.45). Participants undertaking VISFRA for both <75 and ≥75 minutes per week also had small sample numbers achieving optimal glycaemic control.

As shown in Table 4.45, results indicated that work involving VIA appeared to have an association with glycaemic control. Surprisingly, those who were not involved in work-related VIA tended to have better glycaemic control than those who were. Only four (8.2%) out of the 49 participants involved in work-related VIA achieved optimal glycaemic control. The other physical activity factor which appeared to have an association with glycaemic control was the number of minutes per week that a participant spent walking to get to and from places. Participants who walked for ≥150 minutes per week also tended to have better glycaemic control than those who walked for <150 minutes per week. Although a greater proportion of participants who were involved in work-related MIA for ≥150 minutes per week appeared to have optimal glycaemic control than those not doing this level of activity, the difference did not reach statistical significance. Whether a participant achieved good glycaemic control appeared not to be associated with the overall measure of amount of physical activity, other than walking.

Table 4.45 Association of physical activity with poor glycaemic control (HbA1c > 7.0%).

Variable	HbA1c categories		
	≤7.0 (N [%])	>7.0 (N [%])	p-value[#]
Work-related MIA for at least 10 minutes			0.259
No	47 (22.2)	165 (77.8)	
Yes	26 (17.3)	124 (82.7)	
Minutes of MIA at work/week			0.052
<150	5 (9.4)	48 (90.6)	
≥150	21 (22.1)	74 (77.9)	
Performs MISFRA for at least 10 minutes			0.055
No	67 (22.5)	231 (77.5)	
Yes	6 (9.4)	58 (90.6)	
Minutes of MISFRA/week			0.620
<150	5 (10.4)	43 (89.6)	
≥150	1 (6.3)	15 (93.8)	
Work-related VIA for at least 10 minutes			0.047
No	69 (22.0)	244 (78.0)	
Yes	4 (8.2)	45 (91.8)	
Minutes of VIA at work/week			0.592*
<75	2 (12.5)	14 (87.5)	
≥75	2 (6.3)	30 (93.8)	
Performs VISFRA for at least 10 minutes			0.503
No	68 (20.6)	262 (79.4)	
Yes	5 (15.6)	27 (84.4)	
Minutes of VISFRA/week			0.626*
<75	1 (8.3)	11 (91.7)	
≥75	4 (20.0)	16 (80.0)	
Walks to get to and from places for at least 10 minutes			0.916
No	16 (19.8)	65 (80.2)	
Yes	57 (20.3)	224 (79.7)	
Minutes of walking/week			0.049
<150	20 (15.6)	108 (84.4)	
≥150	36 (25.4)	106 (74.6)	
Amount of physical activity/week			0.582
Sufficient	44 (21.8)	158 (78.2)	
Insufficient	18 (16.8)	89 (83.2)	
None	11 (20.8)	42 (79.2)	

[#]The p-values were obtained from the Chi-square statistic, and assess the strength of association. *Fisher's Exact Test; MIA = Moderate-intensity activities; MISFRA = moderate-intensity sports, fitness and recreational activities; VIA = vigorous-intensity activities; VISFRA = *v*igorous-intensity sports, fitness and recreational activities

Univariate logistic regression analysis of lifestyle factors (other than physical activity) indicated that betel nut exposure was the most important factor influencing glycaemic control (Table 4.46). Participants who had never chewed betel nut had poorer glycaemic control compared to their counterparts who had chewed betel nut. For those who had never chewed betel nut, the odds of poor glycaemic control was almost twice that of those who had done so. However, those who had quit the habit had a lower chance of poor glycaemic control than those who were current chewers. The other betel nut chewing characteristics which showed a weak trend were the number of nuts chewed per day and the number of years of chewing, but neither of these reached statistical significance. As shown in Table 4.46, those who chewed betel nut for 25 years or less had twice the odds of poor glycaemic control and those who chewed five or fewer nuts per day were less likely to have poor glycaemic control.

Smoking appeared to be associated with glycaemic control but was a less important factor compared to betel nut chewing. Participants who had ever smoked appeared to have a lower risk of having poor glycaemic control compared to those who had never smoked.

Although the number of days of consuming vegetables did not reach statistical significance, participants who consumed vegetables for five or fewer days in a typical week tended to have a higher chance of poor glycaemic control, and this risk was significant when comparing those who consumed vegetables for 6-7 days with those who consumed vegetables for 3-5 days. Those who consumed vegetables for 3-5 days were twice as likely to have poor glycaemic control. Participants who consumed two or more servings of fruit appeared to have a lower chance of poor glycaemic control. However, this was not statistically significant (Table 4.46).

Table 4.46 Univariate logistic regression analysis of lifestyle factors associated with poor glycaemic control (HbA1c > 7.0%)

Variable	Crude OR	95% CI	p-value
Betel nut exposure			0.027
Never	1 (reference)		
Quit	0.30	0.13 - 0.68	0.004
≤5 nuts/day	0.45	0.20 - 0.99	0.047
>5 nuts/day	0.64	0.25 - 1.61	0.340
Years of chewing betel nut			0.261
≤25	2.39	0.52 - 10.85	
>25	1 (reference)		
Smoker status			0.137
Current smoker	1 (reference)		
Never a smoker	1.68	0.63 - 4.49	0.304
Quit	0.97	0.34 - 2.75	0.949
Smoker history			0.046
Ever	0.58	0.34 - 0.99	
Never	1 (reference)		
Number of vegetable-eating days in a typical week			0.077
0-2	1.56	0.82 - 2.99	0.178
3-5	2.02	1.06 - 3.84	0.031
6-7	1 (reference)		
Fruit servings/day			0.436
<2 serves	1 (reference)		
≥2 serves	0.80	0.46 - 1.40	
Number of fruit-eating days in a typical week			0.313
0-2	1 (reference)		0.316
3-5	1.44	0.71 - 2.93	0.206
6-7	1.89	0.71 - 5.06	

The dependent variable was HbA1c > 7.0%; HbA1c = glycated haemoglobin

As shown in Table 4.47, the only physical activity variable which had any significant influence on glycaemic control was work-related VIA. Results indicated that the odds ratio of those performing work-related VIA having poor glycaemic control was three-fold higher than those who did not. Although the odds of having poor glycaemic control was almost three-fold in participants who performed work-related MIA for <150 minutes per week compared with those performing ≥150 minutes per week, this did not reach statistical significance. Participants who had walked to and from places for <150 minutes per week were almost twice as likely to have poor glycaemic control compared to those who walked for ≥150 minutes per week but this difference also did not reach statistical significance.

Table 4.47 Univariate logistic regression analysis of physical activities associated with poor glycaemic control (HbA1c > 7.0%)

Variable	Crude OR	95% CI	p-value
Work-related MIA for at least 10 minutes			0.260
No	1 (reference)		
Yes	1.36	0.80 - 2.31	
Minutes of MIA at work/week			0.059
<150	2.72	0.96 - 7.71	
≥150	1 (reference)		
Work-related VIA for at least 10 minutes			0.036
No	1 (reference)		
Yes	3.18	1.11 – 9.16	
Minutes of walking/week			0.051
<150	1.83	0.99 - 3.37	
≥150	1 (reference)		
Performs MISFRA for at least 10 minutes			0.022
No	1 (reference)		
Yes	2.80	1.16 - 6.78	

The dependent variable was HbA1c > 7.0%; HbA1c = glycated haemoglobin; MIA = moderate-intensity activity; VIA = vigorous-intensity activity; MISFRA = moderate-intensity sports, fitness and recreational activity

Lifestyle factors with a significant, or near significant, association with glycaemic control, as highlighted by the univariate analyses, were entered into the multivariate logistic regression model to determine which factors were independently associated with poor glycaemic control.

Results indicated that performing MISFRA, minutes of work-related MIA and the number of days/week on which participants had vegetables were each independently associated with glycaemic control, however, the only significant lifestyle variable which appeared to influence glycaemic control was the number of minutes that work-related MIA was undertaken in a typical week (Table 4.48). Those who were walking for <150 minutes per week were four times more likely to

have poor glycaemic control than those who walked for ≥150 minutes per week. Participants who did not consume vegetables, and those who had vegetables for up to 5 days appeared to be more likely to have poor glycaemic control compared to those who had vegetable for 6-7 days in a week. However, this did not reach statistical significance. Those who performed MISFRA were five times more likely to have poor glycaemic control when compared with those who did not. However, like the association between number of days of vegetable consumption and poor glycaemic control, this did not reach statistical significance. Betel nut chewing was not an independent factor for poor glycaemic control.

Table 4.48 Multivariate logistic regression analysis of lifestyle factors associated with poor glycaemic control (HbA1c > 7.0%)

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Performs MISFRA for at least 10 minutes				0.132
No	231/298 (77.5)	1 (reference)		
Yes	58/64 (90.6)	5.06	0.61-41.64	
Minutes of MIA at work/week				0.036
<150	48/53 (90.6)	4.18	1.10-15.88	
≥150	74/95 (77.9)	1 (reference)		
Number of vegetable-eating days in a typical week				0.056
0-5 days	172/204 (84.3)	2.77	0.98-7.86	
6-7 days	117/156 (75.0)	1 (reference)		

The dependent variable was HbA1c > 7.0%; HbA1c = glycated haemoglobin; *The column showing 'n/N (%)' shows the number of people (and percentage) within each variable with poor glycaemic control (HbA1c > 7.0); MIA = moderate-intensity activity; MISFRA = moderate-intensity sports, fitness and recreational activity

4.3.9.3 Univariate analysis of medical and physical factors associated with glycaemic control

Variables such as hypoglycaemic medications, co-medications for co-morbidities, other types of management, number of years living with diabetes and physical characteristics were tested for an association with glycaemic control.

As shown in Table 4.49, using a hypoglycaemic medication over the preceding three months had an influence on glycaemic control. Participants who were prescribed

hypoglycaemic medications for their diabetes were more likely to have poor glycaemic control when compared to their counterparts who were not prescribed these medications.

Usage of, and the daily dosage of, glibenclamide also had an influence on glycaemic control (Table 4.49) Those who were prescribed glibenclamide were more likely to have poor glycaemic control compared to those who were not (either diet-controlled or other hypoglycaemic agents). Participants prescribed the lowest dose of glibenclamide appeared to have more optimal glycaemic control, compared to those prescribed higher doses. The -prescription of metformin and the number of hypoglycaemic medications prescribed by participants did not affect glycaemic control, as shown in Table 4.49.

Glycaemic control was examined at four different thresholds of adherence, namely: 100% (complete adherence with hypoglycaemic treatment), 95%, 90% and 80%. Glycaemic control also was examined at a glycaemic control of HbA1c greater than 10.0% (abnormally high = poor control) and greater than 8.0%. The cut-off for HbA1c of ≤10.0% was previously accepted as good glycaemic control but a cut-off of ≤8.0% is now accepted as good glycaemic control, in clinical practice.[4]

Apart from Chi-square testing, the distribution of levels of HbA1c achieved, according to different levels of adherence to treatment, was examined. HbA1c levels were categorised at three different levels of glycaemic control. These HbA1c levels were ≤7.0% (optimal), 7-10% (high) and >10.0% (abnormally high). Percentages of participants who were categorised under these different levels were calculated. (Figure 4.4)

Figure 4.4 shows that, as the level of adherence decreased the percentage of participants who achieved optimal glycaemic control also decreased, in general. There was a significant impact of adherence on glycaemic control when the level of adherence fell from 100% to 90% but there was no significant impact when adherence fell from 90% to 80%, as shown in Figure 4.4

Table 4.49 Association of hypoglycaemic and co-medication variables with optimal glycaemic control (HbA1c > 7.0%)

Variable	HbA1c (%) categories		
	≤7.0 (N [%])	>7.0 (N [%])	p-value[#]
Hypoglycaemics used in the previous three months			0.017
No	10 (38.5)	16 (61.5)	
Yes	63 (18.9)	271 (81.1)	
Hypoglycaemic doses missed			0.504
No	28 (20.6)	108 (79.4)	
Yes	35 (17.7)	163 (82.3)	
Metformin doses/day			0.322
None	28 (18.9)	120 (81.1)	
≤500 mg	9 (25.5)	27 (75.0)	
750–1,000 mg	25 (24.5)	77 (75.5)	
>1,000 mg	10 (14.1)	61 (85.9)	
Metformin doses missed			0.496
No	22 (23.2)	73 (76.8)	
Yes	22 (19.3)	92 (80.7)	
Glibenclamide dose/day			0.002
None	30 (29.4)	72 (70.6)	
≤5 mg	11 (28.9)	27 (71.1)	
7.5–15 mg	25 (17.2)	120 (82.8)	
>15 mg	6 (8.2)	67 (91.8)	
Glibenclamide doses missed			0.588
No	19 (17.8)	88 (82.2)	
Yes	23 (15.2)	128 (84.8)	
Number of hypoglycaemics used			0.383
1	37 (20.6)	143 (79.4)	
2 or 3	25 (16.8)	124 (83.2)	
Co-medications used			0.137
No	23 (16.0)	121 (84.0)	
Yes	47 (22.4)	163 (77.6)	

[#]The p-values were obtained from the Chi-square statistic, and assess the strength of association.

Figure 4.4 Percentages of patients attaining different HbA1c targets

The impact of adherence to the use of hypoglycaemic medications on glycaemic control was tested at two different levels of glycaemic control using chi-square statistics at the level of optimal control (HbA1c ≤ 7.0%) and abnormally high levels (HbA1c > 10.0%).

Results indicated that, when the impact of adherence on glycaemic control was examined using the optimal glycaemic control cut-off of HbA1c ≤ 7.0%, glycaemic control was found not to be associated with level of adherence used. However, when glycaemic control was examined using an HbA1c of ≤10.0%, results indicated that missing any dose had an impact on glycaemic control. Those who were 100% adherent were more likely to have an HbA1c of ≤10.0% (p=0.003), as shown in Table 4.50.

Using the currently acceptable glycaemic control of HbA1c ≤ 8.0, there appeared to be no difference in glycaemic control across different levels of adherence.

Table 4.50 Associations of different levels of hypoglycaemic medication adherence with two levels of glycaemic control

Level of Adherence tested	HbA1c (%) categories					
	≤7.0 (N%])	>7.0 N[%])	p-value	≤10.0 (N%])	>10.0 (N[%])	p-value[#]
100%			0.504			0.003
Adherent	28 (20.6)	108 (79.4)		105 (77.2)	31 (22.8)	
Non-adherent	35 (17.7)	163 (82.3)		122 (61.6)	76 (38.4)	
95%			0.535			0.230
Adherent	43 (18.9)	185 (81.1)		159 (69.7)	69 (30.3)	
Non-adherent	16 (16.0)	84 (84.0)		63 (63.0)	37 (37.0)	
90%			0.362			0.198
Adherent	50 (18.9)	214 (81.1)		183 (69.3)	81 (30.7)	
Non-adherent	9 (14.1)	55 (85.9)		39 (60.9)	25 (39.1)	
80%			0.381			0.126
Adherent	53 (18.7)	230 (81.3)		196 (69.3	87 (30.7)	
Non-adherent	6 (13.3)	39 (86.7)		26 (57.8)	19 (42.2)	

[#]The p-values were obtained from the Chi-square statistic, and assess the strength of association.

Results indicated that those who had had diabetes for five years or less were more likely to have optimal glycaemic control than their counterparts who had had

diabetes for more than five years (p=0.009). Other physical measurements were not associated with glycaemic control, as shown in Table 4.51.

Table 4.51 Associations of physical measurements and number of years living with diabetes, with optimal glycaemic control (HbA1c > 7.0%)

Variable	HbA1c (%) categories		
	≤7.0 (N [%])	>7.0 (N [%])	p-value[#]
BMI category			0.873
Underweight	1 (12.5)	7 (87.5)	
Normal weight	23 (20.9)	87 (79.1)	
Overweight	25 (18.4)	111 (81.6)	
Obese	19 (21.6)	69 (78.4)	
SBP (mmHg)			0.867
≤130	17 (19.5)	70 (80.5)	
>130	55 (20.4)	215 (79.6)	
DBP (mmHg)			0.094
≤80	39 (24.1)	123 (75.9)	
>80	33 (16.9)	162 (83.1)	
Waist circumference			0.204
Normal	26 (24.3)	81 (75.7)	
Above normal	47 (70.1)	208 (81.6)	
No. of years living with diabetes			0.009
≤5 years	50 (25.3)	148 (74.7)	
>5 years	23 (14.1)	140 (85.9)	

[#]The p-values were obtained from the Chi-square statistic, and assess the strength of association; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; Normal waist circumference is 88 cm (females) and 102 cm (males)

For univariate logistic regression analysis, BMI was regrouped into a 2-category group (<25 kg/m^2 and ≥25 kg/m^2).

Results of univariate logistic regression analysis indicated that the medical variables which had an influence on glycaemic control were usage of hypoglycaemic medications over the preceding three months, glibenclamide use and number of years living with diabetes (Table 4.52).

Participants who were using both one and two or three hypoglycaemic medications were two and three times more likely, respectively, to have poor glycaemic control compared to their counterparts who were not taking any hypoglycaemic medications. Those taking a glibenclamide dose of >15 mg daily were four times more likely to have poor glycaemic control, while those on 7.5-15 mg/day were twice as likely.

Those who had lived with diabetes for >5 years had twice the odds of having poor glycaemic control. Physical measurements such as BMI, waist circumference and blood pressure did not influence HbA1c. DBP appeared to be associated with HbA1c but this did not reach statistical significance. Although taking co-medications lowered the odds of poor glycaemic control, this also did not reach statistical significance, as can be seen in Table 4.52.

Table 4.52 Univariate logistic regression analysis of medical variables associated with poor glycaemic control (HbA1c > 7.0%)

Variable	Crude OR	95% CI	p-value
Hypoglycaemics used in the previous three months			0.048
0	1 (reference)		
1	2.42	1.01-5.76	0.047
2 or 3	3.10	1.26-7.62	0.014
Co-medications used			0.139
No	1 (reference)		
Yes	0.66	0.38-1.14	
Glibenclamide dose/day			0.004
None	1 (reference)		
≤5 mg	1.02	0.45-2.32	0.957
7.5–15 mg	2.00	1.09-3.67	0.025
>15 mg	4.65	1.82-11.88	0.001
Number of years living with diabetes			0.010
≤5 years	0.49	0.28-0.84	
>5 years	1 (reference)		
BMI (kg/m^2)			0.437
<25	0.80	0.45-1.41	
≥25	1 (reference)		
Waist circumference			0.206
Normal	0.70	0.41-1.21	
Above normal	1 (reference)		
DBP (mmHg)			0.095
≤80	0.64	0.38-1.08	
>80	1 (reference)		

The dependent variable was HbA1c > 7.0%. HbA1c = glycated haemoglobin; BMI = body mass index; DBP = diastolic blood pressure; Normal waist circumference is 88 cm (females) and 102 cm (males)

Results of univariate logistic regression analysis examining 100% adherence and abnormally high HbA1c indicated that missing any dose had an influence on glycaemic control with respect to abnormally high HbA1c (HbA1c > 10.0%). Participants who did not miss any doses were less likely to have an abnormally high HbA1c (Crude OR = 0.474, 95% CI = 0.29-0.78, p=0.003).

4.3.9.4 Multivariate logistic regression analysis of medical and physical factors and glycaemic control

Multivariate logistic regression analysis was performed for different levels of adherence with hypoglycaemic medications to investigate which level of adherence influenced an abnormally high HbA1c (>10%). Each participant was classified into their level of adherence, and the dependent variable was HbA1c > 10%.

Odds Ratios for the adherence levels were expressed relative to the completely adherent subjects. This analysis showed explicitly that the odds of abnormally high HbA1c was greater than one for all levels of non-adherence, but only significantly higher for the adherence levels 95-99%, and <80% (Table 4.53).

Table 4.53 Multivariate logistic regression analysis: The influence of medication adherence on abnormally high HbA1c (>10.0%).

Adherence level	HbA1c > 10% n/N (%)*	Odds Ratio	95% Confidence Interval	p-value
100%	31/136 (22.8)	1 (reference)		
95-99%	38/92 (41.3)	2.4	1.3 - 4.2	0.003
90-94%	12/36 (33.3)	1.7	0.8 - 3.8	0.197
80-89%	6/19 (31.6)	1.6	0.5 - 4.5	0.403
<80%	19/45 (42.2)	2.5	1.2 - 5.1	0.012

The dependent variable was HbA1c > 10.0%. HbA1c = glycated haemoglobin; *The column showing 'n/N (%)' shows the number of people (and percentage) within the given adherence level who had high HbA1c.

According to multivariate logistic regression analysis, medical and physical factors which were independently associated with glycaemic control were glibenclamide use, co-medication use, DBP, number of years diagnosed with diabetes and BMI. However, DBP did not reach statistical significance, as shown in Table 4.54. Participants who were prescribed >15 mg of glibenclamide were five times more likely to have poor glycaemic control. There was no statistically significant difference in association between being prescribed ≤5 to 15 mg of glibenclamide daily and not being prescribed any glibenclamide. Participants not prescribed co-medications and those diagnosed with diabetes for more than five years were twice as likely to have poor glycaemic control.

Table 4.54 Multivariate logistic regression analysis of medical factors associated with poor glycaemic control (HbA1c > 7.0%)

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Glibenclamide dose/day				0.046
None	72/102 (70.6)	1 (reference)		
≤5 mg	27/38 (71.1)	1.21	0.30 - 4.28	0.812
7.5–15 mg	120/145 (82.8)	1.77	0.73 - 4.28	0.223
>15 mg	67/73 (91.8)	5.62	1.60 - 19.69	0.013
Co-medication use				0.031
No	121/144 (84.0)	2.23	1.08 - 4.62	
Yes	163/210 (77.6)	1 (reference)		
No. of years diagnosed with diabetes				0.034
≤5	148/198 (74.7)	1 (reference)		
>5	140/163 (85.9)	2.10	1.06 - 4.17	
DBP (mmHg)				0.058
≤80	123/162 (75.9)	1 (reference)		
>80	162/195 (83.1)	1.88	1.06 - 4.17	
BMI (kg/m^2)				0.011
<25	75/98 (76.5)	1 (reference)		
≥25	180/224 (80.4)	2.42	1.22 - 4.79	

The dependent variable was HbA1c > 7.0%; HbA1c = glycated haemoglobin; *The column showing 'n/N (%)' shows the number of people (and percentage) within each variable with poor glycaemic control (HbA1c > 7.0); DBP = diastolic blood pressure; BMI = body mass index

4.3.10 Multivariate logistic regression analysis of all factors which had an influence on glycaemic control

Hypoglycaemic medication variables were combined to form a new four-category variable. These variables were: no hypoglycaemic medication, metformin only, glibenclamide only and combination. Insulin only was not included because of the small sample number of participants using this hypoglycaemic agent. The variable 'minutes of work-related MIA' was regrouped into three categories to include those who did not participate in work-related MIA at all.

As shown in Table 4.55, variables which independently influenced glycaemic control in this study were gender, betel nut exposure, MISFRA, work-related MIA, hypoglycaemic medication use and DBP.

Those at risk of poor glycaemic control were females, those who never chewed betel nut or those who chewed >5 nuts daily, those who participated in MISFRA, those diagnosed with diabetes for more than five years, those taking single or combined hypoglycaemic agents and those with high DBP.

Female participants had twice the risk of having poor glycaemic control compared to their male counterparts.

Those who quit betel nut chewing were less likely to have poor glycaemic control. Those who chewed ≤5 betel nuts daily also tended to be less likely to have poor glycaemic control but this failed to achieve statistical significance. There was no difference in association of poor glycaemic control between those who never chewed betel nut and those who chewed >5 nuts daily.

Participants who performed any MISFRA were three times more likely to have poor glycaemic control. Those with DBP > 80 mmHg and diagnosed with diabetes more than five years ago had twice the risk of poor glycaemic control compared to their counterparts. Interestingly, taking metformin, glibenclamide or a combination of hypoglycaemic agents was associated with poor glycaemic control. Those on

glibenclamide and those on a combination of hypoglycaemic agents both had six times the odds of having poor glucose control compared to those using metformin, with only thrice the odds. However the association between metformin use as a single agent and poor glycaemic control was of borderline significance.

Other variables that were independently associated with poor glycaemic control but were of borderline significance were number of vegetable-eating days in a typical week, number of minutes of work-related MIA and use of co-medications. Both consuming vegetables for five days or less in a week and not taking co-medications appear to be associated with poor glycaemic control. In regard to work-related MIA, those who were spending <150 minutes performing such physical activities in a week were four times more likely to have poor glycaemic control; an association which was statistically significant.

Table 4.55 Multivariate logistic regression analysis of factors independently associated with poor glycaemic control (HbA1c > 7.0%)

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Gender				0.024
Female	190/228 (83.3)	2.19	1.11-4.32	
Male	99/134 (73.9)	1 (reference)		
Betel nut exposure				0.025
Never	77/87 (88.5)	1 (reference)		
Quit	53/76 (69.7)	0.33	0.12 - 0.89	0.028
≤5 nuts/day	86/111 (77.5)	0.39	0.15 - 1.01	0.051
>5 nuts/day	54/65 (83.1)	1.28	0.41 - 4.01	0.669
Performs MISFRA for at least 10 minutes				0.016
No	231/298 (77.5)	1 (reference)		
Yes	58/64 (90.6)	3.89	1.29-11.69	
Work-related MIA for at least 10 minutes				0.050
None	165/212 (77.8)	1 (reference)		
<150 minutes	48/53 (90.6)	4.55	1.80-54.80	0.014
≥150 minutes	74/95 (77.9)	1.18	0.54-2.60	0.685
Hypoglycaemic medication use				0.029
None	16/26 (61.5)	1 (reference)		
Metformin	39/58 (67.2)	3.75	0.93-15.13	0.063
Glibenclamide	88/105 (83.8)	6.59	1.68-25.87	0.007
Combination	128/153 (83.7)	6.42	1.75-23.59	0.005
DBP (mmHg)				0.047
≤80	123/162 (75.9)	1 (reference)		
>80	162/195 (83.1)	2.28	1.01-5.11	
Number of years diagnosed with diabetes				0.010
≤5	148/198 (74.7)	1 (reference)		
>5	140/163 (85.9)	2.71	1.27-5.81	
Number of vegetable-eating days in a typical week				0.069
0-5	172/204 (84.3)	1.87	0.95-3.67	
6-7	117/156 (75.0)	1 (reference)		
Co-medication used				0.079
No	121/144 (84.0)	2.03	0.92-4.47	
Yes	163/210 (77.6)	1 (reference)		

The dependent variable was HbA1c > 7.0%; HbA1c = glycated haemoglobin; *The column showing 'n/N (%)' shows the number of people (and percentage) within each variable with poor glycaemic control (HbA1c > 7.0). MIA = moderate-intensity activity; MISFRA = moderate-intensity sports, fitness and recreational activity; DBP = diastolic blood pressure

4.4 Discussion

4.4.1 Demographic characteristics

A majority of the total 385 participants were from the Southern region (76.4%) and were urban dwellers (55.1%). The predominance of participants from the Southern region and from urban dwellings may have been because of the location of the PMGH Diabetes Clinic. The finding that the majority of participants were from the Southern region is similar to that of Benjamin et al, [5] whose study was conducted in the same setting. The PMGH Diabetes Clinic also serves those from the Central province (Southern region). It is possible that there are more people living with T2DM in urban areas, such as the city of Port Moresby, where there are more predisposing factors than in rural areas. Previous studies in PNG have demonstrated higher prevalence rates of T2DM in urban areas compared to rural areas.[6-9] Furthermore, studies have also shown differences in T2DM risk factors, such as lipids or obesity, between urban and rural dwellers.[10, 11] Those living with diabetes in rural areas may have once lived in urban areas because, in PNG, most of those employed in the cities and towns retire to their childhood villages where they own land.

A high proportion (32.5%) of participants was either homemakers or unemployed (15.3%), which may be a reflection of the levels of education achieved. More than 40% of the participants had only completed basic primary education or had not completed even that. In general, the higher the level of education, the more likely it is that a person will be employed and therefore the high proportion of homemakers or unemployed may have been due to low levels of education. The high number of females in the study may have also contributed to the high proportion of homemakers. The high percentage of females being homemakers may also be due to cultural norms and expectations in PNG where women are responsible for taking care of the family. The observation that a high proportion of participants were either homemakers or unemployed may have been because their time was more flexible to allow participation in the study.

The highest proportion (37.7%) of participants in the current study was aged 50-59 years. As the categories of age increased, the number of participants increased up

to the age group 50-59 years and then decreased after that age group. The increase is due to the fact that T2DM is commonly a maturity-onset disease. The decrease in the number of participants after the ages 50-59 years may be due to deaths. The life expectancy at birth for Papua New Guineans has been reported to be 65.5 and 61.2 years for females and males, respectively.[12]

4.4.2 Lifestyle factors

4.4.2.1 Alcohol consumption

The number of participants who reported consuming alcohol in this study was small and therefore valid conclusions could not be drawn. However, alcohol consumption appeared to be influenced by age, gender and employment status. Participants younger than 50 years, males and those who were employed (paid and self-employed) appeared to be more likely to consume alcohol. On the other hand, those who had not completed basic education and those who had only completed primary education appeared to be less likely to consume alcohol. In PNG, from personal knowledge, consumption of alcohol is not common among females, mostly due to cultural reasons. There were more females in this study, which may have therefore contributed to the low levels of alcohol consumption. It may also be that participants may have quit alcohol as part of their diabetes management. This study did not gather information on whether or not participants had quit alcohol consumption.

4.4.2.2 Tobacco smoking

Like alcohol consumption, the percentage of those who smoked tobacco was small (6.2%). The finding that the prevalence of smoking was low in this study is similar to other studies that have found low prevalence of smoking by those with T2DM compared with those who do not have diabetes.[13, 14] A Malaysian study [14] showed 8% of those with T2DM were smokers. Kengne et al [15], however, reported a similar prevalence of current smokers in both their cohorts with and without diabetes. Smoking appeared to be affected by age in the present study, but sample numbers for those who were classified as smokers were too small to draw any valid conclusions.

4.4.2.3 Vegetable and fruit consumption

Participants were requested to think of a typical week in the preceding three months when they had consumed vegetables or fruit, and recall both the number of days and the number of cups of fruit or vegetables consumed on those days. For each person, the number of cups was converted to number of servings using the show card (Appendix 9) for fruit and vegetable intake.

Results of this study indicated that vegetable and fruit consumption was poor, with 92% and 70.4% of the participants reporting that they consumed less than three and less than two servings of vegetables and fruits, respectively. There are no national guidelines on the amount of fruit or vegetables to be consumed daily; rather recommendations from Australia have been adapted. PNG traditionally has a diet rich in leafy vegetables, so this finding of the study possibly indicates indirectly that diet is changing in PNG. Studies have shown changes in diet of Papua New Guineans which have been attributed to urbanisation and westernisation. [16, 17] There has been a shift from garden food to processed food. The cost of feeding a large family with processed food is usually cheaper than feeding them with garden food sold either in the local markets or grocery shops. The cost of living in Port Moresby therefore may also be contributing to low levels of fruit and vegetable intake.

Consuming a diet poor in fruit and vegetables further increases the risk of cardiovascular diseases in these participants with T2DM. [18-20] Fruit and vegetables are high in antioxidants which boost immunity and protect against other nutrient deficiencies. Studies also have shown that a high intake of dietary fibre improves glycaemic control, decreases hyperinsulinaemia and plasma lipid concentrations in patients with T2DM. [21, 22] Therefore, poor consumption of fruit and vegetable may contribute to poor glycaemic control among the participants of the present study.

4.4.2.4 Physical activity

Fifty six percent of participants reported doing a sufficient amount of physical activity, which was mostly contributed to by the high proportion of participants

walking as their mode of travel. The most common type of physical activity was walking for travel, with 296 (76.9%) participants reporting that they walked to get to and from places. The only significant demographic factor which influenced this type of physical activity was gender. Females were more likely to walk, but the amount of walking (minutes per week) they did was less than that of their male counterparts. Area of residence and years of residence in Port Moresby had a significant influence on the amount of walking, while the influence of age was of borderline significance. Compared to those who were born in Port Moresby and had spent their entire lifetimes there, rural village dwellers and those who had migrated to the city were significantly more likely to do more walking.

Twenty percent of participants of this study were from rural villages where there are hardly any motor vehicles. In many rural areas of PNG, the most common types of motor vehicle in the villages are public motor vehicles, which are usually open-backed trucks. These vehicles are used to transport passengers to and from the towns. Therefore, those residing in the villages are more likely to walk to get to and from places. For those who live in Port Moresby, walking for travel may have been further influenced by the limited transport system in the National Capital District. Usually, people have to walk long distances to the nearest bus stop. (Personal knowledge)

As the intensity of physical activity increased, the number of participants undertaking those activities decreased. One hundred and sixty participants (41%) did work-related MIA while only fifty three (13.8%) did work-related VIA. Similarly, the prevalence of those doing MISFRA was higher than that of VISFRA. These results were influenced by age. Univariate (Chi-square) analysis indicated that age was associated with participation in sports, fitness and recreational activities but not work-related MIA and VIA. As age increased, the number of participants taking part in sports, fitness and recreational activities significantly decreased. As age increases, there is a natural trend to reduce physical activity. Although this study did not document the type of work-related activity, this may be a reflection of employment status. More than 70% of participants were either unpaid or unemployed and therefore had to find a means of survival if they lived in the city. If they lived in their rural villages, they could depend on subsistence farming or fishing

for their livelihoods. The small number of those performing leisure-time physical activities may also indicate that people would rather put their time towards work-related activities than leisure-time physical activities because of the need to provide food, shelter and other necessities. Additionally, as the present study cohort was comprised of those with T2DM, complications or factors related to this disease may have contributed to decreased physical activity among these participants. Safe participation in physical activity such as exercise in those with T2DM can be complicated by the presence of disease-related complications such as cardiovascular disease, hypertension, neuropathy or microvascular changes. [23] Other studies have reported a high number of T2DM patients are inactive. [24, 25] It is important that T2DM engage in physical activity at a level of intensity that is comfortable and safe for them.

4.4.3 Medical factors

4.4.3.1 Diabetes management

The change of diabetes management of 48 (12.5%) participants from diet-controlled to pharmacological agents in the preceding three months indicates a need for better glycaemic control for these participants. . This is the usual progressive management for T2DM because, as time passes and diabetes advances, there is loss of β-cell function and, therefore, a greater need for pharmacological agents to deal with the resulting hyperglycaemia. Although 25% were advised about their diet, none of the participants were on a prescribed diet. This is a reflection of services available for those living with diabetes in PNG. From personal knowledge, since a 2001 report [26], there are still insufficient resources, such as nutritional and dietetic services, and specialist endocrinologists to support diabetes management in the country. The reason for the availability of a limited range of hypoglycaemics (glibenclamide, metformin and insulin) through the public health care system during the time of the study is because the list of medicines purchased is based on the WHO Model List of Essential Medicines. The use of essential medicines only is to ensure affordable medicines are widely available.

Participants were requested to report management of their T2DM when they were initially diagnosed with the disease. The reduction in the number of patients on insulin over time may have been partly due to changing from inpatient services to outpatient services. Some of these participants may have received insulin while in hospital at the time of initial diagnosis but may have been discharged on oral hypoglycaemic medications. It is also possible that T2DM patients who require insulin may not be able to use insulin for reasons such as the storage requirements of this medication. Usage of insulin in PNG is limited by its requirement for refrigeration. As seen in this study, about 20% of the participants lived in rural areas and 20% lived in peri-urban areas. In rural PNG, only a few homes have portable electricity generators but electricity is produced mostly for smaller appliances and lighting purposes only. Some peri-urban areas may not have consistent electricity supplies and, in particular, may not have refrigerators.

4.4.3.2 Medication adherence

Adherence to medications is of paramount importance because there are strong correlations between medication adherence, patient outcomes and treatment costs. [27-30]

The type of medication adherence investigated by the present study was omission of doses, which is the most common type of non-adherence. [31] This may be intentional or non-intentional. A high proportion of participants (59.6%) reported omitting at least some of their doses. This is consistent with the trends that have been reported elsewhere. [32-36]

The only significant factor which affected adherence to medication regimens was age. Those aged 60 years or older were more likely to be adherent to their diabetes medications. Younger people tend to have other priorities in their lives and lead busier lives than the elderly, because of employment and other social activities. This may partly explain why the younger age group was less adherent to their hypoglycaemic medications than the older age group in the present study.

Older people also may have been more adherent within this study population because the study setting has a medication supply policy that exempts those aged 60 years or older from medication fees. Furthermore, in a society like PNG's where extended family usually live together in a single household, care of the elderly may have led to better adherence by those aged 60 years and older. This finding, that older people are more adherent, is consistent with other studies showing that better hypoglycaemic medication adherence is associated with increased age. [34, 37, 38] A Scottish study, however, reported that younger people were more adherent in taking their hypoglycaemic medications, compared to their older counterparts.[39]

There is evidence that strong psychosocial support improves medication adherence.[40] Participants in this study were living in a society where extended families usually live in the one house. Family ties are strong and, usually, younger family members care for their elder relatives within the family home. With the advantage of strong psychosocial support in PNG, patients and their family carers may have better opportunity to develop good routines in medication behaviour, as it has been shown that developing such routines usually leads to higher levels of adherence.[40]

The most common reasons cited by participants for omitting doses were patient- and health care system-related. The most common patient-related reason for omitting doses cited by participants was that they simply forgot to take their medications. The next most common patient-related factor was participants not refilling their medications, despite having prescriptions. This group of participants did not elaborate further on their reasons for not doing so.

All participants who had problems with access to the diabetes clinic reported that they were waiting for their next medical review to pick up their new prescriptions. This led to them not continuing their medications as required. The contributing factors to this were: increase in the number of patients attending the clinic, scheduling of appointments, the number of clinic days and hours per week, cancellation/rescheduling of clinic times, shortage of staff at the clinic and closure of the clinic from the beginning of December to the end of January every year. Scheduling of review dates for each individual patient depends on availability of an appointment time. Even if a doctor wants to see a patient one month later, for

example, the next available appointment may not be until two weeks after that. This may lead to a patient missing out on their medications for two weeks, because the doctor will usually prescribe only one month's supply of medication based on the understanding that the patient will be seen again after a month. Despite the increase in the number of people diagnosed with diabetes, this clinic was still only open for three hours per week. To make matters worse, shortages in staff (both nursing and medical) often led to cancellation of appointments or scaling down of the clinic's operations. (personal observation)

Cost of medications is a crucial issue in medication adherence, especially for those who have been diagnosed with chronic diseases like T2DM, because therapy is ongoing (life-long). A further cost burden is often incurred due to the complications associated with diabetes. Most patients in PNG do not have private medical insurance but all patients benefit from subsidised medications through the public health system. Despite minimal medicine costs, many patients still cannot afford medications. There are also associated costs, such as consultation fees and the cost of transport to the clinic. Almost 20% of the participants in this study lived in rural villages where the cost of transport is even more than the cost of medicines. Apart from transport costs, those who live in the rural areas have to find temporary accommodation in the city where the diabetes clinic is situated. Studies elsewhere have shown that the cost of medications contributes to reduced adherence.[36, 41, 42] Similarly, the inconvenience of travel and the cost of travel also play a role.

There are three main policies which affect access to hypoglycaemic medications in PNG. Hypoglycaemic medications are only available in hospitals, which makes access more expensive for those living in rural villages. Another policy involves pharmacy fee exemptions. Patients with chronic diseases like cardiovascular diseases and asthma are exempted from paying for their disease-related medications but the same concession is not available, in general, for patients with diabetes. The exception is that patients who are 60 years and older are exempted from the costs of all medical problems. This policy may need revising to improve adherence to hypoglycaemic medications. The third policy concerns the total quantities dispensed per patient. Pharmacy departments usually only dispense one month's supply, even if the prescriber makes a request for three month's supply, for

example. Patients are then required to travel to the hospital pharmacy more often for their monthly refills.

4.4.4 Physical measurements

4.4.4.1 Blood pressure

The high prevalence of systolic (74.5%) and diastolic (53.5%) hypertension in this cohort was not surprising as it is well known that hypertension is associated with T2DM. Susceptibility of hypertension in Papua New Guineans may also be contributed to by genetic polymorphisms.[43] The observation from this study that the majority of diabetes patients have poorly-controlled hypertension is similar to other studies.[44-46] Findings of a systematic review of observational studies by McLean et al [45] reported that only 12% of T2DM patients had their blood pressures adequately controlled (≤130/85 mmHg). Some of the studies referenced in the review did not report the age groups included and some studies also included those with type 1 diabetes mellitus.

Univariate analysis indicated that factors which influenced SBP in the current study were age, employment status, tobacco smoking, duration of MISFRA, BMI and use of co-medications. After adjusting for each other, the factors with an independent significant influence on SBP were age, smoking and co-medications taken with hypoglycaemic drugs. High SBP was observed in those aged 50 years and older, smokers and quitters, and those taking co-medications, even after adjusting for confounders.

Due to the small number of smokers, no valid conclusion could be drawn regarding the influence of smoking on blood pressure in the study cohort. Studies have shown that any independent chronic effect of smoking on blood pressure is small [47] and smoking is associated with hypertension in a dose-dependent manner [48] Cigarette smoking is said to exert a hypertensive effect mainly through stimulation of the sympathetic nervous system.[49]

The finding of higher SBP with increasing age is consistent with those reported elsewhere.[50-53]. Ageing is associated with progressive loss of the visco-elastic properties of conduit vessels, increased atherosclerotic arterial disease, and

hypertrophy and sclerosis of muscular arteries and arterioles; factors which contribute to amplification of systolic pressure and a fall in diastolic pressure.[54, 55] Age-related changes in blood pressure are also due to a progressive decline in organ function and other pathophysiological processes. The ability of the kidneys to secrete salt loads efficiently, for example, declines with age, thereby resulting in increasing blood pressure.[56] Total and renal vascular resistance also increase, and cardiac output, heart rate, stroke volume, intravascular volume, renal blood flow and plasma renin activity are reduced.[54, 57] Further, the present study cohort includes those with T2DM; a disease which not only adversely affects kidney function [58] but also accelerates vascular injury. [59, 60] More than 80% of the participants had poorly controlled T2DM, increasing the risk of endothelial dysfunction and subsequent arterial stiffness.

Use of co-medications was probably associated with a high SBP because the most common class of co-medications used by participants was an antihypertensive, and not because of any adverse effect of co-medications on blood pressure per se.

None of the physical activities investigated were significantly associated with SBP in this study. However, undertaking MISFRA for less than 150 minutes per week appeared to be associated with a high SBP. Performing MISFRA and VISFRA appeared to have a beneficial influence on SBP but this did not reach significance. These findings, that none of the physical activities were significantly associated with SBP are contrary to other studies which have reported a beneficial association between physical activity and SBP. [24, 61] A meta-analysis [61] of 42 randomised control studies reported an improvement in blood pressure in association with supervised exercise among those with T2DM. That study did not find a significant association between SBP and either aerobic or resistance exercise alone, but a significant association was observed when aerobic and resistance exercises were combined.

Factors influencing DBP were gender, age, employment status and BMI, with gender, age and BMI remaining significant after adjusting for other confounders. As previously indicated females and those aged 50 years or older were significantly less likely to have a high DBP, compared to those who were younger. Those who had a BMI ≥25 kg/m^2 were more likely to have a high DBP. Compared to SBP, a

number of studies have reported that DBP is either maintained or decreases with increased age. [50-52] The present study found that DBP decreased with increasing age, while SBP increased with increasing age. The trend in blood pressure changes with age observed in the present study is different to what has been reported earlier in rural areas of PNG where people live a traditional life. [11, 62-64] A PNG survey [62] in the Highlands of PNG in the 1960s showed a decrease in both SBP and DBP with increasing age. The authors attributed the falling blood pressure to a fall in body build after the third decade of age in that population. In 1985, another survey [63] in the Highlands of PNG showed little evidence of an association between either age or adiposity and blood pressure. Studies conducted in remote rural areas of PNG and other countries where the lifestyle is more traditional, have observed the same findings that there is little or no increase in BP with increasing age.[64, 65] This perhaps indicates the role of urbanisation (or modernisation) and its consequent dietary changes on BP, as observed in the present study.

Obesity is recognised as a major risk factor for high blood pressure. The pathogenic associations of obesity include the stimulatory effects of insulin and leptin on the sympathetic nervous system and activation of the renin-angiotensin-aldosterone system (RAAS) in obesity.[66] The prevalence of high SBP among this cohort was almost similar to the prevalence of poor glycaemic control, increased BMI and waist circumference.

4.4.4.2 Measures of obesity and adiposity

In the present study, BMI was used as an indicator for general obesity while waist circumference was an indicator for central obesity. Lipid profiles were only available for a few participants.

More than 60% of participants were either overweight or obese. Region of origin of participants, betel nut exposure and age were significant independent factors associated with BMI. Although gender was an independent factor, the association was not significant. Those from the New Guinea Islands and the Momase regions were twice as likely to have a BMI ≥25kg/m^2, but this was not significant. However, being from the Highlands region was significantly associated with a BMI ≥25kg/m^2.

The increasing trend of obesity among the urban Highlanders in PNG is different to what has been observed in rural Highlanders living a more traditional lifestyle.[62-64 64, 67, 68] This is an indication of lifestyle changes as a result of residing in urban areas.

When age was regrouped into two categories and entered into the logistic regression models, it became a significant independent factor affecting BMI. Those aged ≥50 years of age were significantly associated with a higher BMI after adjusting for other confounders. Studies have shown that obesity increases progressively from 20 to 60 years and decreases after 60 years of age.[69, 70] It would have been useful to examine the association with an age cut-off at 60 years. A decline in physical activity and hence total energy expenditure may partly be contributing to the gradual increase in body fat with advancing age in the present cohort. This study observed a decline in physical activity with advancing age.

This study showed that a high proportion (70.1%) of participants had an abnormally high waist circumference. The most important factor influencing waist circumference was gender. Females were nine times more likely to have a waist circumference above normal, compared to the males. This finding is inconsistent with other findings that males are more likely to have central adiposity compared to females.[71] One possible reason for this finding in PNG is parity. Papua New Guineans usually have large families predisposing mothers to central adiposity. Studies have reported an adverse influence of having three or more children on waist circumference. [72, 73] However, in rural villages of PNG, even women who have many children usually do not put on weight or have central obesity. The finding that women are more likely to have increased waist circumference or BMI is different to what has been observed in rural areas, especially on the mainland of Papua New Guinea, where females are more likely to have a BMI or waist circumference within the normal limits. This is mostly due to increased habitual/occupational physical activity in rural areas.[11, 74, 75] The inconsistencies in studies investigating factors associated with obesity reflect the multifactorial risks of this disorder and, in some cases, the predominance of certain risk factors.

4.4.5 Betel nut chewing

4.4.5.1 Prevalence of betel nut chewing

Fifty five percent of the participants in this study were betel nut chewers. A review of literature found only one study reporting the prevalence of betel nut chewing among those living with T2DM. The PNG study [5 76] which was also conducted at the PMGH Diabetes clinic, reported a higher prevalence (74%) of betel nut chewing. That study included a smaller sample (n = 210) than the present study.

4.4.5.2 Demographic factors associated with betel nut chewing

Betel nut chewing for this cohort was associated with the participant's area of residence, the region of origin of the participant, years of residence in Port Moresby and level of education. Age also appeared to have an influence on the prevalence of betel nut chewing but the association was not significant.

Rural village dwellers had the highest proportion of betel nut chewers. This finding is similar to that of a comparison between rural and urban males in Sri Lanka, where the prevalence of betel nut chewing in the rural district was ten times that of the urban district. [77] Betel nut trees are grown in rural areas and, therefore, the nuts are more readily available and may be cheaper for rural dwellers. Urban dwellers mostly have to pay for betel nuts, so chewing betel nut may be a strain on the budget. However, employment did not have an influence on betel nut chewing, so it is more likely that the high prevalence of betel nut chewing may have been as a result of availability rather than cost.

Those from the Southern region were more likely to chew betel nut, most probably because betel nut is readily available and accessible for those from the Southern region, especially for those from the Central and Gulf provinces because these two provinces are linked to Port Moresby by road. This prevalence may have been correlated to area of residence, since those from the rural villages were those from the Southern region.

In terms of years of residence in Port Moresby and its association with betel nut chewing, the habit was more prevalent in those residing outside of the city of Port Moresby and those who had been in Port Moresby for a lifetime. Those who indicated that they had spent their lifetimes in Port Moresby were mostly those living in urban villages, who usually have family in rural villages, which increases their access to betel nut.

The lowest prevalence of betel nut chewing was observed among those who did not complete basic primary education, compared to all other categories of education level. There was no difference observed among all other higher levels of education. It is not known why those with this level of education were least likely to chew betel nut. Although this may be a reflection of the affordability of betel nut, employment status did not influence the prevalence of betel nut chewing. One of the reasons for this is that betel nut is commonly shared, as a gesture of goodwill, during meet and greet events and other social gatherings, and as a sign of friendship or kinship.

4.4.5.3 Lifestyle factors associated with betel nut chewing

Alcohol, smoking, work-related MIA and amount of physical activity per week were significantly associated with betel nut chewing. Walking as a means of travel, work-related VIA and number of vegetable servings also appeared to be associated with betel nut chewing but the association did not reach significance. After adjusting for other confounding factors, alcohol consumption, work-related MIA and smoking were independent factors influencing betel nut chewing. The influence of smoking however was not significant. This may be because of the small number of participants who were smokers.

The finding that alcohol and smoking are associated with betel nut is consistent with findings in settings where betel nut chewing is endemic. [77-82] However, the finding that betel nut chewers are more physically active is in contrast with what has been reported in Taiwan.[79] In PNG, alcohol, tobacco products and betel nut are commonly shared and consumed during social gatherings.

4.4.5.4 Physical factors associated with betel nut chewing

Although those who had chewed betel nut for more than 25 years appeared more likely to have a high SBP in comparison to their counterparts, this was not statistically significant. Betel nut chewing did not influence DBP. Consequently, betel nut chewing did not influence blood pressure among this cohort of T2DM. This finding is different to that reported elsewhere in population-based studies.[78, 82] This indicates that there are more important risk factors, other than betel nut chewing, affecting blood pressure among those with T2DM.

Betel nut chewing was significantly associated with BMI. Quitting the habit and chewing ≤5 nuts per day had a beneficial effect on BMI. Never having chewed betel nut appeared to have a beneficial effect but this did not reach significance when compared with those who chewed >5 nuts per day. When adjustments were made for other confounding factors, the overall significance of betel nut chewing on BMI remained, but it was less significant. It appears that, apart from the beneficial effects of never having chewed or quitting the habit, a lower dose of betel nut chewing also has a beneficial influence on BMI in those with T2DM.

Although betel nut chewing did not have an influence on waist circumference, based on the univariate analysis, adding waist circumference to the multivariate logistic regression models demonstrated an independent association with betel nut chewing, but this was of borderline significance. Never having chewed betel nut, chewing ≤5 nuts per day, and quitting the habit had beneficial influences on waist circumference in comparison to chewing >5 nuts per day. These results indicate a dose effect of betel nut on obesity in those with T2DM. The finding that betel nut chewing is associated with BMI and waist circumference is consistent with findings among non-diabetic populations. [78-81, 83-85] but a beneficial influence appears to result from a low dose of betel nut; too much of it may predispose the chewer to a higher BMI.

Animal studies reporting the effects of betel nut on cholesterol or obesity have been inconsistent. Several studies have reported a favourable effect [86-88] of betel nut or arecoline on lipids while Boucher et al [89] have reported the reverse. Zhou et al [87] reported a significant reduction in total cholesterol and increased HDL by low dose

of areca oil plus arecoline in rats. Iqbal et al [90], however reported a low dose of betel nut causing a significant increase on total cholesterol while a high dose had no effect in a rat model. Animal studies have demonstrated that betel nut inhibits activity on cholesterol absorption in high cholesterol diets resulting in reduced plasma lipid concentrations [88, 90]

4.4.6 Glycaemic control

The present study showed that only a small number of participants (18.3%) achieved the optimal target for glycaemic control of ≤7.0%. The proportion of participants achieving optimal glycaemic control in the present study is lower than that reported elsewhere [41, 91, 92] In comparison with some recent reports from the Pacific Island Countries (PICs), the prevalence of optimal glycaemic control in the present cohort is similar to what has been reported in the neighbouring Solomon Islands (17.0%) and Nauru (20.0%) but less than that reported in those from Vanuatu (28.0)%. [93]. An earlier study [94] in PNG showed 64% (N = 83) had poor glycaemic control (HbA1c >10.0%). That study, however, used a higher HbA1c cut-off than the present study. Differences in prevalence rates of poor glycaemic control may partly be explained by the different cut-offs for appropriate glycaemic control. Studies elsewhere using the optimal target of HbA1c ≤7.0% have reported higher prevalence rates of poor glycaemic control than that observed in the present study. [95-98]

4.4.6.1 Influence of demographic factors

Using Chi-square statistics, the demographic factors which appeared to have an association with glycaemic control were gender, age and employment. Logistic regression analysis indicated that females and those younger than 50 years had poor glycaemic control while those who had retired exhibited better glycaemic control.

It is possible that older aged patients with T2DM who have been diagnosed much later in their life, may have had no or minimal risk factors for much of their lives, at least until later in life. Further, older aged T2DM patients may have had relatively

good glycaemic control after diagnosis and, therefore, lived longer than those who did not. Hsieh et al [99] reported an association between glycaemic control and age at diagnosis, with those diagnosed later in life having better glycaemic control. In the present study, better glycaemic control may be partly explained by better medication adherence among older participants (≥60 years). Female participants of the present study may have had poor glycaemic control because this group of participants appeared to be more likely to have a higher than normal BMI and waist circumference, both of which are risk factors for T2DM. The finding that female participants had poor glycaemic control, compared to their male counterparts, is consistent with other studies [100, 101], although not all studies have found an association of gender with glycaemic control. [102] One of these studies reporting poorer glycaemic control among women, compared to their male counterparts, was a Saudi Arabian cross-sectional study of 1,000 diabetes patients. Apart from the finding that females had poorer control than males, the study also found that females were more obese than their male counterparts. Further, the current study found that females significantly had an abnormally higher waist circumference, which is a risk factor for poor glycaemic control. However, results of the present study indicated that waist circumference was not associated with poor optimal glycaemic control.

4.4.6.2 Influence of lifestyle factors

Lifestyle factors which had an association with glycaemic control were smoking status, work-related VIA and minutes of walking to get to and from places. The associations of performing MISFRA and minutes of work-related MIA were of borderline significance.

Participants who had never smoked tobacco were more likely to have poor glycaemic control, compared to those who did.

Interestingly, results of this study indicated that those who did work-related VIA and MISFRA were more likely to have poor glycaemic control. Those whose work involved VIA, or who were performing MISFRA, were three times more likely to have poor glycaemic control compared to those who did not participate in these activities.

This may have been due to compensatory over-eating after such physical activities. This compensatory over-eating may have had a cultural component as well because from personal knowledge, a person who works hard for income or brings food home for a family is rewarded with a large meal, for those who can afford such meals. In this study, work was not merely employment-related but also included activities such as household chores, gardening and fishing, for example. It is also possible that those who are physically active develop bigger appetites. Participants of this study who were physically active were probably consuming low energy meals before engaging in physical activity. Hubert et al [103] reported that low energy breakfast increased hunger and increased energy intake. Further, that study reported that low energy breakfast failed to generate the inhibitory satiety signals. High dose exercise however does not induce hunger. [104] Martins et al argue that the effect of exercise on energy intake and appetite is a controversial area because the mechanisms that operate to regulate appetite are complex. [105]

The present study requested that participants think of a typical week when they performed physical activity and answer questions related to such activities. Participants may have remembered only a week when they were most physically active. The responses included in this study were self-reported, possibly explaining why results observed were different to studies involving directly-observed physical activities and their associations with glycaemic control. However, other studies involving self-reported activities have reported that physical activity had a beneficial influence on glycaemic control. [24] Effects of exercise interventions have also reported a beneficial effect on glycaemic control. [106, 107] A meta-analysis [108] of controlled trials reported that all forms of exercise training conferred small benefits on HbA1c.

Genetics also may have played a role in the results observed. A recent study [109] has shown that genes may play a part in affecting the outcomes of physical activity on glycaemic control. That study reported an association between the glucagon gene and both moderate and high-intensity physical activity, whereby those with the C-C genotype who did moderate or high-intensity physical activity had a reduced risk of T2DM. The study further reported that those with the T-T haplotype who did high-intensity physical activity had increased risk of T2DM. The glucagon gene

encodes glucagon, glucagon-like peptides 1 and 2, and oxyntomodulin proteins which are involved in glucose metabolism homeostasis. More research on these genes may assist in devising programs for the prevention of T2DM and also appropriate management programs aiming at achieving optimal glycaemic control for those with T2DM.

4.4.6.3 Influence of physical and medical factors

Use of hypoglycaemic medications, glibenclamide dose per day and number of years living with T2DM were important factors influencing glycaemic control.

SBP did not influence glycaemic control and the influence of DBP was of borderline significance. After adjusting for other medical confounders, the significant influence of daily dose of glibenclamide and number of years living with T2DM remained. The borderline significant influence of DBP also remained but the significance increased. Those with high DBP were more likely to have poor glycaemic control compared to their counterparts. The association of high DBP with poor glycaemic control has been reported elsewhere.[110]

Although BMI was not associated with glycaemic control in the univariate analysis, adding this variable to the multivariate logistic regression models resulted in BMI having an independent influence on glycaemic control. Obesity is a contributing factor to insulin resistance which is one of the underlying problems leading to T2DM.[111]

It is well known that, as T2DM progresses, β-cell function declines and may decline faster in poorly controlled T2DM. The association of poor glycaemic control with longer disease progression observed in the present study has been reported elsewhere. [99, 112] Further, disease progression is associated with complications of the disease. [93]

It is known that hypoglycaemic medications lower blood glucose. For this reason, it was unexpected in the present study that being prescribed hypoglycaemic medication was adversely associated with glycaemic control. As the number of prescribed hypoglycaemic medications increased, the likelihood of poor glycaemic control also increased. This is probably an indication of the progressive nature of

the disease. As T2DM progresses, the likelihood of being prescribed hypoglycaemic medications or a combination of them increases. Those on diet-controlled management are usually those who have had a shorter duration of T2DM and appropriate glycaemic control that does not require drug therapy. It is also possible that those prescribed hypoglycaemic medications are not complying with other aspects of management, such as lifestyle modification, because they are more reliant on medications to lower blood glucose while eating carelessly. It is also possible that hypoglycaemic regimens prescribed for those in this study may have been insufficient to control hyperglycaemia. An overstretched and poorly resourced clinic further adds to the problem because these factors may be contributing to inadequate follow up of patients. The observation of poor glycaemic control in those prescribed hypoglycaemic drug therapy has been reported elsewhere. [110] The UKPDS study [113] reported that the need to increase the number of hypoglycaemic medications is indicative of the progressive decline of β-cell function. The study further reports that by three years of diagnosis, 50% of T2DM patients will need more than one pharmacological agent and by nine years, 75% will need multiple therapies. The present study showed that more than 50% of the participants who had lived with diabetes for more than five years were taking one or no hypoglycaemic medication. This indicates that more than half of these patients were receiving insufficient therapy for their diabetes.

4.4.6.4 Influence of betel nut chewing

Betel nut chewing history/status exhibited an association with glycaemic control. The beneficial influence of betel nut chewing on glycaemic control also tended to be dose-related.

Using never chewers as the reference, those who had quit and those who chewed ≤5 nuts per day were significantly more likely to have better glycaemic control. Although chewing >5 nuts per day appeared to be associated with better glycaemic control in comparison to those who had never chewed, this association was not significant. After controlling for other confounders, betel nut chewing continued to be associated with glycaemic control and, therefore, betel nut independently influenced glycaemic control.

A search of the literature did not find any studies on glycaemic control among betel nut chewers with T2DM in other countries where the habit is prevalent. The only similar study was a PNG study by Benjamin et al. [5] That study reported that 73% of those with poor glycaemic control were betel nut chewers, a finding that is contradictory to that of the present study The blood glucose levels used in the study were reported to be the most recent blood glucose measurements recorded in medical notes, with no specific indication of time between measurements and data collection. Benjamin et al [5] did not further investigate whether or not betel nut chewing was independently associated with poor glycaemic control, which was defined in that study as blood glucose ≥10 mmol/L.

Other studies which have investigated the association between betel nut chewing and glycaemic control in the general populations of other countries have also reported an influence of betel nut chewing on poor glycaemic control. [79, 114] Tung et al [114] further reported a dose-dependent influence of betel nut on glycaemic control. Tseng reported an association between betel nut chewing and incident T2DM. [85] However, those studies did not investigate the glycaemic effects of betel nut chewing in relation to T2DM but were focussed on the general population. Further, most of these studies included males only and have been conducted in Taiwan. The beneficial association of betel nut chewing observed in the present study is similar to that observed in a small study by Chempakan [115] involving humans who were subcutaneously administered injections of arecoline.

Findings from animal studies also have been inconsistent. These studies have not only investigated the glycaemic effect of betel nut or its chemical constituents but also that of PBL. Boucher et al [89] reported glucose intolerance in adult mice fed with betel nut. Ling et al [86] reported a decreased level of fasting blood glucose in Wistar rats after treating these rats with different doses of arecoline. Using PBL extract, Arambewela et al [116] reported hypoglycaemic effects in normoglycaemic and diabetes-induced rats. That study reported a glucose-lowering effect comparable to tolbutamide, a hypoglycaemic drug. Iqbal et al, [90] however, demonstrated no effect of betel nut on glucose and body weight in a normoglycaemic rat model. In diabetes-induced rats, oral administration of a betel nut extract for 30 days demonstrated that the nut possesses antidiabetic properties which are comparable

to gliclazide, an oral hypoglycaemic drug. [117] Possible mechanisms of betel nut and additives on glycaemic control have already been discussed in the literature review.

In the present study, a low dose of betel nut had a beneficial influence on general and central obesity, both of which are known risk factors for T2DM or poor glycaemic control.

4.5 Conclusions

The present study observed a high prevalence of betel nut chewing among those with T2DM. The prevalence of poor glycaemic control was high (82.0%). Significant independent factors associated with glycaemic control were gender, betel nut exposure, MISFRA, work-related MIA, number of years diagnosed with T2DM, DBP and hypoglycaemic medication use. Of these factors, physical activity had a significant association with betel nut chewing. Betel nut chewing had a significant independent association with glycaemic control, with chewers and quitters being more likely to have better glycaemic control than those who had never chewed; a finding that contradicts what has been reported among the general population in Taiwan.

In conclusion, low dose of betel nut chewing has a beneficial influence on glycaemic control among those with T2DM. This study is a cross-sectional study and, therefore, has limitations in explaining any mechanism of action for the glucose lowering effects of betel nut in T2DM.

4.6 References

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Chapter V: Glycaemic effects of betel nut chewing and its associated factors in a non-T2DM cohort

5.1 Objectives

The main objectives of this part of the research, involving a cohort of participants without T2DM, were to:

1 Identify their characteristics with a focus on their demographics, lifestyle behaviours, and physical and biochemical measurements.
2 Estimate the prevalence of betel nut use.
3 Identify demographic, lifestyle, biochemical [as measured by bioelectric impedance analysis (% body fat)] and physical factors associated with betel nut chewing.
4 Determine the effects of factors associated with betel nut chewing on glucose control [as measured by oral glucose tolerance (OGT) and fasting capillary blood glucose (FCBG)].
5 Determine whether betel nut chewing is associated with poor glucose control and whether the association, if any, is independent of other confounding factors included in this research.

5.2 Methodology

5.2.1 Study setting

This study was undertaken in the National Capital District (NCD), where the Port Moresby General Hospital (PMGH) Diabetes Clinic is situated. The study included two urbanised suburbs and one peri-urban area in the NCD.

5.2.2 Data collection

Data for this phase was taken from the World Health Organization (WHO) STEPwise approach to surveillance (STEPS) survey.[1] The survey used a standardised method for collecting data in many developing countries. In PNG, the

study was completed on the 22nd of March 2007 to the 30th of March 2008 by HOPE worldwide PNG (Papua New Guinea), in association with the PNG National Department of Health, with funding from the WHO.

Data collection for this survey is described elsewhere [1] and was modified for PNG (Appendix 13). Briefly, data collected for this survey was in relation to behavioural and other health risk factors for non-communicable diseases such as diabetes and hypertension. Data was collected in a step-wise approach, commencing with behavioural risk factors, followed by physical measurements and then biochemical measurements.

5.2.3 Statistics

Data was obtained from HOPE worldwide PNG in an Excel format and was imported into SPSS version 22.0 for data analysis. Those people excluded from analysis were those whose information was discrepant, those who reported being diagnosed with diabetes or were undergoing treatment for diabetes and women who were pregnant.

All statistical analyses outlined in chapter IV that were performed on participants with diabetes were repeated on the STEPS data for non-diabetic participants.

5.2.4 Ethics

Approval for the study was granted by the Curtin University Human Research Ethics Committee (approval number HR 38/2011), the University of PNG's School of Medicine and Health Sciences Research and Ethics Committee, and the Medical Research Advisory Committee of the National Department of Health of PNG.

Data was received from HOPE worldwide PNG in de-identified format and, therefore, consent was not required from participants in this survey.

Permission to use the data for this study was granted by HOPE worldwide PNG.

5.3 Results

5.3.1 Study setting

This study was undertaken in NCD, the same district where PMGH is located. The study included participants from three selected suburbs in the NCD, one of which was a peri-urban suburb.

5.3.2 Demographic characteristics

Of the 922 participants, 511 (55.4%) were females and most of the participants were either from the Southern (39.9%) or the Highlands (37.7%) regions. The mean age for participants was 36.6±13.0, with ages ranging from 15 to 67 years. The highest number of participants were in the age group <30 – 39 years while the least number of participants was in the age group 60 – 69 years.

Participants of this study resided in the urban and peri-urban areas of the NCD, with more than half (67.5%) of the participants in urban areas. Three hundred and seventy seven (40.9%) participants had lived in the Port Moresby suburb from where they were recruited for more than 10 years. The number of years of living in that suburb was used as an estimate for the number of years of living in Port Moresby.

Of the 922 participants, 188 (20.4%) either had no formal education or had not completed basic primary education (Grades 6 or 8). Three hundred and forty seven (37.6%) participants had completed basic primary education and 355 (38.5%) attained a secondary school certificate by completing Grades 10 and 12.

Five hundred and thirty three participants were either in non-paid employment (homemakers, volunteers, students) or were unemployed (Table 5.1). Two hundred and fifty (27.1%) participants were in regularly paid employment, either in the government or non-government sectors, while 114 (12.4%) were self-employed.

Table 5.1 Demographic characteristics of study participants (N = 922)

Characteristic	n*	Percentage
Gender		
Male	411	44.5
Female	511	55.4
Age category		
< 40	647	70.2
40 – 49	132	14.3
50 – 59	108	11.7
60 – 69	35	3.8
Region of origin		
Southern	368	39.9
Momase	117	12.7
Highlands	348	37.7
New Guinea Islands	86	9.3
Level of education		
No formal education	89	9.7
Less than Grade 6	99	10.7
Grade 6	177	19.2
Grade 8	170	18.4
Grade 10/vocational	248	26.9
Grade 12	107	11.6
Tertiary education	26	2.8
Area of residence		
Urban	622	67.5
Peri-urban	300	32.5
Employment status		
Homemaker	177	19.2
Retired	11	1.2
Unpaid	5	0.5
Self-employed	114	12.4
Unemployed, able to work	214	23.2
Unemployed, unable to work	24	2.6
Government	94	10.2
Non-government	156	16.9
Student	113	12.3
Years of residence in Port Moresby		
1 – 2	79	8.6
3 – 5	116	12.6
6 – 10	277	30.0
> 10	377	40.9

*The number may not add up to the total because of missing values for some categories.

5.3.3 Lifestyle characteristics

The lifestyle characteristics, which were recorded, included alcohol consumption, tobacco smoking, betel nut chewing, fruit and vegetable consumption and physical activity.

5.3.3.1 Alcohol consumption

Almost half (41.4%) of the 922 participants had consumed alcohol in the preceding 12 months.(Table 5.2) Of those who consumed alcohol in the preceding 12 months, more than half (61.3%) had consumed alcohol in the preceding 30 days.

One hundred and thirty nine (36.4%) participants consumed alcohol at least once per week. Of those who consumed alcohol in the preceding 12 months, 51.3% reported consuming 10 drinks or less on a single occasion, while 38.7% had consumed more.

For males in this subgroup, the mean number of days on which they had consumed five or more standard drinks in a single day over the preceding 12 months was 6.2±6.0 days (n = 107 participants). In comparison, the mean number of days for which female participants had consumed four or more standard drinks in a single day was 3.3±3.5 days (n = 54).

The most common source of alcohol was friends/relatives (46.6%), followed by participants buying their own alcohol (45.5%). More than 50% of the participants who had consumed alcohol recorded more than 10 alcoholic drinks as their largest number of drinks on a single occasion.

Table 5.2 Alcohol consumption amongst participants

Variable	n/N*	Percentage
Alcohol consumed in the previous 12 months		
No	540/922	58.6
Yes	382/922	41.4
Frequency of having at least one drink in the previous 12 months		
1 - 7 days/week	139/382	36.4
1 - 3 days/month	67/382	17.5
Less than once a month	146/382	38.2
Alcohol consumed in the previous 30 days		
No	140/382	36.6
Yes	234/382	61.3
Alcohol consumed in the previous 7 days		
No	206/382	53.9
Yes	176/382	46.1
Average number of alcoholic drinks at any one time in a day		
≤ 5	67/382	17.5
6 - 10	129/382	33.8
>10	148/382	38.7
Largest number of drinks on a single occasion in the last 12 months		
1 - 10	115/382	30.1
11 - 20	109/382	28.5
>20	109/382	28.5
Source of alcohol*		
Bought by self	174/382	45.5
Friends/relatives	178/382	46.6
Homebrew	8/382	2.1

*May not add up to the total because of missing values

The Chi-square statistic was used to test for any association between alcohol consumption and the demographic factors (categorical variables). Those variables which were found to show some association ($p < 0.05$) were entered into a multivariate logistic regression model to investigate both the direction of the associations for different categories of each variable and factors independently associated with alcohol consumption in the preceding 12 months.

Gender, age, education and employment had statistically significant associations with alcohol consumption in the preceding 12 months, while gender, employment

and area of residence had significant influences on alcohol consumption in the preceding 30 days (Table 5.3).

For those who had consumed alcohol in the preceding 12 months, the likelihood of consuming alcohol varied with age. Those aged <50 years were more likely to consume alcohol, compared to those aged 50 years or older. Male participants were more likely to have consumed alcohol in the preceding 12 months or 30 days, compared to their female counterparts.

Those who had completed tertiary education and those in regular paid employment were more likely to have consumed alcohol in the preceding 12 months.

Using “yes, alcohol consumed in the previous 12 months” as the dependent variable, multivariate logistic regression analysis indicated that age, gender, level of education, employment status, smoking and betel nut exposure were independently associated with alcohol consumption, with age, gender, smoking and betel nut exposure being the most important factors (Table 5.4). For multivariate analysis, a 4-employment status was collapsed into two categories because of the small sample number for those who were retired. Those who had retired were included in the unpaid/unemployed category and self-employed participants were combined with those in paid employment to create the category “employed”.

Those younger than 50 years were six times more likely to consume alcohol, compared to their counterparts aged 60 years and older. Female participants had lower odds of consuming alcohol in comparison to their male counterparts. Although education had an independent influence on alcohol consumption, the association was only significant when comparing those who had completed basic primary education with those who had not. Those who were employed and those who were betel nut chewers were more likely to consume alcohol, compared to their counterparts. Heavy betel nut chewers (>5 nuts/day) were more likely to consume alcohol compared to those who never chewed, those who had quit and those who chewed ≤5 nuts/day.

Table 5.3 Associations of demographic factors with alcohol consumption

Variable	Alcohol consumed in the previous 12 months		p-value	Alcohol consumed in the previous 30 days		p-value[#]
	No	Yes		No	Yes	
Gender			<0.001			<0.001
Female	385 (75.3)	126(24.7)		64(52.9)	57(47.1)	
Male	155 (37.7)	256(62.3)		76(30.0)	177(70.0)	
Age			<0.001			0.741
<50	432 (55.5)	347(44.5)		128(37.5)	213(62.5)	
50 - 59	80 (74.1)	28(25.9)		9(33.3)	18(66.7)	
≥60	28 (80.0)	7(20.0)		3(50.0)	3(50.0)	
Level of Education			<0.001			0.093
Did not complete basic education	111 (59.0)	77(41.0)		34(47.2)	38(52.8)	
Primary basic education	232 (66.9)	115(33.1)		45(39.8)	68(60.2)	
Secondary/ Vocational	182 (51.3)	173(48.7)		54(31.4)	118(68.6)	
Tertiary	11 (42.3)	15(57.7)		7(46.7)	8(53.3)	
Employment status			<0.001			0.001
Paid	114 (45.6)	136(54.4)		32(23.0)	102(76.1)	
Unpaid/ unemployed	351 (65.9)	182(34.1)		81(45.8)	96(54.2)	
Retired	6 (54.5)	5(45.5)		2(40.0)	3(60.0)	
Self-employment	64 (56.1)	50(43.9)		21(42.9)	28(57.1)	
Area of residence			0.920			0.034
Urban	365(58.7)	257(41.3)		87(33.9)	170(66.1)	
Peri-urban	175(58.3)	125(41.7)		53(45.3)	64(34.7)	
Region of origin			0.481			0.711
Southern	211 (57.3)	157(42.3)		53(34.4)	101(65.6)	
NGI	48 (55.8)	38(44.2)		15(36.6)	26(63.4)	
Momase	76 (65.0)	41(35.0)		57(41.0)	82(59.0)	
Highlands	204 (58.6)	144(41.4)		14(36.8)	24(63.2)	
Years of residence in Port Moresby			0.141			0.997
≤10	289 (61.2)	183(38.8)		66(36.7)	114(63.3)	
>10	212 (56.2)	165(43.8)		59(36.6)	102(63.4)	
Smoker status			<0.001			0.182
Current	92 (26.3)	258 (73.7)		89 (34.8)	167(65.2)	
Quit	65 (69.1)	29 (30.9)		9 (34.6)	17 (65.4)	
Never	379 (80.3)	93 (19.7)		41 (45.6)	49 (54.4)	
Betel nut exposure			<0.001			0.805
Never	124 (88.6)	16 (11.4)		7 (43.8)	9 (56.3)	
Quit	25 (83.3)	5 (16.7)		1 (25.0)	3 (75.0)	
≤5 nuts/day	250 (62.0)	153 (38.0)		59 (39.6)	90 (60.4)	
>5 nuts/day	129 (39.2)	200 (60.8)		71 (36.0)	126(64.0)	

[#] The p-values were obtained from the Chi-square statistics and assess the strengths of associations. NGI = New Guinea Islands

Table 5.4 Multivariate logistic regression analysis of demographic risk factors for alcohol consumption within the previous12 months

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Age				
<50	347/779 (44.5)	7.68	2.44 - 24.14	<0.001
50 - 59	28/108 (25.9)	2.92	0.83 – 10.20	<0.001
≥60	7/35 (20.0)	1 (reference)		0.094
Gender				<0.001
Female	126/511(24.7)	0.26	0.18 - 0.37	
Male	256/411(62.3)	1 (reference)		
Level of Education				0.005
Did not complete basic education	77/188 (41.0)	1 (reference)		
Primary basic education	115/347 (33.1)	0.43	0.26 - 0.71	0.001
Secondary/Vocational	173/355 (48.7)	1.02	0.63 - 1.65	0.930
Tertiary education	15/26 (57.7)	2.34	0.77 - 7.27	0.132
Employment status				0.017
Employed	186/364 (51.1)	1 (reference)		
Unpaid/unemployed	187/544 (34.4)	0.64	0.44 – 0.92	
Smoker status				<0.001
Current	258/350 (73.7)	1 (reference)		
Quit	29/94 (30.9)	0.25	0.14 – 0.45	<0.001
Never	93/472 (19.7)	0.16	0.11 -0.23	<0.001
Betel nut exposure				<0.001
Never	16/140 (11.4)	0.16	0.09 – 0.32	<0.001
Quit	5/30 (16.7)	0.21	0.06 – 0.71	0.013
≤5 nuts/day	153/403 (38.0)	0.49	0.33 – 0.71	0.001
>5 nuts/day	200/329 (60.8)	1 (reference)		

The dependent variable was the answer "Yes" to alcohol consumption in the previous 12 months; *The column 'n/N (%)' shows the number (and percentage) of alcohol consumers within each variable who had consumed alcohol.

5.3.3.2 Tobacco smoking

Three hundred and fifty (38.0%) participants reported currently smoking tobacco. Of these smokers, 312 (89.1%) were daily smokers. Four hundred and seventy two (51.2%) participants had never smoked tobacco, while 444 (48.2%) had 'ever' been smokers (either currently or had quit). Of these, 94 (21.2%) participants had quit the habit.

For those classified as smokers, the median age was 29 with a minimum of 15 and a maximum of 67 years. For this subgroup, the median age for onset of smoking was 17, with a minimum of 10 and a maximum of 42 years. The median number of years of daily smoking was 9, with a minimum of 0 (<1 year) and a maximum of 45 years. For participants who had quit smoking, the median age at which these participants had given up the habit was 25, with a minimum age of 13 and a maximum of 47 years. Seventy (20.0%) participants who were smokers had been smoking for more than 20 years.

Manufactured cigarettes were the most common type of tobacco products used. Of the 350 smokers, 299 (85.4%) used manufactured cigarettes. Of those who smoked manufactured cigarettes, 256 (85.6%) smoked 20 cigarettes or less per day, while 116 (99.1%) of those who smoked hand-rolled cigarettes smoked less than 10 per day.

Table 5.5 Frequency of tobacco smoking and the characteristics of participants

Variables	Frequency* n/N (%)
Current smoker	
No	566/922 (61.4)
Yes	350/922 (38.0)
Smoking status	
Never	472/922 (51.2)
Quit	94/922 (10.2)
Current	350/922 (38.0)
Smoking history	
Never	472/922 (51.2)
Ever	444/922 (48.2)
Number of years of smoking	
≤ 10	185/350 (52.9)
11 - 20	72/350 (20.6)
21 - 30	45/350 (12.9)
>30	25/350 (7.1)
Number of manufactured cigarettes smoked/day	
1 - 10	235/299 (78.6)
11 - 20	21/299 (7.0)
>20	43/299 (14.4)
Number of hand-rolled cigarettes smoked/day	
1 - 10	116/117 (99.1)
11 - 20	1/117 (0.9)
>20	0/117 (0.0)
Number of pipes of tobacco smoked/day	
<5	8/12 (66.7)
≥5	4/12 (33.3)

*May not add up to the total because of missing values

As shown in Table 5.6, tobacco smoking was influenced by gender, age and employment status, alcohol consumption in the previous 12 months and betel nut exposure. Male participants were more likely to smoke, compared to their female counterparts. As age increased, the number of participants who smoked decreased. Those who were retired were more likely to smoke tobacco, but it must be noted that the sample number for this category was small. When comparing the categories of employment, those who were employed (both paid and self-employment) were more likely to smoke, compared to those in the unpaid/unemployed category. Betel nut chewers, betel nut chewers who chewed all three components of the betel nut and those who had consumed alcohol in the previous 12 months were more likely to smoke.

For multivariate analysis, whether or not a participant chewed betel nut was used in the model, rather than betel nut exposure, because the number of those who had quit betel chewing and were smokers was too small (<5) for logistic regression modelling. Gender, alcohol consumption in the last 12 months and betel nut chewing independently influenced tobacco smoking (Table 5.7). Male participants were four times more likely to smoke tobacco, compared to their female counterparts. Those who had consumed alcohol in the last 12 months and those who were current betel nut chewers were six times more likely to smoke, compared to those who did not consume alcohol or chew betel nuts.

Table 5.6 Factors associated with tobacco smoking

Variable	Current tobacco smoker		p-value[#]
	No	Yes	
Gender			<0.001
Female	385 (75.9)	122 (24.1)	
Male	181 (44.3)	228 (55.7)	
Age			0.014
<50	463 (59.8)	311 (40.2)	
50 - 59	77 (71.3)	31 (28.7)	
≥60	26 (76.5)	8 (23.5)	
Level of Education			0.769
Did not complete basic education	119 (63.6)	68 (36.4)	
Primary basic education	208 (60.5)	136 (39.5)	
Secondary/Vocational	218 (61.8)	135 (38.2)	
Tertiary education	18 (69.2)	8 (30.8)	
Employment status			0.008
Paid	140 (56.5)	108 (43.5)	
Unpaid/unemployed	350 (66.0)	180 (34.0)	
Retired	3 (30.0)	7 (70.0)	
Self-employed	67 (58.9)	47 (41.2)	
Area of residence			0.157
Urban	391 (63.4)	226 (36.6)	
Peri-urban	175 (58.5)	124 (41.5)	
Region of origin			0.259
Southern region	221 (60.7)	143 (39.3)	
New Guinea Islands	55 (64.0)	31 (36.0)	
Momase	81 (69.8)	35 (30.2)	
Highlands	208 (59.9)	139 (40.1)	
Years of residence in Port Moresby			0.870
≤10	291 (62.0)	178 (38.0)	
>10	230 (61.5)	144 (38.5)	
Alcohol consumption in the previous 12 months			<0.001
No	444 (82.8)	92 (17.2)	
Yes	122 (32.1)	258 (67.9)	
Betel nut exposure			<0.001
Never	132 (94.3)	8 (5.7)	
Quit	26 (86.7)	4 (13.3)	
≤5 nuts/day	272 (67.5)	131 (32.5)	
>5 nuts/day	130 (39.5)	199 (60.5)	
Betel nut chew components			<0.001
Betel nut + PBI + lime	196 (41.9)	272 (58.1)	
Betel nut ± PBI or lime	192 (75.6)	62 (24.4)	
Betel nut only	19 (90.5)	2 (9.5)	

[#]The p-values were obtained from the Chi-square statistics, and assess the strengths of associations. PBI = *Piper betel* inflorescence

Table 5.7 Multivariate logistic regression analysis of factors associated with tobacco smoking

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Gender				<0.001
Female	122/507 (24.1)	0.44	0.31 – 0.62	
Male	228/409 (55.7)	1 (reference)		
Consumed alcohol in the previous 12 months				<0.001
No	92/536 (17.2)	1 (reference)		
Yes	258/380 (67.9)	6.72	4.80 – 9.40	
Betel nut chewer				<0.001
No	12/171 (7.0)	1 (reference)		
Yes	337/744 (45.3)	6.89	3.59 – 13.20	

The dependent variable was the answer "Yes" to tobacco smoker; *The column 'n/N (%)' shows the number (and percentage) of tobacco smokers within each variable.

5.3.3.3 Betel nut chewing

Of the 922 participants, 745 (80.8%) reported that they were current betel nut chewers. One hundred and forty (15.2%) participants reported never chewing betel nut, while 30 (3.3%) had quit chewing betel nut. Overall, of all the participants studied, 775 (84.1%) had chewed betel nut at some time in their lives.

Of all the betel nut chewers, more than 60% of the participants chewed betel nut with lime and *Piper betle* inflorescence (PBI) and only 21 (2.8%) chewed the nut without lime or PBI (Table 5.8).

The survey asked participants how many times they chewed betel nut daily. For the purposes of analysis, the number of times a participant chewed betel nut daily was renamed quantity of betel nuts chewed daily, as it was assumed that participants chewed only one betel nut each time they chewed betel nut.

The mean number of betel nuts chewed by betel nut chewers per day was 6.6±5.7 (range: 1 - 50). For this category of participants, 403 (54.1%) chewed five or less and 29.4% chewed 10 or more betel nuts per day.

Table 5.8 Frequency of betel nut chewing and characteristics of participants

Variables	Frequency* n/N(%)
Betel nut chewer	
No	171/922 (18.5)
Yes	745/922 (80.8)
Mean number betel nut chewed/day ± SD	6.6 ± 5.7
Number of betel nuts/day†	
≤5	403/745 (54.1)
6 - 9	123/745 (16.5)
≥10	219/745 (29.4)
Betel nut chewing history	
Never	140/922 (15.2)
Quit	30/922 (3.3)
Current	745/922 (80.8)
Betel nut chewing status	
Never	140/922 (15.2)
Ever	775/922 (84.1)
Frequency of chewing betel nut with lime and PBI	
Always	469/745 (63.0)
Sometimes	205/745 (27.5)
Rarely	49/745 (6.6)
Never	21/745 (2.8)
Betel nut chewing components	
Betel nut + PBI + lime	469/745 (63.0)
Betel nut ± PBI or lime	254/745 (34.1)
Betel nut only	21 (2.8)

*****May not add up to the total because of missing values; †Equivalent to average number of times betel nut used daily; PBI = *Piper betle* inflorescence

Results indicated that gender, age, level of education, area of residence and region of origin were associated with betel nut chewing. (Table 5.9) As age increased, the prevalence of betel nut chewing decreased. Male participants, those who had completed basic and secondary education, those from urban areas and those from the Southern region were more likely to chew betel nut. Employment status and

number of years residing in Port Moresby were not associated with betel nut chewing.

Table 5.9 Demographic factors associated with betel nut chewing

Variable	Betel nut chewer		p-value[#]
	No	Yes	
Gender			0.002
Female	113 (22.2)	395 (77.8)	
Male	58 (14.2)	350 (85.8)	
Age			<0.001
<50	127 (16.4)	647 (83.6)	
50 - 59	32 (29.6)	76 (70.4)	
≥60	12 (35.3)	22 (64.7)	
Level of Education			0.002
Did not complete basic education	50 (26.7)	137 (73.3)	
Primary basic education	58 (16.9)	286 (83.1)	
Secondary/vocational	53 (15.0)	300 (85.0)	
Tertiary education	8 (30.8)	18 (69.2)	
Employment status			0.224
Paid	47 (19.0)	201 (81.0)	
Unpaid/Unemployed	95 (17.9)	435 (82.1)	
Retired	0 (0.0)	10 (100.0)	
Self-employed	27 (23.7)	87 (76.3)	
Area of residence			0.001
Urban	96 (15.6)	521 (84.4)	
Peri-urban	75 (25.1)	224 (74.9)	
Region of origin			<0.001
Southern	41 (11.2)	324 (88.8)	
Momase	21 (18.1)	95 (81.9)	
Highlands	92 (26.6)	254 (73.4)	
New Guinea Islands	16 (18.6)	70 (81.4)	
Years of residence in Port Moresby			0.845
≤10	89 (19.0)	380 (81.0)	
>10	69 (18.4)	305 (81.6)	

[#] The p-values were obtained from the Chi-square statistics and assess the strengths of associations.

Analyses of the association of betel nut chewing with other lifestyle factors indicate that betel nut chewing is associated with alcohol consumption ($p<0.001$) , smoking ($p<0.001$) , vegetable and fruit servings per day and number of days that fruit ($p = 0.010$) and vegetables ($p < 0.001$) are consumed in a typical week. From these

analyses, it was found that those who had consumed alcohol and were current smokers were more likely to chew betel nut and that those who had quit smoking were less likely to chew betel nut, compared to their counterparts who had not. Those who were betel nut chewers were more likely to consume vegetables for only two days or less, in a typical week, compared to non-chewers. Furthermore, betel nut chewers were more likely to consume less than three vegetable servings on any day when they had vegetables, compared to non-chewers. This finding was similar for fruit consumption. Those who were betel nut chewers were more likely to consume fruit for two days or less in a typical week, compared to non-chewers. Furthermore, they were more likely to consume less than two serves of fruit on any day that they had fruit, but this was of borderline significance ($p = 0.059$). The number of natural teeth also influenced the prevalence of betel nut use. Those who still had all of their natural teeth were more likely to chew betel nut, compared to those who had lost some ($p < 0.001$).

Multivariate analysis indicated that region of origin, alcohol consumption in the previous 12 months, smoking, number of days that vegetables were consumed in a typical week and number of natural teeth, were each independently associated with betel nut chewing. (Table 5.10) Although those from the Momase and New Guinea Islands regions were less likely to chew betel nut, compared to their counterparts from the Southern region, the differences were not statistically significant. Highlanders were significantly less likely to chew betel nut, compared to those from the Southern region. Those who were alcohol consumers were almost four times more likely to chew betel nut, compared to those who were not. Those who were smokers were almost eight times more likely to chew betel nut, compared to those who were not smokers. Having full sets of natural teeth positively influenced betel nut chewing; that is, those who had all their natural teeth were two times more likely to chew betel nut compared to those who had lost some of their natural teeth. Betel nut chewers were more physically active in terms of walking to get to and from places and participating in MISFRA.

Table 5.10 Multivariate analysis of factors associated with betel nut chewing

Variable	n/N (%)	Adjusted OR	95% CI	p-value
Region of origin				<0.001
Southern	324/365 (88.8)	1 (reference)		
Momase	95/116 (81.9)	0.72	0.38 – 1.33	0.291
Highlands	254/346 (73.4)	0.36	0.26 – 0.56	<0.001
New Guinea Islands	70/86 (81.4)	0.64	0.31 – 1.30	0.212
Alcohol in the previous 12 months				<0.001
No	385/535 (72.0)	1 (reference)		
Yes	360/381 (94.5)	3.60	2.11 – 6.15	
Smoker status				< 0.001
No	407/566 (71.9)	1 (reference)		
Yes	337/349 (96.6)	7.54	3.84 – 14.82	
Number of vegetable-eating days/week				0.018
0 - 2	175/194 (90.2)	2.06	1.16 – 3.67	
3 - 5	233/278 (83.8)	1.57	1.01 – 2.42	0.013
6 - 7	333/437 (76.2)	1 (reference)		0.044
Number of natural teeth				<0.001
All of them	527/621 (84.9)	2.10	1.42 – 3.11	
Some missing	214/290 (73.8)	1 (reference)		
Participates in MISFRA for at least 10 minutes				0.006
No	484/625 (77.4)	1 (reference)		
Yes	257/287 (89.5)	1.90	1.20 – 3.01	
Walks to get to and from places				0.006
No	67/102 (65.7)	1 (reference)		
Yes	672/808 (83.2)	2.02	1.22 – 3.34	

The dependent variable was the answer "Yes" to betel nut chewer; *The column 'n/N (%)' shows the number (and percentage) of betel nut chewers within each variable.

5.3.3.4 Vegetable and fruit consumption

Table 5.11 shows that vegetable and fruit consumption was poor amongst the study cohort. Ninety two per cent of the participants reported consuming less than three servings of vegetables per day in a typical week. Despite eating less serves of vegetables, 47.6% of the participants reported eating vegetables for 6 - 7 days in a typical week. When compared with vegetable consumption, 70% of the participants

consumed fruit on two days or less in a typical week, and 66.6% had less than two serves of fruit on any day that they consumed fruit (Table 5.11).

Table 5.11 Frequencies of fruit and vegetable consumption characteristics (N=922)

Variables	Frequency n (%)*
Vegetable servings/day	
<3	848 (92.0)
≥3	66 (7.2)
Number of vegetable-eating days/week	
0 - 2	196 (21.3)
3 - 5	279 (30.3)
6 - 7	439 (47.6)
Fruit servings/day	
<2	614 (66.6)
≥2	273 (29.6)
Number of fruit-eating days/week	
0 - 2	646 (70.1)
3 - 5	207 (22.5)
6 - 7	62 (6.7)

*May not add up to total because of missing values

Chi-square statistics indicate that the number of vegetable servings was influenced by area of residence and betel nut chewing (Table 5.12). The number of vegetable servings also tended to be associated with level of education. Those who did not complete basic education were more likely to consume ≥3 serves of vegetables in a day compared to those in other categories of level of education. Participants residing in peri-urban areas were more likely to consume ≥3 serves of vegetables in a day, compared to their urban counterparts. Those who were betel nut chewers were less likely to consume ≥3 serves of vegetables, compared to those who were not. The association of the number of vegetable serves consumed with employment status was of borderline significance.

Chi-square statistics also indicate that the number of vegetable and fruit consumption days was influenced by betel nut chewing (not shown). Those who were betel nut chewers were more likely to consume vegetables for only two days or less in a typical week, compared to non-chewers ($p < 0.001$). This finding was similar for fruit consumption. Those who were betel nut chewers were more likely to

consume fruit for only two days or less in a typical week, compared to non-chewers (p = 0.010).

Table 5.12 Factors associated with vegetable servings consumed

Variable	Vegetable servings		p-value[#]
	<3	≥3	
Gender			0.259
Female	466 (91.9)	41 (8.1)	
Male	382 (93.9)	25 (6.1)	
Age			0.637
<50	718 (93.1)	53 (6.9)	
50 - 59	98 (90.7)	10 (9.3)	
≥60	32 (91.4)	3 (8.6)	
Level of Education			0.043
Did not complete basic education	165 (88.2)	22 (11.8)	
Primary basic education	324 (94.2)	20 (5.8)	
Secondary/vocational	331 (94.3)	20 (5.7)	
Tertiary education	24 (92.3)	2 (7.7)	
Employment status			0.099
Paid	223 (90.7)	23 (9.3)	
Unpaid/Unemployed	499 (94.3)	30 (5.7)	
Retired	11 (100.0)	0 (0.0)	
Self-employed	102 (89.5)	12 (10.5)	
Area of residence			<0.001
Urban	588 (95.3)	29 (4.7)	
Peri-urban	260 (87.5)	37 (12.5)	
Region of origin			0.144
Southern	344 (94.0)	22 (6.0)	
Momase	108 (93.1)	8 (6.9)	
Highlands	311 (90.4)	33 (9.6)	
New Guinea Islands	82 (96.5)	3 (3.5)	
Years of residence in Port Moresby			0.940
≤10	434 (92.9)	33 (7.1)	
>10	348 (92.8)	27 (7.2)	
Alcohol consumed in the previous 12 months			0.873
No	497 (92.9)	38 (7.1)	
Yes	351 (92.6)	28 (7.4)	
Smoker status			0.181
No	517 (91.8)	46 (8.2)	
Yes	325 (94.2)	20 (5.8)	
Betel nut chewer			0.025
No	149 (88.7)	19 (11.3)	
Yes	694 (93.7)	47 (6.3)	
Number of natural teeth			0.562
All of them	579 (93.1)	43 (6.9)	
Some missing	265 (92.0)	23 (8.0)	

[#] The p-values were obtained from the Chi-square statistics and assess the strengths of associations.

The sample number for those who were retired was very small, so this group was amalgamated with the unpaid/unemployed category, leading to the three-category employment variable shown in Table 5.13. Results of multivariate logistic regression analysis indicate that consuming ≥3 servings of vegetables per day was associated with employment status and area of residence. Those who were in the unpaid/unemployed group were statistically less likely to consume ≥3 servings per day, compared to those who were in paid employment. Those who were self-employed consumed vegetables similarly to those in paid employment.

Table 5.13 Multivariate logistic regression of factors associated with vegetable servings

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Employment status				0.042
Paid	23/246 (9.3)	1 (reference)		
Unpaid/unemployed	30/540 (5.6)	0.50	0.28 – 0.90	0.020
Self-employed	12/114 (10.5)	0.94	0.43 – 2.04	0.875
Area of residence				<0.001
Urban	29/617 (4.7)	1 (reference)		
Peri-urban	37/297 (12.5)	3.46	2.04 – 5.89	

The dependent variable was ≥3 vegetable servings per day; *The column 'n/N (%)' shows the number (and percentage) of participants who consumed ≥3 serves of vegetables per day within each variable group.

Factors associated with the number of fruit servings consumed were level of education, employment and smoking status. The association of betel nut chewing and area of residence with the number of fruit servings per day were of borderline significance (Table 5.14). Those who completed tertiary and secondary/vocational education were more likely to consume ≥2 serves of fruit per day, compared to those who did not complete or only completed primary basic education. No other demographic variables appear to influence fruit consumption.

Table 5.14 Factors associated with fruit servings consumed

Variable	Fruit servings		p-value[#]
	<2	≥2	
Gender			0.914
Female	342 (69.4)	151 (30.6)	
Male	272 (69.0)	122 (31.0)	
Age			0.879
<50	523 (69.5)	229 (30.5)	
50 - 59	69 (67.6)	33 (32.4)	
≥60	22 (66.7)	11 (33.3)	
Level of Education			0.013
Did not complete basic education	136 (73.1)	50 (26.9)	
Basic primary basic education	248 (73.4)	90 (26.6)	
Secondary/vocational	212 (63.1)	124 (36.9)	
Tertiary education	14 (60.9)	9 (39.1)	
Employment status			0.001
Paid	142 (60.2)	94 (39.8)	
Unpaid/Unemployed	373 (72.4)	142 (27.6)	
Retired	11 (100.0)	0 (0.0)	
Self-employed	80 (71.4)	32 (28.6)	
Area of residence			0.062
Urban	397 (67.2)	194 (32.8)	
Peri-urban	217 (73.3)	79 (26.7)	
Region of origin			0.201
Southern	254 (72.2)	98 (27.8)	
Momase	70 (62.5)	42 (37.5)	
Highlands	235 (69.5)	103 (30.5)	
New Guinea Islands	53 (64.6)	29 (35.4)	
Years of residence in Port Moresby			0.302
≤10	309 (67.5)	149 (32.5)	
>10	255 (70.8)	105 (29.2)	
Alcohol consumed in the previous 12 months			0.150
No	353 (67.4)	171 (32.6)	
Yes	261 (71.9)	102 (28.1)	
Smoking status			<0.001
No	358 (64.7)	195 (35.3)	
Yes	251 (76.5)	77 (23.5)	
Betel nut chewer			0.059
No	104 (63.0)	61 (37.0)	
Yes	506 (70.6)	211 (29.4)	
Number of natural teeth			0.176
All of them	410 (67.9)	194 (32.1)	
Some missing	202 (74.2)	77 (27.6)	

[#] The p-values were obtained from the Chi-square statistics and assess the strengths of associations.

For multivariate logistic regression analysis of demographic factors and fruit servings, level of education was re-categorised because of the small number of participants who were in the tertiary education category. Tertiary education was combined with the secondary/vocational category because there was little difference between the two groups in the proportions who consumed two or more servings of fruit per day.

As shown in Table 5.15, multivariate logistic regression analysis indicates that employment and smoking independently influence the number of servings of fruit consumed. Those in paid employment were more likely to consume ≥2 servings of fruit per day, in a typical week, than those who were in the unpaid/unemployed category. Those who were self-employed were less likely to consume ≥2 servings of fruit per day compared to those who were in paid employment. Smokers were less likely to consume ≥2 servings of fruit per day compared to those who did not smoke.

Table 5.15 Multivariate logistic regression of factors associated with consumption of ≥2 fruit servings/day

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Employment status				0.001
Paid	94/236 (39.8)	1 (reference)		
Unpaid/unemployed	142/526 (27.0)	0.53	0.38 – 0.74	<0.001
Self-employed	32/112 (28.6)	0.60	0.37 – 0.98	0.042
Smoker status				<0.001
No	195/553 (35.3)	1 (reference)		
Yes	77/328 (23.5)	0.55	0.38 – 0.74	

The dependent variable was ≥2 fruit servings per day; *The column 'n/N (%)' shows the number (and percentage) of participants who consumed ≥2 servings of fruit per day, within each variable.

5.3.3.5 Physical activity

As shown in Table 5.16, results indicated that walking, to get to and from places, was the most common physical activity, with 88.0% (n = 811) of participants reporting that they walked for at least 10 minutes continuously to get to and from places. The number of participants involved in work-related physical activity was higher than those involved in physical activity through sports, fitness and recreational activities. More than 60% (n = 634) of participants reported undertaking sufficient physical activity.

For those who reported undertaking vigorous-intensity physical activity, more than 60% performed work-related vigorous-intensity activity (VIA) and vigorous-intensity sports, fitness and recreational activity (VISFRA) for ≥75 minutes per week. For participants involved in moderate-intensity activities (MIA), more than 50% performed them as work-related activities, while only 33.9% were involved in sports, fitness and recreational activities for ≥150 minutes per week.

Using the Chi-square statistics, the amount of physical activity, which includes all the different types of physical activity, was further examined to determine whether there was any association and, if so, the strength of the association, with demographic factors. Furthermore, the Chi-square statistics also were used to determine whether there was an association between either age or employment status with the different types of physical activity.

Table 5.16 Frequencies of self-reported physical activity

Variables	Frequency* n/N (%)
Work-related VIA for at least 10 minutes	
No	428/922 (46.4)
Yes	484/922 (52.5)
Minutes of work-related VIA/week	
<75	89/484 (18.4)
≥75	354/484 (73.1)
Performs VISFRA for at least 10 minutes	
No	597/922 (64.8)
Yes	316/922 (34.3)
Minutes of VISFRA/week	
<75	102/316 (32.3)
≥75	210/316 (66.5)
Work-related MIA for at least 10 minutes	
No	359/922 (38.9)
Yes	548/922 (59.4)
Minutes of work-related MIA/week	
<150	191/548 (34.9)
≥150	315/548 (57.5)
Performs MISFRA for at least 10 minutes	
No	626/922 (67.9)
Yes	289/922 (31.3)
Minutes of MISFRA/week	
<150	183/289 (63.3)
≥150	98/289 (33.9)
Walks to get to and from places for at least 10 minutes	
No	102/922 (11.1)
Yes	811/922 (88.0)
Minutes walking/week	
<150	367/811 (45.3)
≥150	368/811 (45.4)
Amount of physical activity/week	
Sufficient	634/922 (68.8)
None/Insufficient	239/922 (25.9)

*May not add up to total because of missing values; VIA = vigorous-intensity activity; MIA = moderate-intensity activity; VISFRA = vigorous-intensity sports, fitness and recreational activity; MISFRA = moderate-intensity sports, fitness and recreational activity

Results indicated that the factors which were associated with the amount of physical activity were age, gender, area of residence and region of origin (Table 5.17). The association of level of education with amount of physical activity was of borderline significance.

Table 5.17 Demographic factors associated with amount of physical activity

Variable	Amount of physical activity		p-value[#]
	Sufficient	None/Insufficient	
Age			0.044
<50	545 (74.3)	189 (25.7)	
50 - 59	68 (64.8)	37 (35.2)	
≥60	21 (61.8)	13 (38.2)	
Gender			<0.001
Female	320 (66.4)	162 (33.6)	
Male	314 (80.3)	77 (19.7)	
Level of Education			0.059
Did not complete basic education	117 (66.5)	59 (33.5)	
Primary basic education	251 (76.5)	77 (23.5)	
Secondary/Vocational	245 (72.7)	92 (27.3)	
Tertiary education	16 (61.5)	10 (38.5)	
Employment status			0.620
Paid	174 (75.3)	57 (24.7)	
Unpaid/unemployed	360 (70.7)	149 (29.3)	
Retired	7 (70.0)	3 (30.0)	
Self-employed	80 (73.4)	29 (26.6)	
Area of residence			0.012
Urban	444 (75.3)	146 (24.7)	
Peri-urban	190 (67.1)	93 (32.9)	
Region of origin			0.010
Southern	268 (78.1)	75 (21.9)	
New Guinea Islands	54 (66.7)	27 (33.3)	
Momase	87 (75.0)	29 (25.0)	
Highlands	223 (67.6)	107 (32.4)	
Years of residence in Port Moresby			0.160
≤10	342 (76.0)	108 (24.0)	
>10	255 (71.6)	101 (28.4)	

[#]The p-values were obtained from the Chi-square statistics and assess the strengths of associations. *Fisher's Exact Test

Work-related VIA, MISFRA and VISFRA were associated with age. (Table 5.18) Those younger than 50 years were more likely to participate in both work-related VIA and sports, fitness and recreational activities, compared to those who were 50 years and older. Walking to get to and from places and work-related MIA were not associated with age.

Table 5.18 Association of age with physical activity

Variable	Age category (years)			p-value[#]
	<50	50 – 59	≥60	
Walks to get to and from places for at least 10 minutes				0.882
No	87 (11.3)	12 (11.1)	3 (8.6)	
Yes	683 (88.7)	96 (88.9)	32 (91.4)	
Work-related VIA for at least 10 minutes				0.034
No	349 (45.4)	56 (51.9)	23 (65.7)	
Yes	420 (54.6)	52 (48.1)	12 (34.3)	
Work-related MIA for at least 10 minutes				0.654
No	299 (39.1)	47 (43.5)	13 (37.1)	
Yes	465 (60.9)	61 (56.5)	22 (62.9)	
Performs VISFRA for at least 10 minutes				<0.001
No	466 (60.5)	96 (88.9)	35 (100.0)	
Yes	304 (39.5)	12 (11.1)	0 (0.0)	
Performs MISFRA for at least 10 minutes				<0.001
No	497 (64.4)	97 (89.8)	32 (91.4	
Yes	275 (35.6)	11 (10.2)	3 (8.6)	
Amount of physical activity				0.044
Sufficient	545 (74.3)	68 (64.8)	21 (61.8)	
None/Insufficient	189 (25.7)	37 (35.2)	13 (38.2)	

[#] The p-values were obtained from the Chi-square statistics and assess the strengths of associations; VIA = vigorous-intensity activity; MIA = moderate-intensity activity; VISFRA = vigorous-intensity sports, fitness and recreational activities; MISFRA = moderate-intensity sports, fitness and recreational activities

The number of participants who were retired was small, so a three-category employment variable was created. Participants that had been classified as retired were included in the unpaid/unemployed category to increase category size.

Results indicated that participants who were unpaid/unemployed were more likely to walk, to get to and from places, and to undertake work-related MIA and MISFRA (Table 5.19). Those who were self-employed were more likely not to participate in MISFRA and VISFRA.

Table 5.19 Association of employment status with physical activity

Variable	Employment category			p-value[#]
	Paid	Unpaid/ unemployed	Self-employed	
Walk to get to and from places for at least 10 minutes				0.016
No	35 (14.2)	48 (8.9)	19 (16.7)	
Yes	212 (85.8)	490 (91.1)	95 (83.3)	
Work-related VIA for at least 10 minutes				0.376
No	109 (44.1)	262 (48.8)	50 (43.9)	
Yes	138 (55.9)	275 (51.2)	64 (56.1)	
Work-related MIA for at least 10 minutes				0.004
No	119 (48.6)	192 (36.0)	45 (39.5)	
Yes	126 (51.4)	342 (64.0)	69 (60.5)	
Performs VISFRA for at least 10 minutes				0.002
No	157 (63.6)	340 (63.2)	91 (79.8)	
Yes	90 (36.4)	198 (36.8)	23 (20.2)	
Performs MISFRA for at least 10 minutes				0.004
No	170 (68.8)	354 (65.6)	93 (81.6)	
Yes	77 (31.2)	186 (34.4)	21 (18.4)	
Amount of physical activity				0.412
Sufficient	174 (75.3)	367 (70.7)	80 (73.4)	
None/Insufficient	57 (24.7)	152 (29.3)	29 (26.6)	

[#] The p-values were obtained from the Chi-square statistics and assess the strengths of associations. VIA = vigorous-intensity activity; MIA = moderate-intensity activity; VISFRA = vigorous-intensity sports, fitness and recreational activity; MISFRA = moderate-intensity sports, fitness and recreational activity

Level of education, area of residence and region of origin were associated with the likelihood of walking to get to and from places (Table 5.20). Employment status also tended to be a factor. Those who had completed basic primary and secondary/vocational education, as well as those who had not completed basic education, were more likely to walk to get to and from places than those with a tertiary education. However, the association was only significant when comparing those who had completed basic primary and secondary/vocational education with those who had completed tertiary education. Although those who had not

completed basic education were twice as likely to walk to get to and from places, this did not reach statistical significance. Those who were in the unpaid/unemployed category of employment and those who had retired had twice the odds of walking to get to and from places but this did not reach statistical significance for those who were retired. Participants who were in paid or self-employed work were less likely to walk to get to and from places. Those from the New Guinea Islands and Highlands regions were less likely to walk, compared to their counterparts from the Southern region. Although those from the Momase region were less likely to walk to get to and from places, this did not reach statistical significance. Those from the peri-urban areas were less likely to walk to get to and from places, compared to their urban counterparts.

Although level of education, area of residence, region of origin and employment status all were associated with walking to get to and from places, these factors were not associated with the amount of time spent walking (Table 5.21). The number of minutes spent walking to get to and from places was associated with gender. Female participants were less likely to walk, compared to their male counterparts.

Table 5.20 Univariate analysis of demographic factors affecting whether or not a participant walked to get to and from places

Variable	Crude OR	95% CI	p-value
Age			0.883
<50	1 (reference)		
50 - 59	1.02	0.54 – 1.93	0.954
≥60	1.36	0.41 – 4.53	0.618
Gender			0.756
Female	0.94	0.62 – 1.42	
Male	1 (reference)		
Level of Education			0.014
Did not complete basic education	2.16	0.83 – 5.62	0.116
Primary basic education	3.99	1.55 – 10.28	0.004
Secondary/Vocational	3.05	1.21 – 7.74	0.019
Tertiary education	1 (reference)		
Employment status			0.043
Paid	1.21	0.66 – 2.23	0.537
Unpaid/unemployed	2.04	1.15 – 3.64	0.015
Retired	2.00	0.24 – 16.56	0.520
Self-employed	1 (reference)		
Area of residence			0.002
Urban	1 (reference)		
Peri-urban	0.52	0.34 – 0.79	
Region			0.001
Southern	1 (reference)		
New Guinea Islands	0.36	0.17 – 0.75	0.006
Momase	0.57	0.27 – 1.18	0.128
Highlands	0.35	0.21 – 0.58	<0.001
Years of residence in Port Moresby			0.313
≤10	1.25	0.81 – 1.95	
>10	1 (reference)		

The dependent variable was the answer “Yes” to walks to get to and from places.

Table 5.21 Univariate analysis of demographic factors associated with number of minutes spent walking to get to and from places

Variable	Crude OR	95% CI	p-value
Age			0.978
<50	1 (reference)		
50 - 59	1.03	0.66 – 1.59	0.911
≥60	1.07	0.52 – 2.20	0.854
Gender			
Female	0.68	0.51 – 0.91	0.009
Male	1 (reference)		
Level of Education			0.359
Did not complete basic education	2.30	0.82 – 6.48	0.114
Primary basic education	2.10	0.77 – 5.75	0.149
Secondary education	1.85	0.68 – 5.07	0.231
Vocational/Tertiary	1 (reference)		
Employment status			0.722
Paid	0.92	0.55 – 1.54	0.756
Unpaid/unemployed	0.88	0.55 – 1.40	0.597
Retired	1.86	0.44 – 7.94	0.400
Self-employed	1 (reference)		
Area of residence			0.592
Urban	1 (reference)		
Peri-urban	1.09	0.80 – 1.49	
Region			0.438
Southern	1 (reference)		
New Guinea Islands	0.75	0.44 – 1.27	0.284
Momase	1.20	0.76 – 1.89	0.435
Highlands	1.12	0.80 – 1.55	0.520
Years of residence in Port Moresby			0.509
≤10	1.1	0.82 – 1.50	
>10	1 (reference)		

The dependent variable was ≥150 minutes per week spent walking.

5.3.4 Physical measurements and medical characteristics

Characteristics analysed included physical measurements (such as weight, waist and hip circumferences, and blood pressure), biochemical measurements (capillary blood glucose, 2-hour oral glucose tolerance) and bioelectrical impedance (percentage body fat).

As shown in Table 5.22, the mean FCBG and 2-hour oral glucose tolerance levels were within the ideal values of <6.0 and <8.9 mmol/L, respectively. The mean body mass index (BMI) was above normal (>25 kg/m^2), while systolic and diastolic blood

pressures (SBP and DBP, respectively) were within the normal range (≤130 and ≤80 mmHg, respectively). However, as shown in Table 5.23, 258 (28.0%) and 259 (28.1%) participants had abnormally high SBP and DBP, respectively. Sixty five per cent of participants were either overweight or obese. The mean waist circumference was within normal values (102 cm) for males but was higher than normal (88 cm) for females.

Table 5.23 also shows that, of the 918 participants whose capillary blood glucose (CBG) was measured, 897 (97.7%) of the blood glucose levels were fasted while 21 (2.3%) were random (not fasted). Participants with random blood glucose levels were excluded in any analysis requiring fasting blood glucose results. Of the 897 participants who fasted, 60.1% had normal FCBG, 22.1% had impaired fasting glucose (IFG) and 17.8% had CBG indicating a possibility of T2DM. Of the 471 participants who did the 2-hour oral glucose tolerance test, 82.2% had normal glucose tolerance while 14.4% had impaired glucose tolerance (IGT) and 1.7% had levels indicating a possibility of T2DM. Based on the PNG Diabetes Clinical Guidelines 2012, the prevalence of postprandial hyperglycaemia and hyperglycaemia were 4.9% and 17.8%, respectively.

Table 5.2 Medical characteristics of participants (N = 922)

Variable	n (%)*	Mean	SD
Weight (kg)	913 (99.0)	70.0	13.2
Waist circumference (cm)	914 (99.1)	89.1	15.3
Female	507 (99.2)	91.3	16.2
Male	407 (99.0)	86.3	13.7
Hip circumference (cm)	914 (99.1)	96.9	14.4
BMI (kg/m^2)	912 (98.9)	27.5	5.9
SBP (mmHg)	915 (99.2)	123.7	14.8
DBP (mmHg)	915 (99.2)	73.8	11.2
CBG (mmol/L)	918 (99.6)	5.5	1.5
Fasting	897/918 (97.7)	5.5	1.5
Random	21/918 (2.3)	5.3	0.8
OGT† (mmol/L)	471 (51.1)	7.7	2.9
Bioelectric impedance (% body fat)	908 (98.5)	24.9	8.5

*Percentages do not add up to 100 because of missing values; †Only a selected number of participants were required to undergo this test; BMI = body mass index; SBP = systolic blood pressure; DBP= diastolic blood pressure; CBG = capillary blood glucose level; OGT = oral glucose tolerance

Table 5.23 Physical and biochemical characteristics of participants

Variable	Frequency [n/N (%)*]
Systolic Blood Pressure (mmHg)	
≤130	657/922 (71.3)
>130	258/922 (28.0)
Diastolic Blood Pressure (mmHg)	
≤80	656/922 (71.1)
>80	259/922 (28.1)
Body Mass Index category 1	
Underweight	18/922 (2.0)
Normal weight	291/922 (31.6)
Overweight	356/922 (38.6)
Obese	247/922 (26.8)
Body Mass Index category 2 (kg/m^2)[#]	
<25	291/904 (32.2)
≥25	603/904 (66.7)
Waist circumference	
Normal	595/922 (64.5)
Above normal	319/922 (34.9)
Fasting capillary blood glucose (mmol/L)	
<5.6 (normal)	539/897 (60.1)
5.6 – 6.0 (impaired fasting glucose)	198/897 (22.1)
≥6.1 (T2DM)[†]	160/897 (17.8)
OGT for diagnosis of T2DM (mmol/L)	
<11.1	448/471 (95.1)
≥11.1 (T2DM)	23/471 (4.9)
OGT; impaired glucose tolerance (mmol/L)	
<8.9	387/471 (82.2)
8.9 – 12.1 (impaired glucose tolerance)	68/471 (14.4)
>12.1 (T2DM)	16/471 (1.7)

*May not add up to total because of missing values; [#]Excludes those who were underweight

T2DM = type 2 diabetes mellitus; OGT= oral glucose tolerance; [†]Diagnosis arrived at if glucose level associated with signs and symptoms of T2DM occurred in repeated tests; Normal waist circumference is ≤102cm (male) and ≤88cm (female).

5.3.4.1 Blood pressure

Blood pressure was categorised according to the PNG Diabetes Clinical Guidelines 2012, in which an SBP >130 mmHg and a DBP >80 mmHg are classified as being high (abnormal).

Two hundred and fifty eight (28.0%) participants had high SBP, while 28.1% had a high DBP (Table 5.23).

As shown in Table 5.24, SBP was influenced by age, body mass index (BMI), waist circumference and number of years living in the suburb (Port Moresby). Younger participants (<50 years of age) were less likely to have an abnormally high SBP, with those aged 50 – 59 years having twice the odds of having an abnormally high SBP. Although those aged 60 years and older also had almost twice the odds of having a high SBP compared to those less than 50 years of age, this did not reach statistical significance.

Those with BMI ≥25 kg/m^2 and those with an abnormally large waist circumference had twice the odds of having an abnormally high SBP compared to their counterparts. Those who had lived in Port Moresby for more than 10 years had almost twice the odds of having an SBP >130 mmHg compared to those who had lived there for 10 years or less.

Using logistic regression (backwards elimination) to determine which demographics and physical measurements were independently associated with high SBP, results indicated that age, BMI, waist circumference and number of years living in Port Moresby were independently associated with an SBP >130 mmHg (Table 5.25).

Participants aged 50 – 59 years, and 60 years and older, had twice the odds of having an SBP of >130 mmHg but this was only significant when comparing those younger than 50 years with those aged 50 – 59 years.

Those with a BMI ≥25 kg/m^2 were twice as likely to have an SBP >130 mmHg and, similarly, those with a waist circumference above normal were almost twice as likely to have an SBP >130 mmHg. Those who had lived in Port Moresby for more than 10 years also were almost twice as likely to have an SBP >130 mmHg.

Table 5.24 Univariate logistic regression of demographic factors and physical measurements associated with high SBP (>130 mmHg).

Variable	Crude OR	95% CI	p-value
Gender			0.285
Female	0.85	0.64 – 1.14	
Male	1 (reference)		
Age			<0.001
<50	1 (reference)		
50 - 59	2.56	1.69 – 3.86	<0.001
≥60	1.84	0.90 – 3.73	0.094
Level of Education			0.279
Did not complete basic education	0.72	0.31 – 1.68	0.447
Basic primary education	0.54	0.24 – 1.23	0.141
Secondary/Vocational	0.67	0.29 – 1.52	0.332
Tertiary	1 (reference)		
Employment status			0.178
Paid	1 (reference)		
Unpaid/unemployed	0.99	0.70 – 1.39	0.941
Retired	3.21	0.95 – 10.85	0.061
Self-employed	1.28	0.79 – 2.08	0.310
Area of residence			0.791
Urban	1 (reference)		
Peri-urban	1.04	0.77 – 1.42	
Region of origin			0.110
Southern	1 (reference)		
Momase	0.91	0.56 – 1.48	0.696
Highlands	1.39	1.00 – 1.93	0.050
New Guinea Islands	1.44	0.87 – 2.40	0.158
Years of residence in Port Moresby			0.001
≤10	1 (reference)		
>10	1.67	1.23 – 2.25	
BMI category			<0.001
Underweight	0.16	0.04 – 0.73	0.017
Normal weight	0.29	0.19 – 0.42	<0.001
Overweight	0.48	0.34 – 0.68	<0.001
Obese	1 (reference)		
BMI (kg/m^2)			<0.001
<25	1 (reference)		
≥25	2.40	1.71 – 3.36	
Waist circumference			<0.001
Normal	1 (reference)		
Above normal	2.09	1.56 – 2.81	

The dependent variable was SBP >130 mmHg; SBP = systolic blood pressure; BMI = body mass index; Normal waist circumference is ≤102 cm (male) and ≤88cm (female)

Table 5.25 Multivariate analysis of demographics and physical measurements independently associated with abnormally high SBP (SBP >130 mmHg)

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Age (years)				0.001
<50	195/773 (25.2)	1 (reference)		
50 - 59	50/108 (46.3)	2.12	1.35 – 3.32	0.001
≥60	13/34 (38.2)	2.05	0.95 – 4.44	0.068
BMI (kg/m^2)				<0.001
<25	54/309 (17.5)	1 (reference)		
≥25	203/603 (33.7)	2.07	1.41 – 3.04	
Waist circumference				0.001
Normal	136/595 (22.9)	1 (reference)		
Above normal	122/319 (38.2)	1.76	1.26 – 2.45	
Years of residence in Port Moresby				0.007
≤10	109/467 (23.3)	1 (reference)		
>10	126/375 (33.6)	1.55	1.13 – 2.13	

The dependent variable was SBP >130 mmHg; *The column 'n/N (%)' shows the number (and percentage) of participants with SBP >130 mmHg within each variable; SBP = systolic blood pressure; BMI = body mass index; Normal waist circumference is ≤102cm (male), ≤88cm (female)

When examining the associations of lifestyle factors (tobacco smoking, vegetable and fruit consumption) with SBP, results indicated that fruit servings and number of days in a week that fruits were consumed tended to have an influence (Table 5.26).

Those who consumed less than two servings of fruit per day and those who consumed fruit for two days or more per week tended to have a higher SBP compared to their counterparts.

Table 5.26 Univariate logistic regression of lifestyle factors (alcohol, vegetable and fruit consumption, and tobacco smoking) associated with high SBP (>130 mmHg).

Variable	Crude OR	95% CI	p-value
Alcohol consumption in the previous 12 months			0.081
No	1.30	0.97 – 1.75	
Yes	1 (reference)		
Smoker status			0.162
Current	1 (reference)		
Never	1.33	0.97 – 1.82	0.073
Quit	1.39	0.84 – 2.29	0.203
Vegetable servings/day			0.116
<3	1.65	0.88 – 3.08	
≥3	1 (reference)		
Number of vegetable-eating days in a typical week			0.520
0 - 5	0.91	0.68 – 1.21	
6 - 7	1 (reference)		
Fruit servings/day			0.010
<2	1.55	1.11 – 2.17	
≥2	1 (reference)		
Number of fruit-eating days in a typical week			0.030
0 - 1	0.72	0.53 – 0.97	
2 - 7	1 (reference)		

The dependent variable was SBP >130 mmHg. SBP = systolic blood pressure

Betel nut chewing was associated with SBP (Table 5.27). Results of univariate logistic regression analysis indicated that those who were not current betel nut chewers and those who had never chewed were more likely to have an SBP >130 mmHg. When comparing those who had quit the habit and those who chewed ≤5 nuts per day with those who chewed >5 nuts per day, the association was not significant. For those classified as betel nut chewers, the quantity chewed per day and the components of betel nut chewing were not associated with SBP.

Table 5.27 Univariate logistic regression of betel nut chewing and high SBP (>130 mmHg)

Variable	Crude OR	95% CI	p-value
Betel nut chewer			0.003
No	1.70	1.19 – 2.41	
Yes	1 (reference)		
Betel nut chewing history			0.004
Current	1 (reference)		
Never	1.89	1.30 – 2.75	0.001
Quit	1.03	0.45 – 2.35	0.943
Betel nut chewing status			0.001
Never	1.89	1.30 – 2.74	
Ever	1 (reference)		
Betel nut exposure			0.008
Never	2.03	1.33 – 3.10	0.001
Quit	1.11	0.48 – 2.59	0.811
≤5 nuts/day	1.11	0.80 – 1.56	0.529
>5 nuts/day	1 (reference)		
Quantity of betel nuts chewed/day[†]			0.882
≤5	1.06	0.73 – 1.54	0.775
6 - 9	0.94	0.57 – 1.57	0.823
≥10	1 (reference)		
Betel nut chew composition			0.235
Betel nut, lime and PBI	0.79	0.30 – 2.08	0.632
Betel nut ± PBI or lime	1.06	0.40 – 2.84	0.909
Betel nut only	1 (reference)		

The dependent variable was SBP >130 mmHg; [†]Only includes those who were betel nut chewers; SBP = systolic blood pressure; PBI = *Piper betle* inflorescence

When examining any association of SBP with physical activity, results indicated that those who participated in MISFRA and VISFRA for at least 10 minutes per day appeared to be less likely to have an SBP >130 mmHg (Table 5.28). The amount of time (minutes) spent on these activities, however, did not influence SBP. Although participants who performed insufficient physical activities in a week had four times the odds of having an abnormally high SBP, this did not reach statistical significance. All other physical activities were not associated with SBP.

Table 5.28 Univariate logistic regression analysis of physical activity characteristics associated with high SBP (>130 mmHg)

Variable	Crude OR	95% CI	p-value
Work-related MIA for at least 10 minutes			0.379
No	0.87	0.65 – 1.18	
Yes	1 (reference)		
Minutes of work-related MIA/week			0.498
<150	1.15	0.77 – 1.70	
≥150	1 (reference)		
Performs MISFRA for at least 10 minutes			0.007
No	1.57	1.13 – 2.17	
Yes	1 (reference)		
Minutes of MISFRA/week			0.810
<150	1.08	0.59 – 1.97	
≥150	1 (reference)		
Work-related VIA for at least 10 minutes			0.660
No	0.94	0.70 – 1.25	
Yes	1 (reference)		
Minutes of work-related VIA/week			0.314
<75	1.29	0.78 – 2.14	
≥75	1 (reference)		
Performs VISFRA for at least 10 minutes			<0.001
No	1.93	1.40 – 2.68	
Yes	1 (reference)		
Minutes of VISFRA/week			0.307
<75	1.35	0.76 – 2.40	
≥75	1 (reference)		
Walks to get to and from places for at least 10 minutes			0.389
No	0.81	0.50 – 1.31	
Yes	1 (reference)		
Minutes of walking/week			0.570
<150	1.10	0.80 – 1.51	
≥150	1 (reference)		
Amount of physical activity/week			0.118
Sufficient	1 (reference)		
None/Insufficient	1.30	0.94 – 1.79	

The dependent variable was SBP >130 mmHg; SBP = systolic blood pressure; MIA = moderate-intensity activity; MISFRA = moderate-intensity sports, fitness and recreational activity; VIA = vigorous-intensity activity; VISFRA = vigorous-intensity sports, fitness and recreational activity

Results of multivariate logistic regression analysis indicated that the lifestyle factors which were independently associated with an SBP >130 mmHg were fruit servings, number of days in a week that fruits were consumed, betel nut exposure and VISFRA (Table 5.29). Of all these factors, VISFRA was the most important influencing factor, with results indicating that those who did not perform any VISFRA were more likely to have a high systolic blood pressure (>130 mmHg). Participants who never chewed betel nut, those who consumed less than two serves of fruit and those who consumed fruit for more than one day per week were more likely to have a high SBP.

Table 5.29 Multivariate analysis of lifestyle factors independently associated with elevated SBP (>130 mmHg)

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Fruit servings/day				0.005
<2	180/612 (29.4)	1.65	1.16 – 2.34	
≥2	60/270 (22.2)	1 (reference)		
Number of fruit-eating days in a typical week				0.023
0 - 1	91/375 (24.3)	0.69	0.50 – 0.95	
2 - 7	165/535 (30.8)	1 (reference)		
Betel nut exposure				0.027
Never	56/140 (40.0)	1 (reference)		
Quit	8/30 (26.7)	0.60	0.25 – 1.47	0.265
≤5 nuts/day	107/400 (26.8)	0.62	0.40 – 0.94	0.024
>5 nuts/day	81/328 (24.7)	0.51	0.33 – 0.79	0.003
Performs VISFRA for at least 10 minutes				<0.001
No	193/594 (32.5)	1.85	1.31 – 2.60	
Yes	63/316 (19.9)	1 (reference)		

The dependent variable was SBP >130 mmHg; *The column 'n/N (%)' shows the number (and percentage) of participants with SBP >130 mmHg within each variable; SBP = systolic blood pressure; VISFRA = vigorous-intensity sports, fitness and recreational activity

When demographic, lifestyle and medical factors were adjusted for each other using multivariate logistic regression analysis (backward elimination), results indicated that the factors independently associated with SBP were age, number of years living in Port Moresby, betel nut exposure, fruit servings, body mass index and waist circumference (Table 5.30).

Table 5.30 Multivariate analysis of demographic, lifestyle and medical factors independently associated with abnormally high SBP (SBP >130 mmHg)

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Age (years)				0.010
<50	195/773 (25.2)	1 (reference)		
50 - 59	50/108 (46.3)	1.96	1.22 – 3.17	0.006
≥60	13/34 (38.2)	1.93	0.84 – 4.44	0.124
BMI (kg/m^2)				0.002
<25	54/309 (17.5)	1 (reference)		
≥25	203/603 (33.7)	1.85	1.25 – 2.74	
Waist circumference				0.002
Normal	136/595 (22.9)	1 (reference)		
Above normal	122/319 (38.2)	1.75	1.23 – 2.48	
Years of residence in Port Moresby				0.023
≤10	109/467 (23.3)	0.68	0.49 – 0.95	
>10	126/375 (33.6)	1 (reference)		
Betel nut exposure				0.021
Never	56/140 (40.0)	1 (reference)		
Quit	8/30 (26.7)	0.43	0.15 – 1.25	0.122
≤5 nuts/day	107/400 (26.8)	0.63	0.40 – 0.98	0.042
>5 nuts/day	81/328 (24.7)	0.48	0.30 – 0.78	0.003
Fruit servings/day				0.020
<2	180/612 (29.4)	1.55	1.07 – 2.24	
≥2	60/270 (22.2)	1 (reference)		

The dependent variable was SBP >130 mmHg; *The column 'n/N (%)' shows the number (and percentage) of participants with SBP >130 mmHg within each variable; SBP = systolic blood pressure; BMI = body mass index; Normal waist circumference is ≤102 cm (male) and ≤88cm (female)

As shown in Table 5.31, age, BMI, waist circumference and number of years living in Port Moresby were the most important factors influencing a high DBP (>80 mmHg). Area of residence, level of education and region of origin also appear to affect DBP. Gender and employment status were not associated with DBP. Those aged 50 years and older were more likely to have an abnormally high DBP (> 80 mmHg) compared to their younger counterparts. The association, however, was only significant when comparing those aged <50 years with those aged 50 – 59 years but not with those aged 60 years and older. Participants with a BMI ≥25 kg/m^2 had almost twice the odds of having an abnormally high DBP, compared to their counterparts. Those with a waist circumference above normal were three times more likely to have an abnormally high DBP.

Table 5.31 Univariate logistic regression of demographic and physical factors associated with high DBP (>80 mmHg)

Variable	Crude OR	95% CI	p-value
Age (years)			<0.001
<50	1 (reference)		
50 - 59	2.54	1.68 – 3.83	<0.001
≥60	1.82	0.90 – 3.71	0.098
Level of Education			0.002
Did not complete basic education	0.50	0.22 – 1.13	0.096
Primary basic education	0.29	0.13 – 0.64	0.002
Secondary/Vocational	0.44	0.20 – 0.98	0.044
Tertiary	1 (reference)		
Area of residence			0.003
Urban	1 (reference)		
Peri-urban	1.59	1 – 2.14	
Region of origin			0.011
Southern	1 (reference)		
Momase	1.25	0.77 – 2.02	0.362
Highlands	1.70	1.22 – 2.37	0.002
New Guinea Islands	1.74	1.05 – 2.90	0.033
Years of residence in Port Moresby			<0.001
≤10	1 (reference)		
>10	1.81	1.33 – 2.45	
BMI (kg/m^2)			<0.001
<25	1 (reference)		
≥25	1.82	1.31 – 2.51	
Waist circumference			<0.001
Normal	1 (reference)		
Above normal	2.60	1.93 – 3.50	

The dependent variable was DBP >80 mmHg; DBP = diastolic blood pressure; BMI = body mass index; Normal waist circumference is ≤102cm (male) and ≤88cm (female)

The most important lifestyle factors (other than betel nut chewing) influencing DBP were numbers of days per week that any vegetables were consumed, work-related MIA and VIA, MISFRA and VISFRA, and walking to get to and from places (Table 5.32). Other factors which had an association with DBP were tobacco smoking and the amount of time spent doing work-related MIA. Those who did not perform work-related MIA and VIA, MISFRA and VISFRA, and did not walk to get to and from places, were more likely to have an abnormally higher DBP than those who did. Those who undertook work-related MIA for less than 150 minutes per week were less likely to have a DBP >80 mmHg. Participants who did a sufficient amount of physical activity per week were significantly less likely to have an abnormally high

DBP. All other lifestyle factors (other than betel nut chewing) did not have an association with DBP.

Table 5.32 Univariate logistic regression of lifestyle factors associated with high DBP (>80 mmHg)

Variable	Crude OR	95% CI	p-value
Smoker status			0.013
Current	1 (reference)		
Never	1.27	0.93 – 1.74	0.135
Quit	2.05	1.27 – 3.32	0.003
Number of vegetable-eating days in a typical week			<0.001
0 - 5	0.55	0.41 – 0.74	
6 - 7	1 (reference)		
Work-related MIA for at least 10 minutes			<0.001
No	2.01	1.50 – 2.70	
Yes	1 (reference)		
Minutes of work-related MIA/week			0.017
<150	0.573	0.36 – 0.90	
≥150	1 (reference)		
Performs MISFRA for at least 10 minutes			<0.001
No	2.24	1.59 – 3.15	
Yes	1 (reference)		
Work-related VIA for at least 10 minutes			<0.001
No	1.81	1.35 – 2.42	
Yes	1 (reference)		
Performs VISFRA for at least 10 minutes			<0.001
No	2.20	1.58 – 3.05	
Yes	1 (reference)		
Walks to get to and from places for at least 10 minutes			<0.001
No	2.21	1.45 – 3.36	
Yes	1 (reference)		
Amount of physical activity/week			0.001
Sufficient	1 (reference)		
None/Insufficient	1.70	1.23 – 2.33	

The dependent variable was DBP >80 mmHg; DBP = diastolic blood pressure; MIA = moderate-intensity activity; MISFRA = moderate-intensity sports, fitness and recreational activity; VIA = vigorous-intensity activity; VISFRA = vigorous-intensity sports, fitness and recreational

Participants who were not betel nut chewers, or those who had never chewed, were more likely to have a DBP> 80 mmHg when compared to their counterparts who chewed betel nut (Table 5.33). Those who never chewed betel nut had twice the odds of having a DBP >80 mmHg. When comparing daily betel nut use, those who chewed less than 10 nuts per day were less likely to have an abnormally high DBP, but the association only reached statistical significance when comparing those who

chewed 6-9 nuts with those who chewed ≥10 nuts per day. Those who chewed ≤5 nuts per day were significantly less likely to have a DBP> 80 mmHg compared to their counterparts who chewed ≥10 nuts per day.

Table 5.33 Univariate logistic regression analysis of betel nut chewing variables associated with high DBP (>80 mmHg)

Variable	Crude OR	95% CI	p-value
Betel nut chewer			<0.001
No	2.38	1.68 – 3.36	
Yes	1 (reference)		
Betel nut chewing history			<0.001
Current	1 (reference)		
Never	2.35	1.62 – 3.41	<0.001
Quit	2.33	1.11 – 4.88	0.025
Betel nut chewing status			<0.001
Never	2.26	1.56 – 3.28	
Ever	1 (reference)		
Betel nut exposure			<0.001
Never	1.87	1.24 – 2.81	0.003
Quit	1.85	0.86 – 3.95	0.113
≤5 nuts/day	0.63	0.45 – 0.89	0.008
>5 nuts/day	1 (reference)		
Quantity of betel nuts chewed/day[#]			0.008
≤5	0.55	0.38 – 0.80	0.002
6 - 9	0.69	0.42 – 1.14	0.145
≥10	1 (reference)		
Betel nut chew composition			0.126
Betel nut, lime and PBI	0.92	0.35 – 2.43	0.872
Betel nut ± PBI or lime	0.63	0.23 – 1.72	0.370
Betel nut only	1 (reference)		

The dependent variable was DBP >80 mmHg; DBP = diastolic blood pressure; PBI = *Piper betle* inflorescence

As can be seen in Table 5.34, multivariate logistic regression analysis indicated that age, area of residence, years of living in Port Moresby, waist circumference, betel nut chewing status, walking to get to and from places and minutes of undertaking work-related MIA were independently associated with DBP. However, the association between years of living in Port Moresby and high DBP did not reach statistical significance. Participants aged 50 years and older had twice the odds of having a DBP >80 mmHg compared to their younger counterparts. However, this was only statistically significant when comparing those aged 50 years or less with those aged 50 – 59 years. Those who had an abnormally large waist circumference were twice as likely to have a DBP >80 mmHg. Participants who never chewed betel nut were almost twice as likely to have a DBP >80 mmHg, compared with those who quit, having an adjusted odds ratio of 1.80. Not walking to get to and from places predisposed participants to an abnormally high DBP. Those who did not walk were three times more likely to have an abnormally high DBP, compared to those who did. Undertaking work-related MIA for less than 150 minutes per week was less likely to predispose a participant to an abnormally high DBP. Participants residing in peri-urban areas had twice the odds of having an abnormally high DBP.

Table 5.34 Multivariate analysis of factors independently associated with high DBP (>80 mmHg).

Variable	n/N (%)	Adjusted OR	95% CI	p-value
Age (years)				0.008
<50	196/773 (25.4)	1 (reference)		
50 - 59	50/108 (46.3)	2.67	1.39 – 5.11	0.003
≥60	13/34 (38.2)	2.18	0.73 – 6.50	0.163
Area of residence				0.003
Urban	155/616 (25.2)	1 (reference)		
Peri-urban	104/299 (34.8)	2.12	1.28 – 3.50	
Years of residence in Port Moresby				0.082
≤10	105/467 (22.5)	1 (reference)		
>10	129/375 (34.4)	1.52	0.95 – 2.45	
Waist circumference				0.004
Normal	127/575 (21.3)	1 (reference)		
Above normal	132/319 (41.4)	2.06	1.26 – 3.38	
Betel nut status				0.030
Never	61/140 (43.6)	2.19	1.20 – 3.98	0.010
Quit	13/30 (43.3)	1.80	0.51 – 6.36	0.360
Current	183/740 (24.7)	1 (reference)		
Walk to get to and from places for at least 10 minutes				0.049
No	45/102 (44.1)	3.48	1.01 – 2.02	
Yes	213/808 (26.4)	1 (reference)		
Minutes of MIA at work/week				0.035
<150	32/190 (16.8)	0.57	0.34 – 0.96	
≥150	82/314 (26.1)	1 (reference)		

The dependent variable was DBP > 80 mmHg; *The column 'n/N (%)' shows the number (and percentage) of participants with SBP >130 mmHg within each variable; DBP = diastolic blood pressure; MIA = moderate-intensity activity; Normal waist circumference is ≤102cm (male) and ≤88cm (female)

5.3.4.2 Body mass index

As was shown in Table 5.23 earlier, more than 60% of participants were either overweight (38.6%) or obese (26.8%) and 31.6% had normal weight. To determine any association between demographic and lifestyle variables and BMI those who were underweight were excluded from analysis.

Univariate logistic regression analysis indicated that age, gender, region of origin and employment status influenced BMI (Table 5.35). Those younger than 50 years were less likely to be overweight or obese, however, there was no statistically significant difference between this age category and those aged 60 years or older.

Female participants were more likely to have a BMI ≥25 kg/m^2 when compared to their male counterparts. Participants who were in paid employment and those in the unpaid/unemployed category were significantly less likely to have a BMI ≥25 kg/m^2. Although retirees were two times more likely to have a BMI ≥25 kg/m^2, this did not reach statistical significance.

Those from the Highlands and Momase regions were more likely to have a BMI ≥25 kg/m^2, compared to their counterparts from the Southern region. Participants from the Highlands region were twice as likely to have a BMI ≥25 kg/m^2 when compared with those from the Southern region. There was no statistically significant difference in having a BMI≥ 25 kg/m^2 between those from the Southern and New Guinea Islands regions.

Table 5.35 Univariate logistic regression analysis of demographic factors associated with abnormally high BMI (≥25 kg/m^2).

Variable	Crude OR	95% CI	p-value
Age (years)			0.001
<50	1 (reference)		
50 - 59	2.66	1.57 – 4.51	<0.001
≥60	1.37	0.63 – 3.01	0.428
Gender			<0.001
Female	1.75	1.32 – 2.32	
Male	1 (reference)		
Level of Education			0.410
Did not complete basic education	0.49	0.18 – 1.36	0.169
Primary basic education	0.46	0.17 – 1.26	0.132
Secondary/Vocational	0.43	0.16 – 1.18	0.100
Tertiary education	1 (reference)		
Employment Status			0.003
Paid	0.39	0.22 – 0.66	0.001
Unpaid/unemployed	0.44	0.27 – 0.73	0.002
Retired	2.03	0.24 – 16.92	0.512
Self-employed	1 (reference)		
Area of residence			0.333
Urban	1 (reference)		
Peri-urban	1.16	0.86 – 1.57	
Region			<0.001
Southern	1 (reference)		
New Guinea Islands	1.36	0.82 – 2.23	0.232
Momase	1.64	1.05 – 2.58	0.031
Highlands	2.41	1.74 – 3.35	<0.001
Years of residence in Port Moresby			0.247
≤10	1.19	0.89 – 1.60	
>10	1 (reference)		

The dependent variable was BMI ≥25kg/m^2; BMI = body mass index

Tobacco smoking, alcohol consumption and the number of days that participants consumed fruit in a typical week had associations with BMI (Table 5.36). Participants who never smoked tobacco and never consumed alcohol were more likely to have a BMI ≥25 kg/m^2. There was no statistically significant difference in having a BMI ≥25 kg/m^2 between current tobacco smokers and those who had quit smoking. Those who did not consume fruit and those who consumed fruit for one day in a typical week were less likely to have a BMI ≥25 kg/m^2.

Table 5.36 Univariate logistic regression analysis of lifestyle factors associated with abnormally high BMI (≥25 kg/m^2).

Variable	Crude OR	95% CI	p-value
Smoking history			<0.001
Current	1 (reference)		
Never	2.09	1.55 – 2.80	<0.001
Quit	1.54	0.95 – 2.49	0.078
Alcohol consumed in the previous 12 months			<0.001
No	1.90	1.43 – 2.53	
Yes	1 (reference)		
Vegetable servings/day			0.626
<3	1.14	0.67 – 1.94	
≥3	1 (reference)		
Vegetable-eating days/week			0.373
0 - 5	1.14	0.86 – 1.50	
6 - 7	1 (reference)		
Fruit servings/day			0.219
<2	1.21	0.89 – 1.65	
≥2	1 (reference)		
Fruit-eating days/week			<0.001
0 - 1	0.52	0.39 – 0.69	
2 - 7	1 (reference)		

The dependent variable was BMI ≥25 kg/m^2; BMI = body mass index

Betel nut chewing had an association with BMI (Table 5.37). Participants who never chewed betel nut were more likely to have a BMI ≥25 kg/m^2 when compared to their counterparts who were betel nut chewers. When comparing the number of betel nuts chewed by those classified as per day betel nut chewers, results indicated that those chewing 6 - 9 betel nuts per day were more likely to have a BMI ≥25 kg/m^2. Components chewed with betel nut also affected BMI. Those who chewed betel nut with or without PBI or lime were more likely to have an abnormally high BMI compared to those who always chewed betel nut with both PBI and lime. There was no difference in association between BMI and current betel nut chewers or those who had quit the habit.

Table 5.37 Univariate logistic regression analysis of betel nut chewing variables associated with abnormally high BMI (≥25 kg/m^2).

Variable	Crude OR	95% CI	p-value
Betel nut chewer			0.024
No	1.54	1.06 – 2.23	
Yes	1 (reference)		
Betel nut chewing history			0.003
Current	1 (reference)		
Never	1.95	1.27 – 2.98	0.002
Quit	0.59	0.28 – 1.25	0.169
Betel nut chewing status			0.002
Never	1.99	1.30 – 3.04	
Ever	1 (reference)		
Betel nut exposure			0.005
Never	1.77	1.11 – 2.80	0.015
Quit	0.54	0.25 – 1.16	0.112
≤5 nuts/day	0.85	0.62 – 1.15	0.286
>5 nuts/day	1 (reference)		
Quantity of betel nuts chewed/day[#]			0.011
≤5	1.09	0.78 – 1.54	0.608
6 - 9	2.08	1.26 – 3.43	0.004
≥10	1 (reference)		
Betel nut chew composition			0.027
Betel nut, lime and PBI	1 (reference)		
Betel nut ± PBI or lime	1.55	1.11 – 2.15	0.009
Betel nut only	0.84	0.35 – 2.04	0.703

The dependent variable was BMI ≥ 25 kg/m^2; BMI = body mass index; PBI = *Piper betle* inflorescence

Physical activities associated with BMI were work-related MIA and VIA, MISFRA and VISFRA, and the number of minutes undertaking work-related VIA (Table.38). Surprisingly, participants who undertook work-related MIA or VIA were more likely to have a BMI ≥25 kg/m^2, compared to those who did not. In comparison, those who were involved in MISFRA and VISFRA were less likely to have a BMI ≥25 kg/m^2. Those who performed work-related VIA for <75 minutes per week were less likely to have a BMI ≥25 kg/m^2.

Table 5.38 Univariate logistic regression analysis of physical activity performance associated with abnormally high BMI (≥25 kg/m^2).

Variable	Crude OR	95% CI	p-value
Amount of physical activity			0.246
Sufficient	1 (reference)		
None/Insufficient	0.83	0.61 – 1.14	
Work-related VIA for at least 10 minutes			0.003
No	1 (reference)		
Yes	1.52	1.15 – 2.02	
Minutes of work-related VIA/week			0.040
<75	0.59	0.36 – 0.98	
≥75	1 (reference)		
Performs VISFRA for at least 10 minutes			<0.001
No	2.06	1.54 – 2.75	
Yes	1 (reference)		
Minutes of VISFRA/week			0.258
<75	0.76	0.46 – 1.23	
≥75	1 (reference)		
Work-related MIA for at least 10 minutes			<0.001
No	1 (reference)		
Yes	1.74	1.31 – 2.32	
Minutes of work-related MIA/week			0.298
<150	0.81	0.54 – 1.21	
≥150	1 (reference)		
Performs MISFRA for at least 10 minutes			<0.001
No	1 (reference)		
Yes	0.54	0.41 – 0.73	
Minutes of MISFRA/week			0.058
<150	0.61	0.37 – 1.02	
≥150	1 (reference)		
Walks to get to and from places for at least 10 minutes			0.330
No	1.26	0.79 – 2.00	
Yes	1 (reference)		
Minutes walking/week			0.095
<150	0.77	0.56 – 1.06	
≥150	1 (reference)		

The dependent variable was BMI ≥25 kg/m^2; BMI = body mass index; VIA = vigorous-intensity activity; MIA = moderate-intensity activity; VISFRA = vigorous-intensity sports, fitness and recreational activity; MISFRA = moderate-intensity sports, fitness and recreational activity

As demonstrated in Table 5.39, results indicated that region of origin, tobacco smoking, number of days/week that fruit and vegetables were consumed, VISFRA and the number of minutes of work-related VIA in a week were independently associated with BMI.

Those from the Highlands region had three times the odds of having a BMI ≥25 kg/m^2 when compared to those from other regions. Although betel nut exposure was an independent factor, the association did not reach statistical significance. There was, however, a significant association when comparing those who had chewed >5 nuts per day with those who had chewed ≤5 nuts per day. Those who chewed ≤5 nuts per day were less likely to have a BMI ≥25 kg/m^2, compared to those who chewed >5 nuts. Those who never smoked and those who had quit were three and two times more likely to have a BMI ≥25 kg/m^2, respectively. Not participating in VISFRA and undertaking work-related VIA for ≥75 minutes per week were both associated with a BMI ≥25 kg/m^2.

Participants who consumed vegetables for less than 6 - 7 days in a week were more likely to have a BMI ≥25 kg/m^2. In comparison, those who consumed fruit for less than two days in a week were less likely to have a BMI ≥25 kg/m^2.

Those who never smoked tobacco were almost four times more likely to have a BMI ≥25 kg/m^2 compared to their counterparts who were tobacco smokers. Although those who had quit the habit had twice the odds of having a BMI ≥25 kg/m^2, this did not reach statistical significance.

Table 5.39 Multivariate logistic regression analysis of demographic and lifestyle factors associated with abnormally high BMI (≥25 kg/m^2).

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Region of origin				0.004
Southern	202/363 (55.6)	1 (reference)		
Momase	79/116 (68.1)	1.56	0.76 – 3.22	0.225
Highlands	265/345 (76.8)	3.12	1.70 – 5.73	<0.001
New Guinea Islands	54/85 (63.5)	1.51	0.66 – 3.27	0.314
Betel nut exposure				0.064
Never	109/140 (77.9)	0.46	0.19 – 1.13	0.090
Quit	15/29 (51.7)	0.46	0.04 – 5.36	0.537
≤5 nuts/day	251/400 (62.8)	0.49	0.29 – 0.84	0.010
>5 nuts/day	217/326 (66.6)	1 (reference)		
Smoker status				<0.001
Never	341/467 (73.0)	3.73	2.21 – 6.63	<0.001
Quit	62/93 (66.7)	2.43	0.85 – 6.00	0.067
Current	196/347 (56.5)	1 (reference)		
Number of vegetable-eating days/week				0.029
0 - 5	316/470 (67.2)	1.79	1.06 – 3.00	
6 - 7	282/436 (64.7)	1 (reference)		
Number of fruit-eating days/week				<0.001
0 - 1	213/373 (57.1)	0.36	0.22 – 0.57	
2 - 7	386/534 (72.3)	1 (reference)		
Performs VISFRA for at least 10 minutes				0.030
No	426/594 (71.7)	1.71	1.05 – 2.77	
Yes	173/313 (55.3)	1 (reference)		
Minutes of work-related VIA/week				0.021
<75	55/89 (61.8)	0.57	0.29 – 0.90	
≥75	258/353 (73.1)	1 (reference)		

The dependent variable was BMI ≥ 25 kg/m^2; *The column 'n/N (%)' shows the number (and percentage) of participants with BMI ≥25 kg/m^2 within each variable; BMI = body mass index; VISFRA = vigorous-intensity sports, fitness and recreational activity; VIA = vigorous-intensity activity

5.3.4.3 Waist circumference

Waist circumference was categorised into normal and above normal. The normal waist circumference used for females was ≤88cm and, for males, was ≤102cm, based on the PNG Diabetes Clinical Guidelines 2012.

As Table 5.23 showed earlier, 319 (34.9%) participants had a larger than normal waist circumference.

Univariate logistic regression analysis indicated that age, gender, level of education and area of residence were associated with waist circumference (Table 5.40). Participants aged 50 – 59 years were four times more likely to have an abnormally large waist circumference compared to those aged 60 years and older. Although those younger than 50 years appeared to be more likely to have an abnormally large waist circumference when compared to those aged 60 years and older, this did not reach statistical significance. Female participants had 10 times the odds of having a larger than normal waist circumference, compared to their male counterparts.

Results indicated that betel nut exposure, tobacco smoking, consumption of alcohol in the preceding 12 months, vegetable servings per day and number of days per week that vegetables were consumed affected waist circumference (Table 5.41). Participants who never chewed betel nut had almost twice the odds of having an abnormally large waist circumference, compared to betel nut chewers and those who had quit the habit. Current tobacco smokers were less likely to have a waist circumference above normal compared to those who never smoked or those who had quit smoking. Participants who had consumed alcohol in the preceding 12 months were less likely to have a waist circumference above normal. Those who did not consume vegetables or those who consumed vegetables for up to five days per week were less likely to have an abnormally large waist circumference compared to those who consumed vegetables for six to seven days per week. Furthermore, participants who consumed ≥3 serves of vegetables per day were twice as likely to have a waist circumference above normal.

Table 5.40 Univariate logistic regression analysis of demographic factors associated with abnormally large waist circumference

Variable	Crude OR	95% CI	p-value
Age (years)			0.001
<50	1.94	0.83 – 4.51	0.125
50 - 59	3.86	1.55 – 9.61	0.004
≥60	1 (reference)		
Gender			<0.001
Female	10.11	7.05 – 14.51	
Male	1 (reference)		
Level of Education			0.035
Did not complete basic education	1 (reference)		
Primary basic education	0.61	0.42 – 0.88	0.009
Secondary/Vocational	0.63	0.44 – 0.91	0.014
Tertiary education	0.96	0.42 – 2.20	0.923
Employment Status			0.095
Paid	1 (reference)		
Unpaid/unemployed	1.32	0.96 – 1.82	0.090
Retired	0.22	0.03 – 1.71	0.147
Self-employed	0.99	0.62 – 1.60	0.981
Region			0.180
Southern	0.91	0.55 – 1.50	0.716
Momase	0.96	0.53 – 1.73	0.886
Highlands	1.27	0.78 – 2.09	0.341
New Guinea Islands	1 (reference)		
Years of residence in Port Moresby			0.064
≤10	0.76	0.57 – 1.02	
>10	1 (reference)		
Area of residence			0.009
Urban	1 (reference)		
Peri-urban	1.46	1.10 – 1.95	

The dependent variable was waist circumference above normal; Normal waist circumference is ≤102cm (male) and ≤88cm (female).

Table 5.41 Univariate logistic regression analysis of tobacco smoking, and fruit and vegetable consumption variables, associated with abnormally large waist circumference

Variable	Crude OR	95% CI	p-value
Smoking history			<0.001
Current	0.44	0.27 – 0.72	0.001
Never	1.13	0.72 – 1.78	0.599
Quit	1 (reference)		
Alcohol consumed in the previous 12 months			<0.001
No	1 (reference)		
Yes	0.45	0.33 – 0.60	
Vegetable servings/day			0.002
<3	1 (reference)		
≥3	2.25	1.36 – 3.73	
Number of vegetable-eating days/week			<0.001
0 - 5	0.50	0.38 – 0.66	
6 - 7	1 (reference)		
Fruit servings/day			0.769
<2	1 (reference)		
≥2	1.05	0.78 – 1.41	
Number of fruit-eating days/week			0.058
0 - 1	0.763	0.58 – 1.01	
2 - 7	1 (reference)		

The dependent variable was waist circumference above normal; Normal waist circumference is ≤102cm (male) and ≤88cm (female).

Table 5.42 demonstrates that betel nut chewing was associated with waist circumference. Those who never chewed betel nut were more likely to have a waist circumference above normal. For the subgroup classified as betel nut chewers, those who chewed ≤5 nuts per day were significantly less likely to have a waist circumference above normal, compared to those who chewed 10 or more. For the same subgroup, the components chewed with betel nut did not have an association with waist circumference. When comparing those who were current chewers with those who had quit the habit, the difference in association with waist circumference did not reach statistical significance.

Table 5.42 Univariate logistic regression analysis of betel nut chewing variables associated with abnormally large waist circumference

Variable	Crude OR	95% CI	p-value
Betel nut chewer			<0.001
No	2.04	1.45 – 2.85	
Yes	1 (reference)		
Betel nut chewing history			<0.001
Current	1 (reference)		
Never	2.29	1.59 – 3.30	<0.001
Quit	1.08	0.50 – 2.34	0.847
Betel nut chewing status			<0.001
Never	2.28	1.58 – 3.28	
Ever	1 (reference)		
Betel nut exposure			<0.001
Never	1.85	1.24 – 2.76	0.003
Quit	0.87	0.40 – 1.92	0.739
≤5 nuts/day	0.66	0.48 – 0.90	0.008
>5 nuts/day	1 (reference)		
Quantity of betel nuts chewed/day[#]			0.001
≤5	0.53	0.37 – 0.75	<0.001
6-9	0.57	0.35 – 0.91	0.020
≥10	1 (reference)		
Betel nut chew composition[#]			0.787
Betel nut, lime and PBI	0.97	0.38 – 2.45	0.945
Betel nut ± PBI or lime	0.86	0.34 – 2.23	0.761
Betel nut only	1 (reference)		

The dependent variable was waist circumference above normal; Normal waist circumference is ≤102cm (male) and ≤88cm (female); [#]Includes only those who were betel nut chewers; PBI = *Piper betle* inflorescence

As highlighted in Table 5.43, the amount of physical activity, including work-related MIA and VIA, MISFRA and VISFRA, and walking to get to and from places, was associated with waist circumference. Although these activities had an impact on waist circumference, the amount of time spent on these activities did not. Those who undertook these activities were less likely to have a waist circumference above normal, compared to those who did not.

Table 5.43 Univariate logistic regression analysis of association between physical activity and abnormally large waist circumference

Variable	Crude OR	95% CI	p-value
Amount of physical activity			<0.001
Sufficient	1 (reference)		
None/Insufficient	1.91	1.41 – 2.60	
Work-related VIA for at least 10 minutes			0.016
No	1.40	1.06 – 1.84	
Yes	1 (reference)		
Minutes of work-related VIA/week			0.753
<75	1.08	0.66 – 1.79	
≥75	1 (reference)		
Performs VISFRA for at least 10 minutes			<0.001
No	2.01	1.52 – 2.80	
Yes	1 (reference)		
Minutes of VISFRA/week			0.295
<75	1.33	0.78 – 2.28	
≥75	1 (reference)		
Work-related MIA for at least 10 minutes			<0.001
No	1.67	1.26 – 2.21	
Yes	1 (reference)		
Minutes of work-related MIA/week			0.457
<150	0.86	0.58 – 1.28	
≥150	1 (reference)		
Performs MISFRA for at least 10 minutes			<0.001
No	2.14	1.56 – 2.93	
Yes	1 (reference)		
Minutes of MISFRA/week			0.440
<150	1.27	0.70 – 2.30	
≥150	1 (reference)		
Walks to get to and from places for at least 10 minutes			0.034
No	1.57	1.03 – 2.38	
Yes	1 (reference)		
Minutes of walking/week			0.116
<150	1.28	0.94 – 1.74	
≥150	1 (reference)		

The dependent variable was waist circumference "above normal"; Normal waist circumference is ≤102 cm (male) and ≤88 cm (female); VIA = vigorous-intensity activity; VISFRA = vigorous-intensity sports, fitness and recreational activity; MIA = moderate-intensity activity; MISFRA = moderate-intensity sports, fitness and recreational activity

Results indicated that age, gender, area of residence, betel nut exposure, number of vegetable-eating days and VISFRA appeared to be independently associated with waist circumference (Table 5.44).

Those aged 50 – 59 years old had twice the odds of having a waist circumference above normal, compared to those younger than 50 years. The association, however, did not reach statistical significance when comparing those younger than 50 years with those aged 60 years and older.

Female participants were 14 times more likely to have a waist circumference above normal, compared to their male counterparts. Those who chewed ≤5 nuts/day were significantly less likely to have a waist circumference above normal, compared to those who never chewed. The association, however, did not reach statistical significance when comparing those who chewed >5 nuts/day and those who had quit the habit with those who never chewed betel nut.

Those who either didn't consume vegetables or those who consumed vegetables for up to five days per week appeared to be less likely to have a waist circumference above normal, and those who did not do VISFRA had twice the odds of a higher than normal waist circumference.

Table 5.44 Multivariate logistic regression analysis of demographic and lifestyle risk factors independently associated with abnormally large waist circumference

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Age (years)				0.049
<50	258/772 (33.4)	1 (reference)		
50 - 59	54/108 (50.0)	2.14	1.16 – 3.96	0.015
≥60	7/34 (54.4)	0.90	0.22 – 3.61	0.877
Gender				<0.001
Female	276/507 (54.4)	14.29	8.77 – 23.27	
Male	43/407 (10.6)	1 (reference)		
Area of residence				0.006
Urban	197/615 (32.0)	1 (reference)		
Peri-urban	122/299 (40.8)	1.88	1.20 – 2.95	
Betel nut exposure				0.019
Never	72/140 (51.4)	1 (reference)		
Quit	10/30 (33.3)	1.05	0.28 – 3.95	0.946
≤5 nuts/day	109/400 (27.3)	0.44	0.25 – 0.77	0.004
>5 nuts/day	119/327 (36.4)	0.70	0.40 – 1.23	0.212
Vegetable-eating days/week				0.039
0 - 5	128/470 (27.2)	0.64	0.42 – 0.98	
6 - 7	188/438 (42.9)	1 (reference)		
Performs VISFRA for at least 10 minutes				<0.001
No	238/594 (40.1)	2.15	1.40 – 3.31	
Yes	77/315 (24.4)	1 (reference)		

The dependent variable was waist circumference above normal. Normal waist circumference is ≤102 cm (male) and ≤88 cm (female); *The column 'n/N (%)' shows the number (and percentage) of participants with abnormally large waist circumference within each variable; VISFRA = vigorous-intensity sports, fitness and recreational activity

5.3.4.4 Fasting blood glucose

Analysis for FCBG excluded those participants who did not fast (random CBG). FCBG was grouped into different categories of hyperglycaemia according to the PNG Diabetes Clinical Guidelines 2012. Using those guidelines for definition of T2DM, one of the FCBG variables was created with a cut-off of 6.1, where a FCBG of 6.1 mmol/L or higher would indicate that the participant could have T2DM. FCBG levels were also categorised according to PNG Diabetes Clinical Guidelines 2012 as <5.6, 5.6 - 6.0 and >6.0 mmol/L, indicating normal, IFG and possible T2DM, respectively.

As shown in Table 5.45, participants aged ≥60 years, and those who were retired, had the highest mean FCBG compared to the other age groups. The minimum and maximum FCBG for all participants were 3.5 and 27.7 mmol/L, respectively. Those who had completed tertiary education, those who were self-employed and those who resided in peri-urban areas tended to have lower FCBG ranges.

As can be seen in Table 5.46, age was the only demographic factor that was associated with a FCBG of >6.0 mmol/L. Those aged 60 years and older were more likely to have T2DM, compared to their younger counterparts. Those residing in urban areas and those who had lived in Port Moresby for 10 years or less appeared to have a FCBG of >6.0 mmol/L more often, but none of these associations reached statistical significance.

Table 5.45 Mean, standard deviation and range values of FCBG of participants (N = 897)

Variable	n (%)*	Mean	SD	Range
All participants	897 (100.0)	5.50	1.53	3.5 – 27.7
Gender				
Female	447 (49.8)	5.49	1.28	3.5 – 21.1
Male	360 (40.1)	5.51	1.73	3.5 – 27.7
Age (years)				
<50	680 (75.8)	5.42	1.03	3.5 – 14.4
50 - 59	93 (10.4)	5.65	1.91	3.5 – 21.1
≥60	31 (3.5)	6.83	4.82	3.5 – 27.7
Level of education				
Did not complete basic education	163 (18.2)	5.53	1.99	3.5 – 27.7
Primary basic education	313 (34.9)	5.53	1.28	3.5 – 17.5
Secondary/Vocational	310 (34.6)	5.46	1.45	3.6 – 21.1
Tertiary education	21 (2.3	5.48	0.67	4.4 – 7.1
Employment Status				
Paid employment	219 (24.4)	5.49	1.35	3.5 – 17.5
Unpaid/unemployed	471 (52.6)	5.45	1.32	3.5 – 21.1
Retired	11 (1.2)	7.20	6.83	4.1 – 27.7
Self-employed	106 (11.8)	5.58	0.98	3.5 – 8.6
Area of residence				
Urban	542 (60.4)	5.58	1.72	3.5 – 27.7
Peri-urban	265 (29.5)	5.34	0.87	3.5 – 8.5
Region of origin				
Southern	320 (35.7)	5.51	1.38	3.5 – 17.5
New Guinea Islands	72 (8.0)	5.52	2.05	3.6 – 21.1
Momase	107 (11.9)	5.62	2.35	3.5 – 27.7
Highlands	308 (34.3)	5.44	1.03	3.5 – 11.3
Years of residence in Port Moresby				
≤10	452 (50.4)	5.52	1.33	3.5 – 21.1
>10	355 (39.6)	5.47	1.69	3.5 – 27.7

*May not add up to total because of missing values; FCBG = fasting capillary blood glucose

Table 5.46 Demographic factors associated with T2DM

Variable	Fasting capillary blood glucose (mmol/L)		p-value[#]
	Non-T2DM ≤6.0 (N [%])	T2DM >6.0(N [%])	
Gender			0.765
Female	405 (81.8)	90 (18.2)	
Male	332 (82.6)	70 (17.4)	
Age (years)			0.033
<60	730 (82.7)	153 (17.3)	
≥60	24 (68.6)	11 (31.4)	
Area of residence			0.084
Urban	482 (80.6)	116 (19.4)	
Peri-urban	255 (85.3)	44 (14.7)	
Years of residence in Port Moresby			0.052
≤10	367 (79.6)	94 (20.4)	
>10	308 (84.8)	55 (15.2)	

[#]The p-values were obtained from the Chi-square statistics and assess the strengths of associations; T2DM = type 2 diabetes mellitus

Of all the demographic factors, only age tended to be associated with IFG. Those aged 50 - 59 years appeared more likely to have IFG, while those aged 60 years and older appeared more likely to have FCBG of >6.0 mmol (χ^2, p=0.032), indicating that the latter were more likely to have T2DM. Lifestyle factors, such as tobacco smoking and alcohol, vegetable and fruit consumption, did not have an impact on FCBG. Neither tobacco smoking nor fruit consumption had an impact on FCBG. However, the number of days in a week that vegetables were consumed did appear to have an impact on FCBG, with those consuming vegetables for 6 - 7 days being more likely to have normal FCBG (χ^2, p=0.011). Participants who consumed more than two serves of fruit in a week appeared to be more likely to have IFG but this did not reach statistical significance (χ^2, p=0.088).

As shown in Tables 5.47 and 5.48, none of the betel nut chewing variables was associated with FCBG.

Table 5.47 Betel nut chewing variables associated with T2DM

Variable	Fasting capillary blood glucose		
	Non-T2DM ≤6.0 (N [%])	T2DM >6.0 (N [%])	p-value[#]
Betel nut chewer			0.318
No	141 (84.9)	25 (15.1)	
Yes	592 (81.7)	133 (18.3)	
Betel nut chewing history			0.593
Current	592 (81.7)	133 (18.3)	
Never	116 (85.3)	20 (14.7)	
Quit	24 (82.8)	5 (17.2)	
Betel nut exposure			0.767
Never	116 (85.3)	20 (14.7)	
Quit	24 (82.8)	5 (17.2)	
≤5 nuts/day	324 (82.2)	70 (17.8)	
>5 nuts/day	258 (81.1)	60 (18.9)	
Betel nut chew composition[†]			0.380
Betel nut, lime and PBI	366 (80.3)	90 (19.7)	
Betel nut ± PBI or lime	210 (84.3)	39 (15.7)	
Betel nut only	17 (85.0)	3 (15.0)	

[#]The p-values were obtained from the Chi-square statistics, and assess the strengths of associations; T2DM = type 2 diabetes mellitus; FCBG = fasting capillary blood glucose; PBI = *Piper betle* inflorescence; [†]Includes only those who were classified as betel nut chewers

Table 5.48 Betel nut chewing variables associated with IFG and T2DM

Variable	Fasting capillary blood glucose (mmol/L)			p-value[#]
	Normal <5.6 (N [%])	IFG 5.6 - 6.0 (N [%])	T2DM >6.0 (N [%])	
Betel nut chewer				0.606
No	103 (62.0)	38 (22.9)	25 (15.1)	
Yes	434 (59.9)	158 (21.8)	133 (18.3)	
Betel nut chewing history				0.577
Current	434 (59.9)	158 (21.8)	133 (18.3)	
Never	88 (64.7)	28 (20.6)	20 (14.7)	
Quit	15 (51.7)	9 (31.0)	5 (17.2)	
Betel nuts exposure				0.713
Never	88 (64.7)	28 (20.6)	20 (14.7)	
Quit	15 (51.7)	9 (31.0)	5 (17.2)	
≤5 nuts/day	232 (58.9)	92 (23.4)	70 (17.8)	
>5 nuts/day	193 (60.7)	65 (20.4)	60 (18.9)	
Betel nut chew composition[†]				0.115
Betel nut, lime and PBI	280 (61.4)	86 (18.9)	90 (19.7)	
Betel nut ± PBI or lime	142 (57.0)	68 (27.3)	39 (15.7)	
Betel nut only	12 (60.0)	5 (25.0)	3 (15.0)	

[#]The p-values were obtained from the Chi-square statistics, and assess the strengths of associations; [†]Includes only those who were classified as betel nut chewers; IFG = impaired fasting glucose; T2DM = type 2 diabetes mellitus; FCBG = fasting capillary blood glucose; PBI = *Piper betle* inflorescence

As demonstrated in Table 5.49, of all the physical activities investigated in this study, work-related VIA was the only variable associated with FCBG. Those whose work involved VIA were more likely to have FCBG >6.0 mmol/L compared to those who did not.

When FCBG was classified into three categories (<5.6, 5.6 - 6.0 and >6.0 mmol/L), the physical activities which were associated with FCBG were work-related MIA and VIA (Table 5.50). Those who were involved in work-related MIA were more likely to have IFG compared to those who did not. Those involved in work-related VIA were more likely to have FCBG >6.0 mmol/L.

Table 5.49 Association of physical activity with T2DM.

Variable	Fasting capillary blood glucose		p-value[#]
	Non-T2DM ≤6.0 (N [%])	T2DM >6.0 (N [%])	
Work-related MIA for at least 10 minutes			0.185
No	295 (84.5)	54 (15.5)	
Yes	432 (81.1)	101 (18.9)	
Performs MISFRA for at least 10 minutes			0.307
No	236 (84.3)	44 (15.7)	
Yes	497 (81.5)	113 (18.5)	
Work-related VIA for at least 10 minutes			0.004
No	361 (86.2)	58 (13.8)	
Yes	369 (78.8)	99 (21.2)	
Performs VISFRA for at least 10 minutes			0.410
No	473 (81.6)	107 (18.4)	
Yes	258 (83.8)	50 (16.2)	
Walks to get to and from places for at least 10 minutes			0.850
No	80 (81.6)	18 (18.4)	
Yes	651 (82.4)	139 (17.6)	
Amount of physical activity/week			0.857
Sufficient	519 (82.3)	112 (17.7)	
None/Insufficient	197 (82.8)	41(17.2)	

[#]The p-values were obtained from Chi-square statistics, and assess the strengths of associations; T2DM = type 2 diabetes mellitus; MIA = Moderate-intensity activities; MISFRA = Moderate-intensity sports, fitness and recreational activities; VIA = Vigorous-intensity activities; VISFRA = Vigorous-intensity sports, fitness and recreational activities

Table 5.50 Physical activities associated with IFG and T2DM

Variable	Fasting capillary blood glucose (mmol/L)			p-value[#]
	Normal <5.6 (N[%])	IFG 5.6 - 6.0 (N [%])	T2DM >6.0 (N [%])	
Work-related MIA for at least 10 minutes				0.017
No	231 (66.2)	64 (18.3)	54 (15.5)	
Yes	302 (56.7)	130 (24.4)	101 (18.1)	
Performs MISFRA for at least 10 minutes				0.263
No	357 (58.5)	140 (23.0)	113 (18.5)	
Yes	180 (64.3)	56 (20.0)	44 (15.7)	
Work-related VIA for at least 10 minutes				0.006
No	273 (65.2)	88 (21.0)	58 (13.8)	
Yes	262 (56.0)	107 (22.9)	99 (21.2)	
Performs VISFRA for at least 10 minutes				0.277
No	339 (58.4)	134 (23.1)	107 (18.4)	
Yes	197 (64.0)	61 (19.8)	50 (16.2)	
Walks to get to and from places for at least 10 minutes				0.808
No	61 (62.2)	19 (19.4)	18 (18.4)	
Yes	475 (60.1)	176 (22.3)	139 (17.6)	
Amount of physical activity /week				0.836
Sufficient	379 (60.1)	140 (22.2)	112 (17.7)	
None/Insufficient	148 (62.2)	49 (20.6)	41 (17.2)	

[#]The p-values were obtained from the Chi-square statistics, and assess the strengths of associations; MIA = moderate-intensity activity; MISFRA = moderate-intensity sports, fitness and recreational activities; VIA = Vigorous-intensity activities; VISFRA = Vigorous-intensity sports, fitness and recreational activities; IFG = impaired fasting glucose; T2DM = type 2 diabetes mellitus

The only medical factors associated with FCBG were BMI and waist circumference (Table 5.51). Participants with a BMI ≥25 kg/m^2 and those with abnormally large waist circumferences were more likely to have a FCBG of >6.0 mmol/L that indicated a possibility of T2DM. Blood pressure was not associated with FCBG.

Table 5.51 Medical factors associated with T2DM

Variable	Fasting capillary blood glucose		
	Non-T2DM ≤6.0 (N [%])	T2DM >6.0 (N [%])	p-value[#]
Body mass index (kg/m^2)			0.004
<25	264 (87.4)	38 (12.6)	
≥25	466 (79.7)	119 (20.3)	
Waist circumference			0.016
Normal	489 (84.6)	89 (15.4)	
Above normal	243 (78.1)	68 (21.9)	
Systolic blood pressure (mmHg)			0.961
≤130	529 (82.4)	113 (17.6)	
>130	204 (82.3)	44 (17.7)	
Diastolic blood pressure (mmHg)			0.961
≤80	529 (82.4)	113 (17.6)	
>80	204 (82.3)	44 (17.7)	

[#] The p-values were obtained from the Chi-square statistics, and assess the strengths of associations; T2DM = type 2 diabetes mellitus; Normal waist circumference is ≤102cm (male) and ≤88cm (female)

When FCBG was grouped into three categories, BMI and waist circumference were associated with FCBG (Table 5.52). However, those with a BMI ≥25 kg/m^2 and those who had a waist circumference above normal were more likely to be associated with FCBG >6.0 mmol/L rather than having an IFG of 5.6 – 6.0 mmol/L. When comparing those who were normal with the overweight and obese, results indicated that, as the BMI increased, the percentage of those with FCBG >6.0 mmol/L increased. Those who were underweight were less likely to have a normal or IFG but were more likely to have a FCBG >6.0 mmol/L when compared with the other categories of BMI. The sample number (n=16; 2 missing) for the former was very small.

Table 5.52 Medical factors associated with IFG (5.6 - 6.0 mmol/L) and T2DM (>6.0 mmol/L)

Variable	Fasting capillary blood glucose			p-value[#]
	Normal <5.6 (N [%])	IFG 5.6 - 6.0 (N [%])	T2DM >6.0 (N [%])	
BMI category				0.024
Underweight	9 (56.3)	2 (12.5)	5 (31.3)	
Normal	183 (64.0)	70 (24.5)	33 (11.5)	
Overweight	207 (60.2)	73 (21.2)	64 (18.6)	
Obese	136 (56.4)	50 (20.7)	55 (22.8)	
BMI (kg/m^2)				0.016
<25	192 (63.6)	72 (23.8)	38 (12.6)	
≥25	343 (58.6)	123 (21.0)	119 (20.3)	
Waist circumference				0.025
Normal	351 (60.7)	138 (23.9)	89 (15.4)	
Above normal	185 (59.5)	58 (18.6)	68 (21.9)	
SBP (mmHg)				0.994
≤130	387 (60.3)	142 (22.1)	113 (17.6)	
>130	150 (60.5)	54 (21.8)	44 (17.7)	
DBP (mmHg)				0.958
≤80	386 (60.1)	143 (22.3)	113 (17.6)	
>80	151 (60.9)	53 (21.4)	44 (17.7)	

[#] The p-values were obtained from the Chi-square statistics, and assess the strengths of associations; IFG = impaired fasting glucose; T2DM = type 2 diabetes mellitus; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; Normal waist circumference is ≤102cm (male) and ≤88cm (female)

Factors significantly associated with FCBG were entered into a univariate logistic regression model to determine the direction of association. Results indicated that work-related via, BMI and waist circumference had a significant influence on FCBG (Table 5.53). Participants who performed work-related VIA and those who had a BMI >25 kg/m^2 and an abnormally high waist circumference were more likely to have a FCBG of >6.0 mmol/L. Those aged 60 years and older had twice the odds of having a FCBG >6.0 mmol/L but the impact of age on FCBG was only significant when comparing those aged 60 years and older with those younger than 50 years.

Table 5.53 Univariate logistic regression analysis of factors associated with abnormally high FCBG (>6.0 mmol/L).

Variable	Crude OR	95% CI	p-value
Age (years)			0.099
<50	1 (reference)		
50 - 59	0.87	0.49 – 1.52	0.617
≥60	2.16	1.03 – 4.51	0.041
Number of vegetable-eating days in a typical week			0.177
0 - 2	1.29	0.82 – 2.01	0.271
3 - 5	1.44	0.97 – 2.14	0.070
6 - 7	1 (reference)		
Work-related MIA for at least 10 minutes			0.185
No	0.78	0.55 – 1.13	
Yes	1 (reference)		
Work-related VIA for at least 10 minutes			0.005
No	0.60	0.42 – 0.85	
Yes	1 (reference)		
BMI (kg/m^2)			0.004
<25	1 (reference)		
≥25	1.77	1.20 – 2.63	
Waist circumference			0.016
Normal	1 (reference)		
Above normal	1.54	1.08 – 2.18	

The dependent variable was FCBG >6.0 mmol/L; FCBG = fasting capillary blood glucose; BMI = body mass index; MIA = moderate-intensity activity; VIA = vigorous-intensity activity; Normal waist circumference is ≤102cm (male) and ≤88cm (female)

As can be seen in Table 5.54, multivariate logistic regression analysis indicated that age, work-related VIA, BMI and waist circumference independently had an impact on FCBG.

Participants aged 60 years had two times the odds of having a FCBG >6.0 mmol/L. Those involved in work-related vigorous-intensity were almost twice as likely to have a FCBG >6.0 mmol/L. Waist circumference had a more significant impact on FCBG than BMI. The association between BMI and FCBG appeared to be statistically significant

Table 5.54 Multivariate logistic regression analysis factors independently associated with high FCBG (>6.0 mmol/L)

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Age (years)				0.023
<50	136/777 (17.5)	1 (reference)		
50 - 59	17/106 (16.0)	0.78	0.44 – 1.39	0.394
≥60	11/35 (31.4)	2.69	1.25 – 5.77	0.011
Work-related VIA for at least 10 minutes				0.005
No	60/427 (14.1)	0.59	0.41 – 0.86	
Yes	101/481 (21.0)	1 (reference)		
BMI (kg/m^2)				0.050
<25	38/307 (12.4)	1 (reference)		
≥25	123/601 (20.5)	1.53	1.00 – 2.34	
Waist circumference				0.035
Normal	92/592 (15.5)	1 (reference)		
Above normal	69/318 (21.7)	1.51	1.03 – 2.21	

The dependent variable was FCBG >6.0mmol/L; *The column 'n/N (%)' shows the number (and percentage) of participants who had FCBG >6.0 mmol/L within each variable; FCBG = fasting capillary blood glucose; BMI = body mass index; VIA= vigorous-intensity activity; Normal waist circumference is ≤102cm (male) and ≤88cm (female)

5.3.4.5 Oral glucose tolerance

As with FCBG, 2-hour oral glucose tolerance (OGT) was grouped into different categories of hyperglycaemia according to the PNG Diabetes Clinical Guidelines 2012. One of the variables was created with a cut-off of 11.0, where an OGT >11.0 mmol/L indicated that the participant could have T2DM. OGT was also categorised according to PNG Diabetes Clinical Guidelines 2012 as <8.9, 8.9 - 12.1 and >12.1 mmol/L, indicating normal, IGT and possibleT2DM, respectively.

OGT was not normally distributed and, therefore, are reported as median and range in Table 5.55. As shown in this Table, median values for all age categories were within the normal OGT of <8.9 mmol/L but these levels ranged from 3.7 to 32.9 mmol/L.

The highest median OGT value was observed in those aged 60 years and older. This subgroup also had the highest minimum OGT value compared to those who

were younger. Participants who had completed tertiary education and those who were self-employed had the narrowest and the second narrowest range of values, respectively.

The only factor associated with abnormally high OGT was age (Table 5.56). As age increased, the prevalence of having an abnormally high OGT also increased. Those aged 60 years and older appeared to have an abnormally high OGT, however the sample number for this subgroup was small.

Table 5.55 Median and range values of oral glucose tolerance test levels of participants (N = 471)

Variable	n (%)*	Median	Range
All participants	471 (100.0)	7.2	3.7 – 32.9
Gender			
Female	242 (51.4)	7.2	3.8 – 32.9
Male	186 (39.5)	7.2	3.7 – 30.0
Age (years)			
< 50	352 (74.7)	7.1	3.7 – 31.8
50 - 59	58 (12.3)	7.4	4.8 – 32.9
≥ 60	18 (3.8)	8.3	5.7 – 30.0
Level of education			
Did not complete basic education	83 (17.6)	7.6	3.8 – 30.0
Primary basic education	174 (36.9)	7.0	3.7 – 26.0
Secondary/Vocational	158 (33.5)	7.8	4.6 – 32.9
Tertiary education	13 (2.8)	7.2	5.3 – 9.5
Employment status			
Paid employment	110 (23.4)	7.3	3.7 – 26.0
Unpaid/unemployed	246 (52.2)	7.2	3.8 – 32.9
Retired	7 (1.5)	7.5	4.9 – 30.0
Self-employed	65 (13.8)	6.9	4.8 – 12.7
Area of residence			
Urban	296 (62.8)	7.1	3.9 – 32.9
Peri-urban	132 (28.0)	7.6	3.7 – 18.8
Region of origin			
Southern	177 (37.6)	7.4	3.7 – 31.8
New Guinea Islands	40 (8.5)	6.9	4.8 – 32.9
Momase	57 (12.1)	7.4	5.1 – 30.0
Highlands	154 (32.7)	7.0	3.8 – 18.8
Years of residence in Port Moresby			
≤10	231 (49.0)	7.2	3.8 – 32.9
>10	197 (41.8)	7.2	3.7 – 31.8

*May not add to total because of missing values

Table 5.56 Demographic factors associated with possible T2DM (OGT >11.0 mmol/L).

Variable	OGT levels (mmol/L)		p-value[#]
	Non-T2DM ≤11.0 (N [%])	T2DM >11.0(N [%])	
Gender			0.428
Female	252 (95.8)	11 (4.2)	
Male	196 (94)	12 (5.8)	
Age (years)			<0.001
<50	376 (97.2)	11 (2.8)	
50 - 59	56 (87.5)	8 (12.5)	
≥60	16 (80.0)	4 (20.0)	
Level of education			0.533
Did not complete basic education	92 (94.8)	5 (5.2)	
Primary basic education	178 (96.2)	7 (3.8)	
Secondary education/Vocational	160 (93.6)	11 (6.4)	
Tertiary education	16 (100.0)	0 (0.0)	
Employment status			0.264*
Paid	114 (95.0)	6 (5.0)	
Unpaid/unemployed	255 (94.8)	14 (5.2)	
Retired	6 (85.5)	1 (14.3)	
Self-employed	68 (98.6)	1 (1.4)	
Area of residence			0.127
Urban	302 (94.1)	19 (5.9)	
Peri-urban	146 (97.3)	4 (2.7)	
Region of origin			0.136*
Southern	181 (92.8)	14 (7.2)	
New Guinea Islands	42 (93.3)	3 (6.7)	
Momase	57 (96.6)	2 (3.4)	
Highlands	166 (97.6)	4 (2.4)	
Years of residence in Port Moresby			0.093
≤10	227 (96.6)	8 (3.4)	
>10	188 (93.1)	14 (6.9)	

[#]The p-values were obtained from the Chi-square statistics, and assess the strengths of associations; *Fisher's exact test; OGT = oral glucose tolerance; T2DM = type 2 diabetes mellitus

When OGT was grouped into three categories, demographic factors such as age and area of residence tended to affect OGT (Table 5.60). Participants aged 50 - 59 years and those aged 60 years and older were more likely to have IGT and T2DM, respectively.

Sample numbers for those aged 60 years and older, and those with OGT >12.1 were small. Those in peri-urban areas tended to have a higher prevalence of IGT, while their counterparts in urban areas tended to have OGT levels indicating T2DM.

The demographic factors associated with IGT were age and area of residence with age being the most important. Those aged 50-59 years (χ^2, $p<0.001$) and those residing in the peri-urban areas (χ^2, $p=0.022$) were more likely to have IGT

Tobacco smoking was associated with OGT but this association was only significant when participants were classified as smokers or non-smokers (Table 5.57). When participants were categorised as current, never or quit smokers, the association of smoking with OGT was not significant. Those who reported being smokers were less likely to have OGT >11.1 mmol/L.

Of the participants who consumed alcohol, vegetables or fruits, only the number of days/week that fruit was consumed appeared to have an association with an abnormally high OGT. Those who did not consume fruit or consumed fruits for up to two days per week were more likely to have an abnormally high OGT compared to those who consumed fruits for more than two days per week. However, the association was of non-significance.

Using the three-category OGT, results indicated that tobacco smoking and the consumption of alcohol, vegetables and fruit were not associated with OGTT abnormalities (Table 5.58).

Table 5.57 Tobacco smoking and alcohol, vegetable and fruit consumption variables associated with possible T2DM (OGT >11.0 mmol/L)

Variable	Capillary OGT (mmol/L)		p-value[#]
	Non-T2DM ≤11.0 (N [%])	T2DM >11.0(N [%])	
Alcohol in the previous 12 months			0.220
No	274 (94.2)	17 (5.8)	
Yes	174 (96.7)	6 (3.3)	
Vegetable servings/day			1.000*
<3	408 (94.9)	22 (5.1)	
≥3	36 (97.3)	1 (2.7)	
Number of vegetable-eating days in a typical week			0.838
0 - 2	97 (96.0)	4 (4.0)	
3 - 5	134 (94.4)	8 (5.6)	
6 - 7	213 (95.1)	11 (4.9)	
Fruit servings/day			0.238
<2	302 (94.4)	18 (5.6)	
≥2	129 (97.0)	4 (3.0)	
Number of fruit-eating days in a typical week			0.050
0 - 2	299 (93.4)	21 (6.6)	
3 - 5	111 (98.2)	2 (1.8)	
6 - 7	34 (100.0)	0 (0.0)	
Current smoker			0.031
No	285 (93.8)	19 (6.2)	
Yes	161 (98.2)	3 (1.8)	

[#]The p-values were obtained from the Chi-square statistics, and assess the strengths of associations; *Fisher's exact test; T2DM = type 2 diabetes mellitus; OGT = oral glucose tolerance

Table 5.58 Lifestyle (alcohol, vegetable and fruit consumption, and tobacco smoking) risk factors associated with IGT and T2DM

Variable	Capillary OGT (mmol/L)			p-value[#]
	Normal <8.9 (N [%])	IGT 8.9 - 12.1 (N [%])	T2DM >12.1 (N [%])	
Alcohol in the previous 12 months				0.509
No	236 (81.1)	43 (14.8)	12 (4.1)	
Yes	151 (83.9)	25 (13.9)	4 (2.2)	
Vegetable servings/day				0.480
<3	352 (81.9)	62 (14.4)	16 (3.7)	
≥3	31 (83.8)	6 (16.2)	0 (0.0)	
Number of vegetable-eating days in a typical week				0.738*
0 - 2	81 (80.2)	18 (17.8)	2 (2.0)	
3 - 5	118 (83.1)	18 (12.7)	6 (4.2)	
6 - 7	184 (82.1)	32 (14.3)	8 (3.6)	
Fruit servings/day				0.229
<2	258 (80.6)	49 (15.3)	13 (4.1)	
≥2	115 (86.5)	16 (12.0)	2 (1.5)	
Number of fruit-eating days in a typical week				0.278*
0 - 2	257 (80.3)	49 (15.3)	14 (4.4)	
3 - 5	99 (87.6)	12 (10.6)	2 (1.8)	
6 - 7	27 (79.4)	7 (20.6)	0 (0.0)	
Current smoker				0.201
No	248 (81.6)	43 (14.1)	13 (4.3)	
Yes	138 (84.1)	24 (14.6)	2 (1.2)	
Smoker history				0.319
Current	138 (84.1)	24 (14.6)	2 (1.2)	
Never	215 (81.7)	38 (14.4)	10 (3.8)	
Quit	33 (80.5)	5 (12.2)	3 (7.3)	

[#]The p-values were obtained from the Chi-square statistics, and assess the strengths of associations; OGT = oral glucose tolerance; IGT = impaired glucose tolerance; T2DM = type 2 diabetes mellitus

Betel nut chewing was associated with abnormally high OGT (Table 5.9). Those who did not chew betel nut were more likely to have an abnormally high OGT (>11.0 mmol/L) when compared with chewers. Current betel nut chewers, ever chewers ('current' and 'quit') and those who chewed betel nut with lime and PBI were less likely to have an abnormally higher OGT. When investigating the impact of daily quantities of betel nut chewed, among those who were classified as betel nut

chewers, results indicated that the quantity of betel nut chewed per day did not influence OGT.

Table 5.59 Betel nut chewing variables associated with possible T2DM (OGT >11.0 mmol/L)

Variable	Capillary OGT (mmol/L)		p-value[#]
	≤11.0 (N [%])	>11.0(N [%])	
Betel nut chewer			0.023*
No	84 (90.3)	9 (9.7)	
Yes	363 (96.5)	13 (3.5)	
Betel nut chewing history			0.029*
Current	363 (96.5)	13 (3.5)	
Never	74 (90.2)	8 (9.8)	
Quit	9 (90.0)	1 (10.0)	
Betel nut chewing status			0.038*
Never	74 (90.2)	8 (9.8)	
Ever	372 (96.4)	14 (3.6)	
Betel nut exposure			0.082*
Never	74 (90.2)	8 (9.8)	
Quit	9 (90.0)	1 (10.0)	
≤5 nuts/day	190 (96.4)	7 (3.6)	
>5 nuts/day	167 (96.5)	6 (3.5)	
Betel nut chew composition[†§]			0.037
Betel nut, lime and PBI	223 (97.4)	6 (2.6)	
Betel nut ± PBI or lime	129 (95.6)	6 (4.4)	
Betel nut only	10 (83.3)	2 (16.7)	

[#]The p-values were obtained from the Chi-square statistics, and assess the strengths of associations; *Fisher's Exact Test; [†]Includes only those classified as betel nut chewers; [§]data for 1 participant missing; OGT = oral glucose tolerance; PBI = *Piper betle* inflorescence

Using the three-category OGT, results indicated that betel nut chewing was not associated with OGT (Table 5.60). Sample numbers were small, especially for the category of OGT >12.1 mmol/L and therefore, a two-category variable (<8.9 and ≥8.9 mmol/L) with a cut-off of 8.9 mmol/L was created to investigate the association of betel nut chewing with OGT around this cut-off. Using this cut-off, results indicated that none of the betel nut chewing variables were associated with an OGT >8.9 mmol/L (Table 5.61).

Table 5.60 Association of betel nut variables with IGT (OGT = 8.9 - 12.1 mmol/L) and T2DM (OGT >12.1mmol/L)

Variable	Capillary OGT (mmol/L)			p-value[#]
	Normal <8.9 (N [%])	IGT 8.9 - 12.1 (N [%])	T2DM >12.1 (N [%])	
Betel nut chewer				0.329
No	73 (78.5)	15 (16.1)	5 (5.4)	
Yes	314 (83.5)	52 (13.8)	10 (2.7)	
Betel nut chewing history				0.409*
Current	314 (83.5)	52 (13.8)	10 (2.7)	
Never	64 (78.0)	13 (15.9)	5 (6.1)	
Quit	8 (80.0)	2 (20.0)	0 (0.0)	
Betel nut exposure				0.679*
Never	64 (78.0)	13 (15.9)	5 (6.1)	
Quit	8 (80.0)	2 (20.0)	0 (0.0)	
≤5 nuts/day	162 (82.3)	30 (15.2)	5 (2.5)	
>5 nuts/day	146 (84.4)	22 (12.7)	5 (2.5)	
Betel nut chew composition[†]				0.353
Betel nut, lime and PBI	194 (84.7)	31 (13.5)	4 (1.7)	
Betel nut ± PBI or lime	110 (81.5)	20 (14.8)	5 (3.7)	
Betel nut only	9 (75.0)	2 (16.7)	1 (8.3)	

[#]The p-values were obtained from the Chi-square statistics, and assess the strengths of associations; *Fisher's Exact Test; [†]Includes only those classified as betel nut chewers; OGT = oral glucose tolerance; IGT = impaired glucose tolerance; T2DM = type 2 diabetes mellitus

Table 5.61 Association of betel nut chewing with IGT

Variable	Capillary OGT (mmol/L)		p-value[#]
	<8.9 (N [%])	≥8.9 (N [%])	
Betel nut chewer			0.254
No	73 (78.5)	20 (21.5)	
Yes	314 (83.5)	62 (16.5)	
Betel nut chewing history			0.488
Current	314 (83.5)	18 (22.0)	
Never	64 (78.0)	2 (20.0)	
Quit	8 (80.0)	62 (16.5)	
Betel nut chewing status			0.245
Never	64 (78.0)	18 (22.0)	
Ever	322 (83.4)	64 (16.6)	
Quantity of betel nuts chewed/day[†]			0.544
≤ 5	162 (82.2)	35 (17.8)	
6 - 9	54 (81.8)	12 (18.2)	
≥ 10	98 (86.7)	15 (13.3)	
Betel nut exposure			0.666
Never	64 (78.0)	18 (22.0)	
Quit	8 (80.0)	2 (20.0)	
≤5 nuts/day	162 (82.2)	35 (17.8)	
>5 nuts/day	146 (84.4)	27 (15.6)	
Betel nut chew composition[†]			0.538
Betel nut, lime and PBI	194 (84.7)	35 (15.3)	
Betel nut ± PBI or lime	110 (81.5)	25 (18.5)	
Betel nut only	9 (75.0)	3 (25.0)	

[#]The p-values were obtained from the Chi-square statistics, and assess the strengths of associations; [†]Includes only those classified as betel nut chewers; PBI = *Piper betle* inflorescence; IGT = impaired glucose tolerance; OGT = oral glucose tolerance

As Table 5.62 demonstrates, none of the different types of physical activities included in this study had an association with abnormally high OGT (>11.0 mmol/L) but the number of minutes spent on MISFRA tended to influence OGT. Those who did this type of activity for <150 minutes per week were less likely to have an OGT >11.0 mmol/L. When OGT was divided into three categories none of the physical activities included in this study influenced OGT.

Table 5.62 Physical activity variables associated with possible T2DM

Variable	Non-T2DM ≤11.0 (N [%])	T2DM >11.0 (N [%])	p-value[#]
Work-related MIA for at least 10 minutes			0.443
No	177 (94.1)	11 (5.9)	
Yes	268 (95.7)	12 (4.3)	
Minutes of work-related MIA/week			0.747*
<150	94 (96.9)	3 (3.1)	
≥150	153 (95.6)	7 (4.4)	
Performs MISFRA for at least 10 minutes			0.168
No	308 (94.2)	19 (5.8)	
Yes	138 (97.2)	4 (2.8)	
Minutes of MISFRA/week			0.027*
<150	81 (100.0)	0 (0.0)	
≥150	53 (93.0)	4 (7.0)	
Work-related VIA for at least 10 minutes			0.969
No	211 (95.0)	11 (5.0)	
Yes	234 (95.1)	12 (4.9)	
Minutes of work-related VIA/week			0.128*
<75	44 (100.0)	0 (0.0)	
≥75	169 (93.9)	11 (6.1)	
Performs VISFRA for at least 10 minutes			0.127
No	300 (94.0)	19 (6.0)	
Yes	145 (97.3)	4 (2.7)	
Minutes of VISFRA/week			0.314*
<75	45 (100.0)	0 (0.0)	
≥75	99 (96.1)	4 (3.9)	
Walks to get to and from places for at least 10 minutes			1.000
No	53 (96.4)	2 (3.6)	
Yes	392 (94.9)	21 (5.1)	
Minutes of walking/week			0.433
<150	174 (95.6)	8 (4.4)	
≥150	181 (93.8)	12 (6.2)	
Amount of physical activity/week			0.494
Sufficient	306 (95.3)	15 (4.7)	
Insufficient/None	120 (93.8)	2 (6.2)	

[#]The p-values were obtained from Chi-square statistics, and assess the strengths of associations; *Fisher's Exact Test; OGT = oral glucose tolerance; MIA = moderate-intensity activities; MISFRA = moderate-intensity sports, fitness and recreational activities; VIA = vigorous-intensity activities; VISFRA = vigorous-intensity sports, fitness and recreational activities

As shown in Table 5.63, SBP, BMI and waist circumference tended to be associated with abnormally high OGT (>11.0 mmol/L). Those with a BMI ≥25 kg/m^2 and a waist circumference above normal were more likely to have an abnormally high OGT.

Participants with SBP >130 mmHg were more likely to have an OGT >11.0 mmol/L. DBP did not affect OGT.

Table 5.63 Medical factors associated with possible T2DM (OGT >11.1 mmol/L)

Variable	Capillary OGT (mmol/L)		p-value[#]
	Non-T2DM ≤11.0 (N [%])	T2DM >11.0 (N [%])	
BMI category			0.019
Underweight	5 (83.3)	1 (16.7)	
Normal	140 (98.6)	2 (1.4)	
Overweight	173 (95.6)	8 (4.4)	
Obese	125 (91.2)	12 (8.8)	
BMI (kg/m^2)			0.048
<25	145 (98.0)	3 (2.0)	
≥25	298 (93.7)	20 (6.3)	
Waist circumference			0.045
Normal	285 (96.6)	10 (3.4)	
Above normal	159 (92.4)	13 (7.6)	
SBP (mmHg)			0.007
≤130	311 (96.9)	10 (3.1)	
>130	133 (91.1)	13 (8.9)	
DBP (mmHg)			0.390
≤80	308 (95.7)	14 (4.3)	
>80	136 (93.8)	9 (6.2)	

[#]The p-values were obtained from Chi-square statistics, and assess the strengths of associations; OGT = oral glucose tolerance; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; Normal waist circumference is ≤102cm (male) and ≤88cm (female).

Using the three-category OGT to investigate which medical factors were associated with IGT (8.9 – 12.1 mmol/L), if any, results indicated that BMI was associated with IGT, with participants having a BMI ≥25 kg/m^2 being more likely to have IGT (Table 5.64). Those with an SBP ≤130 mmHg appeared to be more likely to have IGT, while those with an SBP >130 mmHg were more likely to have an abnormally high OGT (>12.1 mmol/L).

Table 5.64 Medical factors associated with IGT and T2DM

Variable	Capillary OGT (mmol/L)			p-value[#]
	Normal <8.9 (N [%])	IGT 8.9 - 12.1 (N [%])	T2DM >12.1 (N [%])	
BMI category				0.002*
Underweight	4 (66.7)	1 (16.7)	1 (16.7)	
Normal	129 (90.8)	13 (9.2)	0 (0.0)	
Overweight	147 (81.2)	26 (14.4)	8 (4.4)	
Obese	103 (75.2)	27 (19.7)	7 (5.1)	
BMI (kg/m^2)				0.007
<25	133 (89.9)	14 (9.5)	1 (0.7)	
≥25	250 (78.6)	53 (16.7)	15 (4.7)	
Waist circumference				0.103
Normal	251 (85.1)	36 (12.2)	8 (2.7)	
Above normal	133 (77.3)	31 (18.0)	8 (4.7)	
SBP (mmHg)				0.008
≤130	263 (81.9)	52 (16.2)	6 (1.9)	
>130	121 (82.9)	15 (10.3)	10 (6.8)	
DBP (mmHg)				0.762
≤80	264 (82.0)	48 (14.9)	10 (3.1)	
>80	120 (82.8)	19 (13.1)	6 (4.1)	

[#]The p-values were obtained from Chi-square statistics, and assess the strengths of associations; *Fisher's exact test; OGT = oral glucose tolerance; IGT = impaired glucose tolerance; T2DM = type 2 diabetes mellitus; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; Normal waist circumference is ≤102cm (male) and ≤88cm (female).

Variables associated with OGT using the two- and the three-category OGT were entered into a univariate logistic regression model to determine the direction of association. The variable MISFRA was dropped because the sample number of participants with OGT >11.0 mmol/L was too small to enter into the model.
The results, outlined in Table 5.65, indicated that age was the important factor which influenced OGT. Other factors were betel nut chewing, smoking and SBP. As participant age increased, the likelihood of having an abnormally high OGT increased. Participants aged 50 – 59 years and 60 years and older were four and eight times, respectively, more likely to have an OGT >11.0 mmol/L, compared to their younger counterparts.

Participants who never chewed betel nut had almost three times the odds of having an OGT >11.0 mmol/L. Although the association between betel nut chew composition and OGT did not reach statistical significance, a significant association was observed when comparing chewing betel nut only with chewing the nut with both PBI and lime. Those who chewed betel nut only were seven times more likely to have an abnormally high OGT when compared with those who chewed the nut with PBI and lime.

Those who had a high SBP had three times the odds of an abnormally high OGT. Having a BMI ≥25 kg/m^2 and waist circumference above normal appeared to have an association with OGT >11.0 mmol/L but this did not reach significance.

Table 5.65 Univariate logistic regression analysis of factors associated with abnormally OGT (>11.0mmol/L)

Variable	Crude OR	95% CI	p-value
Age (years)			<0.001
<50	1 (reference)		
50 - 59	4.88	1.88 – 12.66	0.001
≥60	8.55	2.45 – 29.80	0.001
Area of residence			0.137
Urban	1 (reference)		
Peri-urban	0.44	0.15 – 1.30	
Number of fruit-eating days in a typical week			0.114
0 - 1	1.98	0.85 – 4.61	
2 - 7	1 (reference)		
Betel nut chewer			0.015
No	2.99	1.24 – 7.23	
Yes	1 (reference)		
Betel nut chewing status			0.022
Never	2.87	1.16 – 7.09	
Ever	1 (reference)		
Betel nut chew composition[†]			0.072
Betel nut, lime and PBI	1 (reference)		
Betel nut ± PBI or lime	1.73	0.55 – 5.47	0.352
Betel nut only	7.43	1.33 – 41.56	0.022
Current smoker			0.043
No	3.58	1.04 – 12.28	
Yes	1 (reference)		
SBP (mmHg)			0.010
≤130	1 (reference)		
>130	3.04	1.30 – 7.11	
BMI (kg/m^2)			0.061
<25	1 (reference)		
≥25	3.24	0.95 – 11.09	
Waist circumference			0.050
Normal	1 (reference)		
Above normal	2.33	1.00 – 5.44	

The dependent variable was >11.0 mmol/L; OGT = oral glucose tolerance; PBI = *Piper betle* inflorescence; SBP = systolic blood pressure; BMI = body mass index; Normal waist circumference is ≤102cm (male) and ≤88cm (female)

Age was the most important factor which was independently associated with OGT (Table 5.66). Participants aged 50 years and older were more likely to have an abnormally high OGT.

Although tobacco smoking and SBP were independently associated with OGT, the associations did not reach statistical significance. The sample numbers for the prevalence of OGT >11.0 mmol/L were small so valid conclusions could not be made.

Table 5.66 Multivariate logistic regression analysis of factors independently associated with high OGT (>11.0 mmol/L).

Variable	n/N (%)*	Adjusted OR	95% CI	p-value
Age category (years)				0.004
<50	11/387 (2.8)	1 (reference)		
50 - 59	8/64 (12.5)	4.27	1.62 – 11.25	0.003
≥60	4/20 (20.0)	5.39	1.32 – 21.91	0.019
Current smoker				0.071
No	19/304 (6.3)	3.16	0.91 – 11.04	
Yes	3/164 (1.8)	1 (reference)		
SBP (mmHg)				0.065
≤130	10/321 (3.1)	1 (reference)		
>130	13/146 (8.9)	2.31	0.95 – 5.61	

The dependent variable was >11.0 mmol/L; OGT = oral glucose tolerance; SBP = systolic blood pressure; *The column 'n/N (%)' shows the number (and percentage) of participants who had OGT >11.0 mmol/L within each variable.

5.3.4.6 Bioelectric impedance body composition measurement (% body fat)

Statistical analysis of this variable and factors associated with it used >25.0% as a cut-off for males and >35.0% for females. These cut offs were previously used in a recent Vanuatu study.[2] Other factors affecting percentage body fat were not considered in the analysis because the focus of the current research was on glycaemic control and betel nut chewing.

Considering gender as a factor which affects percentage body fat, Chi-square analysis indicated that no demographic, lifestyle, physical and biochemical factors were associated with percentage body fat in males. The only factor which was associated with percentage body fat in females was age. As age increased in females, the proportion of those with percentage body fat >35% increased from those aged <30 to those 49 years of age. A reduction in the proportion of those with percentage body fat > 35% was observed in those aged 50-59 years compared to those younger than 50 years. For those in the age group 60-69 years, an equal proportion was observed in those with ≤35% and >35% body fat. However the sample number of females in the latter age category was small (n=10, Table 5.67). None of the betel nut variables was associated with percentage body fat in both genders

Table 5.67 Association of age with % body fat in females (p=0.003)

Age category	Percentage body fat [n (%)]	
	≤35.0%	>35.0%
< 30	220 (90.5)	23 (9.5)
30-39	112 (88.2)	15 (11.8)
40-49	56 (86.2)	9 (13.8)
50-59	53 (88.3)	7 (11.5)
60-69	5 (50.0)	5 (50.0)

The p-value was obtained from Chi-square statistics, and assesses the strength of association

5.4 Discussion

5.4.1 Demographic characteristics

The highest numbers of participants were in the age group ≤ 39 years. The majority of participants were from the Highlands (37.7%) and the Southern (39.9%) regions. The region from which the highest numbers of participants were originally from may be reflective of the sites used for the survey. Some of the peri-urban sites used for this survey were squatter settlements belonging to those from the highlands region (Tari and Chimbu blocks) and Kerema in the Southern region. However, as discussed in Chapter IV, a cross-sectional study by Benjamin[3] also reported that the highest numbers of participants were from the highlands (34.0%) and southern (37.7%) regions. That study used a different recruitment process to the current study. These results may be a reflection of which regions of PNG make up the majority of the Port Moresby population. The finding of the present study, that the highest number of participants were 39 years or younger, is consistent with the finding from the study by Benjamin.[3] The study reported that the highest number of participants were aged 40 years or younger. This is also a reflection of the age-specific population in PNG where >80% of the population is in the age group <50 years.[4]

Twenty five percent of participants reported being unemployed, although almost half of these were fit to work. When homemakers, students and those who were in unpaid employment were included as one category (unemployed/non-paid), the largest proportion (56.4%) of participants was in this category. This may be a reflection of the sites selected for the survey, urban drift, age groups included in this study, or extended family culture in PNG. One third of the participants included in this study were from squatter settlements which are the main dwellings for those who migrate to the city, the majority of whom are either unemployed or low income earners. However, due to other socioeconomic issues such as lack of appropriate housing for employees and high costs of housing rentals, a number of middle income earners may reside in these squatter settlements as well. One of the challenges in the City of Port Moresby is urban drift especially by young people. Young people are migrating to the city with the hope of a better life. Furthermore,

those who are unemployed may be immediate or extended family members of those who are employed and living in urban areas.

Almost a quarter of participants did not complete primary basic education. Getting at least basic primary education in PNG is not compulsory and PNG has had one of the lowest literacy rates in the Asia-Pacific region.[5] However, the literacy rate for those aged 15 years and older has increased from 56% reported in the 2000 census[5] to 62.4% in 2011[6]. There are many factors which influence whether or not a child attends school, one of which is cultural.

5.4.2 Lifestyle factors

5.4.2.1 Alcohol consumption

The prevalence rate of alcohol consumption in the preceding 12 months observed in the present study was 41.4%. This finding is similar to that reported by similar studies (STEPS survey) in PICs like Fiji[7] and Nauru[8] but is higher than that reported in the Solomon Islands[9], the Marshall Islands[10], Kiribati[11] and Vanuatu[12], with Vanuatu having the lowest prevalence. The STEPS survey in the Cook Islands[13] however reported a higher (62.9%) prevalence of alcohol consumption.

The finding that males are more likely to consume alcohol is consistent with many other findings in the PICs [7-16] and elsewhere.[17-19] This study also observed that prevalence of alcohol consumption decreased with increasing age with those younger than 50 years having the highest prevalence. Younger people tend to consume alcohol in social gatherings more than their older counterparts. Padrao et al[18] however reported an increasing prevalence of alcohol consumption with increasing age in a Mozambique study in adults aged 25-64 years. Also consistent with the Mozambique study is the finding of this present study that alcohol consumption is influenced by income among men. The positive influence of completing tertiary education on alcohol consumption in the present study is also an indication that those who attain this level of education are more likely to have an income and therefore more likely to consume alcohol. The Mozambique study also reported an increasing prevalence of alcohol consumption with increasing level of education but only in women.

5.4.2.2 Tobacco smoking

The prevalence of tobacco smoking among participants of this study was 38.0%. The prevalence of tobacco smoking seen amongst this PNG cohort is similar to that reported in Melanesian countries like Fiji[7] and the Solomon Islands[9]. Another Melanesian country, Vanuatu[12], however has reported a lower prevalence compared to PNG, Fiji[7] and the Solomon Islands[9]. Other PICs such as Nauru[8] and Kiribati[11] have reported higher prevalence rates of smoking compared to PNG, Fiji, Vanuatu and the Solomon Islands.

Smoking was influenced by gender, age and employment status. The findings of the present study that males are more likely to smoke compared to females, is consistent with many other findings in the PICs [7-16] and elsewhere [17, 20, 21]. The influence of age on tobacco smoking in this study was similar to that seen in alcohol consumption. As with alcohol, the prevalence of tobacco smoking decreased with increasing age which is consistent with another study.[21] The finding that those who retired were more likely to smoke tobacco compared to the other employment status may have been due to the small sample number (n=10) of those who retired. Apart from this, those in paid employment were more likely to smoke which is consistent with another study.[21] The present study was conducted in urban/peri-urban areas where tobacco products cost money compared to rural villages where smokers usually supplement manufactured tobacco products with home-grown tobacco. The cost of manufactured tobacco products may have contributed to the statistically significant influence of paid employment on smoking.

5.4.2.3 Vegetable and fruit consumption

Dietary intake of vegetable and fruit reported by participants was poor. More than 90% of participants consumed <3 vegetable servings and 66.6% consumed <2 fruit servings per day in a typical week. An average of 79.3% of participants consumed <5 combined fruit and vegetable serves. This finding is similar to the Cook Islands[13], a country with a much smaller land mass than PNG. Amongst the Melanesian countries, vegetable and fruit consumption was much worse in the Solomon Islands[9] with 93.6% consuming <5 combined fruit and vegetable serves. Vanuatu[12], however has reported a better dietary intake compared to PNG and the

Solomon Islands[9] with 61.8% consuming < 5 combined fruit and vegetable serves. Other PICs that have reported more than 90% consuming < 5 combined fruit and vegetable serves include Nauru[8], The Marshall Islands[10] and Kiribati[11], with Kiribati reporting the worst (99.3%) vegetable and fruit consumption.

Despite the majority of participants in this study consuming <3 vegetable serves of vegetables per day, almost half (47.6%) of those who consumed vegetables did so for 6-7 days in a typical week. The reverse was seen in the number of days per week fruit was consumed. As the number of days increased, the number of those consuming fruit decreased.

The present study however requested the participants to think of a typical week on which they consumed fruit which may have under or overestimated fruit and vegetable consumption among the participants.

The most important factor which influenced the number of vegetable servings per day was area of residence and betel nut chewing. Those in the peri-urban areas were more likely to consume ≥ 3 vegetable servings compared to their counterparts in urban areas. This may be because those who live in peri-urban areas may have vegetable garden plots on vacant land in surrounding areas while those in urban areas rely mostly on vegetables bought from local vegetable markets or supermarkets.

Those who did not complete basic education tended to be more likely to consume ≥ 3 serves of vegetables compared to the other subgroups. The influence of employment on vegetable servings was of borderline significance. Both those in paid and self-employment were more likely to consume ≥3 vegetable servings compared to the other employment statuses. This may be a reflection of the cost of living in Port Moresby. Those who did not complete basic education may have been living in peri-urban areas and had vegetable garden plots or they may have lived with immediate or extended family members who were employed. Vegetables are generally cheaper than protein especially for those living in urban areas so for many who cannot afford protein in their meals, carbohydrates are usually consumed with vegetables only. In general, the results observed in terms of vegetable and fruit consumption reflects a change in the diet of Papua New Guineans. PNG people

used to have a vegetable-rich diet but as westernisation and urbanisation increases, there is an increasing trend to consume processed food. Processed foods such as rice cost less to feed a large family compared to fresh sweet potatoes and green leafy vegetables from the markets. These findings however may not reflect vegetable consumption in rural areas where those living in these areas thrive on subsistence farming.

The number of fruit servings consumed per day in a typical week when fruit was consumed was influenced by level of education and employment status. The influence of area of residence on fruit serving was of borderline significance. Fruits sold in PNG are either imported from overseas or are grown in rural villages and sold in the supermarkets and local fresh food markets. Imported fruits such as apples, pears and oranges are usually expensive and are therefore usually afforded by those who have some form of income. This is reflected in the observations of the present study that those in paid employment were more likely to have ≥2 fruit servings per day. There was a small difference in those who consumed ≥ 2 fruit servings between those in unpaid/unemployed and those who were self-employed. It is possible that unpaid/unemployed participants may have been living with those who were in paid employment or were involved in the informal economic sector to generate income. The informal economic sector in Port Moresby encourages those who are unemployed to set up minimarkets to sell their goods or produce to make an income. If the unpaid/unemployed were involved in the informal economic sector, vegetables or fruits may have been commodities they were selling for income. Those involved in this sector often buy fresh produce from rural villagers and resell them in the urban markets or their residential minimarkets. Umezaki et al[22] in a study conducted in three PNG settlements found that certain informal sector activities of those in settlements were generating more money per day in comparison to other settlers who were employed in the formal sector. Residents in settlements employed in the formal sector may mostly have been low income earners as observed by Umezaki et al. That study also reported that energy intake but not nutrient intake was closely associated with per adult net earnings in a week.

When comparing lifestyle characteristics such as alcohol consumption, tobacco smoking and vegetable and fruit intake amongst PICs with that of this study cohort,

the findings of this study cohort may not reflect lifestyle characteristics of PNG as a whole as the PNG cohort in this study was made up of those from urban and peri-urban dwellings in Port Moresby, the largest city in PNG. The STEPS surveys in other PICs included those from the rural villages in those countries.

5.4.2.4 Physical activity

The most common physical activity was walking for travel which is consistent with a study among urban black Soweto women.[23] The finding that the most common type of physical activity reported by participants of this study was walking to get to and from places may be a reflection of the inefficient public transport system in Port Moresby. Public buses usually run on the main roads but not through streets of the suburbs. Many of those using public transport therefore have to walk fairly long distances to nearest bus stops. Furthermore, public buses are often overloaded and lack maintenance which discourages use of public transport services.

Walking for travel was more common among the unpaid/unemployed and levels of education lower than tertiary which may be a reflection of income, affordability of public transport or owning a motor vehicle. As the level of education affects the likelihood of employment and the type of employment, the subgroup who completed tertiary education are more likely to have high paying jobs and therefore are more likely to own vehicles or be provided transport by their employers. The employed (paid and self-employed) are therefore less likely to walk to get to and from places.

Sixty eight percent of participants reported doing sufficient physical activity (≥ 75 or 150 minutes of VIA or MIA respectively per week). The high prevalence of sufficient physical activity was contributed to largely by 'walking" as a physical activity. The amount of physical activity was influenced by area of residence and region of origin. Those living in urban areas were more likely to do more sufficient physical activity compared to those in peri-urban areas. This may be due to more availability of sports, fitness and recreational facilities in urban areas but not peri-urban areas.

Age significantly influenced sports, fitness and recreational activity. The prevalence of participating in sports, fitness and recreational physical activity decreased with increasing age. Age also inversely influenced work-related VIA; that is as age

increased, the prevalence of undertaking work-related VIA decreased. These findings are expected because as age increases, the intensity of physical activity a person can comfortably perform also decreases.

Employment had a significant influence on work-related MIA with the unpaid/unemployed and those who were self-employed being more likely to do work-related MIA. This may be a reflection of the type of work done by those in regularly paid employment compared to those are unpaid/unemployed and those self-employed. Those in unpaid/unemployed may have been involved in doing household chores such as cleaning houses or gardening. This also reflects the prevalence of homemakers in this study. Those who were self-employed were less likely to participate in sports fitness and recreational activities compared to those who were unpaid/unemployed and in regularly paid employment. The most obvious reason for those self-employed not participating in sports, fitness and recreational activities may have been due to time or financial constraints to undertake such activities. Although this study did not specify the types of jobs done by those who were employed, it is likely that those who were self-employed were working on a need basis for non-specific duration of time. Those who were self-employed were also less likely to do sufficient physical activity and this may be an indirect indication of the type of jobs done by those who are self-employed.

5.4.3 Physical measurements

5.4.3.1 Blood pressure

Twenty eight per cent of participants of this study had hypertension. This is similar to that found in Fiji[7], lower than that in Vanuatu[12] and the Cook Islands[13] and higher than in the Solomon Islands[9], the Marshall Islands[10], Kiribati[11] and Nauru[8]. However, in these PICs, high blood pressure (BP) cut-offs were higher (SBP > 140, DBP >90 mmHg) than that used for this study (SBP >130, DBP>80 mmHg) and therefore the prevalence may have been lower if higher BP cut-offs were used for the PNG cohort.

The likelihood of a high SBP and DBP increased with age but was slightly lower in those aged 60 years or more possibly because of the small sample of participants in

this age group. The finding that the likelihood of high SBP and DBP are associated with increasing age is consistent with other studies.[23-26] It is known that as age increases, the risk of high BP increases as a consequence of the ageing process in organ systems.[27-29]. Other studies have reported that as age increases, SBP increases while DBP either decreases or is maintained.[30-32]

The odds of having a high SBP and DBP significantly increased with increasing BMI and waist circumference which is consistent with other studies [24, 26, 33-35] reporting an association of obesity or weight gain with hypertension.

The finding that consuming ≥2 serves of fruit has a beneficial effect on systolic blood pressure is consistent with other studies demonstrating an association of fruit consumption with blood pressure.[36, 37]. The study by Gibbons[36] however used six to eight servings of potassium rich fruits in a follow up study of 6 weeks of African Americans. Berry et al [38] however reported that increased potassium intake from fruits and vegetables did not lower BP in 57 UK men and women.

The present study found that occupational physical activity did not influence SBP but moderate and vigorous-intensity leisure-time physical activities did with an increase in likelihood of a high SBP in those who did not perform these activities. Further, not taking part in all of the different physical activities included in this study increased the likelihood of having a high DBP. The finding that leisure-time physical activity reduces blood pressure is consistent with other findings.[39-41] However, undertaking work-related MIA for >150 minutes per week was associated with an increased risk of high DBP; for reasons which are unclear. Diastolic blood pressure is affected by peripheral resistance and increases with increased resistance. It is not known why this result was observed. It may have arisen by chance.

Living in urban Port Moresby for 10 years or more was associated with a high DBP. This is in agreement with another study [42] that longer duration of residing in urban areas increases the likelihood of high BP. This may be related to modernisation of way of life in urban areas increasing risk factors for high BP such as sedentary lifestyles, obesity and dietary changes.[43] Physical activity, obesity and diet are major influences of high blood pressure.[44-47]

5.4.3.2 Measures of obesity and adiposity

In the present study, obesity was determined by BMI, waist circumference and percentage body fat. Using BMI, more than 60% of participants were either overweight or obese (38.6% overweight, 26.8% obese). The prevalence of abnormally high waist circumference was 34.9%.

The pattern of obesity indicated by BMI is consistent with findings of two studies[3, 48] conducted in PNG by Benjamin. The prevalence of overweight observed in this study is similar to that reported in the Marshall Islands[10] but higher than that reported in Vanuatu[12]. The prevalence of obesity (BMI ≥ 30 kg/m^2) is much higher than that reported in Fiji[7]. Other PICs have reported higher prevalence rates of obesity than PNG. [8, 11, 13, 15, 16]

BMI is a measure of general obesity. In the present study, it was influenced by demographic factors such as age, gender, employment status and region of origin, and lifestyle factors such as smoking, alcohol consumption, betel nut consumption, physical activity and diet. After adjusting for each other, the important independent and significant factors which influenced BMI were region of origin, smoking, dietary factors, physical activity and betel nut chewing. The loss of significance of the influence of gender on BMI after adjusting for other confounding factors suggests that there are other important interacting factors affecting BMI in this study population.

Waist circumference is a measure of central obesity. After adjusting for each other, the significant independent factors affecting waist circumference were age, gender, area of residence, betel nut chewing, physical activity, and frequency of vegetable intake. Although level of education was associated with waist circumference, it was not an independent factor. The same was observed for smoking, alcohol, vegetable servings, and frequency of fruit consumption.

Percentage body fat is a measure of adiposity. There are many factors which are known to affect percentage body fat and therefore acceptable values in different populations have been reported to vary. A literature search for current recommended acceptable percentage body fat values for Papua New Guineans did

not find any. Therefore, the acceptable cut-off values for percentage body fat used study[2] of a Melanesian population of Vanuatu were used for analysis. In the present study, none of the demographic, lifestyle, physical and biochemical factors affected percentage body fat in male participants. The only factor which appeared to influence percentage body fat in female participants was age. Age has been reported to be one of the most important factors influencing percentage body fat.[49, 50]

The common significant factor which affected BMI and waist circumference was physical activity. Performing VISFRA was independently associated with a normal waist circumference suggesting that MIA and occupational physical activity are not sufficient to have a beneficial impact on waist circumference in this population, especially in the presence of usual dietary patterns. Surprisingly, performing leisure-time physical activity had a beneficial effect on BMI while occupational physical activity had an adverse effect. The duration of work-related VIA also had an independent adverse effect on BMI. This may be due to increased food intake influenced by culture. As already discussed in Chapter IV, in PNG, it is usual or cultural for the person who does vigorous-intensity work to be served large quantities of food as a token of appreciation for bringing food or money home for family, for example. This is also observed during feasting where those who work hard are appreciated with large quantities of food. Similar appreciation is not usually given to those involved in leisure-time activity. Therefore cultural reasons may be the reason for such a finding. (personal knowledge)

The finding that females were more likely to have a waist circumference in this cohort is the same as that in the T2DM cohort of this study. Possible reasons for the association of gender with waist circumference above normal have already been discussed in Chapter IV (Section 4.4.4.2).

Age had an independent influence on waist circumference in this cohort compared to the T2DM cohort where gender appeared to be the most important adverse factor. The highest association of age with waist circumference was in the age group 50-59 years with no difference between those aged <50 and ≥60 years. As age increased, the likelihood of an elevated percentage body fat increased with age with a peak at 50-59 years and decreased from 60 years. Smoking only had an independent beneficial effect on BMI and not waist circumference. This suggests

that smoking may confer a protective effect on BMI. The likelihood of having a BMI ≥25 kg/m^2 was doubled in those who quit and tripled in those who never smoked. It is well known that smoking is associated with a reduction in food intake and subsequent lower body weight. The finding that those who quit smoking have a high BMI is consistent with a follow up study by Munafo et al[51] and other studies[52] which found that BMI in those who quit smoking increases over time. For those who quit and return to smoking, research has also shown weight loss after returning to smoking.[52] The beneficial influence of smoking on BMI is most likely a result of appetite suppression by nicotine in cigarettes[53] which is probably mediated by the central nervous system[54] and levels of leptin [55]. In the study by Moffat et al[52], an increase in percentage body fat was observed in those who quit smoking but after 30 days of quitting, the percentage remained the same up to the 60th day.

A surprise finding from this study is that eating fruit for less than 2 days a week had a beneficial effect on BMI even after adjusting for other confounding factors suggesting an increase in frequency of fruit consumption may have an adverse effect on BMI. Although consumption of vegetable did not have a significant influence on BMI in the univariate analysis, it became a significant independent factor when it was entered into the multivariate logistic regression model with other confounding factors. Consuming vegetables for 6 to 7 days in a week had a beneficial influence on BMI. Although this finding is based on the number of days which may not accurately quantify vegetable consumption, this suggests that an increased frequency of vegetable consumption has a beneficial effect on BMI. Studies have reported conflicting results on the association of vegetable and fruit intake with weight gain.[56-58] The conflicting findings on the association of vegetable and fruit consumption with measures of obesity may partly be due to the fact that weight gain or obesity is multifactorial.

PNG has different indigenous groups. Although classified as Melanesians, those from the Central Province are more Polynesian than Melanesian and therefore may be of different ethnicity. The finding that those from the Southern region (mainly from Central Province), were more likely to be leaner (BMI) than those from other regions is surprising as it has been reported that Polynesians have a stronger association with increased body weight. Perhaps the frequent visits to rural villages

by those from the Southern region (Gulf and Central Provinces) living in urban Port Moresby confers a beneficial effect on BMI as a consequence of interchange between refined foods and a traditional diet while in the village. Physical activity may also increase while in the village. The study by Benjamin showed that 52% of rural villagers from the Central Province had a BMI <20kg/m^2.[48]

5.4.3.3 Potential mechanisms linking obesity to high blood pressure

BMI and waist circumference are measures of adiposity which were significantly associated with high BP (both SBP and DBP) and this relationship remained after adjusting for other confounders such as age. More than 50% of those included in this study were overweight or had increased adiposity. This suggests a high risk of cardiovascular and metabolic disorders in this population

There are many potential mechanisms linking obesity to high BP. These include dietary factors, metabolic, endothelial and vascular dysfunction, neuroendocrine imbalances, sodium retention, glomerular hyperfiltration, proteinuria and maladaptive immune and inflammatory responses.[59, 60]. Adipose tissue is the site of production of important molecules and hormones such as adiponectin, leptin, resistin, TNF and IL-6, all of which have been linked to cardiovascular and metabolic disorders. Visceral adipose tissue not only is the site of altered secretion for these molecules and hormones but also becomes resistant to insulin and leptin.[59]. Recent studies have also reported a role of gut microbiota on metabolism which may affect BP.[61, 62]

5.4.4 Betel nut chewing

5.4.4.1 Prevalence of betel nut chewing

The present study reports an 80% crude prevalence of betel nut chewing amongst Papua New Guineans in NCD, Port Moresby. The prevalence of betel nut chewing in this study is much higher than what was reported by an earlier study[3] conducted in the same district. The low prevalence of betel nut chewing (13.0%) reported by Benjamin[3] may be low because the majority (78%) of participants were Seventh Day Adventist church followers who usually do not chew betel nut. The prevalence of betel nut chewing varies in different regions or within countries where the habit is

practised. The prevalence rates of betel nut chewing from STEPS surveys [9, 10, 12, 63] in the Pacific Islands have been reported to range from 0.1% to 62.6% making PNG the highest consumers of betel nut in the region. Another smaller study consisting 315 participants in the Solomon Islands reported a prevalence rate of 76.8%.[64] In Taiwanese population-based studies[17, 65, 66] including men only, the prevalence of betel nut chewing reported ranges from 14.4% to 20.4% . These studies indicated that women had very low prevalence rates of betel nut chewing; findings which are different to what have been observed in PNG. In Bangladesh[67], the prevalence reported in both men and women in selected rural areas was 33.2% and a Sri Lankan study[68] reported an average of 9.6% in males living in both rural and urban residences (rural 17.6%, urban 1.7%). These figures show a large variation in prevalence rates of betel nut chewing not only between different countries but also within countries.

5.4.4.2 Demographic factors associated with betel nut chewing

The present study indicated that the factors associated with betel nut chewing were age, gender, level of education, area of residence and region of origin. Other factors reported by other studies to be associated with the prevalence of betel nut chewing include types of employment[65, 67], income level[69], level of education[65, 67, 69], physical activity[65], smoking[17, 65, 67, 69, 70], alcohol consumption[17, 65, 68-70] and, fruit and vegetable consumption[17, 65].

Results of this study support the finding by Yen et al [65] that the prevalence of betel nut chewing is higher in lower levels of education. The study by Yen et al reported that those with less years of education, those who are unemployed and those who are manual labourers or have service trade jobs are more likely to chew betel nut compared to teachers, officer holders, military personnel and business or professional workers. This study did not report details of types of employment but employment status did not influence prevalence of betel nut chewing. As previously discussed in Chapter IV, betel nut chewing is a social habit and betel nut is usually shared. A possible reason for the higher prevalence of betel nut chewing amongst those with lower levels of education than tertiary education is that those with lower level of education may be more likely to sell betel nuts to make an income.

The finding that males were more likely to chew betel nut in this study is consistent with findings elsewhere [17, 65, 66]. The prevalence of betel nut chewing among males was only slightly higher than that of the females. The small difference in prevalence of betel nut chewing between males and females is similar to that found in Bangladesh.[67] Other studies conducted in different population groups have reported large differences in prevalence of betel nut chewing among males and females.[17, 65, 66, 69, 71, 72]

Urban dwellers were more likely to chew betel nut compared to peri-urban dwellers. There is now a ban on the sale of betel nuts in places other than designated markets out of the urban areas of Port Moresby. Furthermore, the ban of betel nut chewing in public places has been reinforced. This study was conducted before the ban which came into effect in 2013. Before the current ban on betel nut chewing in public places and sale of betel nut at residential premises, many residences in urban areas had mini-markets within their premises. Most of these mini markets were selling betel nuts and therefore increased the availability. The unemployed or homemakers living in those residences often manned the mini markets. The cost of a betel nut can be expensive during seasons when the supplies are low and therefore it is mostly those who can afford betel nut who chew or buy and share with those who cannot afford it.

Region of origin may have influenced betel nut chewing because of increased availability and affordability. In terms of the influence of region of origin on betel nut chewing, those from the Southern region were more likely to chew betel nut. The most important reasons for this are firstly because betel nut trees are grown in rural villages and those from the region are more likely to have access through relatives or family living in the rural villages. Secondly, betel chewing has been practised in the Southern region for a long time. Betel nut is grown locally in the rural villages of Central Province and the nearby Gulf province which is the only other Southern region province connected to Port Moresby by road. One of the sites for this study was the Kerema block of which its inhabitants are from Gulf province, the only betel nut growing province connected to Port Moresby by road. Those from the Highlands region were statistically significantly less likely to chew betel nut. This is because betel nut trees do not grow in higher altitudes such as that of the highlands of PNG.

This habit is a recent introduction to those from the highlands region by those from the coastal regions.

As age increased, the prevalence of betel nut chewing decreased therefore the habit is more common in those aged <50 years. This may be due to dental reasons. Chewing betel nut requires fairly good sets of strong teeth as some of the nuts chewed may be hard in texture. This study found that betel nut chewing was significantly associated with the number of intact teeth a chewer has with those missing some teeth having a less likelihood of chewing betel nut. The finding of this study that the prevalence of betel nut chewing decreased with increasing age or that younger people are more likely to chew betel nut is consistent with findings in other PICs[9, 12, 63] and elsewhere [65, 66, 69, 70, 72] where the habit is practised. In countries other than those in the Pacific islands, the current finding that betel nut chewing is more common among younger people are different to what has been reported in Sri Lanka[68] and rural Bangladesh[67] . These studies reported that the prevalence of betel nut increased with increasing age and the highest was among those aged >65 and > 50 years, respectively. The Sri Lankan study however included only male participants.

5.4.4.3 Lifestyle factors associated with betel nut chewing

Alcohol consumption, smoking, and vegetable and fruit consumption were associated with betel nut chewing. Of these, alcohol consumption and smoking were independently associated with betel nut chewing after adjusting for other factors. Alcohol consumption and smoking are also social habits like betel nut chewing. In PNG, betel nut chewing is usually followed by smoking or vice versa. The finding that smoking is associated with betel nut chewing has been reported elsewhere [65, 67, 69, 70]. Many alcohol consumers in PNG usually consume their alcohol with friends or relatives in a group at any one time when alcohol is consumed. During these times of consuming alcohol, betel nut and tobacco products are also shared and used. It is therefore not surprising that the three habits were associated with each other. Other studies have also reported the association of betel nut chewing with alcohol. [17, 65, 68-70]

The finding that betel nut chewers are not eating the recommended amounts of fruit and vegetable is of concern. Instead of eating fruit for example, betel nut chewers are probably chewing betel nut. The habit of chewing betel nut requires money for most and money is probably spent on betel nut instead of a healthy meal consisting of vegetables and instead of snacking on fruits, betel nut is chewed. The observation that betel nut chewers are eating less vegetable has been reported elsewhere.[65]

5.4.4.4 Physical factors associated with betel nut chewing

This study indicated that betel nut was negatively associated with BMI and waist circumference. Non-betel nut chewers were more likely to be overweight or obese and have an abnormally high waist circumference compared to those who did. Those who quit the habit were least likely to be obese but the sample number for this subgroup was small. The finding that betel nut chewers were less overweight or less obese is different to that reported by other studies among Taiwanese. [17, 65, 69-73] Heck et al[67] however did not find any association of betel nut chewing with BMI or overweight.

The finding that betel nut chewing has a beneficial effect on BMI and waist circumference is contradictory to a study by Iqbal et al[74] investigating the effects of betel nut on cardiovascular risk factors in a rat model. That study reported that betel nut ingestion did not affect mean body weights. The finding that betel nut chewing may have a beneficial effect on BMI and waist circumference may be partly supported by two animal studies which demonstrated cholesterol-lowering effects of betel nut extracts. [75, 76] The mechanism by which betel nut is thought to lower cholesterol is by decreasing cholesterol absorption through inhibition of pancreatic cholesterol esterase [75, 76] and intestinal acyl-CoA cholesterol acyltransferase [76].

Chewing betel nut was associated with lower SBP and DBP. Those who never chewed betel nut were more likely to have an abnormally high SBP and DBP. This finding is different to that reported by Heck et al[67] who found that betel nut chewing increased both SBP and DBP or high BP.[17] In the study by Yen et al[65] betel nut chewing was associated with high BP and in another study it was not.[73] Tseng[73] reports that the prevalence of hypertension was significantly lower in the chewers

compared to non-chewers who were males but in women the prevalence of hypertension remained significantly higher in chewers than in non-chewers. However the differences were small for both SBP and DBP in the chewing groups in both genders. The results of these studies indicate inconsistencies on the association of betel nut chewing with blood pressure. Inokuchi et al[77] reported an antihypertensive effect of a tannin fraction from betel nut in rats. Oral administration of the betel nut fraction produced a dose-related antihypertensive effect in spontaneous hypertensive rats; an effect which was comparable to captopril at doses of 30 and 100 mg/kg. In the same study[77], intravenous treatment produced a dose-related inhibition of the pressor responses to angiotensin I and II. Differences in effects of betel nut chewing on BP with regards to angiotensin effects may be partly explained by polymorphisms in the angiotensin converting enzyme gene. Chung et al[78] reported that betel nut chewers with the DD genotype had significantly lower BP, pulse pressure and prevalence of hypertension compared to those with II or ID genotypes. It is well known that genes interact with the environment and therefore environmental factors may be contributing to differences in the association of betel nut with BP. Another study [79] which supports the antihypertensive effect of betel nut shown in this study is one conducted by Gilani et al. That study reported beneficial activities of betel nut on the cardiovascular system. The benefits reported by the study were hypotensive, cardiosuppressant, endothelium-dependent vasodilator and antiplatelet activities. Gilani et al [79] demonstrated a dose-dependent atropine-sensitive fall in the arterial blood pressure of normotensive rats under anaesthesia. That study further reported that only arecoline showed atropine-sensitive cardio-suppressant and vasodilator effects while catechin exhibited atropine-insensitive vasodilator and antiplatelet effects. This indicates that different chemical constituents of betel nut have different effects on the cardiovascular system. A study investigating the effects of PBL on blood pressure further supports the antihypertensive effect of betel nut chewing. [80] Gilani et al[80] from that study suggest that PBL reduces blood pressure by blocking calcium channels. Lin et al, in a study investigating the haemodynamic effects of betel nut showed that betel nut reduced DBP; a finding that is consistent with the present study.[81]

Physical activity was strongly associated with betel nut chewing. Betel nut chewers were more likely to do physical activity compared to their counterparts. This finding

is different to that from a Taiwanese study[65] which reported that less physical activity was reported among betel nut chewers.

5.4.5 Glycaemic control

The study reports a 17.8% prevalence of fasting hyperglycaemia and a 4.9% prevalence of post prandial hyperglycaemia. The prevalence rates for IFG and IGT were 22.1% and 14.4% respectively indicating a high prevalence of pre-diabetes in this study cohort. The study by Benjamin[3] reported a slightly lower prevalence rate (13.0%) of fasting hyperglycaemia. That study used a higher FCBG cut off of 7.0mmol/L compared to the 6.1mmol/L used by the present study. The slightly lower prevalence therefore may have been due to the higher FCBG used by Benjamin.

5.4.6 Factors associated with fasting and post prandial hyperglycaemia

5.4.6.1 Influence of demographic factors on glycaemic control

According to FCBG and OGT, the only statistically significant demographic factor associated with both fasting and postprandial hyperglycaemia, respectively, was age; those aged 60 years and older were more likely to have hyperglycaemia or T2DM compared to those who were younger. After adjusting for other confounders, age continued to be associated with fasting hyperglycaemia. This is consistent with findings from studies in Fiji.[82, 83]. It is well known that the risk of T2DM increases with increasing age. This may be due to declining beta cell function either as a result of ageing or longer exposure to risk factors of T2DM.[84]

Those aged 50-59 years of age were more likely to have IFG and IGT. The finding that this age group (50-59 years) is more likely to have IFG and IGT may partly explain why those aged 60 years or older in this study were more likely to have T2DM. IFG and IGT eventually progress to T2DM. DeFronzo et al[84] reported that the mean age of participants with IGT was 53.3±0.5 years which is consistent with the present study. That study[84] investigated the determinants of glucose tolerance in a study cohort with IGT and demonstrated that the main determinant of progression of normal glucose tolerance to IGT was progressive beta cell failure.

5.4.6.2 Influence of lifestyle factors on glycaemic control

Those consuming vegetables for 5 days or less in a typical week were more likely to have IFG and T2DM. As the number of days during which vegetables were consumed was reduced, the prevalence of IFG and T2DM increased. Consuming ≥2 fruit servings appeared to be associated with IFG but this did not reach statistical significance. Studies investigating the beneficial effects of fruit and vegetable intake on blood glucose control have reported conflicting results which may be largely due to the methodologies used and may also suggest that vegetable and fruit consumption is not a stronger predictor of diabetes risk. Cooper et al[85] in their adjusted analyses reported that quantity of vegetable intake was inversely associated with T2DM; an association which was not observed for fruit intake. This is consistent with findings by Villegas et al [86] in a cohort of Chinese women. Other studies [86-89] have also reported the beneficial influence of vegetable consumption on glycaemic control. The present study found that the number of days vegetables were consumed in a week was inversely associated with T2DM which is consistent with studies reporting a beneficial association of vegetable intake on glycaemic control. A meta-analysis[90] reported that the amount of green leafy vegetables in an individual's diet could help reduce the risk of T2DM but did not find any significant association of fruits, vegetables or a combination of both with the incidence of T2DM. Other studies [87, 88, 91] have found a beneficial association of fruit consumption either on its own or in combination with vegetables on glycaemic control. Cooper et al[85] found that a greater variety of fruit rather than the quantity was inversely associated with incident T2DM after adjusting for other factors.

The only type of physical activity that was significantly associated with fasting hyperglycaemia was work-related VIA. Unexpectedly, those who were involved in work-related VIA were likely to have fasting hyperglycaemia. This may be due to compensatory increases in food intake which may be partly due to cultural reasons (personal knowledge) as previously discussed in Chapter IV (Section 4.4.6.2). Performing VISFRA was not associated with glycaemic control but the amount of VISFRA per week was associated with glycaemic control. Those who did VISFRA for ≥75 minutes per week were appeared to be more likely to have hyperglycaemia. The association however was of borderline significance.

In a genome-wide association study, Li et al[92] demonstrated that genetic polymorphism in rs12104705 of a glucagon gene (GCG) may interact with physical activity to modify the risk of T2DM. The study suggests that moderate and high physical activity with the C-C genotype may be associated with decreased risk of T2DM compared with low physical activity with the genotype. The GCG gene encodes glucagon proteins GLP-1, GLP-2 and oxyntomodulin which are essential for energy metabolism. [92] Genetics may therefore play a role in differences observed in association of lifestyle factors such as physical activity with development of T2DM.

5.4.6.3 Influence of physical measurements on glycaemic control

Those with a BMI ≥25 kg/m^2 and those with a waist circumference above normal were more likely to have FCBG and post prandial hyperglycaemia. This finding is consistent with studies elsewhere.[82, 93] An earlier study[82] in the same ethnic group of Fijian Melanesians showed BMI to be one of the most important predictors of T2DM. A 16-year follow-up of female nurses in England found that the most important risk factor for T2DM was BMI. [94] The study showed that as the BMI increased from 30.0-34.9 kg/m^2 to ≥35 kg/m^2, the relative risk of diabetes increased from 20.1% to 38.8% respectively. T2DM in those who are not obese may be contributed to by predominantly β-cell dysfunction rather than insulin resistance.[95] High BP was not associated with fasting hyperglycaemia but those who had a higher than normal SBP were significantly more likely to have post prandial hyperglycaemia. High SBP appeared to have an independent association with OGT which was of borderline significance. Studies have shown that OGT is a strong predictor of cardiovascular risk.[96-98] Tomiyami et al[99] demonstrated that abnormal glucose tolerance determined by using OGT may have a direct pathological association with endothelial dysfunction. That study included participants with borderline hypertension. Endothelial dysfunction is associated with cardiovascular risk. [100] The present study also observed that obesity was associated with high SBP and postprandial hyperglycaemia which therefore increases the risk of high SBP in the present study cohort.

5.4.6.4 The influence of betel nut chewing on glycaemic control

The present study did not find any association between betel nut chewing and fasting hyperglycaemia but found a beneficial influence on post prandial hyperglycaemia. Further, betel nut chewing was not associated with IFG. This finding is different to an earlier PNG study[3] where fasting hyperglycaemia was more prevalent in betel nut chewers. That study however included a small sample of betel nut chewers.

Using fasting blood glucose of ≥ 6.1 mmol/L to indicate hyperglycaemia, studies in Taiwan among male betel nut chewers have reported an association between betel nut chewing and hyperglycaemia.[65, 66] These studies reported betel nut chewers were more likely to have hyperglycaemia. Tung et al[66] further reported a dose-dependent association of betel nut chewing with T2DM.

Tseng[73] classified chewers as ever or never chewers and reported that the incidence rate for newly diagnosed T2DM was higher in ever chewers than never chewers and the incidence rates increased with increasing age peaking at age 60-69 years. Further the incidence rate in never chewers continued to increase in those aged ≥70 years compared to ever chewers which peaked at age 60-69 years. It is most likely that increasing prevalence of incident T2DM may have been due to increasing age. The present study found that age was the most important demographic factor influencing both fasting and post prandial glycaemic control with risk increasing with increasing age. The study by Tseng did not adjust for other risk factors for T2DM such as age; the only confounding factor which was examined using Chi-square statistic was obesity.

Those who quit and those who never chewed were more likely to have hyperglycaemia or T2DM suggesting that betel nut chewing appears to have a beneficial effect on blood glucose levels. Participants who chewed betel nut only were more likely to have hyperglycaemia or T2DM compared to those who chewed betel nut with PBI and lime or with PBI.

The finding that betel nut chewing has a beneficial influence on blood glucose is in contrast to other studies which have found that betel nut or arecoline causes

hyperglycaemia. [101-103]. Iqbal et al[74] reported no effect on glucose in a normoglycaemic rat model.

Dasgupta et al[104] demonstrated an acute hyperglycaemic effect of arecoline but a hypoglycaemic effect after chronic administration intraperitoneally in mice. This effect has been attributed to the effect of betel nut on adrenal function. Chempakan[105] in a small sample of humans also reported a hypoglycaemic effect of arecoline after subcutaneous administration. Other studies have also reported hypoglycaemic effects of not only arecoline but also some unidentified chemical constituents in PBL. [106, 107]

5.5 Conclusions

The prevalence of betel nut chewing amongst the population in this study is higher than reported elsewhere. The present study found that betel nut chewing is not associated with hyperglycaemia. By contrast to other Asian studies, betel nut chewers had better glycaemic control compared to those who were not current chewers. This finding was related to postprandial glucose but not fasting glucose. This beneficial association however was not independent. Further, betel nut chewing had an independent beneficial influence on important risk factors for T2DM; these risk factors were BMI, waist circumference, SBP and DBP. In terms of lifestyle risk factors for T2DM, betel nut had an independent positive influence on physical activity. The beneficial and non-beneficial association of betel nut chewing with smoking, and vegetable and fruit intake, respectively is however a concern. Although smoking had a beneficial influence on BMI, it is a known health risk.

In conclusion, the positive influence of betel nut chewing on post prandial hyperglycaemia is therefore most probably through its beneficial influence on these other known risk factors. Betel nut chewing in a population with very high prevalence of the habit therefore does not directly influence glycaemic control but exerts its influence through a beneficial effect on adiposity.

5.6 References

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Chapter VI: Comparisons between the T2DM and the non-T2DM cohort

6.1 Objectives

The main objective of this part of the research was to compare and identify any significant differences between the type 2 diabetes mellitus (T2DM) and non-T2DM cohorts in terms of demographics, lifestyle, betel nut chewing, physical measurements and medical characteristics.

6.2 Methodology

Records of the diabetes survey data (N = 385) were compared against the records of those STEPS survey respondents who identified themselves as not having T2DM (N = 922). Univariate comparisons of the key features outlined above were performed using the Chi-square test or t-test, as appropriate. In addition, a multivariate logistic regression model was used to identify variables independently associated with T2DM. Following convention, a p-value of <0.05 was taken to indicate a statistically significant association in all tests.

6.3 Results

6.3.1 Participant characteristics

Participant characteristics that were compared included demographic, lifestyle, physical and medical factors.

6.3.2 Demographic characteristics

There were statistically significant differences in demographic characteristics between the two study cohorts (Table 6.1). The non-T2DM cohort had more participants younger than 50 years while, in the T2DM cohort, the greatest proportion of participants was in the age group 50-59 years. Those with T2DM were more likely to have completed tertiary education compared to those without T2DM. In addition, those who had T2DM were more likely to be retired, compared to those without T2DM. Both cohorts had very similar unpaid/unemployment rates. The

study involving non-T2DM participants included only those in selected urban suburbs and peri-urban areas, while the other study involved T2DM patients from any area of residence. However, in both studies, the highest number of participants resided in urban areas. When comparing the numbers of participants from the two studies who resided in peri-urban areas, the figure was higher for the non-T2DM cohort. There were more highlanders in the non-T2DM cohort.

Table 6.1 Comparison of demographic characteristics between the non-diabetes and diabetes study cohorts

Variable	Study cohort		p-value[#]
	Non-T2DM (N=922) n (%)	T2DM (N=385) n (%)	
Gender			0.017
Female	511 (55.4)	241 (62.6)	
Male	411 (44.6)	144 (37.4)	
Age category (years)			<0.001
<50	779 (84.5)	113 (31.0)	
50 – 59	108 (11.7)	145 (39.7)	
≥60	35 (3.8)	107 (29.3)	
Level of education			<0.001
Did not complete basic education	188 (20.5)	88 (22.9)	
Primary basic education	347 (37.9)	111 (28.9)	
Secondary/vocational	355 (38.8)	115 (29.9)	
Tertiary	26 (2.8)	70 (18.2)	
Employment status			<0.001
Paid	250 (27.5)	81 (21.0)	
Unpaid/Unemployed	533 (58.7)	195 (50.6)	
Retired	11 (1.2)	70 (18.2)	
Self-employed	114 (12.6)	39 (10.1)	
Area of residence			<0.001
Urban	622 (67.5)	212 (55.2)	
Peri-urban	300 (32.5)	77 (20.1)	
Rural	0 (0.0)	80 (20.8)	
Outside Province	0 (0.0)	15 (3.9)	
Region of origin			<0.001
Southern	368 (40.0)	294 (76.4)	
New Guinea Islands	86 (9.4)	36 (9.4)	
Momase	117 (12.7)	26 (6.8)	
Highlands	348 (37.9)	29 (7.5)	

[#]The p-values were obtained from the Chi-square statistics and assess the strengths of associations

6.3.3 Lifestyle characteristics

Lifestyle factors included were alcohol consumption, tobacco smoking, fruit and vegetable consumption, and physical activity.

There were statistically significant differences observed between the cohorts with T2DM and without T2DM cohorts (Table 6.2). These differences were seen in alcohol consumption, smoking and the number of days that participants had consumed fruits in a typical week. However, there were no differences observed in the frequency and number of servings of vegetables consumed.

For the study cohort without T2DM, questions on alcohol consumption requested information in relation to the preceding 12 months but, for the cohort with T2DM, information was requested only for the preceding three months. However, the two studies requested information on whether or not participants had consumed alcohol in the preceding 30 days, so this variable was the one used for comparisons. The prevalence of alcohol consumption within the preceding 30 days was higher in those without T2DM compared to those with T2DM.

Those without T2DM were more likely to smoke compared to those who had T2DM. However, those with T2DM were more likely to have quit smoking compared to those without T2DM.

Table 6.2 Comparison of differences in lifestyle characteristics between the non-T2DM and T2DM study cohorts

Variable	Study cohort		p-value[#]
	Non-T2DM (N=922) n (%)	T2DM (N=385) n (%)	
Alcohol consumption within the past 30 days			<0.001
No	688 (74.6)	354 (91.9)	
Yes	234 (25.4)	31 (8.1)	
Smoking status			0.001
Current	350 (38.2)	24 (6.2)	
Never	472 (51.5)	272 (70.6)	
Quit	94 (10.3)	89 (23.1)	
Smoking history			0.001
Ever	444 (48.6)	113 (29.4)	
Never	472 (51.5)	272 (70.6)	
Vegetable consumption (servings/day)			0.955
<3	848 (92.8)	355 (92.7)	
≥3	66 (7.2)	28 (7.3)	
Vegetable consumption (days/week)			0.071
0 - 5	475 (52.0)	220 (57.4)	
6 - 7	439 (48.0)	163 (42.6)	
Fruit consumption (servings/day)			0.585
<2	614 (69.2)	271 (70.8)	
≥2	273 (30.8)	112 (29.2)	
Fruit consumption (days/week)			0.012
0 - 1	375 (41.0)	186 (48.6)	
2 - 7	540 (59.0)	197 (51.4)	

[#]The p-values were obtained from the Chi-square statistics and assess the strengths of associations

The cohort without T2DM was more physically active than those with T2DM in relation to work and recreational activities with the exception of walking to get to and from places (Table 6.3). In terms of the total amount of physical activity per week, those with T2DM were less likely to undertake sufficient physical activity per week.

When comparing the differences in the number of minutes spent on physical activities between the two cohorts, there was no statistically significant difference in all but work-related VIA. The non-T2DM cohort was more likely to undertake work-related VIA for ≥75 minutes per week (Table 6.3).

Table 6.3 Comparison of physical activity characteristics between the non-T2DM and T2DM study cohorts

Variable	Study cohort		p-value[#]
	Non-T2DM (N=922) n (%)	T2DM (N=385) n (%)	
Amount of physical activity			<0.001
Sufficient	634 (72.6)	234 (60.8)	
Insufficient	239 (27.4)	151 (39.2)	
Work-related VIA for at least 10 minutes			<0.001
No	428 (46.9)	332 (86.2)	
Yes	484 (53.1)	53 (13.8)	
Minutes of work-related VIA/week			0.036
<75	89 (20.1)	17 (32.7)	
≥75	354 (79.9)	35 (67.3)	
Performs VISFRA for at least 10 minutes			<0.001
No	597 (65.4)	351 (91.2)	
Yes	316 (34.6)	34 (8.8)	
Minutes of VISFRA/week			0.320
<75	102 (32.7)	14 (41.2)	
≥75	210 (67.3)	20 (58.8)	
Work-related MIA for at least 10 minutes			<0.001
No	359 (39.6)	225 (58.4)	
Yes	548 (60.4)	160 (41.6)	
Minutes of work-related MIA/week			0.601
<150	191 (37.7)	56 (35.4)	
≥150	315 (62.3)	102 (64.6)	
Performs MISFRA for at least 10 minutes			<0.001
No	626 (68.4)	317 (82.3)	
Yes	289 (31.6)	68 (17.7)	
Minutes of MISFRA/week			0.120
<150	183 (65.1)	51 (75.0)	
≥150	98 (34.9)	17 (25.0)	
Walks to get to and from places			0.349
No	367 (49.9)	133 (46.7)	
Yes	368 (50.1)	152 (53.3)	
Minutes of walking/week			0.349
<150	367 (49.9)	133 (46.7)	
≥150	368 (50.1)	152 (53.3)	

[#]The p-values were obtained from the Chi-square statistics and assess the strengths of associations; VIA = vigorous-intensity activity; VISFRA = vigorous-intensity sports, fitness and recreational activity; MIA = moderate-intensity activity; MISFRA = moderate-intensity sports, fitness and recreational activity.

6.3.4 Medical and physical characteristics

The medical characteristics compared included physical measurements, such as body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), waist circumference and fasting capillary blood glucose (FCBG). Regarding biochemical measurements, the study involving those with T2DM did not include measurements such as the two-hour oral glucose tolerance test and percentage body fat, while the study involving those without T2DM did not include glycated haemoglobin (HbA1c) measurements. Comparisons between the two study cohorts, therefore, only included physical measurements and FCBG. The only physical measurement which was not included in the comparisons was hip circumference. Hip circumference measurements were included in both studies but, because of discrepancies in measurement of this variable in those with T2DM, this variable was not used in comparisons between the two different cohorts.

As shown in Table 6.4, the only statistically significant differences in medical characteristics between the two cohorts were FCBG, SBP and DBP. Those with T2DM were more likely to have high BP, compared to those without T2DM. The cohort with T2DM was also more likely to have FCBG ≥6.1 mmol compared to those without the disease.

Table 6.4 Comparison of medical characteristics between the non-T2DM and T2DM study cohorts.

Variable	Study cohort		p-value[#]
	Non-T2DM (N=922) n (%)	T2DM (N=385) n (%)	
BMI category			0.582
Underweight	18 (2.0)	12 (3.3)	
Normal weight	291 (31.9)	117 (31.8)	
Overweight	356 (39.0)	143 (38.9)	
Obese	247 (27.1)	96 (26.1)	
BMI (kg/m^2)			0.232
<25	309 (33.9)	104 (30.3)	
≥25	603 (66.1)	239 (69.7)	
Waist circumference			0.069
Normal	595 (65.1)	270 (70.3)	
Above normal	319 (34.9)	114 (29.7)	
SBP (mmHg)			<0.001
≤130	657 (71.8)	93 (24.5)	
>130	258 (28.2)	287 (75.5)	
DBP (mmHg)			<0.001
≤80	656 (71.7)	174 (45.8)	
>80	259 (28.3)	206 (54.2)	
FCBG (mmol/L)			<0.001
<6.1	754 (82.1)	36 (9.5)	
≥6.1	164 (17.9)	344 (90.5)	

[#]The p-values were obtained from the Chi-square statistics and assess the strengths of associations; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; FCBG = fasting capillary blood glucose; T2DM = type 2 diabetes mellitus; Normal waist circumference is ≤102cm (male) and ≤88cm (female).

6.3.5 Betel nut chewing

Results indicated that there were statistically significant differences in betel nut chewing habits among those with T2DM and those without T2DM. The non-T2DM cohort was more likely to chew betel nut compared to those with T2DM. For the subgroup of betel nut chewers, this cohort was more likely to chew >5 betel nuts per day and they chewed betel nut with or without *Piper betle* inflorescence (PBI) or lime. Those with T2DM were more likely to have quit betel nut chewing but those that were still chewing were more likely to chew betel nut with PBI and lime (all 3 components) compared to betel nut chewers without T2DM.

Table 6.5 Comparison of betel nut chewing characteristics between the two different study cohorts

Variable	Study cohort		p-value[#]
	Non-T2DM N=922 n (%)	T2DM N=922 n (%)	
Betel nut chewer			<0.001
No	171 (18.7)	173 (44.9)	
Yes	745 (81.3)	212 (55.1)	
Betel nut chewer status			<0.001
Current	745 (81.4)	212 (55.1)	
Quit	30 (3.3)	77 (20.0)	
Never	140 (15.3)	96 (24.9)	
Betel nut exposure			<0.001
Never	140 (15.5)	96 (26.6)	
Quit	30 (3.3)	77 (21.3)	
≤5 nuts/day	403 (44.7)	118 (32.7)	
>5 nuts/day	329 (36.5)	70 (19.4)	
Betel nut chew components*			<0.001
Betel nut, PBI and lime	469 (63.0)	177 (83.9)	
Betel nut ±PBI or lime	254 (34.1)	12 (5.7)	
Betel nut only	21 (2.8)	22 (10.2)	

[#]The p-values were obtained from the Chi-square statistics and assess the strengths of associations; *Includes betel nut chewers only; PBI = *Piper betel* inflorescence; T2DM = type 2 diabetes mellitus.

6.3.6 Factors independently associated with T2DM

Multivariate analysis, with the T2DM cohort being the dependent variable, indicated that the factors independently associated with this cohort were age, smoking, betel nut chew components, work-related VIA, SBP and FCBG (Table 6.6)

The non-T2DM cohort was more likely to be younger, while those with T2DM were more likely to be older than 50 years of age. Those who had never smoked or who had quit the habit were more likely to be those with T2DM compared to those who were current smokers.

Those with T2DM were more likely to chew all three components of the betel nut chew. In terms of work-related VIA, those who did not undertake such activities were more likely to be those with T2DM, compared to those who did. Those who had SBP >130 mmHg or FCBG ≥6.1 mmol/L were more likely to be those with T2DM.

Table 6.6 Multivariate analysis of factors independently associated with T2DM

Variable	Adjusted OR	95% CI	p-value
Age category (years)			<0.001
<50	1 (reference)		
50 - 59	11.97	5.34 – 26.84	<0.001
≥60	11.06	3.91 – 31.26	<0.001
Smoke history			0.001
Current	1 (reference)		
Never	2.65	1.24 – 5.66	0.012
Quit	5.95	2.24 – 15.80	<0.001
Betel nut chew components*			<0.001
Betel nut, PBI and lime	1 (reference)		
Betel nut ±PBI or lime	0.060	0.02 – 0.16	<0.001
Betel nut only	0.88	0.28 – 2.76	0.829
Work-related VIA			<0.001
No	12.56	5.96 – 26.50	
Yes	1 (reference)		
SBP (mmHg)			<0.001
≤130	0.12	0.06 – 0.23	
>130	1 (reference)		
FCBG (mmol/L)			<0.001
<6.1	1 (reference)		
≥6.1	107.72	45.67 – 254.04	

The dependent variable was the T2DM cohort; PBI = *Piper betle* inflorescence; VIA = vigorous-intensity activity; SBP = systolic blood pressure; FCBG = fasting capillary blood glucose; T2DM = type 2 diabetes mellitus.

6.4 Discussion

6.4.1 Demographic differences

There were significant demographic differences between the two cohorts. The T2DM cohort was older, had higher level of education and had the highest proportion in the retired category. The highest proportion of those with T2DM was

from the Southern region while in the non-T2DM cohort, there was an equal proportion from both the Highlands and Southern regions. There were no participants from the rural areas in the non-T2DM cohort and a higher proportion than the T2DM cohort resided in peri-urban areas.

The cohort with T2DM was older because of the fact that T2DM tends to affect those who are 40 years old and older.[1] The risk of T2DM increases with age as has been observed in population based studies.[2, 3] This was also observed among the non-T2DM cohort in the current study which showed that those 60 years and older were more likely to have a FCBG>6.0 mmol/L compared to their younger counterparts. In the same cohort, glucose intolerance (oral glucose tolerance test >11.0mmol/L) increased with age. These results provide evidence of increasing blood glucose levels with age from a PNG population. Furthermore, the results provide evidence that T2DM tends to affect those who are older than 40 years of age. The finding that the T2DM cohort had higher level of education than their counterparts is different to what has been reported in other population groups.[4-6] It has been suggested that those with high educational levels may be receptive to messages of disease prevention, have a greater ability to change their health behaviour and have better use of health care systems.[7-9] It is not certain why the T2DM cohort had a higher level of education than their counterparts in the present study, however one could postulate better education leads to better employment and income which may have adverse effects on lifestyle.

The possible reasons for the highest proportion of the T2DM being from the Southern region have previously been discussed in Chapters IV and V. As previously reported in Chapter V, 70% of the non-T2DM cohort was younger than 40 years old. This may have led to the observation that the T2DM cohort had the highest proportion of participants in the retired category compared to the non-T2DM cohort.

6.4.2 Lifestyle characteristics

The prevalence rates of smoking and alcohol consumption were higher in the non-T2DM cohort than in the T2DM. As discussed in Chapter IV this may be because those with T2DM are quitting these habits as part of their diabetes management.

However, from the study, it is not known whether or not T2DM participants quit smoking after being diagnosed with the disease as further analysis was not done to relate the time the participant quit smoking to the date of diagnosis with T2DM. To a certain extent, the finding that those with T2DM are quitting smoking as part of their disease management may be supported by the observation that the proportion of T2DM participants who quit smoking is higher than in the non-T2DM cohort. The finding that prevalence of current smokers is lower in those with T2DM compared to those without the disease has been reported elsewhere.[10]

The only dietary variable with a significant difference between the two cohorts was the number of fruit-eating days per week. The T2DM cohort had a lower frequency of fruit consumption than their counterparts. The most obvious reason for this may be the fear of fruits increasing blood glucose. It has been found in other countries that the associations with the risk of T2DM differs significantly among individual fruits and that the risk is greater with consumption of fruit juice rather than whole fruits.[11, 12] To date, there are no locally written guidelines on fruit consumption for those with T2DM in PNG but international guidelines form the basis of dietary education for those who are affected (Personal communication).

A significant difference in performance of physical activity was observed between the two cohorts. The non-T2DM cohort was more physically active than those with T2DM in relation to the different physical activities included in this study, with the exception of walking to get to and from places. The observation that there was no difference between the two cohorts in terms of walking for travel, has been discussed in Chapters IV and V. T2DM patients are usually more inactive compared to those without the disease and this has been discussed in Chapter IV. The observation that the T2DM cohort had a greater number of retirees and those 40 years and older compared to the non-T2DM cohort may have contributed to the significant differences in physical activity. It has been reported that overall physical activity appears to decline with retirement.[12, 13]

6.4.3 Physical and biochemical measurements

High BP often co-exists with T2DM, and persistent hyperglycaemia is the underlying issue in this cohort so as expected, the T2DM cohort had a high prevalence of high

BP and high FCBG. Less than 10% of the T2DM cohort achieved optimal fasting glycaemic control.

The prevalence of obesity (both central and general) was similar among the T2DM and non-T2DM cohort. The increase in T2DM may therefore be related to the increasing prevalence of obesity in PNG. In PNG and many PICs where "being fat is good", education is important to shift this culturally accepted mindset.[14] Papua New Guineans without T2DM have a high risk of developing the disease not only because of genetics but because of factors such as obesity, increasing westernisation and urbanisation, and lifestyle behaviours. Obesity also has been linked to genetics. [15] Studies have reported the association between the Pro12Ala substitution and T2DM and/or obesity. [16-18] The polymorphism is said to have a protective effect against obesity and T2DM. In a PNG study, Sakaue et al. [19] investigated the Pro12Ala substitution in PPARγ2 gene among 252 Balopa islanders and their analyses revealed that the substitution was not found in any of the groups (non-obese, overweight and obese). . Sakaue et al.[19] in that PNG study further examined Trp64Arg polymorphism in β3-AR gene and found that the polymorphism was significantly higher in overweight and obese than in non-obese participants. These findings indicate a high risk of obesity among Papua New Guineans as Pro12Ala polymorphism in PPARγ2 is said to have a protective effect against obesity and T2DM while the Trp64Arg polymorphism increases the risk. Genetics is therefore possibly contributing to the increasing prevalence of obesity and T2DM in PNG. The sample population however may not be reflective of PNG as a whole as nutritional factors have been reported to influence expression of PPARγ2 in human adipocytes [20, 21] and also because the sample of participants in the study by Sakaue et al was recruited from one particular island.

6.4.4 Betel nut chewing

Like other behavioural factors such as smoking and alcohol consumption, the prevalence of betel nut chewing was lower in the T2DM cohort compared to the non-T2DM cohort. Again, like smoking, those with T2DM were more likely to quit betel nut chewing compared to their counterparts. As previously discussed in Chapter IV, those with T2DM may be quitting betel nut chewing and smoking as part of their

diabetes management. The study did not investigate reasons for quitting betel nut and did not perform further analysis to correlate the age participants quit betel nut chewing with age at diabetes diagnosis. The diabetes clinic does not advise those with T2DM to quit betel nut chewing. Although the data collection involving the T2DM cohort did not collect data on oral health and dentures, results related to oral health including the non-T2DM cohort indicated that those with some teeth missing were less likely to chew betel nut compared to those with all of their teeth intact. To some extent, this may have contributed to the lower numbers of the T2DM cohort chewing betel nut compared to the non-T2DM cohort because those in the former cohort were older than the latter.

6.5 Conclusions

In conclusion, there were significant differences between the two cohorts, in terms of demographic characteristics, lifestyle behaviour and biochemical and physical measurements. However, there were some similarities between the two study cohorts in terms of prevalence of obesity, vegetable consumption and walking for travel. Some of these differences such as reduced physical activity and physical measurements such as increased prevalence of high BP in the T2DM cohort are a reflection of the impact of T2DM on an individual. Quitting habits such as smoking and betel nut chewing and a lower prevalence of alcohol consumption in the T2DM cohort is an indication that these habits are less common in those with the disease. Although low dose betel nut chewing has been observed to be associated with better glycaemic control in both study cohorts, chronic use can be expensive especially in urban areas and therefore patients may spend much needed funds on the habit rather than on costs associated with diabetes management.

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Chapter VII: Acute glycaemic effect of betel nut chewing in T2DM

7.1 Objectives

The main objectives of this part of the research, involving a cohort of participants with type 2 diabetes mellitus (T2DM), were to:

1 Document their betel nut chewing characteristics
2 Determine the immediate effect of betel nut chewing on blood glucose by measuring capillary blood glucose (CBG) just prior to, and approximately 5-10 minutes after, each chewing occasion.
3 Determine any differences in hourly CBG between the betel nut chewing and non-chewing days

7.2 Methodology

7.2.1 Study setting

This study (Phase 2) was conducted in the pharmacy practice laboratory at the School of Medicine and Health Sciences, University of PNG.

7.2.2 Study design

This study was a single-subject design where each participant served as their own control.

7.2.3 Study participants

Participants included in this study were betel nut chewers recruited from the T2DM cohort. The study protocol was explained verbally for those who requested further information. Participants who understood the study protocol and gave their consent to participate were included. The consent form was signed by both the participant and the investigator. The recruitment process is shown in Figure 7.1 below.

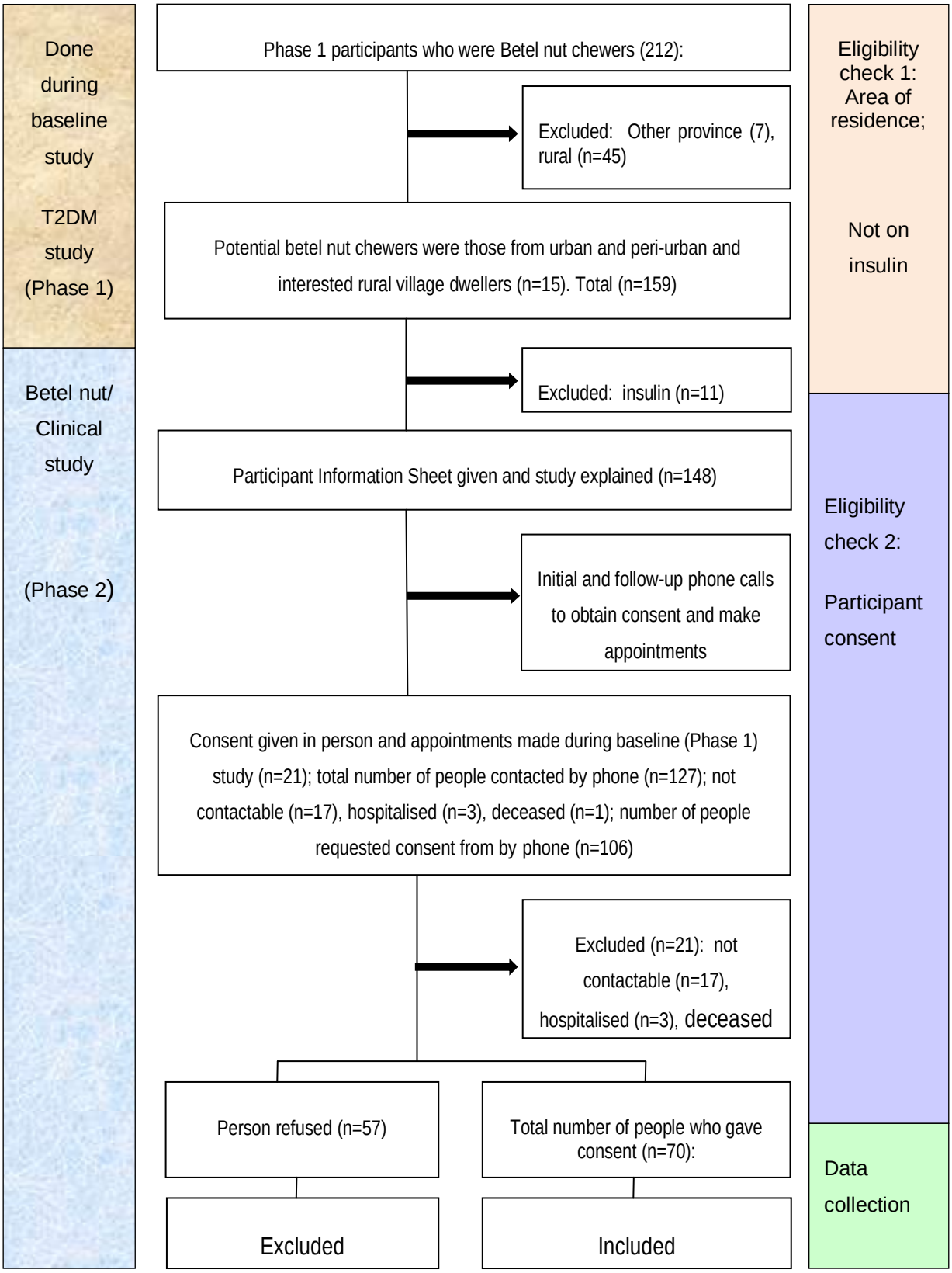

Figure 7.1 Recruitment process

7.2.4 Data collection

Data for this study were collected over 2 days. During Day 1, participants chewed betel nut according to their individual chewing habits and during Day 2, participants abstained from betel nut chewing.

During the study days, different activities such as knitting, watching movies and peer education sessions were organised in the study room. Each day started with a fasting blood glucose measurement followed by a reminder of what was happening during the study period. Participants were under observation by the investigator throughout the study period from 8.00am to 3.30pm.

7.2.4.1 Study tools

An instrument was developed to collect data for this study (Appendix 11). The design of the questionnaire was initially constructed based on the objectives of the study and review of relevant literature. Data collected included fasting CBG and time of measurement, names of medications and time taken, hourly CBG and full details of betel nut chewing activity. This included the time of starting to chew and duration of chewing, as well as details of the chewing habit including: number of nuts chewed, whether they were chewed with other constituents [lime, *Piper betle* leaf (PBL) or inflorescence (PBI)], whether the betel juice was swallowed or spat out, and whether the betel nut was ultimately swallowed or spat out and the time at which the chewing was finished. This information was recorded for each occasion of chewing during the 2 days of the study. CBG was measured just prior to, and approximately 5-10 minutes after, each chewing occasion. The time of the most recent chewing occasion prior to the start of data collection was also recorded.

CBG was measured using a hand-held Omnitest® Plus (B.Braun, Melsungen, Germany) capillary blood glucose meter.

Betel nut was supplied by the researcher to ensure consistency in size and maturity. A standard diet (Appendix 12) was given to participants for breakfast and lunch and this was consistent over the 2 days of the study.

7.2.4.2 Pilot questionnaire and testing of study protocol

The study questionnaire and protocol were pretested on four participants with T2DM at the study venue in October 2011.

7.2.4.3 Final questionnaire and study protocol

The pretesting of the questionnaire and study protocol resulted in minor changes to the final questionnaire and protocol. The times for the CBG and meals were included on the final questionnaire. In terms of the study protocol, participants were initially required to have breakfast at 8.00am and were required to cease the study at 3.00pm. These participants were required to have their fasting CBG measured before 8.00am. After pre-testing the study protocol, the breakfast time was changed to 8.30am and CBG measurements were therefore done by 8.30am. The cessation time for the final study protocol was consequently changed to 3.30pm. The change of time was due to logistical reasons. Most participants were travelling by public transport making it difficult to get to the study setting before 8.00am. As a result of the change in study commencement time, the times for the hourly sugar were changed on the final questionnaire.

7.2.5 Study days

The protocol for the study is shown in Figure 7.2 below

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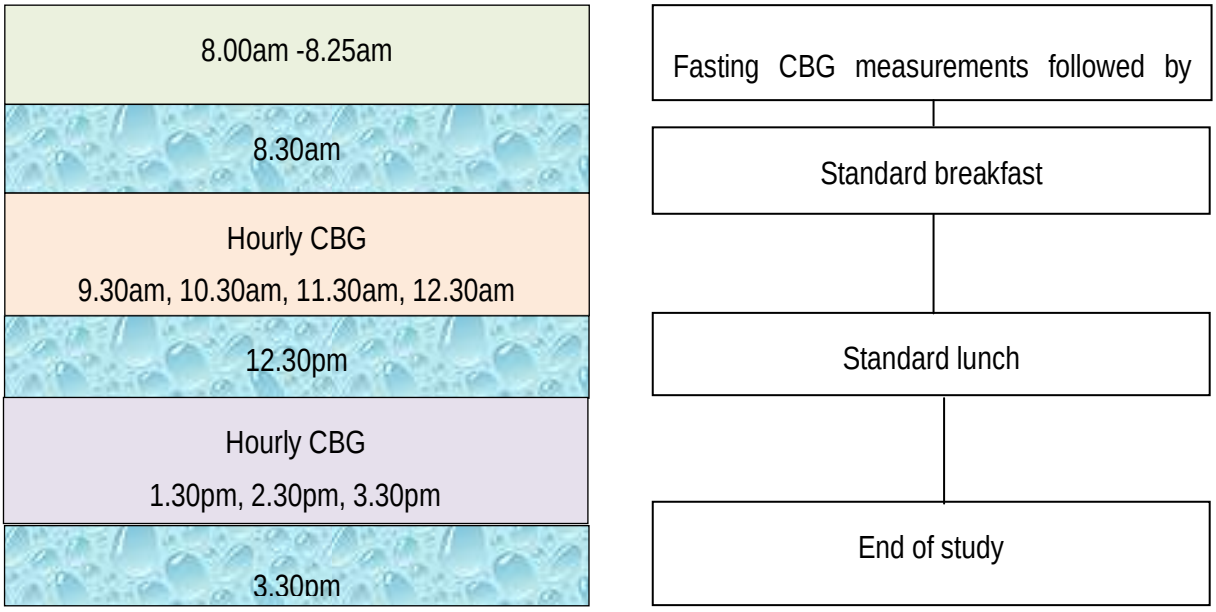

CBG = capillary blood glucose

Figure 7.2 Day 1 and day 2 Study protocol

7.2.5.1 Day 1: Betel nut chewing

Data was collected on the participants' chewing habits and recorded on the questionnaire developed for the study. Participants had to return to their own accommodation after completion of Day 1.

After completion of Day 1, appointments were confirmed for Day 2. Participants were expected to return the next day but for various reasons, many patients were not able to do so and therefore, appointments were made for the next available date.

7.2.5.2 Day 2: Abstinence from betel nut

During this day, the same protocol as in Day 1 was followed except that participants abstained from betel nut chewing for the whole day. In this case hourly CBG levels were measured.

7.2.6 Sample size and sampling

Estimation of an adequate sample size for this study was difficult. There were many measurements of CBG on each participant, and each one of these was an observation as far as the analysis was concerned. However, the correlation between measurements made on the same individuals influenced the estimated sample size. If all measurements were un–correlated, then a sample of approximately N=120 would have been adequate to identify variables exhibiting a moderate effect size, with 80% power and α=0.05. [1] With many observations per person, it was anticipated that a sample of approximately N=70 people may be adequate for this study.

7.2.7 Statistical analysis

Standard descriptive statistics (frequencies and percentages for categorical variables, and means and standard deviations for continuous variables) were used to summarise the profile of the study participants. Similar descriptive statistics were used to describe their betel nut chewing habits.

For the hourly CBG data for Days 1 and 2, the area under the curve (AUC) was calculated using the simple trapezoidal rule (dividing the curve up into blocks and assuming a straight line between the hourly measurements). The difference in AUC from Day 1 to Day 2 was calculated and a paired t-test was used to determine the significance of any difference between Days 1 and 2.

The individual CBG measurements were also compared separately at each hour of the two days. This was performed using a paired t-test to identify any consistent difference between the two days (at each measurement hour).

The Kappa statistic was used to assess agreement between fasting and the average CBG over the day for each person. For this analysis, the CBG was divided into its recommended brackets of <6.0 mmol/L for fasting, and <8.0 mmol/L for appropriate glycaemic control.

A repeated measures analysis was used to identify any relationship between CBG and timing of the betel nut chewing episodes, meals and medications. This analysis was carried out as random effects regression model using SAS version 9.2 statistical software. This analysis took into account the correlations between observations made on the same individuals. A p-value < 0.05 was taken to indicate a statistically significant association in all tests. This analysis was performed in 3 stages – firstly, a gross comparison between the measurements taken on Day 1 and Day 2 was performed not taking into account details of meals or medications. This analysis included all the hourly measurements made on individuals, and aimed to find if there was any detectable difference between the two days. Secondly, the analysis was repeated taking into account time delays between meals, medications and CBG measurements. Thirdly, the data from Day 1 only (BN chewing day) were analysed in the same manner, to identify any relationship between CBG and delays between BN chewing and CBG (as well as delays from meals and medications).

7.2.8 Ethics

Participants were provided with a Participant Information Sheet [(PIS) Appendix 10] which was written in English. Participants had to read the PIS before they were asked if they wanted to participate. The PIS was orally translated or explained in Pidgin for those who were interested in the study but requested more information in the language they were more fluent in.

Approval for the study was granted by the Curtin University Human Research Ethics Committee (approval number HR38/2011), The University of PNG School of Medicine and Health Sciences Research and Ethics Committee, and the Medical Research Advisory Committee of the National Department of Health of PNG. Permission to undertake the study in a pharmacy practice laboratory, University of PNG School of Medicine and Health Sciences was approved by the school.

7.3 Results

7.3.1 Study setting

The Pharmacy Practice Laboratory at the School of Medicine and Health Sciences, University of Papua New Guinea (UPNG), where the study was conducted is located at the Taurama campus of UPNG and is within the grounds of the Port Moresby General Hospital.

7.3.2 Participant recruitment

Of the 385 participants, there were 212 (55%) potential participants (betel nut chewers) for this study. Of these 212, 7(3.3%) were from outside provinces, 60 (28.3%) from rural villages, and 144 (67.9%) from urban and peri-urban areas. Data for the area of residence for one participant was missing. For logistical purposes, that is, ease of travel arrangements to the study vicinity, only participants who resided in the urban and periurban areas were eligible for the study. However, fifteen betel nut chewers from rural villages who expressed interest in the study and were able to organise their own logistics were allowed to participate. After excluding the rest of the rural participants, a total of 159 betel nut chewers (144 urban/peri-urban,15 rural) were therefore potential participants for the study. Eleven of the 159(6.9%) participants on insulin were further excluded on the basis of potential risk of adverse effects on glycaemic control and to avoid it being a confounding factor because of its pharmacology and pharmacokinetics. The PIS was therefore handed to 148 participants.

Of the 148 who were given the PIS, 21(14.2%) gave consent and immediately made appointments to participate before leaving the hospital after the baseline study. Phone calls were made to obtain consent and make appointments for the rest of the participants. Of those who were contacted by phone, 3 (2.4%) were hospitalised, one was deceased and 17 (13.4%) were not contactable and were therefore excluded. Those who were not contactable by phone were excluded after four daily attempts. Consent was therefore sought from 106 (83.5%) of the 127 participants contacted by phone. Of these, 57(53.8%) refused to participate while 49 (46.2%) agreed to participate.

Seventy participants gave consent to participate and of these, 59 (84.3%) appointments were confirmed while the rest were still undecided on convenient days to do the study. Of the fifty nine, 44 (74.6%) participated in the study, but five (11.4%) of them did not complete the study leaving a total of 39 participants completing the study. However, one further participant was subsequently excluded because he ceased medications before and during the second day of the study. The final analysis for this study therefore included only the 38 participants who completed the study.

Common reasons cited for refusal included feeling unwell, babysitting grandchildren, death in the family and fear of travelling to the study location during the civil/political unrest which was occurring in Port Moresby during the time of the study.

7.3.3 Participant characteristics at baseline

Participant characteristics at baseline were those measured and recorded at the Port Moresby General Hospital Diabetes Clinic during a face to face interview. These included demographic, lifestyle and medical and physical characteristics.

7.3.3.1 Demographic characteristics

Of the participants, 76.3% were females and 50% of them were in the age range 50-59 years (Table 7.1). Only four (10.5%) were in paid employment while the rest were unemployed, unpaid or retired. More than 80% of the participants were urban or peri-urban dwellers. The majority of participants (42.1%) were born and had lived in Port Moresby for their lifetime. Thirty-three (86.8%) participants were from the Southern region. Eighteen (47.3%) of the participants either did not complete basic or completed only basic primary education.

Table 7.1 Frequencies of demographic characteristics (N=38)

Characteristics	n*	Percentage*
Gender		
Male	9	23.7
Female	29	76.3
Age		
<50	9	23.7
50-59	19	50.0
≥60	10	26.3
Region of origin		
Southern	33	86.8
Momase	1	2.6
Highlands	2	5.3
New Guinea Islands	2	5.3
Level of education		
Did not complete basic education	4	10.5
Primary basic education	14	36.8
Secondary education	8	21.1
Vocational training	2	5.3
Tertiary education	10	26.3
Area of residence		
Urban	18	47.4
Peri-urban	15	39.5
Rural village	5	13.2
Employment status		
Paid employment	4	10.5
Unpaid/unemployed	26	68.4
Retired	8	21.1
Years of residence in Port Moresby		
0	5	13.2
1-10	4	10.5
>10	10	26.3
Lifetime	16	42.1

*May not add up to total because of missing values

7.3.3.2 Lifestyle characteristics

Only four (10.5%) of the participants consumed alcohol in the preceding 3 months while only one (2.6%) was a current smoker (Table 7.2). In terms of diet, more than 50% of the participants were consuming vegetables for 6-7 days per week but only four (10.5%) were consuming 3 or more servings on days when vegetables were consumed. When comparing fruit and vegetable days, most of the participants (60.5%) were either not consuming fruit at all, or were consuming fruit for no more than 2 days per week. Like servings of vegetables, more participants were

consuming fewer servings of fruit. About half of the participants consumed less than 5 betel nuts per day and about three quarters had consumed betel nut for more than 25 years. Nearly all (94.7%) consumed betel nut with *Piper betle* inflorescence (PBI) and lime.

Table 7.2 Frequencies of lifestyle characteristics at baseline (N=38)

Characteristics	n*	Percentage*
Alcohol consumed in the last 3 months		
No	34	89.5
Yes	4	10.5
Smoker status		
Current	1	2.6
Never	24	63.2
Quit	13	34.2
Vegetable servings /day		
<3	34	89.5
≥3	4	10.5
Number of vegetable days/week		
0-2	8	21.1
3-5	9	23.7
6-7	21	55.3
Fruit servings /day		
<2	22	57.9
≥2	16	42.1
Number of fruit days / week		
0-2	23	60.5
3-5	10	26.3
6-7	5	13.2
Number of betel nuts chewed/day		
≤5	21	55.3
>5	16	42.1
Number of years of chewing betel nut		
≤25	5	13.2
>25	28	73.7
Betel nut chewing components		
Betel nut + PBI + Lime	36	94.7
Betel nut only or with PBI but no lime	2	5.3

PBI = *Piper betel* inflorescence; *May not add to total because of missing values

The most common type of physical activity was walking to and from places with more than 70% reporting undertaking such physical activity (Table 7.3). For those who walked to and from places, about 50% walked for less than 150 minutes in a week. Only a very small number of participants reported participating in vigorous-intensity activity either at work or in sports, fitness and recreation. The same was

seen in the number of participants participating in moderate-intensity sports, fitness and recreational activity (MISFRA). Overall, 57.9% of participants reported sufficient physical activity while the rest either did insufficient or no physical activity in a week.

Table 7.3 Physical activity characteristics of participants at baseline

Characteristics	n	Percentage
Work-related VIA for at least 10 minutes		
No	35/38	92.1
Yes	3/38	7.9
Minutes of work-related VIA/week		
<75	2/3	66.7
≥75	1/3	33.3
Work-related MIA for at least 10 minutes		
No	20/38	52.6
Yes	18/38	47.4
Minutes of work-related MIA/week		
<150	8/18	44.4
≥150	10/18	55.6
Walk to get to and from places for at least 10 minutes		
No	8/38	21.1
Yes	30/38	78.9
Minutes of walking/week		
<150	17/30	56.7
≥150	13/30	43.3
Performs VISFRA for at least 10 minutes		
No	36/38	94.7
Yes	2/38	5.3
Minutes of VISFRA/week		
<75	0/2	0.0
≥75	2/2	100.0
Performs MISFRA for at least 10 minutes		
No	34/38	89.5
Yes	4/38	10.5
Minutes of MISFRA/week		
<150	3/4	75.0
≥150	1/4	25.0
Amount of physical activity/week		
Sufficient	22/38	57.9
Insufficient	12/38	31.6
None	4/38	10.5

VIA=vigorous-intensity activity; MIA = moderate-intensity activity; VISFRA = vigorous-intensity sports, fitness and recreational activity; MISFRA = moderate-intensity sports, fitness and recreational activity.

7.3.3.3 Physical and biochemical characteristics

Physical measurements included body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), weight, and hip and waist circumferences. The number of years a participant had lived with T2DM was also included in this section. As shown in Table 7.4, the median values for continuous physical and biochemical characteristics fell outside the 'healthy' values except for waist circumference. The waist circumference was within the normal values only for male participants (the median for females was high). According to the Diabetes Clinical Practice Guidelines for PNG, the normal waist circumference for males is ≤102 cm while that for females is ≤88 cm. The median DBP was just above target value, however the median SBP significantly above the target value. The median number of years participants were diagnosed with T2DM was 3.0 years with a minimum of 0.5 and a maximum of 30 years.

Table 7.4 Median and range values of continuous physical and biochemical characteristics (N=38)

Characteristics	n (%)	Median	Range
Weight (kg)	37 (97.4)	71.0	52 - 22
Waist circumference (cm)	38 (100.0)	99.5	80 – 141.5
Female	29 (76.3)	104.0	87.0-141.5
Male	9 (23.7)	96.0	80.0-101.0
Hip circumference (cm)	38 (100.0)	101.0	80 - 144.5
BMI (kg/m^2)	37 (97.4)	27.1	19.4 - 47.7
SBP (mmHg)	38 (100.0)	146.5	108 - 200
DBP (mmHg)	38 (100.0)	80.5	51 - 118
HbA1c (%)	37 (97.4)	8.1	5.4 - 12.7
CBG (mmol/L)	38 (100.0)		
Fasting	13 (34.2)	10.0	6.1 - 17.9
Random	20 (52.6)	12.2	5.0 - 27.2
Unknown	5 (13.2)	8.4	8.2 - 15.3
Number of years diagnosed with diabetes	38 (100.0)	3.0	0.5 - 30

BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; CBG = capillary blood glucose

When measurements were classified into categories (widely accepted to indicate 'healthy' or 'unhealthy' behaviour), it appeared that results for the majority of participants fell outside the 'healthy' range. In particular, this was the case for waist circumference, BMI, SBP, DBP and HbA1c. Participants were equally divided with regard to healthy or unhealthy DBP. Twenty six (68.4%) of the participants had been living with T2DM for five years or less. See Table 7.5

Table 7.5 Categorical variables for physical measurements at baseline (N=38)

Characteristics	n	Percentage
Waist circumference (cm)		
Normal	10	26.3
Above normal	28	73.7
BMI (kg/m^2)		
<25	7	18.4
≥25	28	73.7
SBP (mmHg)		
≤130	8	21.1
>130	30	78.9
DBP (mmHg)		
≤80	19	50.0
>80	19	50.0
HbA1c (%)		
≤7.0	9	23.7
>7.0	28	73.7
Number of years diagnosed with diabetes		
≤5	26	68.4
>5	12	31.6

BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; HbA1c = glycated haemoglobin; Normal waist circumference is ≤88cm (females) and ≤102cm (males)

7.3.4 Medications during study

Participants on insulin were excluded from this study and therefore all participants had either diet-controlled diabetes or were on oral hypoglycaemic medications. Nearly 50% (n=18) of participants were on combination oral therapy including glibenclamide and metformin. More than 50% of participants were not on any co-medications (e.g. antihypertensive medication, lipid-lowering agents). Table 7.6

Table 7.6 Hypoglycaemic medications used during study (N=38)

Variable	n	Percentage
Diabetes management		
Diet	5	13.2
Metformin	5	13.2
Glibenclamide	10	26.3
Combination	18	47.4
Co-medications used		
No	17	55.3
Yes	21	44.7

7.3.5 Betel nut chewing characteristics during the study

During the betel nut chewing day, there were 109 occasions on which betel nut was chewed amongst the 38 participants. This corresponded to an average of 2.8 chewing episodes per participant. More than 90% of betel nut chewing episodes included lime and PBI, and swallowing betel nut rather than spitting it out. In more than 60% of episodes of chewing, betel nut juice was swallowed. Usually, one betel nut was chewed at a time (68.8%), with half a nut chewed on most other occasions. Fifty six (51.4%) episodes of betel nut chewing lasted for up to 10 minutes. Table 7.7

Table 7.7 Betel nut chewing characteristics (N=109)

Variable	n(%)
Lime used	
No	7 (6.4)
Yes	102 (93.6)
Piper betle inflorescence	
No	4 (3.7)
Yes	105 (96.3)
Betel nut juice swallowed or spat out	
Spat out	37 (33.9)
Swallowed	72 (66.1)
Betel nut swallowed or spat out	
Spat out	8 (7.3)
Swallowed	101 (92.7)
Number of nuts chewed per episode	
0.5	31 (28.4)
1	75 (68.8)
2	3 (2.8)
Duration of chewing betel nut (minutes)	
≤ 10	56 (51.4)
>10	53 (48.6)

7.3.6 Differences in hourly CBGL during the betel nut chewing and betel nut abstinence days

The mean fasting CBG for the betel nut chewing day was slightly less than that for the betel nut abstinence day but there were no statistically significant differences in CBG between days, when based on the fasting, average or hourly glucose measurements. The data in Table 7.8 below were obtained from a random effects regression model (to adjust for the correlations between observations on the same participant). This is equivalent to a paired t-test on these measurements.

Table 7.8 Differences in the CBG taken at various times during the day, and overall (average CBG measurement), between betel nut chewing and non-chewing days

Variable	Betel nut chewing day Mean (SE)	No betel nut day Mean (SE)	p-value*
Fasting CBG (mmol/L)	7.9 (0.4)	8.4 (0.4)	0.1796
Average CBG (mmol/L)	9.2 (0.4)	9.3 (0.4)	0.4182
Hourly BGL (mmol/L)			
9:30am	10.3 (0.5)	10.9 (0.5)	0.1395
10:30am	11.1 (0.5)	11.5 (0.5)	0.3349
11:30am	9.2 (0.5)	9.4 (0.5)	0.6092
12:30pm	7.7 (0.4)	7.5 (0.4)	0.4870
1:30pm	9.0 (0.4)	9.2 (0.4)	0.5554
2:30pm	9.4 (0.5)	9.1 (0.5)	0.4874
3:30pm	8.6 (0.5)	8.4 (0.5)	0.6369

*P-values were obtained from a 'paired' analysis which took into account the correlations between measurements on the same individual; CBG = capillary blood glucose; SE = standard error.

The CBG was put into categories, and the fasting values tabulated against the average for each day (Table 7.9). The cut-off value for the fasting level was 6.0 mmol/L, while the cut-off for the average was 8 mmol/L. Not surprisingly, there appeared to be some agreement between low values for both fasting and average values, and similarly for the high values. The Kappa statistic was used to assess the agreement between these measures, and the results were: 0.37 and 0.34 for Day 1 and Day 2 respectively. Kappa is a statistic whose value lies between about -0.2 and 1. The values greater than 0.7 are considered to indicate excellent agreement, those from 0.5 to 0.7 show good agreement, while values less than 0.5 indicate fair to poor agreement. In this case, the kappa statistics indicate fair to poor agreement. On examining the data, it appears that over 25% of the participants who

had ‘fasting’ readings which were over 6 mmol/L, had average CBG readings which were under 8 mmol/L, and this discrepancy accounts for most of the disagreement. In summary, it may be that the fasting measurement of CBG is not a very specific predictor of the average CBG throughout the day.

Table 7.9 Fasting and average daily hourly CBG

Variable	Average capillary blood glucose *		kappa
	≤ 8.0	>8.0	
Day 1 fasting CBG			0.37
≤6.0 mmol/L	6 (75.0)	2 (25.0)	
>6.0 mmol/L	8 (28.6)	20 (71.4)	
Day 2 fasting CBG			0.34
≤6.0 mmol/L	5 (71.4)	2 (28.6)	
>6.0 mmol/L	8 (26.7)	22 (73.3)	

*The average capillary blood glucose for each day was different; CBG = capillary blood glucose

7.3.7 Area under the Curve (AUC) analysis

7.3.7.1 Hourly CBG

The difference in AUC from Day 1 to Day 2 was small (+1.37 mmol/L) and a paired Student’s t-test showed that the difference was not significant (p=0.56) indicating that there was no significant change in AUC between a betel nut chewing day and non-chewing day. See Table 7.10.

Table 7.10 Differences in AUC between the betel nut chewing and non-chewing day

Variable	N	Minimum	Median	Maximum	Mean	SD
AUC – 1	38	45.20	67.45	124.40	74.28	20.73
AUC – 2	38	42.55	72.25	122.05	75.65	20.61
Difference	38	-32.50	0.30	55.15	1.38	14.50

AUC = area under the curve.

The differences were calculated for each participant separately, and the t-test was used to identify whether the difference was significantly different from zero (which would indicate a systematic difference). The p-value of 0.56 shows that there was no real difference in CBG between the betel nut-chewing and the non-chewing days.

The difference between CBG before and after chewing betel nut (on Day 1 only) was calculated for each participant by subtracting the CBG after from the CBG before betel nut chewing. The duration of betel nut chewing, from onset of each chewing episode to spitting out or swallowing the chew ranged from 1-33 minutes. Table 7.11 shows the distribution of these differences for each episode of betel nut chewing.

Table 7.11 CBG difference after betel nut chewing

CBG difference (mmol/L)	Frequency	Percentage	Range
< -0.1	51	46.8	¯0.4.5 - ¯0.2
-0.1 – 0.1	14	12.8	¯0.1 – 0.1
> 0.1	44	40.4	0.2 – 5.7

CBG = capillary blood glucose

7.3.8 Random effects regression models

Different random effects regression models using each episode of betel nut chewing were used to determine any glycaemic effect of betel nut.

7.3.8.1 Hourly CBG for betel nut and no betel nut days

The hourly CBG measurements were also analysed using a random effects regression model. This model takes into account the correlations between measurements made on the same individual. The model was applied in different stages. Firstly, a direct comparison of Day 1 (betel nut chewing) to Day 2 (no betel nut) was performed, using the hourly CBG measurements. This model showed that the mean CBG on Day 1 was 9.16 (SE: 0.40), and on Day 2 it was 9.30 (SE: 0.40), and that this difference was not significantly different from zero (p=0.43). This is consistent with the findings from the AUC analysis, but it takes into account the individual measurements rather than the summarising of each individual's observations as the AUC for each day.

7.3.8.2 Association between CBG, medication and meals

A second analysis was performed to identify any association between CBG and the timing of medication and meals. For the purpose of this analysis, the delay between the most recent meal and CBG measurement was calculated, and categorised into: up to 1 hr, 1-2 hrs, 2-4 hrs, more than 4 hrs. Similarly, the delay between medication time and CBG time was calculated and categorised (same categories).
There appeared to be a strong association between the timing of the meal and the CBG; the more recent the meal, the higher the CBG. There is also a strong association between timing of medications and CBG, with the CBG appearing to be lower 2 hours after medication than within the first 2 hours (suggesting that the medication takes at least 2 hours to have effect). The findings from this analysis are shown in Table 7.12

Table 7.12 Comparison of CBG between betel nut chewing and non-chewing days, after adjustment for timings of meals, medications, and blood sampling.

Variable	Mean CBG (adjusted)	95% CI	p-value
Delay from medication			<0.0001*
< 1 hour	10.10	9.18 – 11.02	(reference)
(1,2] hrs[#]	10.51	9.59 – 11.42	0.2162
(2,4] hrs	8.74	7.87 – 9.61	<0.0001
4 or more hours	8.25	7.41 – 9.09	<0.0001
No medication (diet only)	9.54	8.61 – 10.47	0.2008
Delay from most recent meal			<0.0001*
< 1 hour	10.00	9.18 – 11.02	(reference)
(1,2] hrs	10.50	9.68 – 11.31	0.0161
(2,4 hrs	9.27	8.46 – 10.08	0.0004
4 or more hours	7.95	6.94 – 8.97	<0.0001
Betel nut chewing day			0.2917
No (Day 2)	9.36	8.56 – 10.15	
Yes (Day 1)	9.50	8.71 – 10.29	

*Overall p-value. The p-values shown in the table above are all 'after adjustment' for each other. This means that any influence of the meal (for example) is taken into account in calculation of the influence of medication and betel nut chewing (and vice versa); [#] The notation: (1,2] means a delay 'strictly greater than 1 hour, and less than or equal to 2 hours'. Round brackets exclude the endpoint, while square brackets include it; CBG = capillary blood glucose

7.3.8.3 Association between CBG and betel nut chewing, meals and medications

The final analysis was undertaken to focus only on the first day of the study, when betel nut was chewed. In addition to the delay between CBG measurement and timing of medication and meals, the time between the most recent betel nut chew was also calculated. These varied from a few minutes (when CBG was assessed very shortly after an episode of chewing), to an hour or more. The pattern of adjusted CBG was similar for delay from medication and meals, except that the CBG within an hour of meal time was not as high as it was for the whole group (over 2 days). Consequently, the significance of differences from that baseline (meal shortly before CBG assessment) was not as significant as they were previously. The main finding was that there appeared to be no significant association between

timing of betel nut chewing and CBG. The results of this analysis are shown in the Table 7.13

Table 7.13 Analysis of the influence of timing of betel nut chewing on CBG, after adjustment for timings of meals, medications, and blood sampling.

Variable	Mean CBG (adjusted)	95% CI	p-value
Delay from medication			<0.0001*
< 1 hour	10.40	9.20 – 11.61	(reference)
(1,2] hrs[#]	10.70	9.62 – 11.78	0.4740
(2,4] hrs	8.68	7.58 – 9.78	0.0004
4 or more hours	8.84	7.89 – 9.79	0.0001
No medication (diet only)	9.28	7.95 – 10.60	0.1051
Delay from most recent meal			<0.0001*
< 1 hour	9.39	8.39 – 10.40	(reference)
(1,2] hrs	10.61	9.63 – 11.60	<0.0001
(2,4] hrs	9.59	8.58 – 10.61	0.5763
4 or more hours	8.72	7.50 – 9.94	0.1110
Delay from most recent BN			0.8356*
< 1 hour	9.74	8.76 – 10.72	(reference)
(1,2] hrs	9.54	8.40 – 10.68	0.5487
(2,4] hrs	9.51	8.33 – 10.70	0.5642
4 or more hours	9.53	8.55 – 10.52	0.5140

*Overall p-value. The p-values shown in the table above are all 'after adjustment' for each other. This means that any influence of the meal (for example) is taken into account in calculation of the influence of medication and betel nut chewing (and vice versa); [#] The notation: (1,2] means a delay 'strictly greater than 1 hour, and less than or equal to 2 hours'. Round brackets exclude the endpoint, while square brackets include it; CBG = capillary blood glucose BN = betel nut

7.4 Discussion

This part of the research was designed to investigate the immediate glycaemic effects of betel nut chewing. Evidence from animal and cell studies, and epidemiological evaluation indicates there is a link between betel nut, PBL/PBI and arecoline (major constituent of betel nut) and metabolic disorders. Based on evidence from the literature, it was hypothesised that betel nut chewing increases blood glucose. Based on that hypothesis, the overall study was designed to investigate both the long term and acute glycaemic effects of betel nut chewing. It was envisaged that any acute effect would confirm or deny findings from the cross-sectional studies.

Thirty eight participants were included and among them they chewed a total of 109 times which corresponded to an average of 2.8 (range: 1 – 6 episodes) per participant. Participants were not given a set dose of betel nut and were required to chew according to their normal habits. The study was designed this way to investigate if any blood glucose changes were dependent on the dose and the chewing habit. Other studies have reported a dose-dependent effect of betel nut or arecoline on blood glucose. [2-4] Diet and physical activity were controlled, and participants were observed closely during the two study days. Participants moved around the room where the study was conducted but did not leave the room for the duration of the study.

The hypothesis that betel nut chewing increases blood glucose was tested in two different ways; i.e. using AUC and random effects regression models.

7.4.1 AUC and random effects regression models

Using hourly AUC analysis to determine any difference in CBG between Day 1 (the betel nut chewing day) and Day 2 (the non-chewing day), a small non-significant difference was observed. The AUC reflected the overall glycaemic control during the period of the study from 8.30am to 3.30pm. From this analysis, the present study demonstrated that betel nut chewing does not alter blood glucose levels in people with T2DM, and rejects the hypothesis that betel nut chewing increases blood glucose. Random effects regression analysis took into consideration the effect of meals and medication on blood glucose to determine if betel nut chewing was associated with changes in blood glucose. The analysis resulted in no significant association between timing of betel nut chewing and CBG, also rejecting the hypothesis that betel nut chewing increases blood glucose in T2DM.

7.4.2 Difference in CBG immediately before and after each chewing episode

A simple calculation to determine the difference between CBG before and after chewing betel nut indicated that there were three types of responses which were all non-significant; a reduction, no effect and an increase in CBG after betel nut chewing. CBG after chewing was measured 5-10 minutes after swallowing or

spitting out the betel nut chew. The duration of betel nut chewing from onset of each chewing episode to spitting out or swallowing the chew ranged from 1 to 33 minutes. No CBG was measured while the participant was still chewing. The observation that blood glucose increased, stayed the same or decreased indicates individual responses of blood glucose to betel nut chewing. However, this confirms the variable responses and that any acute glycaemic effect of betel nut appears to be short-lived. The finding that the glycaemic effect of betel nut is short-lived is consistent with reports of studies investigating the pharmacokinetics of arecoline in Alzheimer patients. Asthana et al [2] who intravenously infused 5mg arecoline to Alzheimer patients over 30 minutes reported that plasma arecoline concentrations were detectable by 5 minutes and increased to peak by the end of the infusion (30 minutes). That study determined the mean plasma half-lives of arecoline to be 0.95 ± 0.54 ($t^1/_2$) and 9.3 ± 4.5 (SD) ($t^1/_2\beta$) minutes.

7.4.3 Possible reasons for results observed

Those on insulin were excluded from the study as previously mentioned (in the results) due to potential risk of adverse glycaemic events. The two medications used by participants during the study were glibenclamide and metformin. Glibenclamide [5] is a sulphonylurea which increases insulin secretion from the Islets of Langerhan's. It requires a functioning β-cell to exert its effect and it is long acting with a duration of action of 6-24 hours. Its long-acting effect may have had an effect on blood glucose levels, although this was not evident from the random effects regression model.

Metformin [5] is a biguanide with a different mode of action and has a shorter duration of action compared to glibenclamide. It does not stimulate pancreatic insulin secretion but increases insulin action and reduces hepatic glucose production and is therefore useful in reduced β-cell function. Other modes of action include stimulation of tissue uptake of glucose and reduction of gastrointestinal absorption of carbohydrate. There is a possibility that the increased insulin action by metformin may counteract the acute glucose increase caused by adrenaline release stimulated by arecoline in betel nut. Animal/cell studies have shown that arecoline administration increases adrenaline which in turn increases blood glucose. [3, 6, 7]

Although no effect on glucose was observed by the end of the study days, transient effects of betel nut may have been missed. The onset of action has been reported to be within two [8] to 10 minutes [9] Blood glucose in this study was measured at the end of a chewing episode. A chewing episode was from the onset of chewing to the swallowing or spitting out of betel nut. The minimum and maximum duration for chewing was 1 minute and 33 minutes, respectively. Any small non-significant change that was observed would probably have been from systemic absorption rather than buccal absorption while the chew was in the mouth. Buccal absorption avoids first-pass effect. What is usual at the end of chewing is volume of material in the mouth is smaller than when chewing began because during mastication bits of the chew are continuously swallowed. Chronic administration of arecoline has been reported to be hypoglycaemic in animal studies.[3, 10]

7.4.4 Other observations from the study

Although it was not part of the study to observe behaviour of study participants, it was observed during the two study days that when participants were not chewing betel nut, they were feeling sleepy. Some actually fell asleep. On the day of betel nut chewing, none of the participants was sleepy of fell asleep. Several were sweating profusely while they were chewing betel nut. However, participants did not sweat consistently with every betel nut they chewed, which may indicate that not every betel nut was the same chemically. These manifestations are thought to be due to stimulation of the autonomic nervous system. [8, 11]

7.4.5 Acute glycaemic effect of betel nut

A review of the literature did not find any reports on the acute glycaemic effects of betel nut chewing in humans. However, a study [3] using arecoline to investigate both the acute and chronic effects on blood glucose was conducted by Dasgupta using mice. That study administered arecoline intraperitoneally at a dose of 10mg/kg. Serum corticosterone, adrenal adrenaline and noradrenaline, and blood glucose and liver glycogen were measured at 20, 40 and 60 minutes. It was found from this study that serum corticosterone increased at 20 and 40 minutes with no change at 60 minutes. In terms of the increase, this was most significant at 20 minutes as

compared to 40 minutes after administration. The same trend was observed on blood glucose levels with the most significant increase at 20 minutes. Liver glycogen decreased at all times (i.e. 20, 40 and 60 minutes) but the most significant decrease was observed at 20 minutes compared to the other measurement times. There was a difference in levels of adrenal adrenaline and noradrenaline with adrenaline levels relatively higher than noradrenaline. However, levels of both catecholamines increased at 20 minutes without any significant change at 40 or 60 minutes after administration. Although blood glucose was measured only once after chewing, the same pattern of a short-lived effect was observed in the present study. The hourly glucose did not show any difference in glucose levels on the betel nut chewing and non-chewing days. Dasgupta et al [3] provide some understanding of the acute effect of arecoline on adrenal function and blood glucose. Other *in vitro* studies [7] have reported that arecoline or betel nut influences release of catecholamines and Dasgupta et al [3] confirm these findings in their *in vivo* study.

As observed by Dasgupta et al [3], the most significant increase in blood glucose was in the first 20 minutes. The present study measured blood glucose 5-10 minutes after the betel nut chew was spat out or swallowed. The minimum duration of chewing was 1 minute and the maximum was 33 minutes. Perhaps the delay in measuring blood glucose may have contributed to the small observed increases, decreases or no change in blood glucose. Had the measurements been done 5-10 minutes after onset of chewing, a difference in readings would probably have been observed. However, like other studies, this would have been short lived. The finding that blood glucose was similar on the betel nut chewing and non-chewing days indicates that betel nut did not have an overall acute effect on blood glucose.

It appears from other studies that the acute increase in blood glucose is due to catecholamine release or corticosterone in response to the arecoline.[3] It is possible that the increase in blood glucose from catecholamine or corticosterone release triggers insulin release which reduces blood glucose quickly. Jensen et al [12] reported that adrenaline increased blood glucose concentration but the concentration decreased to physiological level within 30 minutes when insulin infusion was initiated. That study included 10 healthy volunteers (5 women and 5 men) who were infused with adrenaline.

The finding that betel nut chewing did not affect blood glucose is inconsistent with what was observed in the two cross-sectional studies performed as part of the present study. The two cross-sectional studies observed that betel nut chewing has beneficial effects on blood glucose levels of those with T2DM as well as those without the disease. Those who never chewed betel nut were more likely to have hyperglycaemia while those who chewed betel nut had better glycaemic control. Better glycaemic control may be partly due to inhibition of catecholamine release as a result of chronic use of betel nut. A study [6] using continuous perfusion of arecoline into an adrenal vein for 60 minutes demonstrated that arecoline inhibits catecholamine release from a rat adrenal gland. That study found that arecoline dose-dependently inhibited catecholamine release. Lower doses did not inhibit catecholamine release but a larger dose did.[6] Dasgupta et al [3], apart from giving one dose of arecoline also administered the drug daily for 15 days to investigate the chronic effects of arecoline. That study found that chronic administration of arecoline was hypoglycaemic. The hypoglycaemic effect of arecoline was demonstrated to be a result of its inhibition of adrenocortical activity at ultrastructural and hormonal levels. Ultrastructural studies showed depletions of noradrenaline and adrenaline containing granules. The study by Dasgupta et al [3] also reported that although corticosterone levels were reduced in the adrenal gland, it was increased in the blood serum.

The mechanism of action of arecoline on adrenaline is suggested to be through the effect of arecoline on the calcium channels.[6, 13] It is suggested that the inhibitory effect of arecoline may be mediated by blocking calcium (Ca^{2+}) influx and not through inhibition of Ca^{2+} release from the cytoplasmic store. [6] Inhibition of catecholamines through inhibition of Ca^{2+} influx may partly be responsible for hypoglycaemia resulting from chronic arecoline administration. There may be other mechanisms by which arecoline causes hypoglycaemia. It has also been demonstrated that arecoline inhibits hepatic gluconeogenesis.[14] The opposite effect is exhibited by adrenaline where it stimulates hepatic glucose release. [15, 16] Yao et al [14] reported that a low dose of arecoline decreased the mRNA expression of hepatic G6Pase, PEPCK, Fox01 and PGC-α in a T2DM rat model thereby inhibiting hepatic glucose release. Fasting blood glucose and total cholesterol were reduced. A high dose of arecoline in that study caused hepatic damage. [14] Arecoline has also

been reported to prevent the dysfunction of β cells of the pancreas induced by high fructose via up-regulation of PDX-1. [4]

7.5 Conclusions

Regardless of how the underlying influence of betel nut chewing on glucose levels occurs and how it was assessed (either using AUC or a random effects regression model) results from the present study indicate that betel nut chewing does not acutely influence the blood glucose of patients with T2DM.

7.6 References

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Chapter VIII: General discussion

8.1 Prevalence of betel nut chewing

The present study has investigated the prevalence of betel nut chewing in Papua New Guinea (PNG) in those with and without type 2 diabetes mellitus (T2DM). Findings of this study report a very high prevalence of betel nut chewing not only in those without the disease but also those with the disease. This finding appears to be the highest reported thus far. However the study included a sample of urban and peri-urban location and the rate may have been less if PNG populations where the habit is not common were included in the study. Those from regions where the habit was not common appear after relocation to have picked up the habit from coastal people where the habit is more prevalent.

8.2 The glycaemic effect of betel nut chewing

Epidemiological studies in Asia have shown an association of betel nut chewing with metabolic syndrome or individual components of this syndrome such as hyperglycaemia and diabetes or obesity.[1-3] The same findings have been reported from two cross-sectional studies in PNG. [4, 5]

It was hypothesised that betel nut chewing increased blood glucose in those with T2DM. This hypothesis was tested in both acute and long term chronic betel nut exposure. In terms of long term chronic betel nut exposure, this hypothesis was not accepted since univariate analysis indicated a positive difference in glycaemic control between betel nut chewers and non-chewers (p=0.027). That is to say, betel nut chewers had better glycaemic control than their counterparts. However the association of non-exposure (never chewed) and high betel nut dose with glycaemic control was similar. A lower dose had a beneficial effect while a higher dose did not. To determine the immediate glycaemic effects of acute exposure, the hypothesis was tested in two different ways; firstly through an area under the curve (AUC) analysis and secondly through a random effects regression analysis. Here again the hypothesis was rejected since AUC analysis (a measure of glycaemic control) did not show any significant difference between the AUC during a day when the participants chewed betel nut compared to a day when they did not chew betel nut.

Furthermore, the hypothesis was also rejected after considering the influence of meals and medication using random effects regression analysis which again failed to show any significant differences in glycaemic control secondary to betel nut chewing. Calculation of the difference in capillary blood glucose (CBG) before and after each chewing episode showed small insignificant changes. The null hypothesis that betel nut has no effect on blood glucose is therefore accepted for the effect of acute betel nut exposure on blood glucose.

T2DM patients already have problems with poor glycaemic control as a consequence of β-cell dysfunction and/or insulin action so to investigate whether betel nut chewing had the same effect in those without the disease, a cohort of non-T2DM was included in the present study. Univariate analysis testing the association of betel nut chewing and glycaemic control in the non-T2DM cohort also resulted in a significant difference in glycaemic control between betel nut chewers and non-chewers. Betel nut chewers had better glucose tolerance than those who were not chewers. Fasting blood glucose however was not associated with betel nut chewing. Further, betel nut chewing did not independently influence glycaemic control in the non-T2DM cohort.

These findings suggest that the beneficial effect of low dose betel nut chewing on glycaemic control may be independent of defects in insulin release and/or action. A higher dose however may adversely affect blood glucose. The finding that betel nut chewing did not independently influence postprandial hyperglycaemia suggests that there are other factors contributing to the problem. Further, the finding that betel nut chewing did not affect fasting hyperglycaemia suggests that betel nut chewing probably does not have any effect on hepatic glucose control.

The findings from this study of the beneficial effects of betel nut chewing, arecoline and *Piper betle* leaf (PBL) or *Piper betle* inflorescence (PBI) on glycaemic control of those with T2DM is in agreement with animal and human studies.[6-10] Yao et al.[10] found that a low dose was beneficial while a high dose caused hepatic damage. However, there are also other studies which are in conflict with the findings of the present study.[3, 11-13]

The finding of this study is in disagreement with the previous study by Benjamin and Margis in T2DM.[4] That study did not perform any further statistical analysis apart from calculating frequencies. The conclusion was based on the observation that 73.0% of the 167 patients with poor glycaemic control were betel nut chewers. Benjamin and Margis used a higher fasting CBG cut-off (CBG>10.0 mmol/L) to define poor glycaemic control compared to the present study. Further, the present study used a different blood glucose parameter [glycosylated haemoglobin (HbA1c)] than used by Benjamin and Margis. The majority of participants in that study were betel nut chewers; only 55 (26.0%) were non-chewers. Although the sample number was smaller than the present study, the strength of that study was random recruitment of participants. However, demographic characteristics of participants of the present study and that of Benjamin and Margis were similar in terms of gender, dispersion of age, region of origin and percentage of participants from rural villages. The study reported a higher prevalence (74.0%) of betel nut chewing compared to the present study (55.0%). Further the prevalence rates of those with tertiary education, alcohol consumption and smoking were higher than the present study. Alcohol consumption, smoking and level of education did not affect glycaemic control in the present T2DM cohort. Given the high prevalence of betel nut chewing reported by Benjamin and Margis, and that the majority of participants were betel nut chewers, it is possible that the report is biased and therefore the finding that betel nut chewing contributes to poor glycaemic control is possibly inconclusive.

The finding of the present study that betel nut chewing had a beneficial influence on glycaemic control in the non-T2DM cohort is also in disagreement with another study by Benjamin.[5] The blood glucose parameter used in that study was fasting CBG while the present study used both fasting CBG and oral glucose tolerance (OGT). As previously reported the present study did not find any association of betel nut chewing with fasting CBG but did with OGT. Benjamin reports a low prevalence (13.0%) of betel nut chewing among 769 participants. The conclusion drawn from the study that betel nut is a risk factor for T2DM was based on a sample that lacks sufficient power to detect any differences. Only 92 betel nut chewers were included in the statistical analysis. The recruitment of participants for that study was conducted at church halls and therefore the lower prevalence of betel nut chewing. Some churches discourage their followers from habits such as betel nut

chewing, smoking and alcohol consumption. The majority (78.0%) of participants were from the Seventh Day Adventist church which discourages such social habits.

The finding of the beneficial effect of betel nut chewing is also in disagreement with three Taiwanese studies. Tung et al.[11] and Yen et al. recruited participants from the same database to investigate the effect of betel nut on T2DM and the metabolic syndrome, respectively. The strength of these studies were their sample sizes (>10,000). Another Taiwanese study by Guh et al[14] was smaller in sample size compared to that by Tung et al.[11] and Yen et al.[15] The finding by Guh et al.[14] was not consistent with that of Tung et al. and Yen et al. but did report hyperglycaemia in women. The prevalence of betel nut chewing in women in that study was 2.3%. In another population-based study in Taiwan, Tseng[3] reported that the incidence of T2DM increased with age but peaked at 60-69 years for "ever" chewers but not "never" chewers. That is, the incidence of T2DM kept increasing beyond 69 years for "never" chewers. A common observation from these studies is that betel nut chewers are younger but diabetes is increasing with increasing age suggesting that age is a factor. Tung et al.[11] also reported that there was no significant difference in blood glucose between non-chewers and chewers who were 40 years or younger. This is an age group that has a high prevalence of betel nut chewing in those studies. This probably agrees with the present study that any effect of betel nut is detected after years of chronic chewing.

8.3 Factors associated with betel nut chewing and their association with hyperglycaemia and T2DM

As reported in Chapter IV for the T2DM cohort, the known modifiable risk factors for poor glycaemic control such as systolic blood pressure (SBP) and waist circumference were not associated with betel nut chewing. The modifiable risk factors for poor glycaemic that had a positive (benefit) effect were physical activity and body mass index (BMI). As reported in Chapter V, for the non-T2DM cohort, risk factors such as SBP, diastolic blood pressure (DBP), physical activity, BMI, waist circumference, percentage body fat, smoking and alcohol were significantly associated with betel nut chewing. These findings further support the potential benefit of betel nut chewing in preventing T2DM.

It has been reported that there are disparities in the prevalence of diabetes and pre-diabetes between fasting glucose and HbA1c data.[16-21] Reductions in HbA1c have been reported to indicate improved β-cell function rather than increased insulin sensitivity.[22] It is also worth mentioning that although T2DM patients at the Port Moresby General Hospital (PMGH) Diabetes Clinic are expected to fast before their blood glucose is measured, the present study found that a proportion of them did not fast. It is important that these patients inform their doctors whether or not their glucose measurement is a fasting level or not, as this affects decisions on diabetes management.

8.4 Possible reasons for differences in glycaemic effects of betel nut chewing

There are several possible mechanisms of action for glycaemic effects of betel nut chewing as discussed in Chapter II. The chemical constituents of betel nut and PBL/PBI as discussed in Chapter II are numerous of which many are yet to be discovered. There are also metabolites which have been discovered but whose mechanisms of action are yet to be determined. Genetics also plays a role in drug metabolism. Differences in genetics, ethnicity, cultures and socioeconomic development affect an individual, the environment that individual lives in and the lifestyle that the individual maintains. The interactions between an individual, the environment and their lifestyle perhaps results in the differences in consequences of betel nut chewing. A possible explanation for any difference between what has been reported in animal studies and humans is interspecies differences. Further, any difference between different ethnic groups in metabolism of chemicals in betel nut and PBI/PBL may be dietary or genetic-related. As discussed in Chapter II, the gut microbiota is probably responsible for some of the differences observed between populations. As such, perhaps one of the reasons for the differences in glycaemic effects of betel nut between Asians and Papua New Guineans may be their diet. The diet of Papua New Guineans is mostly composed of tubers while that of Asians mostly includes rice and noodles. It is also possible that the differences may be due to betel nut chewing methods and the content of arecoline or chemical composition of betel nuts found in Asia compared to PNG. However, an earlier study investigating the arecoline content of Port Moresby betel nuts compared to that of

Indian betel nuts did not show much difference.[23] Arecoline content is also known to differ with betel nut maturity. Betel nut chewers in this study generally had the same method of chewing betel nut with a small proportion chewing the nut only or with PBI but not lime. Further, most Papua New Guineans choose to chew fresh nut rather than dried or cured nut.

There may also be a need to improve research methodologies to confirm the metabolic effects of betel nut chewing and if there are differences among human population groups, the reasons for these differences are important.

8.5 Study limitations

There were limitations of the present study. The cross-sectional surveys requested participants to recall lifestyle behaviours and recall for example the number of days per week a particular physical activity was performed and the frequency of participating in such an activity. The need to recall these events may have led inaccurate recall. The questionnaire used to interview the cohort with T2DM was based on the STEPS survey from which data for the cohort with non-T2DM was obtained but the period of recall was longer for the STEPS survey. When answering lifestyle behaviour questions, participants were requested to think back over the previous 12 months. Recall in the T2DM cohort would probably have been better because they were requested to think back over the previous 3 months. In terms of physical activity and vegetable or fruit consumption, participants were requested to think of a week when such an event occurred and report the amount and frequency of consumption. Participants may have therefore reported the best week in terms of amount and frequency of an event, leading to overestimation.

The timing of glucose measurements to determine the glycaemic effect of acute betel nut exposure may have missed the transient effect of betel nut chewing. Arecoline and arecaidine are rapidly absorbed from the buccal membrane so waiting till the end of the chewing episode could miss the transient effect and arecoline has a very short half-life. However, the finding that a proportion of participants had small increases, decreases or no effect shows that there is individual variability in glycaemic responses to betel nut among those with T2DM.

Most continuous variables were categorised and dichotomised, particularly the main dependent variables of this study; variables of glycaemic control. HbA1c in particular was only assessed as a dichotomised variable because the Siemens/Bayer DCA Vantage point-of-care (POC) HbA1c analyser did not give a continuous reading beyond 14.0%. Any reading more than 14.0% was indicated as >14.0% on the analyser so it was not possible to calculate mean values and perform t-tests for HbA1c. HbA1c was also dichotomised to determine prevalent rates of poor/optimal control according to clinical guidelines. There are several disadvantages of dichotomising continuous variables. The extent of variation in outcome between groups such as the odds of having poor glycaemic control may have been underestimated. Variability may have also been absorbed within each group.

Independent tests to correlate POC and laboratory results for glucose concentration showed that laboratory results for glucose concentration were reasonably well correlated.[24] The values obtained by the DCA Vantage analyser and laboratory testing were identical statistically, analytically and clinically, demonstrating an acceptable accuracy for its use in monitoring glycaemic control in those with T2DM.[24] An internal validation study reported the precision coefficient of variation ranged between 2.6-2.8%.[25] These values are less than 3% indicating that clinically significant changes in serial HbA1c can be detected.[26]

The generalizability of some of the results of this study to other diabetes care facilities with limited care such as those in other provinces of PNG may be limited as this study was in a highly specialised setting. Further, the two study cohorts for the cross-sectional studies were in an urbanised and westernised setting and may not be comparable to settings that are different.

8.6 References

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Chapter IX: Conclusions and recommendations

9.1 Conclusions

This research has investigated the glycaemic effect of betel nut chewing in T2DM. The first part of the research investigated any long term effect of betel nut chewing in T2DM through a cross-sectional study as described in Chapter IV. This research has also investigated the acute glycaemic effect of betel nut chewing in T2DM as described in Chapter VII. The importance of investigating the immediate effects was to establish any acute glycaemic effects and link that with any long term effects to confirm the glycaemic effect of betel nut chewing in T2DM. Further, T2DM patients already have defective glucose homeostasis so it was also important to investigate the issue in those with "normal" (no known T2DM) glucose homeostasis. The importance of any findings of glycaemic effects in non-T2DM (Chapter V) could form part of public health education on the issue of chewing betel nut.

In terms of a long term glycaemic effect of betel nut chewing in T2DM, a strong positive association was observed. That is T2DM betel nut chewers had better glycaemic control than those who were non-chewers. However, this finding should be interpreted with caution. It is possible that there may have been residual confounders which were not included in this study mostly because glycaemic control is multifactorial. Categorical variables were used rather than continuous variables.

The study has found that the acute glycaemic effect of betel nut chewing was non-significant and variable, and overall, no acute glycaemic effect of betel nut chewing was observed in T2DM. However, this finding is important knowledge to those with T2DM that betel nut chewing does not affect glycaemic control, provided they continue to take their medications as required and that they are careful with what they are eating. Diet was controlled during the study. An interesting observation during the research was that all participants of the study investigating acute glycaemic effects of betel nut chewing (Phase 2) were either sleepy or actually fell asleep during the betel nut abstinence study day but were all alert during the betel nut chewing day, reflecting that betel nut is a stimulant.

In terms of glycaemic effect of betel nut chewing in non-T2DM participants, low dose betel nut chewing was associated with better glycaemic control but it was not an independent factor. There were other important factors affecting blood glucose.

In the non-T2DM cohort, betel nut chewing had a strong beneficial independent association with important risk factors for T2DM such as physical activity, BMI, waist circumference and percentage body fat. That is, betel nut chewers were leaner and were more physically active. In T2DM participants, betel nut chewing also had a beneficial influence on physical activity, waist circumference and body mass index.

It is therefore concluded from this study that low dose betel nut chewing improves glycaemic control in terms of glycated haemoglobin and glucose tolerance but it has no effect on fasting blood glucose.

9.2 Recommendations

Although betel nut had a beneficial influence on long term glycaemic control in T2DM and also non-T2DM participants, this data must be interpreted with care. The finding that no acute glycaemic effect of betel nut chewing was observed in T2DM patients must also be interpreted with care.

There is a need to improve methodology to further investigate the issue not only in those with T2DM but also non-T2DM. In terms of methodology, case controlled studies should be employed to further investigate both acute and long term effects of betel nut chewing.

Appendix 1: Ethical clearance with conditions, HREC, Curtin University

Memorandum

Office of Research and Development

Human Research Ethics Committee

TELEPHONE 9266 2784

FACSIMILE 9266 3793

EMAILhrec@curtin.edu.au

To	Professor Jeffery Hughes, School of Pharmacy
From	Miss Linda Teasdale, Manager, Research Ethics
Subject	Protocol Approval HR 38/2011
Date	16 May 2011
Copy	Mrs Stella Tilu Tulo, School of Pharmacy Dr Lloyd Ipai, Diabetes Consultant (Port Moresby General Hospital), Graduate Studies Officer, Faculty of Health Sciences

Thank you for your application submitted to the Human Research Ethics Committee (HREC) for the project titled *"Glycaemic Effects of Betel Nut chewing in type 2 Diabetes Mellitus"*. Your application has been reviewed by the HREC and will be approved subject to the conditions detailed below:

1. Please clarify who will be collecting the blood sample;
2. Please provide further information on why only one day cessation from betel nut chewing would show causation as this has not been identified;
3. Please provide justification for not having a control group;
4. Participant Information Sheets (Phase 1 and Phase 2) requires amendment:
    a. Please consider revising the language to an equivalent Grade 8 in the Flesch-Kincaid Grade Level. i.e.; alternative wording "stop" instead of abstain', "timetable" rather than 'protocol'. Refer to the Ethics Webpage for example http://research.curtin.edu.au/guides/Consent.cfm;
    b. Please ensure that the Consent Form is a separate document for the participant to sign their consent as the Participant Information Sheet should be kept by the participants;
    c. Contact details of the researchers must be included;
    d. The following standard statement must be included;

This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number HR38/2011). The committee is comprised of members of the public, academics, lawyers, doctors, and pastoral carers. Its main role is to protect participants. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing *hrec@curtin.edu.au*.

Please ensure that all documentation to be provided to the participants has the correct Curtin University logo. Refer to the Curtin Brand website http://brand-staff.curtin.edu.au/index.cfm.

Please proof read all documents to be provided to participants for typographical and grammatical errors;

5. Question (xi), Page 7 – please amend to read as Papua New Guinea National Department of Health.

Please do not commence your research until your response to the above conditions has been approved and final clearance has been granted by the Human Research Ethics Committee.

Please note the following:

- Reference Number: HR 38/2011. Please quote this number in any future correspondence.
- The following standard statement must be included in the information sheet to participants:

This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number HR38/2011). The Committee is comprised of members of the public, academics, lawyers, doctors, and pastoral carers. Its main role is to protect the participants. If needed, verification of approval cab be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing *hrec@curtin.edu.au*.

- It is the policy of the HREC to conduct random audits on a percentage of approved projects.

These audits may be conducted at any time after the project starts. In cases where the HREC considers that there may be a risk of adverse events, or where participants may be especially vulnerable, the HREC may request the chief investigator to provide an outcomes report, including information on the follow-up of participants.

Regards,

Miss Linda Teasdale

Manager, Research Ethics

Appendix 2: Response to conditions set by HREC, Curtin University

Memorandum

To: The HREC, Office of Research and Development

From: Stella Tulo, PhD candidate, School of Pharmacy

Subject: Response to conditions set by HREC on application number HR 38/2011

Date: 23 May 2011

I write in response to the conditions set by the HREC on the application submitted to the committee for the research project titled "Glycaemic Effects of Betel Nut chewing in Type 2 Diabetes Mellitus". My response is according to the conditions set by the committee.

1. **Clarification on who will be collecting blood sample.**
   Blood sample collection will be done by finger prick for capillary blood test. For Phase 1, finger pricking and HbA1c testing will be done by the registered nurses as part of routine patient checks at the Diabetes clinic. For Phase 2, I will do the finger pricking for capillary blood tests and I will do the blood sugar measurements using a glucose meter. I will receive training for finger pricks and blood sugar measurements from the registered nurses during phase 1 of the study.
2. **Explanation on why there is only one day cessation of betel nut chewing for the study**
   One day cessation should be sufficient to show any immediate effects of "no betel nut" whilst diet is standardised for participants. Betel nut effect is short lived. A study in humans has shown that the half-life of arecoline, the major constituent in betel nut, is 0.95+-0.54 minutes and the clearance is 13.6+-4.5 L/min. Based on this data it is predicted that arecoline would clear the system in minutes.
3. **Justification for not having a control group**
   The participants will serve as their own controls because the primary interest is the change in BSL within an individual rather than between individuals. Diet will be standardised, names of medications and dosage times will be recorded during the study days to assess compliance. The doses of betel nut will not be standardised on day 1, rather will represent the individual's normal usage pattern. Data will be pooled to see if there is a population effect.
4. **Participant information sheets (Phase 1 and Phase 2) amendments**

a. Language has been simplified (participant information sheets for Phase 1 and 2 are attached)
b. Consent form (attached) has been separated. The same consent form will be used for both Phase 1 and Phase 2
c. Contact details of all investigators have been added on the participant information sheets
d. The HREC approval statement has been added to the participant information sheets
e. Curtin logo has been inserted on the participant information sheets and the consent form
f. All documents to be provided to participants have been proof read.

5. **Question (xi), page 7 which reads PNG Department of Health to read as Papua New Guinea National Department of Health**

   The amendment has been done. See the HREC application form.

Regards,

Stella Tulo

Appendix 3: Final ethical clearance, HREC, Curtin University

Memorandum Office of Research and Development
Human Research Ethics Committee

TELEPHONE 9266 2784
FACSIMILE 9266 3793
EMAILhrec@curtin.edu.au

To	Professor Jeffery Hughes, School of Pharmacy
From	A/Professor Stephen Millett, Chair, Human Research Ethics
Subject	Protocol Approval HR 38/2011
Date	30 May 2011
Copy	Mrs Stella Tilu Tulo, School of Pharmacy Dr Lloyd Ipai, Diabetes Consultant (Port Moresby General Hospital), School of Pharmacy

Thank you for providing the additional information for the project titled *"Glycaemic Effects of Betel Nut chewing in type 2 Diabetes Mellitus"*. The information you have provided has satisfactorily addressed the queries raised by the Committee. Your application is now approved.

- You have ethics clearance to undertake the research as stated in your proposal.
- The approval number for your project is HR 38/2011. Please quote this number in any future correspondence.
- Approval for this project is for a period of twelve months 30-05-2011 to 29-05-2012. To renew this approval a completed Form B (attached) must be submitted before the expiry date 29-05-2012.
- If you are a Higher Degree by Research student, data collection must not begin before your Application for Candidacy is approved by your Faculty Graduate Studies Committee.
- The following standard statement must be included in the information sheet to participants:

This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number HR38/2011). The committee is comprised of members of the public, academics, lawyers, doctors, and pastoral carers. Its main role is to protect participants. If needed, verification of approval can be obtained either by writing to the Curtin University

Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing *hrec@curtin.edu.au*.

Applicants should note the following:

It is the policy of the HREC to conduct random audits on a percentage of approved projects. These audits may be conducted at any time after the project starts. In cases where the HREC considers that there may be a risk of adverse events, or where participants may be especially vulnerable, the HREC may request the chief investigator to provide an outcomes report, including information on the follow-up of participants.

The attached FORM B should be completed and returned to the Secretary, HREC, C/- Office of Research & Development:

When the project has finished, or

- If at any time during the twelve months changes/amendments occur, or
- If a serious or unexpected adverse event occurs, or
- 14 days prior to the expiry date if renewal is required.
- An application for renewal may be made with a Form B three years running, after which a new application form (Form A), providing comprehensive details, must be submitted.

Regards,

A/Professor Stephen Millett

Chairman Human Research Ethics Committee

Appendix 4: Ethical clearance, University of PNG

UNIVERSITY OF PAPUA NEW GUINEA
SCHOOL OF MEDICINE AND HEALTH SCIENCES
DIVISION OF CLINICAL SCIENCES

UPNG TAURAMA FAX NO. 325 0809
P.O.BOX 5623 TEL. NO. 311 2626 / 325 3340
BOROKO, NCD, PAPUA NEW GUINEA

5TH October 2010

Ms. Stella Pihau-Tulo
School of Pharmacy
Curtin University of Technology
Western Australia

Dear Stella

SUBJECT: ETHICAL CLEARNACE FOR YOUR RESEARCH PROPOSAL ON "GLYCAEMIC EFFECTS OF BETEL NUT CHEWING IN TYPE 2 DIABETES MELLITUS"

Thank you for submitting this Research proposal for Ethical Clearance, which is important because this project will ultimately involve patients at Port Moresby General Hospital, Papua New Guinea. Therefore, the details of this project need to be reviewed by the SM&HS Research and Ethics Committee.

Having read through the Research Proposal, I found it was well thought out and well written. Due to the delays you are facing on approval at Curtin University, I am in my capacity as Chairman of the SM&HS Research and Ethics Committee, and on behalf of the Committee ethically clear and approve this study so that you can do your data collection here in PNG.

I will inform our next SMHS Research and Ethics Committee about my administrative clearance for formal record keeping only.

Yours sincerely

Professor Nakapi Tefuarani

Chairman

SM&HS Research and Ethics Committee

Cc: Dr. J.A.K Lauwo, Head, Pharmacy Discipline

Appendix 5: Ethical clearance, the Medical Research Advisory Committee, NDOH, PNG

Government of Papua New Guinea
Medical Research Advisory Committee
National Department of Health

Po Box 807
WAIGANI 131, NCD
Papua New Guinea

Phone: + (675) 3013650
Fax: + (675) 325 1825
Email: urarang_kitur@ health/gov.pg

File: 54-6-2

Date: 22/02/2012

Mrs Stella Tulo
School Of Pharmacy
GPO Box U1987
Curtin University
Western Australia

Dear Ms Tulo

This is to certify that the proposal:

Glycaemic effects of betel nut chewing in Type 2 Diabetes Mellitus

Submitted by you and your colleagues has been examined by the Medical Research Advisory Committee of Papua New Guinea and assigned MRAC No.11.29

Your proposal was initially not approved because your research proposal was incomplete in that a proper comprehensive literature review and referencing was not done. The MRAC is satisfied with your literature recview and and give you clearance to conduct your research.

The MRAC of PNG acts as the National Ethical Clearance Committee and as the Institutional ethical committee for the PNG Institute of Medical Research.

Investigators are reminded of the importance of keeping provincial health and research authorities informed on their study and its progress, and of submitting annual progress and outcome reports to the MRAC.

With best wishes

Dr Urarang Kitur

Chairperson

Appendix 6: Participant information sheet – Phase 1

Curtin University

School of Pharmacy

Participant Information Sheet (Phase 1)

Title of Study: Glycaemic Effects of Betel Nut chewing in Type 2 Diabetes Mellitus

My name is Stella Tulo. I am currently completing a piece of research for my Degree of Doctor of Philosophy in Pharmacy at Curtin University in Perth, Western Australia.

Purpose of Research

I am investigating the effect of betel nut chewing on blood sugar levels of people with type 2 diabetes.

Your role

I am interested in finding out if betel nut affects blood sugar levels. I will ask you questions about your:

- Age
- Education
- Employment
- Tobacco, alcohol and betel nut use
- Fruit and vegetable intake
- Physical activity
- History of diabetes and medicines management.

The interview process will take about **10-15** minutes

Other information I will collect

I will also collect information about you from your clinic notes. The information I will collect will be your:

- Height
- Weight
- Waist and hip circumference
- Blood pressure
- Sugar and fat levels in your blood

Consent to Participate

Your involvement in the research is entirely voluntary. You have the right to withdraw at any stage without it affecting your rights or your care. When you have signed the consent form I will assume that you have agreed to participate and allow me to use your data in this research.

Your rights

It is your right to:

- Decline to take part in the study
- Withdraw your consent at any time
- Decline to answer any questions in the interview that you do not wish to answer

If you decide not to participate in this study, this will not affect your continued management at the diabetes clinic.

Confidentiality

I will write down your name and contact information so that I can contact you if there is any need to follow up with you after the face to face interview is conducted.

Your participation and the information you provide will be kept separate from your personal details, and only myself and my supervisors will have access to this. The interview transcript will not have your name or any other identifying information on it and in adherence to university policy, the interview information will be kept in a locked cabinet for at least 5 years, before a decision is made as to whether it should be destroyed.

Community Benefits

The results of this study will help find out if betel nut affects blood sugar levels in patients with type 2 diabetes. If betel nut is found to affect blood sugar levels, then those with type 2 diabetes will be given appropriate advice. The PNG Department of Health may also use the results of the study in public health programs aimed at reducing development of diabetes and improving blood sugar levels in patients with type 2 diabetes.

Ethical approval

This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number HR38/2011). The committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. Its main role is to protect participants. If needed, verification of approval can be obtained either by writing to the Curtin University Human research Ethics Committee, C/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing hrec@curtin.edu.au

Further information

If you would like further information about the study, please feel free to contact me on 7685 8965 (mobile), 311 2626 (office) or By email sptulo@gmail.com. You can also contact my two supervisors:

1. Professor Jeffery Hughes on +61 8 9266 7369 or J.D.Hughes@curtin.edu.au
2. Dr Lloyd Ipai on 324 8200

Thank you very much for your involvement in this research.
Your participation is greatly appreciated

Appendix 7: Consent form – Phase 1 and Phase 2

School of Pharmacy

Consent Form (Phase 1)

Title of Study: Glycaemic Effects of betel nut in Type 2 Diabetes Mellitus

Investigators: Professor Jeffery Hughes, Dr Lloyd Ipai, Mrs Stella Tulo

- I understand the purpose and procedures of the study
- I have been provided with the participation information sheet
- I understand that the procedure itself may not benefit me
- I understand that my involvement is voluntary and I can withdraw at any time without problem
- I understand that no personal identifying information like my name and address will be used in any published materials
- I understand that all information will be securely stored for at least 5 years before a decision is made as to whether it should be destroyed
- I have been given the opportunity to ask questions about this research
- I agree to take part in the study outlined to me

Name: _____

Signature: _____ Date: _____

Witness: _____

Signature: _____ Date: _____

Appendix 8: Questionnaire for T2DM cross-sectional study (Phase 1)

GLYCAEMIC EFFECTS OF BETEL NUT IN TYPE 2 DIABETES MELLITUS

Participant ID……..
Time of interview……
Date……

1. Family Name……. First Name…….
2. Contact phone number: Home…….
Work……. Mobile…….

PART 1: DEMOGRAPHIC INFORMATION

3. Gender: Male □ Female □2
4. Date of birth: ..... Age in Years: .....
5. Place of origin: District……. Province…….
6. Suburb of residence……
7. If you were not born in Port Moresby, how many years ago did you move here?

No of years

8. Highest level of education completed
   a. No formal schooling…… □1
   b. Less than Grade 6…… □2
   c. Completed Grade 6…….. □3
   d. Completed Grade 8…….. □4
   e. Completed Grade 10…… □5
   f. Vocational training…… □6
   g. Completed Grade 12…… □7
   h. Completed tertiary education…… □8
9. Employment
   a. Government employee…… □1
   b. Non-government employee…… □2
   c. Self-employed…… □3
   d. Non-paid…… □4
   e. Student…… □5
   f. Homemaker…… □6
   g. Retired…… □7
   h. Unemployed (able to work)…… □8
   i. Unemployed (unable to work)..... □9

PART II: BEHAVIOURAL MEASUREMENTS

Now I am going to ask you some questions about various health behaviours. This includes things like smoking, chewing betel nut, drinking alcohol, eating fruits and vegetables, and physical activity. Let's start with tobacco.

10. Do you currently smoke any tobacco products, such as cigarettes, cigars or pipes? [If 'no' go to q15]

Yes □1 No □2

11. If yes, do you currently smoke tobacco products daily?

Yes □1 No □2

12. How old were you when you first started smoking daily?

Age (years)

13. Do you remember how long ago it was?

Number (years)

Number (months)

14. On average, how many of the following do you smoke each day?

Manufactured cigarettes

Hand-rolled cigarettes

Pipes full of tobacco

15. In the past, did you ever smoke daily? [If 'no' go to q17]

Yes □1 No □2

16. If yes, how old were you when you stopped smoking?

Age (years)

17. Do you chew betel nut? [If no, go to question 19]

Yes □1 No □2

18. If yes,

a. How many nuts do you chew per day?

Number of nuts/day

b. How many nuts do you chew each time you chew betel nut?

Number

c. When did you start chewing betel nut?

Age (years)

d. Do you chew betel nut with lime and mustard?

Yes □1 No □2

19. If no,

a. In the past did you ever chew betel nut? [If 'no' go to q20]

Yes □1 No □2

b. When did you start chewing betel nut?

Age (years)

c. When did you stop chewing betel nut?

In years

In months

In weeks

d. Did you chew betel nut with lime and mustard?

Yes □1 No □2

ALCOHOL CONSUMPTION: The next questions ask about consumption of alcohol

20. Have you consumed alcohol (beer, wine, spirits, homebrew) within the past 3 months? .
[If 'no' go to q29]

Yes □1 No □2

21. In the past 3 months, how frequently do you drink at least one drink?

a. Daily □1
b. 5-6 per week □2
c. 1-4 days per week □3
d. 1-3 days per month □4
e. Less than once a month □5

22. When you drink alcohol, on average, how many drinks do you drink at any one time/during one day?

Number

23. During each of the past 7 days, how many standard drinks of any alcoholic drink did you have each day?

a. Monday

b. Tuesday

c. Wednesday

d. Thursday

e. Friday

f. Saturday

g. Sunday

24. Have you consumed alcohol (such as beer, wine, spirits, homebrew) within the past 30 days?

Yes □1 No □2

25. In the past 3 months, what was the largest number of drinks you had on a single occasion, counting all types of standard drinks together?

Largest Number

26. For men only: In the past 3 months, on how many days did you have five or more standard drinks in a single day?

Number of days

27. For women only: In the past 3 months, on how many days did you have four or more standard drinks in a single day?

Number of days

28. Where do you get most of your alcoholic drinks from? Choose one only.

a. I buy from the store □1
b. Friends and relatives give me □2
c. Homebrew □3

DIET. The next questions ask about the fruits and vegetables that you usually eat. I have a nutrition card here that shows you some examples of local fruits and vegetables. Each picture represents the size of a serving. As you answer these questions please think of a typical week in the last 3 months

29. In a typical week, on how many days do you eat fruit?

Number of days

30. How many servings of fruit do you eat on one of those days?

Number of servings

31. In a typical week, on how many days do you eat vegetables?

Number of days per week

32. How many servings of vegetables do you eat on one of those days?

Number of servings

PHYSICAL ACTIVITY. *Next I am going to ask you about the time you spend doing different types of physical activity in a typical week. Please answer these questions even if you do not consider yourself to be a physically active person. Think first about the time you spend doing work. Think of work as the things that you have to do such as paid or unpaid work, study/training, household chores, planting, tending and harvesting food/crops, fishing or hunting for food, marketing, seeking employment. In answering the following questions 'vigorous-intensity activities' are activities that require hard physical effort and cause large increases in breathing or heart rate; 'moderate-intensity activities' are activities that require moderate physical effort and cause small increases in breathing or heart rate.*

33. Does your work involve vigorous intensity activity that causes large increases in breathing or heart rate like carrying or lifting heavy loads, digging or construction work for at least 10 minutes continuously?

Yes □1 No □2

34. In a typical week, on how many days do you do vigorous-intensity activities as part of your work?

Number of days per week

35. How much time do you spend doing vigorous-intensity activities at work on a typical day?

Hours

Minutes

36. Does your work involve moderate-intensity activity that increases in breathing or heart rate such as brisk walking (or carrying light loads) for at least 10 minutes continuously?

Yes □1 No □2

37. In a typical week, on how many days do you do moderate-intensity activities as part of your work?

Number of days

38. How much time do you spend doing moderate-intensity activities at work on a typical day?

Hours

Minutes

39. Do you walk or use a bicycle for at least 10 minutes continuously to get to and from places?

Yes □1 No □2

40. In a typical week, on how many days do you walk or bicycle for at least 10 minutes continuously to get to and from places?

Number of days per week

41. How much time do you spend walking or bicycling for travel on a typical day?

Hours

Minutes

42. Do you do any vigorous-intensity sports, fitness or recreational activities that cause large increases in breathing or heart rate, like running or football or basketball for at least 10 minutes continuously?

Yes □1 No □2

43. In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational activities?

Number of days

44. How much time do you spend doing vigorous-intensity sports, fitness or recreational activities on a typical day?

Hours

Minutes

45. Do you do any moderate intensity sports, fitness or recreational activities that causes a small increase in breathing or heart rate (such as brisk walking, cycling, swimming, volleyball) for at least 10 minutes continuously?

Yes □1 No □2

46. In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational activities?

Number of days

47. How much time do you spend doing moderate-intensity sports, fitness or recreational activities on a typical day?

Hours

Minutes

DIABETES AND MEDICATION MANAGEMENT. Now I am going to ask you questions about diabetes and how you have been using your medicines.

48. In what year were you diagnosed with diabetes?

Year

49. When you were diagnosed with diabetes for the first time, how was your diabetes initially managed?

a. Insulin (Injections) □1
b. Oral medicines □2
c. Special prescribed diet □3
d. Advice or treatment to lose weight □4
e. Advice or treatment to stop smoking □5
f. Advice to start or do more exercise □6
g. Other forms of management List

_____
_____
_____
_____

50. For the last 3 months, what management have you been using for your diabetes?

i. insulin (Injections) □1
ii. Oral medicines □2
iii. Special prescribed diet □3
iv. Treatment to lose weight □4
v. Treatment to stop smoking □5
vi. Exercise □6
vii. Other. List

_____
_____
_____

51. Name of medicines and doses

a. Insulin
   i. Insulin type…….
   ii. Doses per day

Number of units; dose 1

Number of units; dose 2

Number of units; dose 3

Number of units; dose 4

b. Glibenclamide

Strength of tablets

mg

Number of tablets per dose

Number

Doses per day

Number of times

c. Metformin

Strength of tablets

mg

Number of tablets per dose

Number

Doses per day

Number of times

d. Other medicines you are taking including doses [including herbal medicines, if names known]

i._____
ii._____
iii._____
iv._____
v._____

52. Have you ever missed a dose of any of your diabetes medicines in the last 3 months? [If no, go to 54]

Yes □1 No □2

53. If yes, try and think back for the last 3 months.

a. How many times have you missed a dose in the last 3 months?

Number of times

b. Think back of a typical month in the last 3 months. In that month, how often did you miss a dose?

i. Daily □1
ii. Weekly □2
iii. Monthly □3

54. What were the reasons for missing your dose?

i. Forgot □1
ii. Ran out of medicine □2
iii. Did not want to take medicine □3
iv. Other reasons. List

_____
_____
_____

PART III: PHYSICAL MEASUREMENTS

55. Height

centimetres

56. Weight

kilograms

57. Waist circumference

Centimetres

58. Hip circumference

Centimetres

59 Blood pressure

Systolic (mmHg)

Diastolic (mmHg)

PART IV: BIOCHEMICAL MEASUREMENTS

No.	Date	Parameter	Measurement
60		Fasting Blood glucose	
61		Glycosylated Hb	
62		Total cholesterol	
63		Triglycerides	
64		LDL	
65		HDL	
66		Urea	
67		Creatinine	
68		Protein (urine)	
69		Glucose (urine)	

Appendix 9: Examples of show cards used during interview

Diet (Typical Fruit and Vegetables and Serving Sizes)

For use with This show card relates to:

Step	Section	Items
Step 1, diet	D	D1 to D4

VEGETABLES are considered to be:	1 Serving =	Examples
Raw green leafy vegetables	1 cup	Spinach, salad, etc.
Other vegetables, cooked or chopped raw	½ cup	Tomatoes, carrots, pumpkin, corn, Chinese cabbage, fresh beans, onion, etc. 
Vegetable juice	½ cup	

FRUIT Is considered to be:	1 Serving =	Examples
Apple, banana, orange	1 medium size piece	
Chopped, cooked, canned fruit	½ cup	
Fruit juice	½ cup	Juice from fruit, not artificially flavoured

Serving size One standard serving = 80 grams (translated into different units of cups depending on type of vegetable and standard cup measures available in the country).

Note: Tubers such as potatoes and cassava should not be included.

Alcohol Consumption

For use with This show card relates to:

Step	Section	Items
Step 1, alcohol consumption	A	A1 to A9a-g

1 standard drink =

1 standard bottle of **regular beer** (285ml)

1 single measure of **spirits** (30ml)

1 medium size glass of wine (120ml)

1 measure of **aperitif** (60ml)

Note: net alcohol content of a **standard drink is approximately 10g** of ethanol. However, standard drinks in different countries can contain different amounts of ethanol. Therefore, countries may have to adapt this measure according to their own standards and will report this measure if different from the standard mentioned above.

List of Work Status

For use with This show card relates to:

Step	Section	Items
Step 1, demographic information	C	C8

Work Status	Description
Government employee	An individual who is hired by a government office or agency and paid a salary. This includes employees of: • Federal • State, or • Municipal governments and their agencies. • Parastatal enterprises, and • Semi-autonomous institutions (such as social security institutions) that are owned by the government. • Institutions like religious schools (if paid by the government).
Non-government employee	An individual who is hired to work and is paid a salary or wages. This includes any employees not working for the government.
Self-employed	An individual who produces goods for sale or earns an income through provision of services to different people or firms. The individual works alone or with intermittent assistance from others, but does not employ anyone for a paid wage or salary on a regular basis.
Non-paid - subsistence farming etc	An individual who spends significant amount of time working for a volunteer organization, family business, family farm or other similar activity without pay.
Student	An individual whose primary activity is engaging in studies at elementary, secondary, university or technical schools.
Homemaker (household chores)	An individual whose primary activity is in carrying out household tasks without being paid.
Retired	An individual who has earned income during some period in the workforce or as an employer and who is no longer working due to age.
Unemployed - able to work	An individual who could work but does not currently have a job or business (excluding homemaker).
Unemployed - unable to work	An individual who cannot work because of his/her health status.

Typical Physical Activities

For use with This show card relates to:

Step	Section	Items
Step 1, physical activity	P	P to P15

WORK RELATED PHYSICAL ACTIVITY		LEISURE/ SPARE TIME RELATED PHYSICAL ACTIVITY	
MODERATE Intensity Activities Makes you breathe somewhat harder than normal	**VIGOROUS Intensity Activities** Makes you breathe much harder than normal	**MODERATE Intensity Activities** Makes you breathe somewhat harder than normal	**VIGOROUS Intensity Activities** Makes you breathe much harder than normal
Examples: • Cleaning (vacuuming, mopping, polishing, scrubbing, sweeping, ironing) • Washing (beating and brushing carpets, wringing clothes (by hand) • Gardening • Milking cows (by hand) • Planting and harvesting crops • Digging dry soil (with spade) • Weaving • Woodwork (chiselling, sawing softwood) • Mixing cement (with shovel) • Labouring (pushing loaded wheelbarrow, operating jackhammer) • Walking with load on head • Drawing water • Tending animals	**Examples:** • Forestry (cutting, chopping, carrying wood) • Sawing hardwood • Ploughing • Cutting crops (sugar cane) • Gardening (digging) • Grinding (with pestle) • Labouring (shovelling sand) • Loading furniture (stoves, fridge) • Instructing spinning (fitness) • Instructing sports aerobics • Sorting postal parcels (fast pace) • Cycle rickshaw driving	**Examples:** • Cycling • Jogging • Dancing • Horse-riding • Tai chi • Yoga • Pilates • Low-impact aerobics • Cricket	**Examples** • Soccer • Rugby • Tennis • High-impact aerobics • Aqua aerobics • Ballet dancing • Fast swimming

Appendix 10: Participant information sheet – Phase 2

Curtin University

School of Pharmacy

Participant Information Sheet (Phase 2)

Study title: Glycaemic Effects of Betel Nut chewing in Type 2 Diabetes Mellitus

My name is Stella Tulo. I am currently completing a piece of research for my Degree of Doctor of Philosophy in Pharmacy at Curtin University in Perth, Western Australia.

Purpose of Research

I am investigating the effect of betel nut chewing on blood sugar levels in people with type 2 diabetes.

What is Involved

I would like to collect information from a minimum of 120 patients who participated in phase 1 of the study. The place where the study will take place is The School Of Medicine & Health Sciences (Medfac)

If you are willing to stop chewing betel nut for about 15 hours I would like you to participate in this study. I will collect information for this part of the study over 2 days.

Day 1

- On this day all participants will continue chewing betel nut.
- I will ask you to stop chewing betel nut and stop eating by 12 midnight before the study day
- I will ask you to arrive at the study place before 7.30 in the morning.
- When you arrive at the study place, I will take a very small amount of blood by finger prick to measure your blood sugar level.
- After I measure your blood sugar , I will give you a packed breakfast at 8.00am
- I will measure your blood sugar at regular time intervals at 9am, 10am, 11am
- At 12 noon I will give you a packed lunch and I will measure your blood glucose again at 1pm, 2pm and 3pm.
- On this day, whenever you want to chew betel nut, I will record the time you put the betel nut in your mouth. When you want to chew betel nut, I would like you to let me know so that I can record the way you chew betel nut.

- I will measure your blood sugar before you chew betel nut and again after you swallow the betel nut.

Day 2

- I will aske all participants to stop chewing betel nut
- I will ask you to come in for Day 2 on a day that suits you.
- The timetable will be the same as in Day 1
- I will measure your blood sugar every hour as in day 1

Important Information

During this study you will still take your medicines as directed
I will discuss with you when you want to come in for the study and whether or not you will need transport.

I will organise activities for you at the school during the period of study.

Timeframe

The study will require you to be at the School Of Medicine & Health Sciences from about 7.30am till 3.00pm.

Consent to Participate

Your involvement in the research is entirely voluntary. You have the right to withdraw at any stage without it affecting your rights or your care. When you have signed the consent form I will assume that you have agreed to participate and allow me to use your data in this research.

Your rights

It is your right to:

- Decline to take part in the study
- Withdraw your consent at any time
- Decline to answer any questions in the interview that you do not wish to answer

If you decide not to participate in this study, this will not affect your continued management at the diabetes clinic.

Confidentiality

I will write down your name and contact information so that I can contact you if there is any need to follow up with you after the face to face interview is conducted

Your participation and the information you provide will be kept separate from your personal details, and only myself and my supervisors will have access to this. The interview transcript will not have your name or any other identifying information on it and in adherence to university policy, the interview information will be kept in a locked cabinet for at least 5 years, before a decision is made as to whether it should be destroyed

Community Benefits

The results of this study will help find out if betel nut affects blood sugar level in patients with type 2 diabetes. If betel nut is found to affect blood sugar levels, then those with type 2 diabetes will be given appropriate advice. The PNG Department of Health may also use the results of the study in public health programs aimed at reducing development of diabetes and improving blood sugar levels in patients with type 2 diabetes.

Ethical Approval

This study has been approved by the Curtin University Human research Ethics Committee (Approval Number HR38/2011). The committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. Its main role is to protect participants. If needed, verification of approval can be obtained either by writing to the Curtin University Human research Ethics Committee, C/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing hrec@curtin.edu.au

Further information

If you would like further information about the study, please feel free to contact me on 7685 8965 (mobile), 311 2626 (office) or by email sptulo@gmail.com. You can also contact my two supervisors:

1. Professor Jeffery Hughes on +61 8 9266 7369 or J.D.Hughes@curtin.edu.au
2. Dr Lloyd Ipai on 324 8200

Thank you very much for your involvement in this research.
Your participation is greatly appreciated

Appendix 11: Data collection sheet, clinical study (Phase 2)

GLYCAEMIC EFFECTS OF BETEL NUT IN TYPE 2 DIABETES MELLITUS - Phase 2: Clinical Study

DAY 1- Betel nut chewing day

Participant ID……
Date……

Time chewed betel nut before midnight ……
Time of measurement……

Fasting BSL before breakfast……

BSL measurements:

Morning	Afternoon
9.30am……	12.30pm……
10.30am……	1.30pm……
11.30am……	2.30pm……
	3.30pm……

Observations: (E.g. symptoms of hypoglycaemia, symptoms of betel nut withdrawal)

Description of symptom(s)

……

……

Time of event…… BSL at time of event……..

Action(s) taken

……

……

Medication times

Diabetes Medication	Time(s) taken
Glibenclamide……	
Metformin……	
Other medications	
1……	
2……	
3……	
4……	

Meal times

Breakfast……

Lunch……

DAY 2- No betel nut chewing

Participant ID…… Date……

Time chewed betel nut before midnight……

Fasting BSL before breakfast……

BSL (hourly) measurements:

Morning	Afternoon
9.30am……	12.30pm……
10.30am……	1.30pm……
11.30am……	2.30pm……
	3.30pm……

Observations: (E.g. symptoms of hypoglycaemia, symptoms of betel nut withdrawal)

Description of symptom(s)

……

……

Time of event…… BSL at time of event……

Action(s) taken:

……

……

……

Medication times

Diabetes medicines	Time(s) taken
Glibenclamide……	
Metformin……	
Other medicines	
1……	
2……	
3……	
4……	

Meal times

Breakfast……

Lunch……

BETEL NUT CHEWING ACTIVITY RECORD SHEET

Participant ID…… Date……

BETEL NUT CHEWING ACTIVITY RECORD SHEET

Participant ID…… **Date……**

No.	BSL before betel nut chewing		Time participant started chewing betel nut	BSL 5-10 minutes after swallowing or spitting out betel nut		No. of nuts Chewed	Other constituents (√)		Chewing habit (√)				Time betel nut chew swallowed or spat out
	Time BSL done	BSL reading		Time BSL done	BSL reading		Lime	PBL -(Daka leaf) PBI (Daka)	Betel juice swallowed	Betel juice spat out	Betel nut swallowed	Betel nut spat out	
1													
2													
3													
4													
5													
6													
7													
8													
9													
10													
11													
12													
13													
14													
15													

Appendix 12: Standard meals for clinical study (Phase 2)

BREAKFAST

3 slices of wholegrain bread

1 boiled egg

¼ teaspoon margarine

1 cup lady grey tea (medium black)

LUNCH

1/3 cup boiled brown rice

2 small unripe plantain bananas (approx. 100g each)

100g chicken breast (no skin, no fat)

1 cup steamed carrots and broccoli

Water (available throughout the study)

Appendix 13: STEPS survey instrument for Papua New Guinea

STEPS Instrument for 2007 Papua New Guinea Non-Communicable Diseases Risk Factor Survey
Version 2.0

HOPE *worldwide* (PNG)
PO Box 3478, Boroko, NCD, Papua New Guinea

Contact Graham Ogle Graham_Ogle@hopeww.org, tel 61 2 9868 1980, or Augustine Kose akose@datec.com.pg, tel. 675 325 6901

Part of the WHO STEPwise approach to Surveillance of noncommunicable diseases (STEPS)

Modified from the WPRO Steps Instrument for NCD Risk Factors, (Core and Expanded Version 2.0) from Noncommunicable Diseases and Mental Health,
World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland

WHO STEPS Instrument for Chronic Disease

Risk Factor Surveillance

<Papua New Guinea>

Survey Information

Location and Date		Response	Code
1	District code	⌊__⌋	I1
2	Centre/Village name		I2
3	Centre/Village code	⌊__⌋	I3
4	Interviewer Identification	⌊__⌋	I4
5	Date of completion of the instrument	⌊__⌋ ⌊__⌋ ⌊__⌋ dd mm year	I5

✂ ----------

Participant Id Number ⌊__⌋

Consent, Interview Language and Name		Response	Code
6	Consent has been read out to participant	Yes 1 No 2 **If NO, read consent**	I6
7	Consent has been obtained (verbal or written)	Yes 1 No 2 **If NO, END**	I7
8	Interview Language	English 1, Tok Pisin 2, Motu 3, Golin 4, Gulf tokples 5, Manus tokples 6, Mamose tokples 7, Other 8	I8
9	Time of interview (24 hour clock)	⌊__⌋ : ⌊__⌋ hrs mins	I9
10	Family Name		I10
11	First Name		I11
12	Contact phone number where possible		I12
13	Specify whose phone	Work 1 Home 2 Relative/ / Other 3	I13

Record and file identification information (I6 to I13) separately from the completed questionnaire.

Step 1 Demographic Information

Questions		Response		Code
14	Sex (*Record Male / Female as observed*)	Male 1 Female 2		C1
15	What is your date of birth? *Don't Know 77 77 7777*	⌊_⌋⌊_⌋ ⌊_⌋⌊_⌋ ⌊_⌋⌊_⌋⌊_⌋⌊_⌋ *If known, go to C4* dd mm year		C2
16	How old are you?	Years	⌊_⌋⌊_⌋	C3
17	In total, how many years have you spent at school or in full-time study (excluding pre-school)?	Years	⌊_⌋⌊_⌋	C4
18	What is your tribal group?	Simbu, EHP, WHP, Enga SHP Central, Motu-Koitaban NCD Gulf Milne Bay, Oro Morobe, Madang, East and West Sepik Manus NIP, ENBP, WNBP, Other – eg expat, Irian Jaya Refused	1 2 3 4 5 6 7 8 9 77	C5
19	What is the highest level of education you have completed?	No formal schooling Less than Grade 6 Grade 6 completed Grade 8 completed Grade 10 or vocational training completed Grade 12 completed University degree completed Refused	1 2 3 4 5 6 7 8	C6
20	Which of the following best describes your main work status over the last 12 months? *(USE SHOWCARD)*	Government employee Non-government employee Self-employed Non-paid Student Homemaker Retired Unemployed (able to work) Unemployed (unable to work) Refused	1 2 3 4 5 6 7 8 9 77	C7
21	How many people older than 18 years, including yourself, live in your household?	Number of people	⌊_⌋⌊_⌋	C8
22	Does your household have electricity?	Yes No	1 2	X1

23	Does your household have a refrigerator?	Yes 1 No 2	X2
24	Does your household have a car kept at the house overnight?	Yes 1 No 2	X3
25	If you were not born in the district where the study is being done, how many years ago did you move there?	Years ⌊_⌋⌊_⌋	X4

Step 1 Behavioural Measurements

Tobacco Use

Now I am going to ask you some questions about various health behaviours. This includes things like smoking, drinking alcohol, eating fruits and vegetables and physical activity. Let's start with tobacco.

Questions		Response	Code
26	Do you currently smoke any **tobacco products**, such as cigarettes, cigars or pipes?	Yes 1 No 2 *If No, go to T6*	T1
27	**If Yes,** Do you currently smoke tobacco products **daily**?	Yes 1 No 2 *If No, go to T6*	T2
28	How old were you when you **first started** smoking daily?	Age (years) ⌊_⌋⌊_⌋ *If Known,* Don't remember 77 *go to T5a*	T3
29	Do you remember how long ago it was? *(RECORD ONLY 1, NOT ALL 3)* Don't remember 77	In Years ⌊_⌋⌊_⌋ *If Known, go to T5a*	T4a
		OR in Months ⌊_⌋⌊_⌋ *If Known, go to T5a*	T4b
		OR in Weeks ⌊_⌋⌊_⌋	T4c
30	On average, **how many** of the following do you smoke each day? *(RECORD FOR EACH TYPE)*	Manufactured cigarettes ⌊_⌋⌊_⌋⌊_⌋	T5a
		Hand-rolled cigarettes ⌊_⌋⌊_⌋⌊_⌋	T5b
		Pipes full of tobacco ⌊_⌋⌊_⌋	T5c
31	In the past, did you **ever** smoke **daily**?	Yes 1 No 2 *If No, go to T9*	T6
32	**If Yes,** How old were you when you **stopped** smoking **daily**?	Age (years) ⌊_⌋⌊_⌋ *If* Don't remember 77 *Known, go to T9*	T7
33	How **long ago** did you stop smoking daily? *(RECORD ONLY 1, NOT ALL 3)* Don't remember 77	Years ago ⌊_⌋⌊_⌋ *If Known, go to T9*	T8a
		OR Months ago ⌊_⌋⌊_⌋ *If Known, go to T9*	T8b
		OR Weeks ago ⌊_⌋⌊_⌋	T8c

34	Do you **currently use** any betel nut?	Y 1 N 2 *If No, go to T12*	T9
35	**If yes** *Do you use betel nut daily?*	Yes 1 No 2	T10
36	On average, how many **times do you use betel nut daily?**	Number of nuts ⌊__⌋⌊__⌋	T11 d
37	In the past, did you **ever use** betel nut **daily**? **(Only ask if does not use betel nut now – i.e. answer to T9 was No)**	Yes 1 Go to A1 No 2 Go to A1	T12
38	When you use betel nut, do you also use mustard and lime?	Always 1 Sometimes 2 Rarely 3 Never 4	X5

Alcohol Consumption

The next questions ask about the consumption of alcohol.

	Questions	Response	Code
39	Have you consumed alcohol (such as beer, wine, spirits, home brew) within the **past 12 months**? *(USE SHOWCARD OR SHOW EXAMPLES)*	Yes 1 No 2 *If No, go to D1*	A1
40	In the past 12 months, **how frequently** have you had at least one drink? *(READ RESPONSES USE SHOWCARD)*	Daily 1 5-6 days per week 2 1-4 days per week 3 1-3 days per month 4 Less than once a month 5	A2
41	When you drink alcohol, **on average**, how many drinks do you have during one day? One drink = one beer or beer equivalent	Number ⌊__⌋⌊__⌋ Don't know 77	X6
42	Have you consumed alcohol (such as beer, wine, spirits, home brew) within the **past 30 days**? *(USE SHOWCARD)*	Yes 1 No 2 *If No, go to X8*	A4
43	During each of the **past 7 days**, how many standard drinks of any alcoholic drink did you have each day? *(RECORD FOR EACH DAY USE SHOWCARD)* Don't Know 77	Monday ⌊__⌋⌊__⌋	X7a
		Tuesday ⌊__⌋⌊__⌋	X7b
		Wednesday ⌊__⌋⌊__⌋	X7c
		Thursday ⌊__⌋⌊__⌋	X7d
		Friday ⌊__⌋⌊__⌋	X7e
		Saturday ⌊__⌋⌊__⌋	X7f
		Sunday ⌊__⌋⌊__⌋	X7g

44	In the past 12 months, what was the **largest number** of drinks you had on a single occasion, counting all types of standard drinks together?	Largest number ⌊_⌋⌊_⌋		X8
45	**For men only**: In the past 12 months, on how many days did you have **five or more** standard drinks in a single day?	Number of days ⌊_⌋⌊_⌋⌊_⌋		X9
	For women only: In the past 12 months, on how many days did you have **four or more** standard drinks in a single day?	Number of days ⌊_⌋⌊_⌋⌊_⌋		X10
46	Where do you get most of your alcoholic drinks from? (choose one only)	I buy from store	1	X11
	_____	Friends and relatives give to me	2	
		Home-brew	3	

Diet

The next questions ask about the fruits and vegetables that you usually eat. I have a nutrition card here that shows you some examples of local fruits and vegetables. Each picture represents the size of a serving. As you answer these questions please think of a typical week in the last year.

Questions		Response	Code
47	In a typical week, on how many days do you **eat fruit**? *(USE SHOWCARD)*	Number of days ⌊_⌋ *If Zero days, go to D3* Don't Know 8	D1
48	How many **servings** of fruit do you eat on **one** of those days? *(USE SHOWCARD)*	Number of servings ⌊_⌋⌊_⌋ Don't Know 88	D2
49	In a typical week, on how many days do you **eat vegetables**? *(USE SHOWCARD)*	Number of days ⌊_⌋ *If Zero days, go to P1* Don't Know 8	D3
50	How many **servings** of vegetables do you eat on one of those days? *(USE SHOWCARD)*	Number of servings ⌊_⌋⌊_⌋ Don't Know 88	D4

Physical Activity

Next I am going to ask you about the time you spend doing different types of physical activity in a typical week. Please answer these questions even if you do not consider yourself to be a physically active person.

Think first about the time you spend doing work. Think of work as the things that you have to do such as paid or unpaid work, study/training, household chores, planting, tending and harvesting food/crops, fishing or hunting for food, marketing, seeking employment. In answering the following questions 'vigorous-intensity activities' are activities that require hard physical effort and cause large increases in breathing or heart rate, 'moderate-intensity activities' are activities that require moderate physical effort and cause small increases in breathing or heart rate.

	Questions	Response	Code
Activity at work			
51	Does your work involve vigorous-intensity activity	Yes 1	P1
		No 2 *If No, go to P 4*	
52	In a typical week, on how many days do you do vigorous-intensity activities as part of your work?	Number of days ⌊__⌋	P2
53	How much time do you spend doing vigorous-intensity activities at work on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P3 (a-b)
54	Does your work involve moderate-intensity activity, that causes small increases in breathing or heart rate such as brisk walking *[or carrying light loads]* for at least 10 minutes continuously? *[INSERT EXAMPLES] (USE SHOWCARD)*	Yes 1	P4
		No 2 *If No, go to P 7*	
55	In a typical week, on how many days do you do moderate-intensity activities as part of your work?	Number of days ⌊__⌋	P5
56	How much time do you spend doing moderate-intensity activities at work on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P6 (a-b)
Travel to and from places			
	The next questions exclude the physical activities at work that you have already mentioned. Now I would like to ask you about the usual way you travel to and from places. For example to work, for shopping, to market, to school, or to church		
57	Do you walk or use a bicycle for at least 10 minutes continuously to get to and from places?	Yes 1	P7
		No 2 *If No, go to P 10*	
58	In a typical week, on how many days do you walk or bicycle for at least 10 minutes continuously to get to and from places?	Number of days ⌊__⌋	P8
59	How much time do you spend walking or bicycling for travel on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P9 (a-b)

Recreational activities			
The next questions exclude the work and transport activities that you have already mentioned. Now I would like to ask you about sports, fitness and recreational activities			
60	Do you do any vigorous-intensity sports, fitness or recreational activities that cause large increases in breathing or heart rate - like running or football or basketball - for at least 10 minutes continuously? *(USE SHOWCARD)*	Yes 1 No 2 *If No, go to P 13*	P10
61	In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational activities?	Number of days ⌊__⌋	P11
62	How much time do you spend doing vigorous-intensity sports, fitness or recreational activities on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P12 (a-b)

Physical Activity (recreational activities) contd.			
Questions		**Response**	**Code**
63	Do you do any moderate-intensity sports, fitness or recreational activities that causes a small increase in breathing or heart rate such as brisk walking,(cycling, swimming, volleyball) for at least 10 minutes continuously? *(USE SHOWCARD)*	Yes 1 No 2 *If No, go to H1*	P13
64	In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational activities?	Number of days ⌊__⌋	P14
65	How much time do you spend doing moderate-intensity sports, fitness or recreational activities on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P15 (a-b)

History of Raised Blood Pressure				
Questions		**Response**		**Code**
66	When was your blood pressure last measured by a health professional?	Within past 12 months	1	H1
		1-5 years ago	2	
		Not within past 5 years	3	
67	During the past 12 months have you been told by a doctor or other health worker that you have raised blood pressure or hypertension?	Yes	1	H2
		No	2	
68	Are you currently receiving any of the following treatments for raised blood pressure prescribed by a doctor or other health worker as well as any advice?			
	Drugs (medication) that you have taken in the last 2 weeks	Yes	1	H3a
		No	2	
	Special prescribed diet	Yes	1	H3b
		No	2	
	Advice or treatment to lose weight	Yes	1	H3c
		No	2	
	Advice or treatment to stop smoking	Yes	1	H3d
		No	2	
	Advice to start or do more exercise	Yes	1	H3e
		No	2	
69	During the past 12 months have you seen a traditional healer for raised blood pressure or hypertension	Yes	1	H4
		No	2	
70	Are you currently taking any herbal or traditional remedy for your raised blood pressure?	Yes	1	H5
		No	2	

History of Diabetes				
Questions		**Response**		**Code**
71	Have you had your blood sugar measured in the last 12 months?	Yes	1	H6
		No	2	
72	During the past 12 months, have you ever been told by a doctor or other health worker that you have diabetes?	Yes	1	H7
		No	2	
73	Are you currently receiving any of the following treatments for diabetes prescribed by a doctor or other health worker as well as any advice?			
	Insulin	Yes	1	H8a
		No	2	
	Oral drug (medication) that you have taken in the last 2 weeks	Yes	1	H8b
		No	2	
	Special prescribed diet	Yes	1	H8c
		No	2	
	Advice or treatment to lose weight	Yes	1	H8d
		No	2	
	Advice or treatment to stop smoking	Yes	1	H8e
		No	2	
	Advice to start or do more exercise	Yes	1	H8f
		No	2	
74	During the past 12 months have you seen a traditional healer for diabetes?	Yes	1	H9
		No	2	
75	Are you currently taking any herbal or traditional remedy for your diabetes?	Yes	1	H10
		No	2	

Oral Health				
76	How many natural teeth do you have?	All of them	1	X12
		Some of them, but have lost some	2	
		None of them	3	
77	Do you have any removable dentures?	Yes	1	O3
		No	2	
78	Which of the following removable dentures do you have? (can have more than one)	A partial denture	1	O4
		A full upper denture	2	
		A full lower denture	3	
79	How would you describe the state of your teeth	Excellent	1	O5
		Very good	2	
		Good	3	
		Average	4	
		Poor	5	
		Very poor	6	
		Don't know	7	
80	How often do you clean your teeth?	Never	1	O7
		Once a month	2	
		2 to 3 times a month	3	
		Once a week	4	
		2 to 3 times a week	5	
		Once a day	6	
		Twice a day	7	
81	Which of the following do you use to clean your teeth (circle one only – main method)	Toothbrush alone	1	O8
		Toothbrush with toothpaste	2	
		Wooden toothpicks	3	
		Thread (dental floss)	4	
		Ash	5	
		Betel nut skin or other abrasive leaf	6	
		Sand	7	
		Steel wool	8	
		Other	9	
82	Do you use toothpaste?	Yes	1	O9
		No	2	
83	How long is it since you last saw a dentist?	Less than 6 months	1	O10
		6-12 months	2	
		More than 1 year but less than 2 years	3	
		More than 2 years but less than 5 years	4	
		More than 5 years	5	
		Never received dental care	6	
84	Have you experienced any of the following problems, during the last 12 months, because of the state of your teeth? (may have more than one)	Difficulty in chewing/biting foods	1	O12
		Difficulty in speech / trouble pronouncing words	2	
		Persistent pain	3	
		Embarrassment with others	4	
		None	5	

Step 2 Physical Measurements

Height and Weight		Response		Code
85	Interviewer ID		⌊_⌊_⌊_⌋	M1
86	Device IDs for height and weight	Height	⌊_⌋	M2a
		Weight	⌊_⌋	M2b
87	Height	in Centimetres (cm)	⌊_⌊_⌊_⌋.⌊_⌋	M3
88	Weight *If too large for scale, code 666.6*	in Kilograms (kg)	⌊_⌊_⌊_⌋.⌊_⌋	M4
89	***(For women)*** Are you pregnant?	Yes	*1 If Yes, go to M 8*	M5
		No	2	
Waist and Hip				
90	Device ID for waist and hip		⌊_⌋	M6
91	Waist circumference	in Centimetres (cm)	⌊_⌊_⌊_⌋.⌊_⌋	M7
92	Hip circumference	in Centimetres (cm)	⌊_⌊_⌊_⌋.⌊_⌋	M15
Blood Pressure				
93	Interviewer ID		⌊_⌊_⌊_⌋	M8
94	Device ID for blood pressure		⌊_⌋	M9
95	Cuff size used	Medium	2	M10
		Large	3	
96	Reading 1 (If automatic machine used, record heart rate below as well)	Systolic (mmHg)	⌊_⌊_⌊_⌋	M11a
		Diastolic (mmHg)	⌊_⌊_⌊_⌋	M11b
98	Reading 2 (If automatic machine used, record heart rate below as well)	Systolic (mmHg)	⌊_⌊_⌊_⌋	M12a
		Diastolic (mmHg)	⌊_⌊_⌊_⌋	M12b
99	Reading 3 (If automatic machine used, record heart rate below as well)	Systolic (mmHg)	⌊_⌊_⌊_⌋	M13a
		Diastolic (mmHg)	⌊_⌊_⌊_⌋	M13b
100	During the past two weeks, have you been treated for raised blood pressure with drugs (medication) prescribed by a doctor or other health worker?	Yes	1	M14
		No	2	

Heart Rate and Body Composition				
101	Heart Rate (Record if automatic blood pressure device is used)			
	Reading 1	Beats per minute	⌊_⌋⌊_⌋⌊_⌋	M16a
	Reading 2	Beats per minute	⌊_⌋⌊_⌋⌊_⌋	M16b
	Reading 3	Beats per minute	⌊_⌋⌊_⌋⌊_⌋	M16c
102	Bioelectric impedance body composition ent	% fat	⌊_⌋⌊_⌋ . ⌊_⌋	X13

Step 3 Biochemical Measurements

Blood Glucose		Response		Code
103	During the last 12 hours have you had anything to eat or drink, other than water?	Yes No	1 2	B1
104	Technician ID		⌊_⌋⌊_⌋⌊_⌋	B2
105	Device ID		⌊_⌋	B3
106	Time of day blood specimen taken (24 hour clock)	Hours : minutes	⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋ hrs mins	B4
107	Fasting blood glucose	mmol/l	⌊_⌋⌊_⌋ . ⌊_⌋⌊_⌋	B5
	(only fill in if machine cannot give numerical reading)	Low High Unable to assess	1 2 3	B5a
108	Time Glucose Load given (24 hour clock). ONLY DO ON EVEN NUMBER SUBJECTS		⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋	X14
109	Time of day 2 hour blood specimen taken (24 hour clock)		⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋	X15
110	2 Hour Blood glucose	mmol/l	⌊_⌋⌊_⌋ . ⌊_⌋⌊_⌋	X16
	(only fill in if machine cannot give numerical reading)	Low High Unable to assess	1 2 3	X17