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The effect of dietary patterns on blood pressure: insights for clinical practice

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THE EFFECT OF DIETARY PATTERNS ON BLOOD PRESSURE: INSIGHTS FOR CLINICAL PRACTICE

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CERTIFICATION

I declare that this thesis, submitted in fulfilment of the requirements for the award Doctor of Philosophy, in the School of Medicine, University of Wollongong, is wholly my own work unless otherwise referenced or acknowledged. This document has not been submitted for qualifications at any other academic institution.

Rhoda Njeru Ndanuko

Date: 03/10/2017

DEDICATION

To

Dad, Mum and Kelly

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I would like to express my sincere gratitude to all my supervisors for their great support and encouragement throughout the completion of this thesis. I would like to thank my primary supervisor, Professor Linda Tapsell, for her guidance in understanding and conducting dietary patterns research, and also encouraging me to keep going, especially when the going seemed tough. I would also like to thank my co-supervisors, Associate Professor Karen Charlton and Dr Elizabeth Neale for their insightful comments which indeed widened my research perspective. I would like to thank Associate Professor Marijka Batterham for her invaluable advice on various statistical analyses.

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LIST OF ABBREVIATIONS

ACC – American College of cardiology

AHA – American Heart Association

ANZCTRN – Australian and New Zealand Clinical Trial Registry

BMI – Body mass index

BP – Blood pressure

C – Control

CARDIA – Coronary Artery Risk Development in Young Adults

CHEP – Canadian Hypertension Education Program

CKD – Chronic kidney disease

CVD – Cardiovascular disease

DASH – Dietary approaches to stop hypertension

DBP – Diastolic blood pressure

ENCORE – Exercise and Nutrition interventions for CardiOvasculaR hEalth

ESC – European Society of Cardiology

ESH – European Society of Hypertension

FSANZ – Food Standards Australia New Zealand

HDL – High density lipoproteins

HIP – Hypertension Improvement Project

I – Intervention

IOM – Institute of Medicine

IQR – Interquartile range

IV – Inverse Variance

IW – Intervention + walnut

JNC – Joint National Committee

K – Potassium

LDL – Low density lipoproteins

MD – Mediterranean diet

Na – Sodium

Na:K – Sodium-to-potassium ratio

NHMRC – National Health and Medical Research Council

NRV – Nutrient reference values

NUTTAB – NUTrient TABles for use in Australia

PABA – *Para*-aminobenzoic acid

PCA – Principal component analysis

PREDIMED – PREvencio´n con DIeta MEDiterra´nea

PREMIER – Prospective Registry Evaluating Myocardial Infarction: Events and Recovery

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-analyses

RR – Relative risk

SBP – Systolic blood pressure

SUN – Seguimiento Universidad de Navarra

SU.VI.MAX – Supplementation en VItamines et Mine´raux AntioXydants

WHO – World Health Organization

PUBLICATIONS IN SUPPORT OF THIS THESIS

Published papers

1. Ndanuko, R.N., Tapsell, L. C., Charlton, K. E., Neale, E. P., Batterham, M. J. Dietary patterns and blood pressure in adults: A systematic review and meta-analysis of randomized controlled trials. *Advances In Nutrition*. 2016;7:76-89; doi:10.3945/an.115.009753.

2. Ndanuko, R.N., Tapsell, L. C., Charlton, K. E., Neale, E. P., O'Donnell, K. M., Batterham, M. J. Relationship between sodium and potassium intake and blood pressure in a sample of overweight adults. *Nutrition.* 2017;33:285-290: doi: 10.1016/j.nut.2016.07.011.

3. Ndanuko, R.N., Tapsell, L. C., Charlton, K. E., Neale, E. P., Batterham, M. J. Associations between dietary patterns and blood pressure in a clinical sample of overweight adults. *Journal of Academy of Nutrition and Dietetics*. 2017;117:228-239: doi:10.1016/j.jand.2016.07.019.

4. Ndanuko, R.N., Tapsell, L. C., Charlton, K. E., Neale, E. P., Batterham, M. J. Effect of individualised dietary advice for weight loss supplemented with walnuts on blood pressure: The HealthTrack study. *European Journal of Clinical Nutrition.* (under review).

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2. Ndanuko, R.N., Tapsell, L. C., Charlton, E. K., Neale, E. P., Batterham, M. J. Association between urinary sodium intake, sodium-to-potassium ratio and blood pressure in adults. Nutrition Society of Australia. Annual Scientific Meeting, Wellington, New Zealand. 1st – 4th December 2015.

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5. Ndanuko, R.N., Tapsell, L. C., Charlton, E. K., Neale, E. P. Changes in blood pressure, urinary sodium and sodium-to-potassium ratio in a clinical sample of overweight adults. Nutrition Society of Australia. Annual Scientific Meeting, Melbourne, Australia. 29th November – 2nd December 2016.

6. Ndanuko, R.N., Tapsell, L. C., Charlton, E. K., Neale, E. P., Batterham, M. J. Effect of specific dietary advice on change in blood pressure, dietary patterns, food and nutrients in the HealthTrack study. Australian Society for Medical Research. NSW scientific meeting, Sydney, Australia. 2nd June 2017.

Other publications

1. Anil, S., Charlton, K. E., Tapsell, L. C., Probst, Y., Ndanuko, R., Batterham, M. J. Identification of dietary patterns associated with blood pressure in a sample of overweight Australian adults. *Journal of Human Hypertension*. 2016: Nov;30(11):672-678. doi: 10.1038/jhh.2016.10.
2. Neale, E., Probst, Y., McDonnell, K., O'Donnell, K., Javadpour, A., Isip, B., Wibisono, C., Ndanuko, R., Fuller, S., Tapsell, L. Development of a matching file of Australian food databases (AUSNUT2007 to AUSNUT2011-13) for use in the clinical trial context. International Conference on Diet and Physical Activity Methods (ICDAM), Brisbane, Australia. 1st – 3rd September 2015.
3. Charlton K, Anil S, Tapsell L, Probst Y, Ndanuko R & Batterham M (2016). Identification of dietary patterns associated with blood pressure in a sample of overweight Australian adults. Dietitians Association of Australia (DAA) National Conference, Melbourne, Australia. Nutrition & Dietetics; 73(S1):p56
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5. Ndanuko, R. "Diet can help control high blood pressure". Article published in the *Illawarra Mercury*, 23rd October 2015
6. Wibisono, C and Ndanuko, R. Nutrition under the microscope. *Food Australia*. April 2015. Report from the ILSI SEAR Australasia conference held in Sydney on 13th March 2015.

7. Wibisono, C and Ndanuko, R. Sugar in the diet: Is there a sweet spot? *Food Australia*. Dec 2015. Report from the ILSI SEAR Australasia conference held in Sydney on 30th October 2015.

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CANDIDATE CONTRIBUTION TO THE HEALTHTRACK STUDY

Completion of the empirical component of this thesis involved analysing data from the HealthTrack study, a 12-month randomised controlled trial, conducted between May 2014 and June 2016 (see Appendix A and B and Chapters 4-6). The candidate Rhoda Ndanuko was responsible for assessments and counselling a cohort of participants in the trial. All assessments and counselling procedures were carried out according to the HealthTrack study Standard Operating Procedures. As an Accredited Practicing Dietitian (APD), the candidate undertook a health practitioner role, but with overall specific duties as an integral member of the research team as outlined below:

Data collection:

The candidate conducted assessments for the participants allocated to her at baseline, 3, 6, 9 and 12 months. Assessments involved anthropometric measurements and collecting dietary intake data through detailed diet history interviews at all time points. Blood pressure measurements were also conducted at baseline, 3 and 12 months.

Dietary counselling:

Of the 377 participants randomised to the Healthtrack study, 66 were allocated to the candidate for dietary counselling and follow-up for the subsequent 12 months. (Note this was a separate group to those involving assessments described above, so there was no bias introduced between assessment and counselling. The counselling task involved scheduling appointments with the participants and contacting them through emails or telephone after missed appointments to reschedule.

Data entry:

The candidate entered anthropometric and blood pressure data into a quality assured Microsoft Excel spreadsheet managed by the project officer. She also entered dietary data into the Foodworks nutrient analysis software program.

Data checking:

The candidate also contributed to quality assurance procedures for the data associated with the trial. She undertook data checking to identify and correct any errors by cross checking the dietary data entered by other health practitioners involved in the study. Likewise, the data she entered was cross checked by another researcher.

Data analysis:

The primary results of the HealthTrack trial have been published by the chief investigators. This thesis contains secondary analyses of data relating to blood pressure, a registered secondary outcome for the trial. All data analysis reported in this thesis was conducted by the candidate.

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ABSTRACT

Hypertension or high blood pressure has been identified as a major risk factor for developing cardiovascular disease, stroke and kidney disease. To lower blood pressure, lifestyle changes such as following a healthy diet, weight loss and exercise have been recommended. This thesis draws on dietary data from a weight loss trial in which blood pressure was a secondary outcome.

Previous studies investigating the effect of diet on blood pressure have mainly focussed on single nutrients such as sodium and potassium. Whilst this has been informative, food is not consumed as single nutrients but as whole foods, in different combinations which make up dietary patterns. An understanding of the interdependence between nutrients, foods and dietary patterns would help in translating dietary advice in clinical practice especially in food-based recommendations for blood pressure reduction. The central hypothesis of this thesis is that dietary patterns, characterised in terms of nutrients and foods, significantly influence blood pressure in adults.

To assess the current level of evidence on the effect of dietary patterns on blood pressure, a systematic review and meta-analysis of randomised controlled trials was conducted. A dietary pattern characterised by high consumption of fruit, vegetables, whole grains, legumes, seeds, nuts, fish and low-fat dairy and low consumption of meat, sweets and alcohol resulted in significant reductions in systolic (SBP) and diastolic (DBP) blood pressure by 4.26 mm Hg and 2.38 mm Hg, respectively. Whether this would still relate to a clinical sample of overweight adults is an important question for practice.

The first stage in the analysis started with the nutrient aspects of the diet-blood pressure relationship. A secondary analysis of baseline data from a 12 month lifestyle intervention trial (the HealthTrack study) was conducted. The results showed that median urinary sodium and sodium-to-potassium ratio significantly predicted SBP ($P < 0.0005$). Identifying food sources of sodium and potassium then enabled translation from the nutrient level of understanding to that of foods. Cereal based products and dishes; cereal and cereal products; meat, poultry and game products and dishes; and milk products and dishes were identified as the major contributors for dietary sodium. Conversely, vegetable products and dishes; meat, poultry and game products and dishes; and milk products and dishes were the major contributors for dietary potassium intake. Thus, while relationships could be seen with nutrient intakes, the consumption of specific foods was also implicated in this relationship.

The regular consumption of specific foods constitutes a dietary pattern. The next level of analysis therefore investigated the association between dietary patterns and blood pressure. Six dietary patterns were derived using principal component analysis. These included; the "nuts, seeds, fruit and fish", "milk and meat", "breads, cereals and snacks", "cereal based products, fats and oils", "alcohol, eggs and legumes" and "savoury sauces, condiments and meat" dietary patterns. Multiple regression analysis showed that a dietary pattern characterised by nuts, seeds, fruit and fish was significantly and inversely associated with SBP (F (7,320) = 15.248, $P < 0.0005$; adjusted $R^2 = 0.234$), DBP (F (7,320) = 17.351, $P < 0.0005$; adjusted $R^2 = 0.259$) and sodium-to-potassium ratio (F (7,320) = 6.210, $P < 0.0005$; adjusted $R^2 = 0.100$). On the other hand, the association between SBP and DBP with the other dietary patterns was not significant. Thus a dietary pattern that is dominated by

specific foods nuts, seeds, fruit and fish appeared protective. All of these foods are naturally low in sodium and the plant foods are all high in potassium.

The second stage in the analysis assessed the impact of specific dietary advice on change in dietary patterns, food and nutrients. Effects on blood pressure after 3 months were assessed. Participants were randomised to one of three groups: intervention (interdisciplinary intervention with individualised dietary advice), intervention + walnut (interdisciplinary intervention with individualised dietary advice plus a supplement of 30 grams of walnuts/day), or control (usual care). SBP reduced significantly in all groups. The greatest reduction however was observed in the intervention + walnut group (-7.0 mm Hg, $P < 0.001$). The change in SBP was significantly greater in the IW and I groups compared to the control group ($P = 0.022$ and $P = 0.041$, respectively). There was no significant difference in change in SBP between IW and I groups (P = 0.692). Using multiple linear regression, an increase in urinary potassium and decrease in urinary sodium-to-potassium ratio was significantly associated with SBP reduction in the intervention + walnut group ($P = 0.044$ and $P = 0.037$ respectively). In the intervention + walnut group, an increase in the consumption of *seed and nut products and dishes* was significantly associated with a reduction in SBP ($P = 0.034$) while increased intake of *seafood products and dishes* was significantly associated with decreased DBP ($P = 0.024$). This confirmed the associations observed in the cross sectional analysis at baseline.

Lifestyle changes are an important component of the management of hypertension. Losing weight is a significant strategy, but in addition there is value in emphasizing dietary strategies that support lower blood pressure. This thesis provided novel evidence that, in the context of clinical practice for weight loss, specific food choices and nutrient intakes that align with beneficial dietary patterns may also assist in

reducing blood pressure. The evidence is provided by data on (1) intakes of dietary sodium and potassium, (2) food sources of these nutrients, and (3) overall dietary patterns. This data was generated in a practice setting incorporating an interdisciplinary model of care for weight loss. Despite utilising a secondary analysis of trial data where weight loss was the primary outcome, the results demonstrated that blood pressure effects can nonetheless be seen in small clinical samples. In clinical practice, dietary advice based on specific food choices and attention to sodium and potassium intakes could be helpful in not only addressing weight-loss but also high blood pressure. Further research to test this hypothesis in practice would strengthen these findings.

THE ROLE OF NUTRIENTS, FOOD AND DIETARY PATTERNS ON BLOOD PRESSURE

1.1 Introduction

This chapter provides an overview of blood pressure and the definition of high blood pressure (hypertension), its aetiology, consequences and management. It further explains the link between diet and blood pressure by reviewing the body of literature on the role of nutrients, single foods and dietary patterns while also considering the implications of behaviour change and the role of primary healthcare and service delivery models in blood pressure management. This chapter also highlights the gaps in the literature which will be addressed in subsequent chapters of this thesis.

1.2 Blood pressure

Blood pressure refers to the force exerted on the arterial walls of the large arteries by the blood circulating in the cardiovascular system [1]. Prolonged raised blood pressure can lead to serious harm to various parts of the body while low blood pressure may result in fainting due to reduced blood flow to the brain, hence maintaining a fairly constant blood pressure is important [2]. Blood pressure regulation is controlled by the renin-angiotensin system, the sympathetic nervous system and the kidneys through regulation of the volume of body fluids and electrolytes [1]. In approximately 95% of cases, raised blood pressure has no particular identifiable physiological cause, and is known as primary, essential, or idiopathic hypertension. In the other 5%, an underlying kidney or adrenal disease resulting in an impaired renin-angiotensin system, increased adrenal medulla catecholamine secretion or increased adrenal cortex aldosterone secretion may lead to secondary hypertension [3] [2]. In essential hypertension, there are multiple risk

factors for raised blood pressure that affect a wide range of population groups (Figure 1.1).

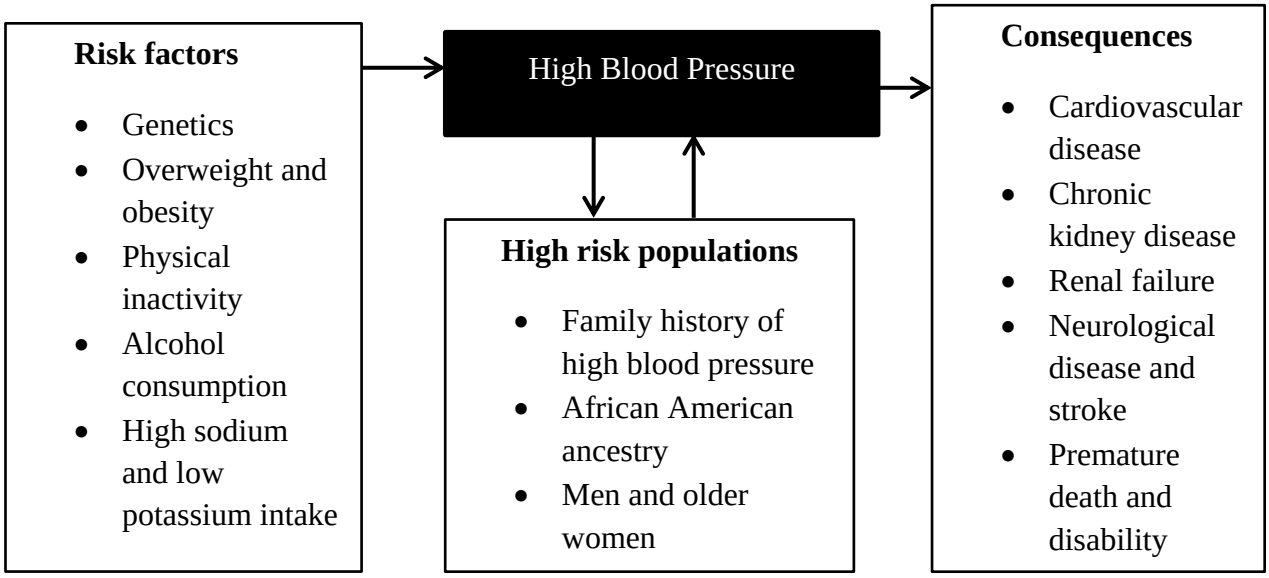

Figure 1.1 High blood pressure: risk factors, consequences, and high-risk groups [1]

Blood pressure within a population does not have a well-defined line between 'normal' and 'abnormal' blood pressure but it is rather a continuous range of blood pressures [2].

1.3 Hypertension: Definition and Health Consequences

Hypertension is the clinical diagnosis of measured and agreed level of 'high blood pressure'. Hypertension has been identified as a major risk factor for developing cardiovascular disease, stroke and kidney disease, with 51% of stroke and 45% of deaths from ischemic heart disease being attributed to high blood pressure [4] [5]. In 2001, high blood pressure was said to cause about 54% of stroke, 47% of ischemic heart disease, 75% of hypertensive disease, and 25% of other cardiovascular diseases [6]. While in 1990 high blood pressure (hypertension) was the fourth leading risk factor for the total burden of disease worldwide, it is currently ranked as the leading

risk factor for mortality and total burden of disease with an estimated 9.4 million deaths per year [7]. The effects of high blood pressure on population health have been experienced both in high and low-income regions such as sub-Saharan Africa and south Asia [7].

Globally, various guidelines exist regarding the measured blood pressure classification of hypertension. Generally, most guidelines classify hypertension as systolic blood pressure (SBP) above 140 mm Hg and/or diastolic blood pressure (DBP) above 90 mm Hg in patients above 18 years, based on a mean of two or more measurements taken while seated. This cut-off is based on the existing evidence which shows that treatment of patients to reduce blood pressure below these values is beneficial [8]. Due to the high day to day variability of blood pressure, the United Kingdom National Institute for Health and Clinical Excellence recommends the use of ambulatory blood pressure monitoring or home blood pressure monitoring to confirm a diagnosis of hypertension in the case that clinic blood pressure is above 140/90 mm Hg [9]. Table 1.1 and 1.2 are examples of hypertension classification [10] [11] while Appendix C and Table 1.3 outline management guidelines proposed by different organizations [5] [8] [10] [12] . The recommendations and blood pressure targets differ according to population groups and the presence or absence of other risk factors such as diabetes and chronic kidney disease.

Table 1.1 Blood pressure classification for adults above 18 years

Classification	SBP (mm Hg)		DBP (mm Hg)
Normal	<120	and	<80
Prehypertension	120-139	or	80-89
Stage 1 hypertension	140-159	or	90-99
Stage 2 hypertension	≥160	or	≥100

Adapted from The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure report [10]

Table 1.2 Definition and classification of office blood pressure levels according to the 2013 ESH/ESC guidelines for the management of arterial hypertension

Category[1]	**Systolic (mm Hg)**		**Diastolic (mm Hg)**
Optimal	<120	and	<80
Normal	120-129	and/or	80-84
High normal	130-139	and/or	85-89
Grade 1 hypertension	140-159	and/or	90-99
Grade 2 hypertension	160-179	and/or	100-109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

[1]The blood pressure category is defined by the highest level of blood pressure, whether systolic or diastolic. Isolated systolic hypertension should be graded 1, 2 or 3 according to systolic blood pressure values in the ranges indicated; ESH, European Society of Hypertension; ESC, European Society of Cardiology.

Table 1.3 Magnitude of blood pressure reduction associated with adherence to lifestyle modifications to manage hypertension

Lifestyle modification	**Recommendation**	**Range of average SBP reduction, mm Hg**
Weight reduction	Maintain normal body weight (BMI 18.5-24.9 kg/m^2)	5 – 20 per 10 kg weight loss
Adopt DASH diet eating plan	Adopt a diet rich in fruits, vegetables and low fat dairy and low in saturated and total fat	8 – 14
Reduced dietary sodium	Restrict dietary sodium to <100 mmol/day (2400 mg sodium or 6 g salt)	2 – 8
Increased physical activity	Regular aerobic exercise such as brisk walking for at least 30 minutes, most days of the week	4 – 9
Moderate alcohol consumption	Consumption of alcohol no more than 2 drinks* for men and 1 drink for women and lighter-weight people	2 – 4

Adopted from JNC 7 guidelines [10]; *1 drink = 375 ml mid strength 3.5% alcohol volume beer, 100 ml wine or 42.5 g 80-proof whiskey; BMI, body mass index; DASH, Dietary Approaches to Stop Hypertension; SBP, systolic blood pressure.

In adults over the age of 50, SBP has been shown to better predict cardiovascular events and renal damage than DBP [8]. In primary care practice, risk scores such as those developed using the Framingham Heart Study data can be used to predict risk of developing hypertension [13] or cardiovascular disease [14] [15] taking into account risk factors such as age, sex, family history, body mass index (BMI), blood pressure, cholesterol levels and other lifestyle factors. Blood pressure is thus seen in the context of total cardiovascular disease risk. In Australia, the majority of individuals have more than one risk factor (including hypertension), for developing chronic disease with about 50% of adults having two or three risk factors [16]. As a result, absolute cardiovascular disease risk scores were developed to be used by general practitioners in primary care setting to assist in the management of multiple individual risk factors [17].

The prevalence of hypertension is increasing. In 2011, about one billion people globally were hypertensive [18] with the prevalence of hypertension predicted to reach 1.56 billion people by 2025 [19]. According to the 2011-2012 Australian Health Survey, the prevalence of hypertension in Australia is about 31.6%, with higher prevalence in men (34.1%) compared to women (29.1%) and in older persons especially those aged above 85 years (87.7%)[20] [20]. Hypertension is therefore an important public health concern both in Australia and globally.

1.4 Effects of lowering blood pressure

Numerous epidemiological studies and randomised controlled trials have demonstrated that reducing blood pressure results in various health benefits. In a meta-analysis of 61 observational studies involving 958,074 participants without any vascular disease at baseline, a 20 mm Hg difference in SBP was associated with a

significantly reduced risk of stroke (RR 0.36, 95% CI 0.32-0.40), ischemic heart disease (RR 0.49, 95% CI 0.45-0.53) and other vascular causes (RR 0.43, 95% CI 0.38-0.48) in adults between 40-49 years, with the risk decreasing with age [21]. In addition, reducing blood pressure has been shown to reduce the risk of coronary heart disease, stroke, and major cardiovascular events [22].

In a recent meta-analysis of 123 randomised controlled trials involving 613,815 participants, lowering SBP by 10 mm Hg through the use of hypertensive medications led to a significant reduction in the risk of stroke (RR 0.73, 95% CI 0.68-0.77), cardiovascular disease events (RR 0.80, 95% CI 0.77-0.83), heart failure (RR 0.72, 95% CI 0.67-0.78), coronary heart disease (RR 0.83, 95% CI 0.78-0.88) and all-cause mortality (RR 0.87, 95% CI 0.84-0.91) across different population subgroups [23]. In the US population, lowering SBP and DBP by 5.0 and 3.0 mm Hg respectively was estimated to result in a 15% reduction in the incidence of coronary heart disease and 27% reduction in stroke incidence [24]. In addition, lowering SBP by 10 mm Hg or DBP by 5 mm Hg through the use of blood pressure lowering medication has been shown to reduce the incidence of coronary heart disease events and stroke by 25% and 30% respectively [25]. Conversely, an increase of 20 mm Hg in SBP and 10 mm Hg in DBP in adults between 40 and 70 years old has been estimated to double the risk of developing cardiovascular disease [10]. Older and overweight individuals with prehypertension are more likely to progress to hypertension thus emphasising the importance of primary preventative interventions for lowering blood pressure [26].

1.5 The role of obesity in hypertension aetiology

Given the high burden of hypertension on health care services and individual risk of disease outcomes, there has been an extensive focus on identifying non pharmacological strategies to prevent its development. In this regard, the relationship between obesity and hypertension is well established. Obesity has been identified as a major risk factor for essential hypertension commonly referred to as obesity-hypertension [27]. In the World Health Organization MONICA (MONItoring of trends and determinants in CArdiovascular disease) Project, BMI was shown to be a significant predictor of SBP accounting for 14% and 32% of variance in men and women respectively after controlling for age [28]. In an 11 year prospective population study, an increase in BMI was significantly associated with an increase in SBP and DBP in 15,971 women and 13,846 men who were not on blood pressure medications, had no diabetes or cardiovascular disease. Further, each 5% weight gain was correlated with a 20-30% increased risk of developing hypertension [29]. In addition, in the Framingham Offspring Study, obesity was identified as a major predictor of hypertension after controlling for baseline blood pressure after 8 years follow-up of 2,027 men and 2,267 women aged between 20 and 49 years [30]. Risk estimates indicated that about 73% and 56% of hypertension cases in men and women respectively were attributed to obesity [30].

The precise mechanism that links obesity and hypertension is not well understood. However, both animal models and human studies have shown that expansion of the blood volume and increased sodium reabsorption in the kidneys play a major role in the development of obesity-hypertension [27]. The increased likelihood of developing hypertension in the obese may be attributed to hyperinsulinemia which

leads to the activation of the sympathetic nervous system which may increase blood pressure either through vasoconstriction or increased sodium retention [31]. Serum leptin, which is elevated in obesity [32], has also been attributed to the development of obesity-hypertension via increasing renal sympathetic nerve activity and reducing sensitivity to appetite inhibition [33]. In prospective studies, greater hospitalisations due to different types of cardiovascular disease have been observed in patients with a higher BMI [34].

Given the high and increasing prevalence of obesity both in industrialized and developing countries [35], body weight management is an important target for hypertension prevention. Approximately 58% of the world's adult population is projected to be overweight or obese by 2030 [36]. Identification of strategies to lower blood pressure in the overweight and obese population is therefore important in reducing the likelihood of developing hypertension over time.

1.6 Diet and blood pressure

As well as energy imbalance (obesity), other dietary factors are known to influence blood pressure through inter-related interactions occurring at various levels between nutrients, foods and dietary patterns. In addition, nutrients, foods and dietary patterns can be influenced by lifestyle factors such as exercise and access to healthcare interventions at the primary healthcare level (Figure 1.2).

Nutrients, foods and dietary patterns are all interconnected. Firstly, nutrients are delivered by foods and are essential for human health, together with other nutritional compounds whose health benefits are being recognised [37]. Focus on the role of nutrients in health previously enabled the understanding and prevention of deficiency diseases [38] which then led to the development of nutrient supplementation

strategies. However, as it is well known, nutrients are delivered from the diet as whole foods. This may also result in food synergy –whereby the combination of nutrients provided through different food matrices may have greater benefits compared to individual nutrients in individual foods themselves [39]. A combination of individual foods leads to the aspect of dietary patterns, which is helpful in enabling easier translation of food based recommendations, such as dietary guidelines and their application in clinical practice [40].

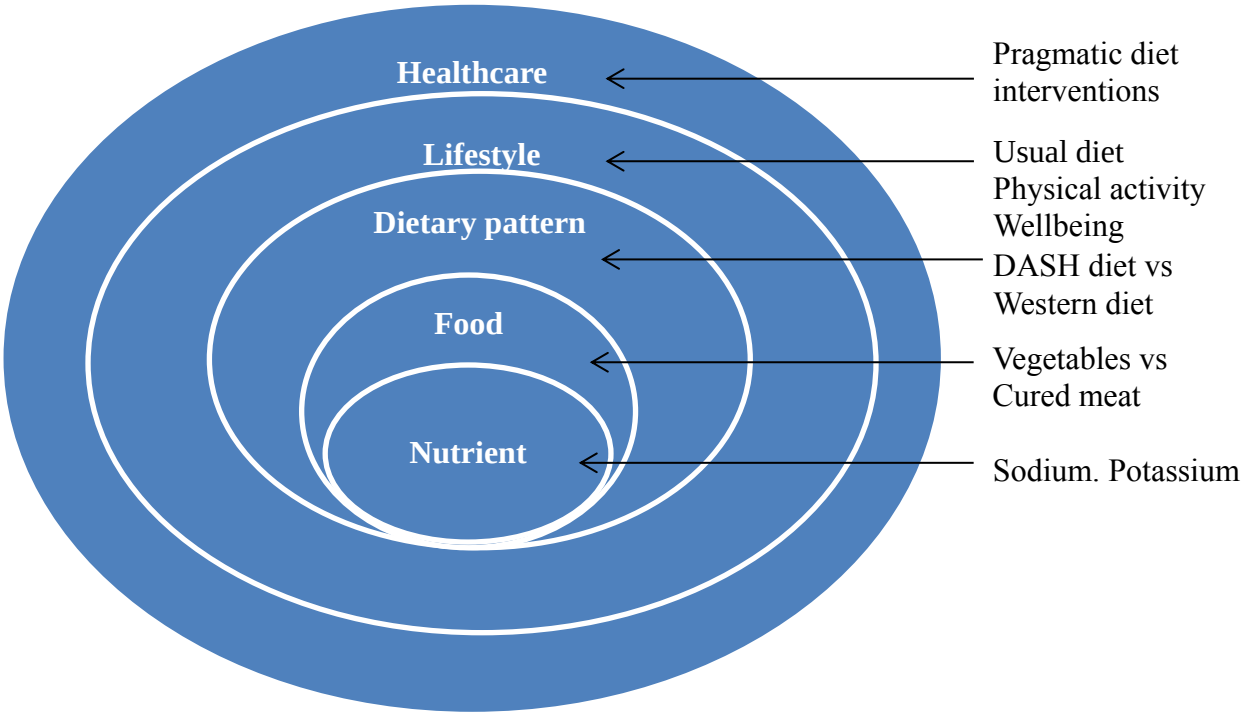

Figure 1.2 Interrelationships between nutrients, foods and dietary patterns

Adapted from: [39] [40] [41] [42].

1.7 The impact of single nutrients on blood pressure

1.7.1 Sodium

Dietary sodium or salt was one of the earliest dietary components to be identified as being associated with blood pressure. In approximately 1700 BC, the Chinese physician Huang Ti Nei Ching Su Wein stated that "therefore if large amounts of salt are taken, the pulse will stiffen and harden", as translated by Wan Ping in AD 762 [43]. Several large epidemiological studies have investigated the relationship between salt intake and blood pressure. Notably in the INTERSALT study, a large international epidemiological study involving 10,074 individuals across 52 centres, higher urinary sodium excretion (difference of 100 mmol) was significantly associated with higher blood pressure values (approximately 3/0 to 6/3 mm Hg) especially in middle aged individuals compared to younger adults [44]. In a meta-analysis investigating the effect of long-term reduction of sodium intake, a reduction to 1,720 mg/day (4.4 g salt/day) resulted in a decrease in blood pressure of 2.0 and 1.0 mm Hg in SBP and DBP respectively in normotensive subjects, with greater reductions of 5.0 and 3.0 mm Hg in SBP and DBP respectively observed in hypertensive subjects [45].

It has been suggested that inconsistencies regarding the impact of increases in sodium intake on the development of hypertension may be the result of differences in the degree of salt sensitivity between individuals [46]. Salt-sensitivity refers to a situation whereby blood pressure is elevated during intake of high dietary sodium and decreases during low sodium intake while in salt-resistant individuals, blood pressure does not change with restriction of sodium intake [47]. Differences in blood pressure response to salt intake in salt-sensitive and salt resistant individuals has been demonstrated in normotensive as well as hypertensive adults [48]. Increased

salt-sensitivity has been linked to the impaired function of the kidneys in sodium excretion whereby in salt-sensitive individuals with hypertension, a higher blood pressure is required to adequately excrete sodium [49]. The application of salt-sensitivity has remained in the research domain, because of difficulties in applying the criteria and a need to hospitalize individuals for the periods of salt restriction or salt loading. The following groups of patients tend to have increased susceptibility to salt-sensitive hypertension, and have been suggested to be targeted for intervention [47]:

• People of African descent

• Elderly people

• Obese persons (not in all studies)

• Patients with type 1 or type 2 diabetes

• Patients treated with calcineurin inhibitors

• Patients with chronic kidney disease

The use of blood pressure as an outcome end-point in studies that investigate the effect of high salt intakes has been subject to various controversies. For instance, in recent studies including the observational cohort - Prospective Urban Rural Epidemiology (PURE) study, using mortality or occurrence of cardiovascular disease events as definitive outcomes to investigate the effects of sodium intake on health have shown that both consumption of salt intakes lower than 7 g salt (2,730 mg sodium) and higher than 14 g salt (5,460 mg sodium) were associated with an increased risk of death and cardiovascular events [50] [51]. The PURE study had various limitations including estimating 24- hour sodium and potassium intake from formula estimate of morning fasting urine samples. In addition, the 2013 Institute of Medicine (IOM) report [52] pointed out that while higher sodium intakes are

associated with the risk of cardiovascular disease, the report concluded that there is insufficient evidence to provide recommendations to lower intakes below 2,300 mg/day. This has raised questions regarding a potential adverse effect of low salt intakes on long term health outcomes.

However, the IOM report did not assess the association of sodium intake with intermediate end-points such as blood pressure. The question of the optimal levels for sodium intake in the general population and in clinical populations, specifically, therefore remains to be further explored. Furthermore, an American Heart Association Science Advisory review of 26 cohort studies that examined the relationship between sodium intake and cardiovascular disease identified various methodological issues arising in the body of evidence. These included random and systematic error in assessment of sodium intake, reverse causality, inadequate follow-up, residual confounding and insufficient power, resulting in inconsistent findings [53]. According to the World Health Organization, the final consensus to date on sodium consumption is a recommendation of less than 2,000 mg of sodium per day (5 g salt) in adults [54].

1.7.2 Potassium

Potassium is another key nutrient which has been shown to play a major role in blood pressure regulation, with an inverse association demonstrated in randomised controlled trials. In a meta-analysis of 32 randomised controlled trials, increasing potassium intake by 780 mg/day without the use of antihypertensive medications was shown to reduce SBP and DBP by 4.9 mm Hg and 2.7 mm Hg, respectively [55]. However, despite these findings, research investigating the association between potassium intake and cardiovascular disease risk factors has provided conflicting results. A significant inverse association was demonstrated between potassium

consumption and stroke incidence in a meta-analysis of 11 cohort studies comprising of 127,038 participants [56]. However in the same study, there was no significant association between potassium intake and the incidence of cardiovascular disease and coronary heart disease. Likewise, there was no significant association between potassium intake and risk of cardiovascular disease events in a prospective observational cohort study of 7,795 adults majority with albuminuria and no history of cardiovascular events at baseline after adjustment for lifestyle and dietary factors [57]. The lack of association in this study may have been due to the high overall median urinary potassium excretion of 70 mmol/24 h which is equivalent to potassium intake of approximately 90 mmol/d. Many populations have intakes much lower than this value, as a result of inadequate fruit and vegetable intakes [58] thus the results may not have wide generalizability.

1.7.3 Sodium-to-potassium ratio

The role of sodium and potassium in influencing blood pressure may be mediated by their effect on a number of synergistic mechanisms of the endothelial system that increase vasodilation, such as production of nitric oxide, endothelium-derived hyperpolarizing factors and prostaglandins [59]. A high sodium intake has been linked to impaired endothelial function [60] while, conversely increased potassium intake enhances endothelial function [61]. In the development of hypertension, excessive sodium and insufficient potassium intake are both shown to play a role since they result in vascular smooth muscle cell contraction which leads to increased peripheral vascular resistance thus causing high blood pressure [62]. A recent review demonstrated that in various randomised controlled trials the sodium-to-potassium ratio had a stronger association with blood pressure than sodium or potassium alone

[63]. The sodium-to-potassium ratio may therefore be a better target for dietary interventions aimed at lowering blood pressure across various geographical regions and cultures [64]. According to the World Health Organization sodium and potassium targets, a sodium-to-potassium molar ratio of 1:1 is implied as optimal although this has not been specified as such [65]. A low sodium-to-potassium ratio may reflect high diet quality, while a high ratio may reflect poorer diet quality. For instance, in 24,807 adults in the United States participating in the National Health and Nutrition Examination Survey 2001-2010, a high consumption of canned vegetable and fruit was associated with a significantly lower sodium-to-potassium ratio of 1.38 compared to a ratio of 1.45 in the low consumption category as assessed through 24-hour dietary recall interviews. The lower sodium-to-potassium ratio was also associated with favourable diet quality as measured by the Healthy Eating Index-2010 [66]. In terms of diet quality and hypertension, a higher diet quality score as measured using the Dietary Guideline Index and Recommended Food Score was inversely associated with hypertension in men in a cross-sectional analysis of the Australian Health Survey 2011-2013 [67].

As a result of the relationship between excessive sodium intake and low potassium intake with increased risk of hypertension and cardiovascular disease, the World Health Organization recommends a population intake target of 2,000 mg of sodium (equivalent to 5 g salt per day) and 3,510 mg of potassium per day [54]. Due to an increase in salt sensitivity in individuals with the metabolic syndrome [68], the Australian National Health and Medical Research Council (NHMRC) further recommends a Suggested Dietary Target of 1,600 mg of sodium for chronic disease prevention [69]. The Nutrient Reference Values for sodium are currently under review by the Australian Government Department of Health in partnership with the

New Zealand Ministry of Health (http://www.health.gov.au/internet/main/publishing.nsf/Content/nutrient-ref-values). In the United States, the Dietary Reference Intakes for potassium is 4700 mg/day and the Upper Limit for sodium is 2300 mg/day which represents a 2:1 ratio [70]. In addition, the American Heart Association and the American College of Cardiology recommends a further reduction to 1500 mg/day for those who need blood pressure lowering [71].

1.7.4 Other nutrients

Other nutrients that may influence blood pressure include dietary fibre [72], calcium [73] and magnesium [74], though research on the effects of these nutrients is inconsistent. Furthermore, it is also well known that nutrients have multiple interactions and may therefore be responsible for blood pressure reduction [24]. For instance, the blood pressure lowering effect of potassium and calcium may be mediated by their ability to increase sodium excretion by the kidneys or through the interactions between sodium and potassium in the sodium-to-potassium ratio [75]. Thus, several nutrients in combination may affect blood pressure rather than a single nutrient alone.

1.8 The impact of single foods on blood pressure

Nutrients are delivered in foods, which also include other components such as plant sterols and polyphenols that investigations have shown to be beneficial to human health [37]. In addition, research into foods and their effect on health has implications for policy development, notably translation into dietary guidelines. We do not consume nutrients in isolation, and as such policies such as dietary guidelines must provide recommendations on consumption of foods, rather than individual

nutrients [40]. As a result, the effect of individual foods on blood pressure has been investigated in randomised controlled trials and observational studies. These foods include fruit and vegetables, dairy foods, nuts, pulses, meat and coffee.

1.8.1 Fruit and vegetables

Fruits and vegetables are rich sources of dietary potassium [76], a nutrient that has been associated with reduced blood pressure [55]. The effect of fruit and vegetables consumption on blood pressure has been investigated in several cohort studies. For example, in the SUpplementation en VItamines et Mine´raux AntioXydants (SU.VI.MAX) study, consumption of more than 642 g per day of fruit and vegetables compared to 228 g per day, resulted in a smaller increase in blood pressure after 5 years of follow-up [77]. The SU.VI.MAX study included 2,341 men and women aged between 35 and 63 years. These results indicate that consumption of more fruit and vegetables could ameliorate changes in blood pressure which occur with age.

A higher fruit and vegetable intake (more than 8 serves of fruit and vegetables per day) was also associated with a significantly reduced risk of hypertension in a large-scale cohort of 28,082 women who were followed up for 12.9 years [78]. However, the association did not remain significant after adjusting for other lifestyle and dietary factors such as smoking, alcohol intake, physical activity, whole grains, red meat, low fat dairy and nuts; highlighting the impact of other lifestyle and dietary factors on blood pressure. This highlights that blood pressure is not only impacted by single foods such as fruits and vegetables, but also by other foods that are consumed in combination.

1.8.2 Dairy foods

Dairy foods are another food category of interest. The foods are rich in protein and bioactive peptides, which through mechanisms such as the influence on the endothelium function, inhibition of angiotensin-I-converting enzyme or effect on body weight, may influence blood pressure [79]. In addition, nutrients such as calcium, magnesium and potassium which are found in dairy foods, have been associated with reduced blood pressure [80] [81].

The association between dairy intake and blood pressure was investigated in a cohort of 5,880 middle aged men and women free of hypertension, cardiovascular disease, diabetes and cancer in the 27-month Seguimiento Universidad de Navarra (SUN) longitudinal prospective study in Spain [82]. Low-fat dairy consumption of more than 2 serves per day (615 g) was associated with 54% lower risk of developing hypertension. In addition, the Rotterdam study investigated the association between dairy intake and hypertension in the Netherlands by following up 2,245 older adults for 2 to 6 years [79]. In this study, intake of 561 g per day (3.7 serves) of low fat dairy was associated with 31% lower risk of hypertension after 2 years of follow-up. After 6 years of follow-up, this association was observed in overweight participants only.

Likewise, the PREvencio´n con DIeta MEDiterra´nea (PREDIMED) study found an inverse association between low-fat dairy intake and blood pressure in 2,290 adults after a 12-month follow-up [83]. In this study, dietary intake was assessed using a semi-quantitative 137-item food frequency questionnaire. In the highest quartile of dairy consumers consuming 632 g per day in the PREDIMED study, SBP and DBP were significantly lower [-4.2 mm Hg (95% CI: -6.9, -1.4) and -1.8 mm Hg (95% CI: -3.2, -0.4] respectively. However, no significant associations were observed with

whole-fat dairy consumption. In addition, in the 1946 birth cohort study in Britain, no association was found between dairy intake, blood pressure and incident of hypertension after 10 years of follow-up in 1,750 adults [84]. The lack of association between whole-fat dairy and blood pressure may be explained by the detrimental effect on the endothelial function asserted by a diet high in saturated fatty acid [85]. Dairy foods are still an important component of diet as they contain nutrients that are implicated for blood pressure control. However, the current body of evidence suggests limiting consumption of whole-fat dairy in the diet would be beneficial.

1.8.3 Nuts

The effect of nut consumption on blood pressure has also been investigated in prospective studies and randomised controlled trials. Nuts contain high amounts of mono- and polyunsaturated fats, magnesium, potassium and fibre and are low in sodium and saturated fats and thus may elicit a blood pressure lowering response [86]. These nutrients and their effects are known but the unique combination and other factors in the nuts may also exert the effect.

In a meta-analysis of four prospective cohort studies involving 40,102 participants and 12,814 hypertension cases, consumption of 1 serving of nuts/day was significantly associated with reduced risk of hypertension (RR: 0.66; 95% CI: 0.44, 1.00; $P = 0.006$) [87]. In a recent meta-analysis of 21 randomised controlled trials, increased nut consumption was shown to lower SBP by 1.29 mm Hg in participants without type 2 diabetes [88]. On the other hand, no association was found between nut intake and development of hypertension after adjustment for sex, age and other confounding factors in the SUN prospective cohort of 9,919 adults [89]. In the SUN study, the effect of nut intake on incidence of hypertension was assessed over a follow-up period of a median 4.3 years using a food frequency questionnaire with

four categories of nut intake (rarely/never, 1-3 times per month, once per week, and 2 or more times per week). Previous studies have investigated the effect of consuming salted or unsalted nuts on blood pressure. For instance, a randomised controlled crossover trial in which participants were randomised to either 30 g/day of raw or dry roasted, lightly salted hazelnuts found that both interventions significantly reduced SBP after 28 days [90]. In most prospective studies, the information on whether the nuts are salted or unsalted is not usually provided [87], thus becoming a limitation to the studies. The effect of nut consumption on blood pressure is therefore not conclusive and it may be influenced by other dietary factors.

1.8.4 Pulses

Blood pressure reductions have also been observed after increasing the consumption of dietary pulses (dried peas and beans). Dietary pulses are rich sources of plant protein, dietary fibre and potassium which have been shown to have blood pressure lowering effects [91]. For instance, in a meta-analysis of eight isocaloric randomised controlled trials which included 554 participants with and without hypertension, intake of dietary pulses (average 162 g/day) were found to significantly lower SBP (-2.25 mm Hg (95% CI, -4.22 to -0.28), $P = 0.03$) [92]. Dietary pulses may therefore have a beneficial effect on lowering blood pressure.

1.8.5 Meat

The effect of meat on blood pressure has been investigated in different studies. Consumption of meat would be expected to impact negatively on blood pressure due to the higher amounts of sodium, saturated fat and nitrates that are negatively associated with blood pressure [93]. In addition, high meat intake might replace other beneficial foods such as fruit and vegetables, whole grains and pulses. On the

contrary, meat consumption may have a blood pressure lowering effect due to the presence of amino acids such as arginine, tryptophan, taurine and tyrosine that impact on the vascular system. L-arginine and taurine were found to lower blood pressure in animal models [94]. In addition, L-arginine infusion in patients with hypertension resulted in reduction of blood pressure through a vasodilatory effect due to an increase in nitric oxide production [95].

In the Coronary Artery Risk Development in Young Adults (CARDIA) prospective study, 4,304 participants aged between 18 and 30 years were followed up for 15 years [93]. The results showed that consumption of red and processed meat more than 1-2 times/day at baseline was positively associated with 20-40% higher risk of developing elevated blood pressure compared to intake less than 0.6 times/day. On the other hand, a higher risk of developing hypertension (OR 1.26, 95% CI, 1.00-1.59) was observed in participants who consumed less meat compared to those who consumed meat more frequently after 4.6 years of follow-up of 3,486 normotensive Japanese male workers [96]. Thus, since red meat has been shown to both positively and negatively impact on blood pressure, its influence may be related to the total dietary pattern in which it is consumed, rather than as a single food in the diet.

1.8.6 Coffee

The effect of coffee consumption on blood pressure has also been investigated in various studies. Coffee may impact on blood pressure negatively through caffeine-induced pressor effects whereby antagonism of endogenous adenosine results in vasoconstriction and raised total peripheral resistance [97]. Increased pressor effects of caffeine are however observed within the first 3 hours after ingestion and diminish thereafter [97] which may result in a lack of association between coffee intake and blood pressure. Coffee is also a good source of antioxidants comparable to red wine

and green tea [98]. Green coffee bean extract has been shown to have antihypertensive properties in animal models due to the presence of polyphenols that influence nitric oxide production [99].

A meta-analysis of 16 randomised controlled trials investigating the effects of coffee and caffeine on blood pressure found a significant increase of 2.04 mm Hg and 0.73 mm Hg in SBP and DBP respectively [100]. However, when coffee and caffeine trials were analysed separately, larger increases were observed for caffeine (SBP: 4.16 mm Hg, DBP: 2.41 mm Hg) compared to the coffee trials (SBP: 1.22 mm Hg, DBP: 0.49 mm Hg). A systematic review and meta-analysis of 10 randomised controlled trials and five cohort studies did not find a significant effect of coffee consumption on blood pressure or the risk of hypertension [101]. Likewise, coffee intake was not associated with incident hypertension in the 12-y prospective cohort Nurses' Health Studies I and II comprising of 155,594 women free from physician-diagnosed hypertension [102]. However in this study, consumption of caffeinated cola beverages including both sugared and diet cola were found to be positively associated with hypertension.

Better understanding of diet-blood pressure associations is warranted, and particularly in at risk groups such as obese and overweight adults. Diets are complex with multiple nutrient interactions, thus making it difficult to isolate the role of individual foods or nutrients in relation to specific health and disease outcomes [103].

1.9 Impact of dietary patterns on blood pressure

While investigating the effect of single nutrients or foods on blood pressure management may have some positive results, individual foods are not consumed in

isolation and are included within a whole diet, resulting in nutrient interactions which may be synergistic [40]. Separating nutrients and foods may therefore not represent the real picture of the combination of foods that people eat and their influence on health. Consequently, dietary pattern analysis has been recommended in nutritional epidemiology as an additional method to better understand relationships between diet and chronic diseases [104]. It is therefore beneficial to assess the effects of entire dietary patterns on blood pressure rather than focusing on single nutrients or single foods.

Perhaps the most well-known study to investigate the impact of dietary patterns on blood pressure was the Dietary Approaches to Stop Hypertension (DASH) trial [24]. The DASH study was a controlled feeding trial that enrolled 459 adults who were supplied with the meals from study centres. The participants were randomised to either the "DASH diet (combination diet)", "fruit and vegetables diet" or the "control diet (typical American diet)". The DASH diet was composed of large amounts of fruit and vegetables, increased low-fat dairy products, whole grains, nuts, legumes and seeds and accompanying small amounts of meat and saturated fat. The "fruit and vegetables diet", was similar to the control diet, though it had larger amounts of fruits and vegetables and less sweets and snacks. In comparison to the typical American control diet, the DASH diet was shown to lower SBP on average by 5.5 mm Hg (-7.4 to -3.7) and DBP by 3.0 mm Hg (-4.3 to -1.6) in all participants. However, the reduction was greater in subjects with hypertension. In the DASH study, weight was kept constant and there was no difference between the sodium content of the three comparator diets. However, the DASH diet led to a reduction of 73 mg in sodium intake compared to a reduction of 232 mg in the fruit and vegetable diet and an increase of 142 mg in the typical American control diet. This may

indicate that the overall dietary pattern has more influence on blood pressure reduction than a single nutrient such as sodium. The effect of reducing sodium was consequently assessed in the DASH-Sodium cross-over parallel group study whereby a significant reduction in SBP was found for participants randomised to both the low sodium (50 mmol sodium/day) and high sodium (150 mmol sodium/day) DASH diets [105]. The low-sodium DASH diet resulted in significant reductions in SBP of 8.9 mm Hg (-6.7 to -11.1) while the DASH diet alone resulted in SBP reduction of 5.5 mm Hg (-7.4 to -3.7) [24], thus showing the additional benefit of lowering sodium in the DASH diet. The DASH-Sodium study therefore showed that having a good quality diet with plenty of fruit and vegetables may be as beneficial as lowering sodium if on a poor American type diet – additive effects of both were less than expected.

The DASH diet can be tailored to include locally produced foods and also consider local food habits. This was demonstrated in a low glycaemic index Brazilian diet whereby the food items were adapted to the local production and dietary habits but incorporated the DASH principles including salt reduction [106]. After 6 months, the intervention group had a net reduction of 6.2 mm Hg in DBP compared to the usual care group. Urinary sodium excretion significantly reduced in the intervention group by 43.4 mmol/24 hours and there was a significant reduction of 1000 mg in sodium intake compared to the control group.

The DASH diet has also been modified to the Australian setting (OZDASH) and investigated in a randomised controlled crossover trial involving 94 community dwelling adults over 25 years of age, with baseline SBP greater than 120 mm Hg or DBP greater than 80 mm Hg [107]. The OZDASH was based on the original DASH diet [24] but had moderate sodium intake (2668 mg per day vs 3000 mg per day in

the DASH diet). After four weeks of intervention, the OZDASH diet led to a reduction in SBP by 1.8 ± 0.5 mm Hg compared to the control diet. In the same study, a low sodium and high potassium diet (1400 mg sodium and 4100 mg potassium) also led to a reduction in SBP and DBP by 4.4 ± 0.8 mm Hg and 2.0 ± 0.6 mm Hg respectively in comparison to the control diet.

Another dietary pattern that has been identified in various randomised controlled trials is the Nordic diet. This diet consists of foods of Nordic origin such as whole grains (rye, barley and oats), rapeseed oil, berries, fruits, vegetables, legumes, fish, nuts and low-fat dairy products [108]. The Nordic dietary pattern's effect on ambulatory blood pressure was examined in a randomised controlled trial. The control diet was based on mean nutrient intake in Nordic countries and comprised wheat products, dairy fat-based spreads such as butter, and low intake of fruits, vegetables and fish. The Nordic diet significantly reduced 24-hour ambulatory DBP by 4.4 mm Hg in the intervention group compared to the control group. In another study, the effect of a healthy Nordic diet, eaten *ad libitum*, on blood pressure was assessed in 88 subjects with mild hypercholesterolemia and with blood pressure less than 145/85 mmHg [109]. The Nordic diet lowered SBP by 6.55 mm Hg after 6 weeks. However, the change did not remain significant after adjusting for weight loss. Likewise, in comparison to an average Danish diet the Nordic diet was shown to have significant reduction in SBP after 26-weeks by 5.13 mm Hg in 181 adults with metabolic syndrome [110]. The Danish diet was composed of refined grains, meat, dairy and cheese, sweets and was low in vegetables and imported fruits.

The Mediterranean dietary pattern is another combination of foods that has been shown to have a beneficial role in blood pressure reduction. The traditional Mediterranean diet is generally characterized by high intake of plant foods such as

fresh fruits, vegetables, legumes, nuts and seeds, unrefined cereals, fish and is low in meat, [111] [112]. It may include moderate amounts of dairy foods, fish and poultry and low amounts of red meat but there may be some variation in food composition between regions. In general though, olive oil is the major source of fat and wine is consumed moderately with meals. The PREDIMED study, a 4-year randomised controlled trial showed that Mediterranean diet supplemented with extra virgin olive oil, and with a daily supplement of 30 g mixed nuts led to significant reductions in DBP by 1.53 mm Hg and 0.65 mm Hg respectively compared to a low fat diet [113]. In a 2-year study investigating the effect of a Mediterranean-style diet on endothelial function and inflammatory markers in 180 patients with metabolic syndrome, a Mediterranean-style diet that included consumption of 25-50 g of walnuts per day significantly reduced SBP by 3 mm Hg and DBP by 2 mm Hg compared to a control prudent diet [114].

The various dietary patterns that have been identified to lower blood pressure consist of different food combinations. Some food components are common across multiple dietary patterns while others are unique to a particular dietary pattern. For example, the Brazilian diet incorporating DASH-Sodium principles is composed of foods of low to moderate glycaemic index (GI<70) that are produced locally and adapted to the local eating habits [106]. However, the DASH diet [24], the OZDASH diet [107], the Brazilian diet, the Nordic diet [109] [115] [108], and the Mediterranean diet [113] all comprise a high intake of fruit, vegetables, nuts and legumes. These diets are high in nutrients such as potassium which has been associated with lowering blood pressure [116]. The DASH diet and Brazilian DASH diet both incorporate approximately 5 serves of fruit and 4 serves of vegetables per day. The Nordic diet emphasizes locally grown foods such as strawberries, blackcurrants, bilberries,

apples, pears and plums. The DASH, Brazilian and Nordic diets are rich in whole grains and include approximately 2 to 3 serves of low-fat dairy per day. As previously highlighted, consumption of dairy products has been associated with reduced blood pressure [117].

Generally speaking, the dietary patterns identified as being beneficial emphasise consumption of less red meat and more white meat as well as more than 3 serves per week of fish. As a result of the diets being high in low-fat dairy and lean meat, they are also low in total fat and saturated fat. The beneficial dietary patterns include consumption of vegetable oils with the use of olive and soya bean oils in the Brazilian diet, rapeseed oil in the Nordic diet and olive oil in the Mediterranean diet. Alcohol is limited to less than 2 drinks per day in the DASH diet while the Mediterranean diet allows consumption of more than 7 glasses of wine per week. Wine is rich in polyphenols and has been linked to a reduction in blood pressure although the results are inconsistent. For example, an open randomised cross-over trial showed a 5.3 mm Hg reduction in postprandial blood pressure after consumption of 250 ml of red wine with the noon meal [118] although the sample size in this study was small (n = 13). On the other hand, another study did not show any reduction in blood pressure after consumption of 560 mg of red wine polyphenols for 4 weeks [119].

There is also limited consumption of sweet snacks and sweetened and carbonated beverages in the four dietary patterns. However, salt intake differs across the four dietary patterns. The DASH diet maintains an intake of 3,000 mg sodium per day while the Brazilian diet has an intake of 2,400 mg sodium per day. The DASH-Sodium includes both low (1150 mg sodium per day) and high (3450 mg sodium per day) sodium variations. The Nordic diet has an intake of 2,730 and 2,340 mg sodium

in men and women respectively. The Brazilian diet uses spices such as garlic, bay leaf, chive, coriander, oregano, parsley leaf and pepper in order to compensate for the reduced salt and enhance flavour in the foods.

As described in this section, blood pressure is influenced by different foods, consumed in combination as different dietary patterns, rather than by single foods. It is therefore more important to focus on dietary patterns in blood pressure management.

1.10 Role of weight loss and exercise in blood pressure

While a focus on dietary patterns and food groups is informative, there is also a body of research on the effect of weight loss on blood pressure. In addition to dietary changes, other behavioural interventions that are recommended for lowering blood pressure include weight loss and increased physical activity [10]. Weight loss has been found to normalize blood pressure levels in obese participants after controlling for other factors such as age, sex, hypertensive drugs and degree of obesity [120]. In addition, a meta-analysis of 3 randomised controlled trials that investigated the effect of weight reducing diets in hypertensive people found that weight loss of about 4 kg led to a reduction of 4.5 mm Hg and 3.2 mm Hg in SBP and DBP respectively [121].

Several studies have focused on the effect of weight loss and exercise, in combination with diet, on blood pressure. An example is the Prospective Registry Evaluating Myocardial Infarction: Events and Recovery (PREMIER) study which investigated the effect of weight loss and exercise, in addition to inclusion of DASH dietary principles in 810 free living subjects who were not on blood pressure medication [122]. Intervention goals included weight loss of about 6.8 kg within the intervention period, reducing sodium intake to 2,300 mg per day, incorporating 180

minutes of moderate exercise per week and reducing daily alcohol intake to less than 2 drinks (28 g pure alcohol) for men and 1 drink (14 g pure alcohol) for women. After 6 months, the behavioural intervention incorporating the DASH diet lowered SBP and DBP by 4.3 mm Hg and 2.6 mm Hg respectively. In the PREMIER study, there was no significant difference between the behavioural intervention group incorporating the DASH diet and behavioural intervention only. Both groups had increased exercise which resulted in weight loss, and both reduced sodium and alcohol intake, which may have resulted in the lack of difference observed between the groups.

In contrast, the 4-month Exercise and Nutrition interventions for CardiOvasculaR hEalth (ENCORE) study found increased benefits of adding weight management changes to the DASH diet [123]. Such interventions included consuming a hypocaloric diet (-500 kcal/ day) and participating in supervised exercise sessions 3 times per week. Compared to the DASH diet only, the DASH diet plus weight loss program significantly lowered SBP and DBP by 5 mm Hg and 3 mm Hg respectively. There is therefore an added advantage of incorporating interventions such as weight loss and exercise to the DASH dietary pattern in blood pressure reduction.

It has been demonstrated that the DASH diet can be followed over the long term [124] but motivation to exercise may decrease especially when supervised exercise sessions are no longer being provided. This was demonstrated in an 8-month follow-up of the ENCORE study participants [125]. Ability to maintain changes in dietary habits, exercise behaviour, weight loss and blood pressure reduction was assessed. The two intervention groups had significant reductions of 6.7 mm Hg in SBP compared to usual care. However, no significant differences were noted between

DASH only and DASH diet plus weight loss groups. It was observed that the DASH diet plus weight loss group had increased caloric intake and reduced energy expenditure compared to DASH only, thus resulting in lack of significant differences between the two intervention groups at follow up. Both DASH groups had lower sodium intake and higher potassium, calcium and magnesium intake compared to the usual care group. Behaviour change strategies including weight loss and exercise may therefore reduce blood pressure in the short term, with longer term effects requiring further investigation.

In this thesis, weight loss and physical activity are some of the lifestyle factors that are controlled for in the analysis in chapters 4, 5 and 6 since they have been shown to independently influence blood pressure.

1.11 Behaviour change in health care settings and blood pressure

Whilst most of the studies described above have been carried out in controlled research settings with well-motivated volunteers, other studies have focused on primary health care settings. The first contact between a patient and a health care provider often occurs in healthcare practices. As a result, the health provider may be required to provide dietary information to the client on the management of their condition. The effect of such a health provider intervention was investigated in the Hypertension Improvement Project (HIP), a 4-arm parallel design randomised controlled trial involving 32 physicians in 8 primary care practices in central North Carolina [41]. The study assessed the adherence of physicians to national guidelines and of patients to behavioural recommendations for reducing blood pressure over a period of 6 months, with further follow-up of patients for 12 months through telephone counselling. The physician intervention included training of physicians on

blood pressure management and lifestyle modification, while the patient intervention component included adherence to a DASH diet, increased physical activity, reduced sodium intake and moderate alcohol intake. The results showed that both the physician and patient interventions combined had the largest effect of lowering SBP by 9.7 ± 12.7 mm Hg and DBP by 5.4 ± 4.6 mm Hg significantly compared to usual care.

On the other hand, there was no effect on blood pressure when a brief 15-minute educational intervention was provided by doctors in 33 general practitioner clinics in Italy [126]. The randomised controlled clinical trial was carried out for 12 months. The goals for the intervention group were to make the following dietary changes: consume more than 5 servings of fruits and vegetables per day, 1 serving of fish per week, use olive oil, consume less than 3 servings of red meat, and consume less snacks and sweets. Control participants received a non-personalised information session with no brochure. The study had a large number of participants (n = 3,186) and the educational intervention was administered on the first visit only, with participants being followed-up for one year without further counselling. This study suggests that the number of contact hours that an individual has with the health provider is an important determinant of behaviour change. More frequent contact may lead to increased motivation for an individual to follow the intervention. However, optimal health provider-patient interaction time, for management of blood pressure has not been identified.

In this thesis, the effects of dietary patterns on blood pressure are examined in clinical participants enrolled in a randomised controlled trial that is based on a service delivery model. This is to establish the relevance of the context to study the relationship between diet and blood pressure in terms of nutrients, foods and dietary

patterns and how this might be implemented by healthcare professionals in clinical practice.

1.12 Summary of evidence and gaps in literature

This review of the literature has identified that the problem of raised blood pressure is of public health concern and therefore needs to be addressed. As has been discussed throughout the chapter, blood pressure is influenced through diet at various levels namely; nutrients, single foods and dietary patterns. However, the results of the influence of diet on blood pressure are inconsistent with some foods showing greater effects than others. There is therefore a need to investigate the current state of evidence on how dietary patterns affect blood pressure in order to inform both population level management of raised blood pressure and individualised clinical practice.

Although various dietary patterns that affect blood pressure have been identified, there is limited data on which dietary patterns have the most beneficial impact on blood pressure in an intervention setting, especially with clinical groups such as overweight adults. In addition, the relevance of dietary patterns to practice and their usefulness in a clinical trial setting is yet to be established.

This chapter has identified the following gaps in the evidence base, which will be addressed in this thesis:

- There is a paucity of research evaluating the current evidence on the relationship between dietary patterns and blood pressure.
- There is little research on which dietary patterns are optimal for blood pressure management in clinical settings.

- There is lack of research on how changes in dietary patterns influence change in blood pressure in clinical settings.

1.13 Hypotheses

Dietary patterns characterised in terms of nutrients and foods, and changes in dietary patterns over time, in a clinical setting significantly influence blood pressure in adults.

1.14 Research questions

1. What is the current evidence on the relationship between dietary patterns and blood pressure?
2. What is the association between sodium and potassium intakes and blood pressure in a clinical sample of overweight adults?
3. What is the association between dietary patterns and blood pressure in a clinical sample of overweight adults?
4. How do changes in dietary patterns affect changes in blood pressure under weight loss conditions in a clinical setting?

1.15 Aims of the study

1. **Study 1** – To assess the current level of evidence on the relationship between dietary patterns and blood pressure by conducting a systematic review and meta-analysis on studies examining the relationship between blood pressure and dietary patterns in adults.

2. **Study 2** – To examine the association between sodium and potassium intake and blood pressure in overweight and obese adults in the context of a lifestyle intervention trial targeting weight loss.

3. **Study 3** – To identify dietary patterns associated with blood pressure in overweight adults in the context of a lifestyle intervention trial targeting weight loss.

4. **Study 4** – To assess how changes in dietary patterns as a result of more specific dietary advice affect changes in blood pressure in the context of a lifestyle intervention trial targeting weight loss.

1.16 Significance of research

The prevalence of hypertension and obesity in adults is increasing. This thesis will expose new knowledge that is relevant to clinical practice by identifying dietary patterns that influence blood pressure in the context of a clinical trial for weight loss. By conducting analyses of changes in blood pressure, a defined secondary outcome in the randomised controlled trial, new approaches for reducing blood pressure concurrently with weight loss will be identified.

1.17 Theoretical framework

The theoretical framework utilised in this thesis is outlined below (Figure 1.3). Study 1 investigated the current level of evidence on the effect of dietary patterns and blood pressure. Study 2 assessed the association between sodium and potassium consumption and blood pressure in overweight adults enrolled in a randomised controlled trial. Study 3 identified dietary patterns associated with blood pressure in

overweight adults, while study 4 assessed the effect of changes in dietary patterns after 3 months in a lifestyle intervention trial.

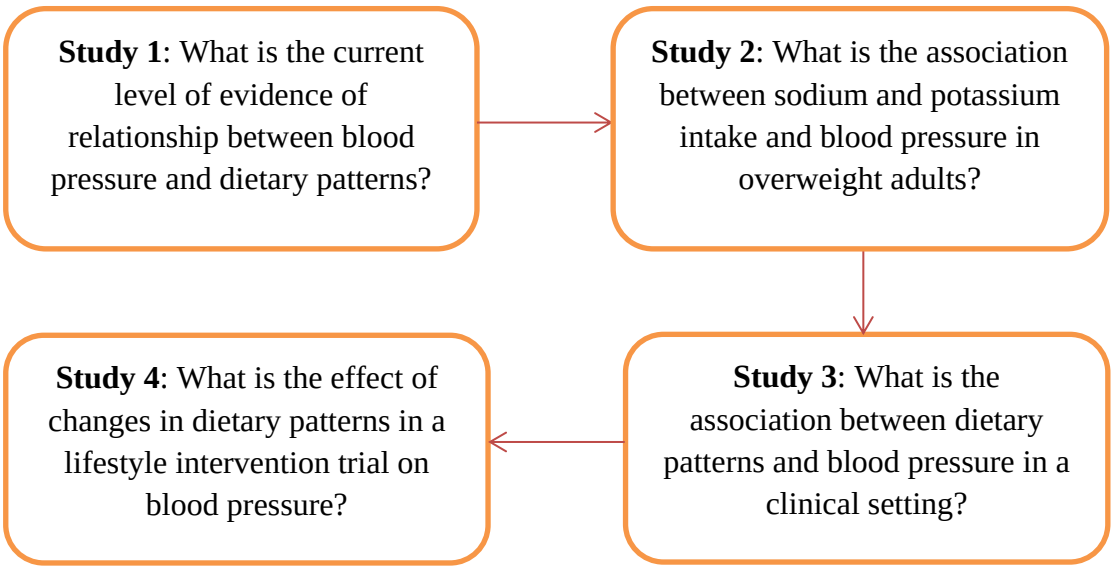

Figure 1.3 Overview of thesis studies

CHAPTER 2 – METHODOLOGY

As discussed in Chapter 1, hypertension is a major public health problem and a risk factor for developing cardiovascular disease, stroke and kidney disease [10]. Dietary components that influence blood pressure including nutrients such as sodium and potassium have been investigated however we do not consume single nutrients in isolation but instead eat whole foods in different combinations that form dietary patterns. In addition to single nutrients, this thesis hypothesizes that clinical settings may be effectively used to intervene upon dietary patterns for hypertension prevention and management. To test this hypothesis, various approaches were used. First, the current body of evidence on the diet-blood pressure relationship was examined applying the methodology of systematic literature review and meta-analysis. Second, a number of studies were conducted involving secondary analysis of data from a randomised controlled trial reflecting the clinical practice setting. Relationships between intakes of nutrients (sodium and potassium), foods or dietary patterns, and blood pressure were examined. These issues are discussed below.

2.1 Systematic reviews and meta-analyses

In order to integrate evidence in nutritional research for translation in clinical practice, systematic reviews and meta-analyses are conducted. Systematic reviews are useful as they enable compilation and synthesis of results from different studies [127]. In the rating of scientific evidence by the Australian health and medical bodies, evidence obtained from systematic reviews of relevant randomised controlled trials is regarded as the highest form (Level I) [128]. These follow established protocols by various expert bodies and groups [129]. The first step in conducting a review is to formulate a research question based on the identified problem. In addition, the Preferred Reporting Items for Systematic Reviews and Meta-analyses

(PRISMA) guidelines [130] offers a checklist and a flow diagram to ensure consistency in reporting systematic reviews and meta-analyses. The protocol details of reviews and meta-analyses are registered on the International Prospective Register of Systematic Reviews (PROSPERO) [131].

In meta-analysis, results from different studies are pooled together and statistically analysed to produce a single effect of an intervention [127]. The importance of conducting a meta-analysis is that there is increased power to detect results as well as increased precision in assessing the effects. In this thesis, results from all relevant randomised controlled trials that met the inclusion criteria were pooled together using computer analysis software, Cochrane Review Manager Software, RevMan [132]. Quality rating for each of the studies included in the meta-analysis is assessed using the "Risk of bias" assessment tool indicating the risk as low, unclear or high [127]. Assessment of risk of bias is important as it can aid in explaining the results of the meta-analysis especially the variation or heterogeneity of results. In clinical practice, systematic reviews and meta-analyses are valuable in offering the evidence that is required for implementation of clinical guidelines.

Meta-analyses can be a valuable component of systematic reviews by increasing statistical power and allowing for the estimation of the effects of interventions [127]. However, there are some limitations to their use. For example, conducting meta-analyses on studies using different techniques in measuring outcome variables or different populations, or combining studies with high levels of bias may lead to misleading results [127] [133]. In addition, publication bias may exist whereby significant results are more likely to be published than non-significant results. These limitations can be minimised through searching through a wide range of literature

including un-published papers, dissertations, and findings in books and professional meetings [133].

In this thesis, a systematic review and meta-analysis was undertaken to investigate the current level of evidence of the relationship between blood pressure and dietary patterns (Chapter 3).

2.2 Secondary analysis of a randomised controlled trial

Randomised controlled trials in nutrition research investigate the cause and effect of relationships that have been identified from research in cross-sectional, case-control and observational cohort studies [134]. Randomised clinical trials are important due to the fact that participants are allocated randomly to intervention groups and also blinded to minimise bias [135]. However, the trials can be expensive and time consuming and may have limitations due to ethical and feasibility concerns [135]. The National Health and Medical Research Council (NHMRC) states that the highest level of evidence in clinical practice including nutrition research should be obtained from systematic review of all relevant randomised controlled trials followed by the evidence from at least one properly designed randomised controlled trial [128].

Randomised controlled trials generate large amount of data which may not all be utilised in the primary analysis. This may therefore necessitate secondary analysis of the trial data in order to answer further questions that may not have been addressed in the primary analysis [136] [137]. Secondary analysis involves using existing data to answer various research questions. The strengths of secondary analysis include the fact that the analysis can reveal important new findings after examining subgroups and relationships not previously analysed [138]. In addition, secondary analysis consumes less time to conduct, can be sourced at minimal cost since the data is

readily available, and is of minimal risk to participants. On the other hand, various limitations of secondary analysis may exist. These include, researchers need to assess whether the data is able to answer the proposed research questions, dealing with incomplete data sets as a result of missing data, variables not measured correctly, and out of date data due to time lag between data collection and data analysis [138].

2.2.1 The HealthTrack study

The results that are reported in this thesis were derived from secondary analysis of data from the HealthTrack study. The study was a single blind randomised controlled trial that was conducted in the Illawarra region, south of Sydney, Australia [139]. The study recruited adults 25-54 years of age through advertisements in local newspapers (Figure 2.1). The sample size was calculated using SAS PROC POWER. One hundred and twenty participants per group were deemed adequate to detect a significant weight loss difference of 2.7 kg between groups. Inclusion criteria were people living in the Illawarra region with a BMI of 25-40 kg/m^2. Participants were not excluded if they had chronic disease risk factors such as family history of coronary heart disease, elevated low-density lipoprotein cholesterol and low high-density lipoprotein cholesterol. Individuals who could not communicate in English, had severe medical conditions that limited their ability to participate in the study, immunodeficiency, had medical conditions that could limit survival to 1 year, reported excessive alcohol intakes (greater than 50 grams of alcohol per day) or illegal drug use, or had difficulties in participating in some parts of the study were excluded.

Participants were randomised to one of three groups:

1. Intervention (interdisciplinary intervention with individualised dietary advice)
2. Intervention + walnut (interdisciplinary intervention with individualised dietary advice plus a supplement of 30 grams of walnuts per day)
3. Control (usual care/ general advice)

Dietary advice in both intervention groups was provided in an individualised manner according to the targeted requirements and usual food habits of the participants. A number of food choices were prescribed from the food groups defined in the Australian Guide to Healthy Eating [140]. This Guide was also used for the controls but advice was given in a general manner. In the intervention + walnut group, walnut supplementation was integrated into diets so as not to provide extra energy but to increase the specificity of the intervention to consume healthy food. The control group received general advice on food choices that enabled them to adjust their usual food patterns to the dietary guidelines [140]. The HealthTrack study was registered with the Australian and New Zealand Clinical Trial Registry (ANZCTRN 12614000581662) (Appendix A) and was approved by the University of Wollongong/Illawarra Shoalhaven Local Health District Human Research Ethics Committee (HE13/189) (Appendix B) including the current analysis in this thesis. All participants provided their informed written consent before participating in the study.

In the HealthTrack study, blood pressure was assessed as a secondary outcome. Details on blood pressure assessment in the trial and the assessment of sodium and potassium dietary intake are discussed in subsequent sections of this chapter.

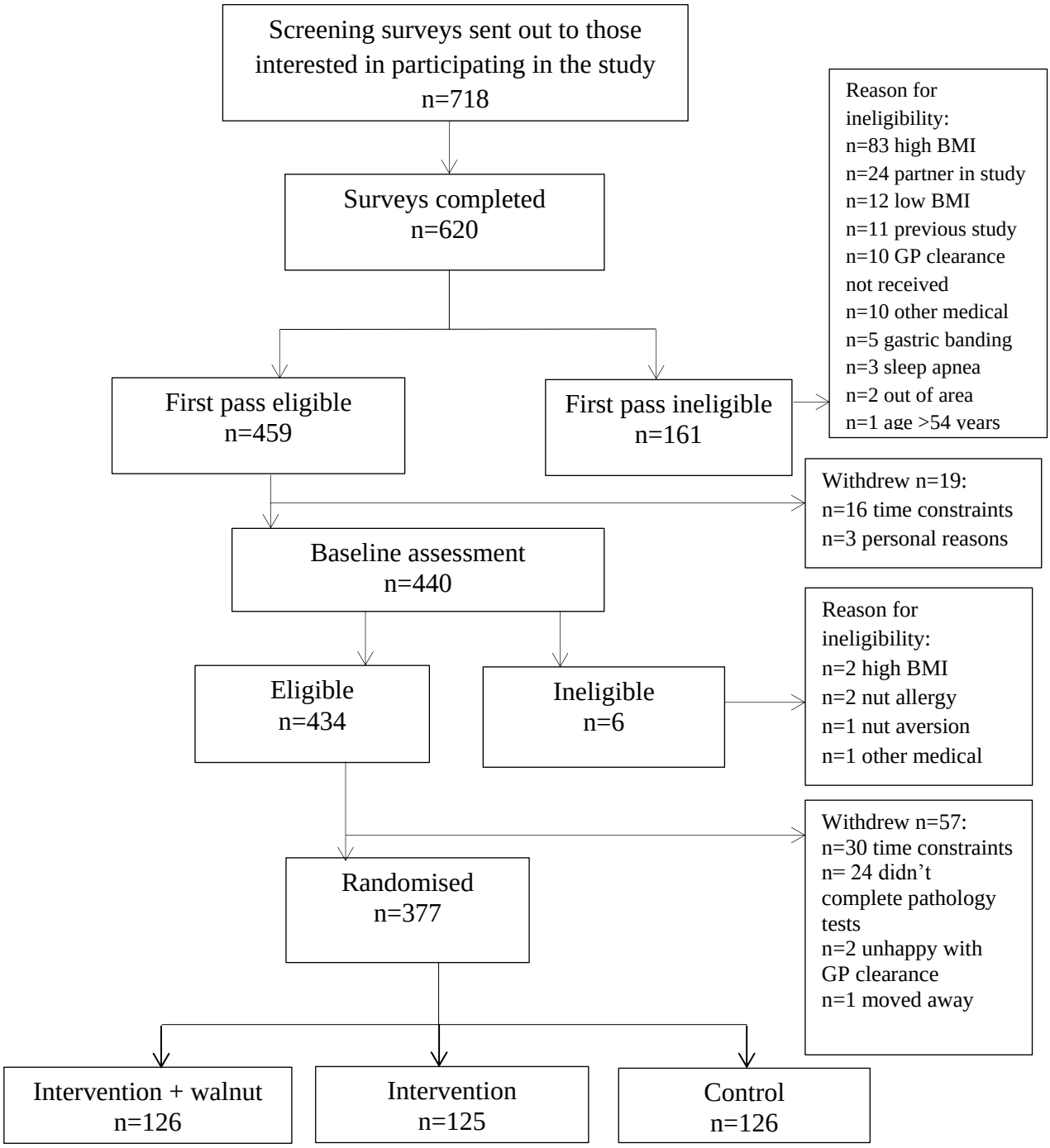

Figure 2.1 Flowchart of the HealthTrack study recruitment

2.3 Dietary intake measurements

Dietary assessment was conducted as a central method in the HealthTrack study. Nutritional epidemiology has progressed over the past years with major contributions to various nutrition-related health problems. Accurate measurement of exposure variables especially diet can however be challenging. As highlighted in Chapter 1, diet can be complex since it is composed of different components and is consumed in different amounts in varying combinations [141].

Different methods are used in nutritional epidemiology for the assessment of dietary intake. These tools include 24-hour dietary recalls, food frequency questionnaires, diet histories, and food records or food diaries. The choice of dietary assessment tool depends on the research design, hypothesis, objectives, study population and resources that are available [142]. Diet histories and food records were utilised in the collection of dietary data that was analysed and reported in this thesis and thus will be discussed in details.

2.3.1 Diet histories

Diet histories were utilised in the HealthTrack study for the assessment of dietary intake. Diet histories are an assessment method that involves a detailed account of an individual's usual dietary intake collected through an in-depth interview with a trained personnel such as a dietitian or nutritionist [142]. Detailed information is collected from the participant such as amounts of food and drinks consumed at every meal, frequency, preparation methods, and may also include a frequency checklist to assist in probing for forgotten items [143]. Advantages of diet histories include the detailed assessment of food consumption for a relatively longer period including meal patterns [143]. However, diet histories have limitations including the fact that

they require trained personnel to administer them and enter the data. They rely on the respondents' memory and may be influenced by recall bias. In addition, participants may tend to underestimate energy, fat, saturated fat and sodium [144]. More details on the appropriateness of diet histories in measuring sodium intake will be discussed in the sections below on measurement of sodium and potassium intake.

2.3.2 Food records

Food records or dietary records were also utilised in the HealthTrack study. Food records involves the participants recording all the foods and drinks consumed for specified number of consecutive days usually 3-7 days including at least one weekend day [143]. However, validity of recording decreases beyond four consecutive days since reported intake reduces due to participants' fatigue [143]. To measure the amount of food and drinks consumed, weighing scales or household items such as cups and spoons are used. Advantages of food records include the fact that they reduce participant's reliance on memory since data is collected at the time of food intake, though the respondents may require being highly motivated due to the burden that is passed on to them [142]. For conversion to nutrient estimates, the information from food records is entered into nutrient analysis software programs which can be time consuming and requires trained personnel [145]. A limitation of food records is that they are usually focussed on short-term food intake and may not be ideal to investigate chronic diseases which require long-term dietary exposure [142]. To overcome this, multiple food records at different time points may be utilised.

2.3.3 Dietary data collection in the HealthTrack study

In the HealthTrack study, the 4-day food records were recorded over four consecutive days, including one weekend day. Participants were instructed by trained health practitioners to record all foods and drinks consumed including amounts and recipes. Quantities of food intakes were determined using common household measures such as cups and spoons that were provided. Information on dietary supplement use was not collected. The records were reviewed for completeness by nutrition trained personnel upon return. In addition, Accredited Practising Dietitians assessed participants' dietary intake through a self-reported diet history interview [146]. Dietary data were entered into the FoodWorks nutrient analysis software program (Xyris software, FoodWorks. 2012: Brisbane, Australia).

2.4 Food composition database

In order to be able to convert food intake data to nutrients, food composition databases are required. In Australia, the Food Standards Australia New Zealand (FSANZ) creates and publishes food and nutrient databases for use by researchers, food manufacturers and by consumers [147]. Two published databases developed by FSANZ include the reference database, NUTrient TABles for use in Australia (NUTTAB), and the survey specific database, AUStralian Food and NUTrient Database (AUSNUT), which contains complete nutrient information for all foods. For this thesis, dietary data was originally analysed using AUSNUT 2007 [148], which was the most recent survey-specific food composition database available at the time of data collection. Due to the subsequent release of AUSNUT 2011-13 [149], dietary data was categorized according to the AUSNUT 2011-13 food groups. A matching file was created to convert the data from AUSNUT 2007 foods to

AUSNUT 2011-13 equivalents using a systematic process which has been published [150].

2.5 Measurement of sodium and potassium intake

Sodium and potassium dietary intake was assessed in the HealthTrack study. The dietary intake can be estimated from dietary intake data. However, studies have shown that individuals tend to under-report and over-report sodium and potassium respectively [151] and the estimates are also subject to recall and recording bias [143]. Furthermore, patients with hypertension have been found to underestimate their sodium intake through dietary recall by 30% to 50% [152]. In addition, dietary assessment methods may not take into account discretionary salt or other sources of sodium such as antacids or sodium containing supplements and medications [153]. A more reliable biomarker of sodium and potassium intake is 24-hour urine excretion since about 90% of the sodium or potassium consumed is excreted in the urine [154]. However, a complete 24-hour sample has to be collected to avoid bias of results due to under- or over collection. Due to the day to day variability in sodium excretion, repeated 24-hour collections are the gold standard but may not be practical as they are labour intensive for participants [154].

To ensure accurate urine collection, detailed verbal and written instructions can be provided to participants, and research personnel can supervise the beginning and end of the collection period [155]. Post collection, various methods can be used for ascertaining completeness such as the use of *para*-aminobenzoic acid (PABA) and urinary creatinine excretion. In the use of PABA, the participant is required to consume one tablet of 80 mg PABA three times a day with meals during the collection period [156]. About 93% of PABA is excreted in urine with completeness

assumed in samples containing above 85% of recovered PABA [157]. Since the timing and subject's age can affect urine excretion [157], an improved method with a high performance liquid chromatography has replaced the calorimetric method allowing the effect of different drugs such as paracetamol to be reduced [158]. In cases where PABA recovery is between 50% and 85%, linear regression equations have been suggested in order to adjust for urinary sodium and potassium [156].

Another method of ascertaining completeness of 24-hour urine samples is use of urinary creatinine excretion. Creatinine excretion models based on an individual's age, sex, weight, and protein intake have been developed, though with low sensitivity, to detect incomplete 24-hour sample collections [159]. Two equations that have been developed include Joosen's equation [160] which considers an individual's sex only and Mage's equation which accounts for age, sex, weight, height and BMI [161]. Other strategies that can be used to ascertain completeness include low urine volume collections, whereby samples with a total volume of less than 500 mL and/or creatinine levels less than 6.0 mmol/d in volumes less than 1000 mL are deemed as incomplete [162]. The use of a single 24-hour urinary sample may however be considered a limitation because of the large day-to-day variability. As a result, greater accuracy of sodium and potassium habitual intake would be obtained from repeated 24-hour urinary collections [163].

In the HealthTrack study, sodium and potassium intake was ascertained via a single 24-hour urine excretion obtained at various time points. Detailed instructions were provided whereby participants discarded the first urine of the day and collected the rest over the 24 hours in standard plastic containers that were provided. The collected samples were delivered to Southern IML pathology and were stored upon receipt at 2-8 degrees. The total volume of urine was measured and recorded.

Sodium and potassium concentrations were determined by indirect ion-specific electrodes whilst the creatinine concentration was determined using the Jaffe reaction colorimetric method [164]. Samples that had a total volume of less than 500 ml and/or creatinine levels less than 6.0 mmol/d, in volumes less than 1,000 ml were excluded as they were classified as incomplete [162].

2.6 Dietary patterns analysis

In dietary pattern analysis, two different approaches are commonly used to derive specific dietary patterns; a priori or hypothesis-oriented approaches, for example diet quality scores; and exploratory or posteriori methods that derive dietary patterns from the data at hand, such as principal component analysis (PCA), exploratory factor analysis, or cluster analysis [165]. In this thesis, PCA was utilised to derive dietary patterns since it had been previously demonstrated that the PCA method can reveal dietary patterns associated with blood pressure in clinical cohorts participating in weight loss trials [166]. As a result, the PCA method will be discussed here including its strengths and limitations.

PCA utilises available dietary data and reduces it into smaller interrelated components (principal components) such as sets of foods or food groups, therefore revealing interrelationships between food components and the dietary habits of a given population [167] [168]. Limitations of PCA include the subjective nature of some of the crucial decisions such as the variables to include, the number of factors to extract, the rotation method and description of the components extracted [169]. However, the use of eigenvalues and examination of the scree plots are helpful in determining the best number of components to extract.

2.7 Blood pressure measurement

Appropriate diagnosis and treatment of blood pressure depends on accurate measurement, using devices that undergo regular calibration and maintenance, and minimization of human errors such as use of inappropriate cuff and incorrect cuff positioning, lack of appropriate rest period prior to taking the measurement, low concentration, digital bias and lack of repeated measurements [170]. Measuring blood pressure in a clinical setting may be challenging due to the 'white coat syndrome' - which refers to blood pressure becoming more elevated than usual in the presence of medical personnel [171]. However, use of automated blood pressure measurement instead of manual office blood pressure in primary care setting has been shown to reduce the 'white coat effect' in hypertensive patients [172]. Moreover, the use of 30-minute office blood pressure measurement, whereby the patient is left alone in a room for thirty minutes and the readings are taken automatically, was shown to further reduce the 'white coat effect' compared to the standard office blood pressure measurement [173]. This may however be challenging to implement in daily primary care practice since additional rooms and more time may be required.

Out of office blood pressure measurement, which includes home blood pressure monitoring and ambulatory blood pressure monitoring is recommended as a more accurate method of measuring blood pressure due to the larger number of readings taken to calculate the average blood pressure [174]. In addition, out of office blood pressure is better at detecting masked hypertension, which refers to a lower blood pressure reading observed in the health care environment [174].

In the HealthTrack study, office SBP and DBP were measured using automatic blood pressure monitor (OMRON BP-203RPE III, OMRON Health Care Co. Ltd, Kyoto, Japan). A test blood pressure reading was taken after participants had rested in the supine position for 5 minutes and a confirmatory reading was taken 10 seconds after the first which was the reading used for the analysis. All blood pressure measurements were performed by trained health practitioners.

2.8 Anthropometric and physical activity measurements

Anthropometric measurements enable assessment of important variables that are used to describe participants' characteristics. In the Healthtrack study, anthropometric measurements were conducted by trained health practitioners. Lightly clad body weight was measured on digital scales [Tanita scales, Tanita Corporation, Tokyo, Japan, UM0703581(1)] to the closest 0.1 kg and percent body fat via bioelectrical impedance recorded to the closest 0.1 %. Height was measured using a wall-mounted stadiometer rounded to the nearest millimetre in accordance with the established anthropometric protocols [175]. Widest part of hip and narrowest waist circumference were measured in accordance with the reported acceptable protocols [175]. BMI was calculated as body weight in kilograms divided by the square of the height in metres.

The International Physical Activity Questionnaire (IPAQ) was used to assess physical activity through the survey's short form questions [176]. IPAQ was deemed appropriate in measuring physical activity due to its acceptable reliability and validity in both developed and developing countries, especially in urban population. However, its application is limited to middle-aged adults (18 to 65 years) and not adolescents or older adults [176].

This chapter has established the methods utilised in this thesis to address the various research questions/ hypotheses of the thesis. A systematic review and meta-analysis was carried out in Chapter 3 to assess the current level of evidence on the relationship between dietary patterns and blood pressure. Measurement of 24-hour urinary sodium and potassium excretion was used in Chapter 4 and dietary pattern analysis was utilised to identify dietary patterns associated with blood pressure in Chapter 5. In each chapter, further details of the specific application of methods used in the specific studies will be provided.

CHAPTER 3 - DIETARY PATTERNS AND BLOOD PRESSURE IN ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

The majority of this chapter is the substantative content of the published work: Ndanuko, R.N., Tapsell, L. C., Charlton, K. E., Neale, E. P., Batterham, M. J., Dietary patterns and blood pressure in adults: A systematic review and meta-analysis of randomized controlled trials. *Advances In Nutrition*. 2016;7:76-89; doi:10.3945/an.115.009753.

The findings of this section were also presented in an oral presentation:

Ndanuko R, Tapsell L & Charlton K (2015). Identifying the effects of dietary patterns on blood pressure: A systematic review. Dietitians Association of Australia, National Conference, Perth, Australia, Nutrition & Dietetics; 72(S1): p32.

CHAPTER 4 – THE RELATIONSHIP BETWEEN SODIUM AND POTASSIUM INTAKE AND BLOOD PRESSURE IN A SAMPLE OF OVERWEIGHT ADULTS

The majority of this chapter is the substantative content of the published work: Ndanuko, R.N., Tapsell, L. C., Charlton, K. E., Neale, E. P., O'Donnell, K. M., Batterham, M. J. Relationship between sodium and potassium intake and blood pressure in a sample of overweight adults. *Nutrition.* 2017;33:285-290: doi: 10.1016/j.nut.2016.07.011.

The findings of this section were also presented in poster presentations:

Ndanuko, R.N., Tapsell, L. C., Charlton, E. K., Neale, E. P., Batterham, M. J. Association between urinary sodium intake, sodium-to-potassium ratio and blood pressure in adults. Nutrition Society of Australia. Annual Scientific Meeting, Wellington, New Zealand. 1st-4th December 2015.

Ndanuko R., Tapsell L, Charlton K & Neale E (2016). Diet history and food records as predictors to urinary sodium, urinary potassium and blood pressure. Dietitians Association of Australia National Conference, Melbourne, Australia. Nutrition & Dietetics; 73(S1):p80.

4.1 Introduction

As discussed in Chapter 1, from a preventive health perspective, lifestyle changes such as reducing dietary sodium, following a healthy diet such as the Dietary Approaches to Stop Hypertension diet and engaging in regular physical activity have been recommended to lower blood pressure [10]. Evidence supporting dietary approaches is provided in meta-analyses that have assessed the effect of sodium and potassium intake on blood pressure [45] [55]. In addition, the ratio of sodium to potassium may better reflect desirable food choices for lowering blood pressure across various geographical regions and cultures [64] but food patterns that reflect an optimal ratio have not been adequately identified.

Despite the recommendations by the World Health Organization for a population sodium intake of 2000 mg of sodium and 3510 mg of potassium per day [54] and Suggested Dietary Target of 1600 mg of sodium for chronic disease prevention recommendations by NHMRC [69] excessive sodium consumption and low potassium intakes have been previously reported [209]. Food sources of sodium may vary according to the dietary habits of different cultures. In the INTERMAP study, major food sources of sodium included bread, grains and cereals in the United States and United Kingdom; added salt in China; and soy sauce, processed fish/ seafood and salted soups in Japan [210].

In the previous chapter, the association between dietary patterns and blood pressure in the published research has been examined. There is need to explore relationships between sodium and potassium intake with blood pressure in a clinical sample. There are few studies examining the relationship between sodium and potassium intakes and blood pressure specifically in clinical overweight populations, whereby

exposing the details of dietary-blood pressure relationships may be informative for primary healthcare practice. The aim of this study was to examine the association between sodium and potassium intakes and blood pressure at baseline in a sample of overweight and obese adults volunteering for a weight loss trial. To address issues of translating dietary advice to practice, sodium and potassium intake is reported, as well as major food sources of these nutrients, in the context of the clinical trial.

4.2 Methods

This chapter utilised baseline data from the 12-month HealthTrack randomised controlled trial. The baseline data was utilised in order to assess the relationship between sodium and potassium intake and blood pressure, consequently leading to analysis of change in nutrients and foods and relationship with blood pressure after 3 months in Chapter 6. The HealthTrack study has been discussed in detail in Chapter 2. Sodium and potassium excretion was estimated from the 24-hour urine. Dietary intake was assessed using 4-day food records (including one weekend day). Participants recorded all foods and drinks consumed including amounts and recipes. In addition, dietary intake was assessed using a self-reported diet history interview administered by accredited practising dietitians. For this analysis, the primary outcomes were SBP and DBP.

4.2.1 Statistical analysis

For this secondary analysis of the Healthtrack data, statistical analysis was performed using the Statistical Package for the Social Sciences (IBM Corp., SPSS for Windows Version 21. 2012: New York, USA). Normality testing was conducted using Shapiro-Wilk test and data was log transformed where possible. For sodium and potassium intake, medians were used as they are less influenced by extreme

values and skewness compared to means. The number and percentage of participants meeting the recommended amounts according to various guidelines was calculated. The percentage contribution of sodium and potassium by AUSNUT 2011-13 major food groups was also determined. Multiple linear regression was used to assess the relationship between urinary sodium and potassium and dietary intake assessed via 4-day food records and via diet histories.

Spearman's rank order correlation was performed to assess the relationship between urinary sodium and potassium excretion and sodium-to-potassium ratio with blood pressure. Stepwise forward multiple linear regression was performed to assess prediction of blood pressure by sodium intake, potassium intake and sodium-to-potassium ratio and prediction of urinary sodium and potassium by dietary sodium and potassium. Covariates that were controlled for include age, sex, BMI and antihypertensive medication. Initial analysis to ensure no violations of the assumptions of normality, linearity, multicollinearity and homoscedasticity were conducted. Data are expressed as mean (standard deviation) unless otherwise stated and as a percentage for the food group contribution of sodium and potassium. Data was considered statistically significant when $P<0.05$.

4.3 Results

4.3.1 Baseline characteristics

A total of 377 participants, predominantly Australian born (82%), were randomised to the HealthTrack study. For the present analysis we included data from 328 participants who had complete dietary data, blood pressure data and 24-hour urine collections at baseline. The main characteristics of the participants are reported in Table 4.1. 26% of the participants (n=85) were hypertensive and of this n=46 were taking antihypertensive medication. Participants were diagnosed as hypertensive if

blood pressure was ≥140/90 mm Hg and/or taking antihypertensives. Median urinary sodium concentrations indicated that dietary intakes were above the recommended targets set by the NHMRC [69] and World Health Organization [54]. Table 4.2 illustrates the number of participants who were compliant with the NHMRC and World Health Organization guidelines for sodium and potassium intake.

Table 4.1 Baseline characteristics of the analysis sample (n=328)

Characteristic	**Mean (SD)**[1]
Male/ female, % (n)	27/73 (89/239)
Age, years	43.6 (8.0)
BMI, kg/m^2	32.4 (4.2)
Blood pressure	
Systolic, mmHg	124.9 (14.5)
Diastolic, mmHg	73.3 (9.9)
Urinary excretion	
Creatinine, mmol/day	8.2 (4.5)
Median sodium, mg/day, (IQR)[2]	3197 (2282-4140)
Median potassium, mg/day, (IQR)	2886 (2223-3549)
Median sodium-to-potassium ratio, (IQR)	1.9 (1.5-2.4)
Median salt intake, g/day (IQR)	8.2 (5.9-10.6)
Dietary intake (4-d food records)	
Median energy, kcal/day, (IQR)	2088 (1745-2500)
Median sodium, mg/day, (IQR)	2682 (2084-3439)
Median potassium, mg/day, (IQR)	3124 (2680-3825)
Medium calcium, mg/day, (IQR)	915 (695-1139)
Medium magnesium, mg/day, (IQR)	370 (304-473)

[1]Data are presented as mean (standard deviation), unless otherwise stated; [2]IQR, Interquartile range.

Table 4.2 Number (%) meeting sodium and potassium urinary excretion targets defined in NHMRC and WHO guidelines

Target value[1]	**Number (%)**
24-h sodium excretion	
≤6 g salt/day (2300 mg Na/day)[a]	86 (26.2)
≤5 g salt/day (2000 mg Na/day)[b]	50 (15.2)
≤4 g salt/day (1600 mg Na/day)[c]	14 (4.3)
24-h potassium excretion	
≥ 97 mmol/day, men (*n* = 89)[e]	32 (36.0)
≥ 72 mmol/day, women (*n* = 239)[f]	111 (46.4)
≥ 90 mmol/day[b]	90 (27.4)

[1]Data presented for n = 328 unless otherwise stated; NHMRC, National Health and Medical Research Council; WHO, World Health Organization. [a]NHMRC upper level; [b]WHO population target; [c]NHMRC suggested dietary target; [e]NHMRC target for men; [f]NHMRC target for women.

4.3.2 Food group contributions to total dietary sodium and potassium intake

Percentage contributions of sodium and potassium by the AUSNUT 2011-13 major food groups from the 4-day food records data were determined (Appendix G). Overall, cereal based products and dishes; cereal and cereal products; meat, poultry and game products and dishes; and milk products and dishes were the major contributors for dietary sodium. On the other hand, vegetable products and dishes;

meat, poultry and game products and dishes; and milk products and dishes were the major contributors for dietary potassium intake.

4.3.3 Prediction of urinary sodium and potassium by dietary intake

A multiple linear regression model established that reported dietary sodium via the 4-day food records significantly predicted urinary sodium excretion adjusted for energy and BMI. The overall model was significant, F (21.8, 3df) $P < 0.01$ accounting for 16.0% of the explained variability in urinary sodium (Figure 4.1). Dietary sodium was a significant predictor, $B = 0.334$, t = 4.032, $P < 0.01$. Likewise, the overall model for predicting urinary potassium from dietary potassium adjusted for energy and BMI was significant, F (29.1, 3df), $p < 0.01$ accounting for 20.5% of the explained variability in urinary potassium (Figure 4.2). Dietary potassium was a significant predictor, $B = 0.67$, t = 8.537, $P < 0.01$. In both sodium and potassium analysis, there was no evidence of multicollinearity and the residual diagnostics indicated the models were a good fit. Dietary intake assessed via 4-day food records showed a stronger relationship with urinary sodium and potassium compared to diet histories (data not shown).

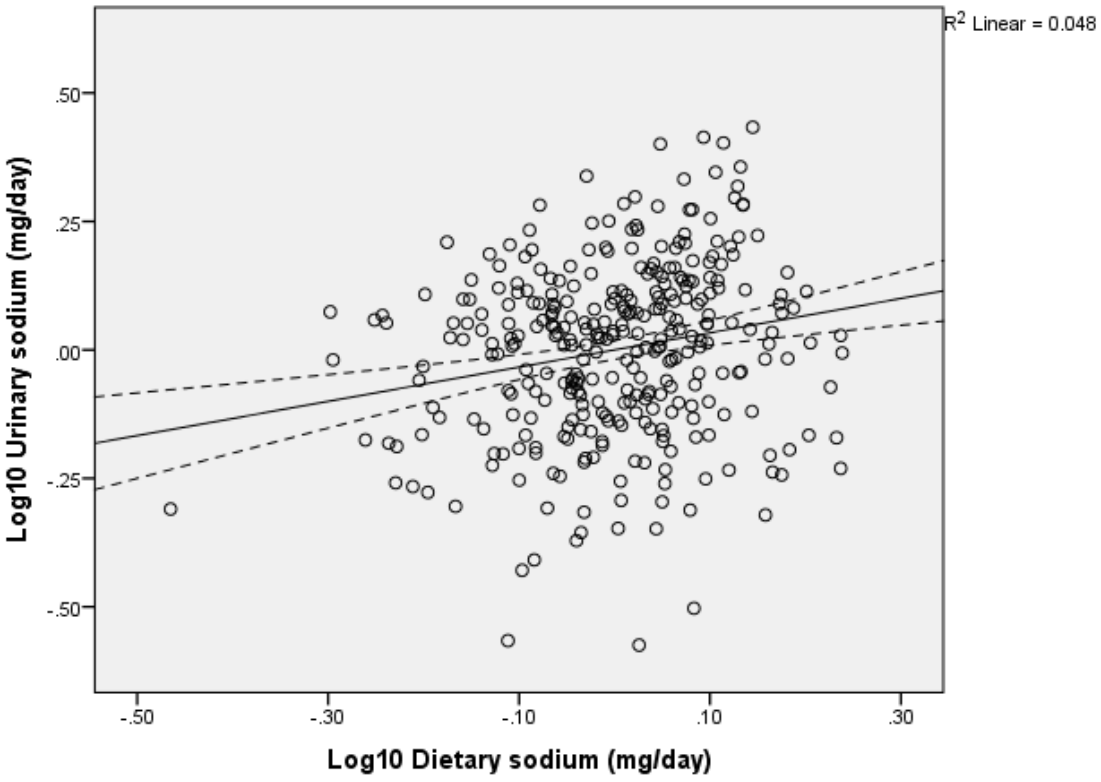

Figure 4.1 Relationship between dietary sodium and urinary sodium excretion. The solid line represents the regression best of line of fit while the dotted lines indicate the 95% confidence limits for mean predicted values.

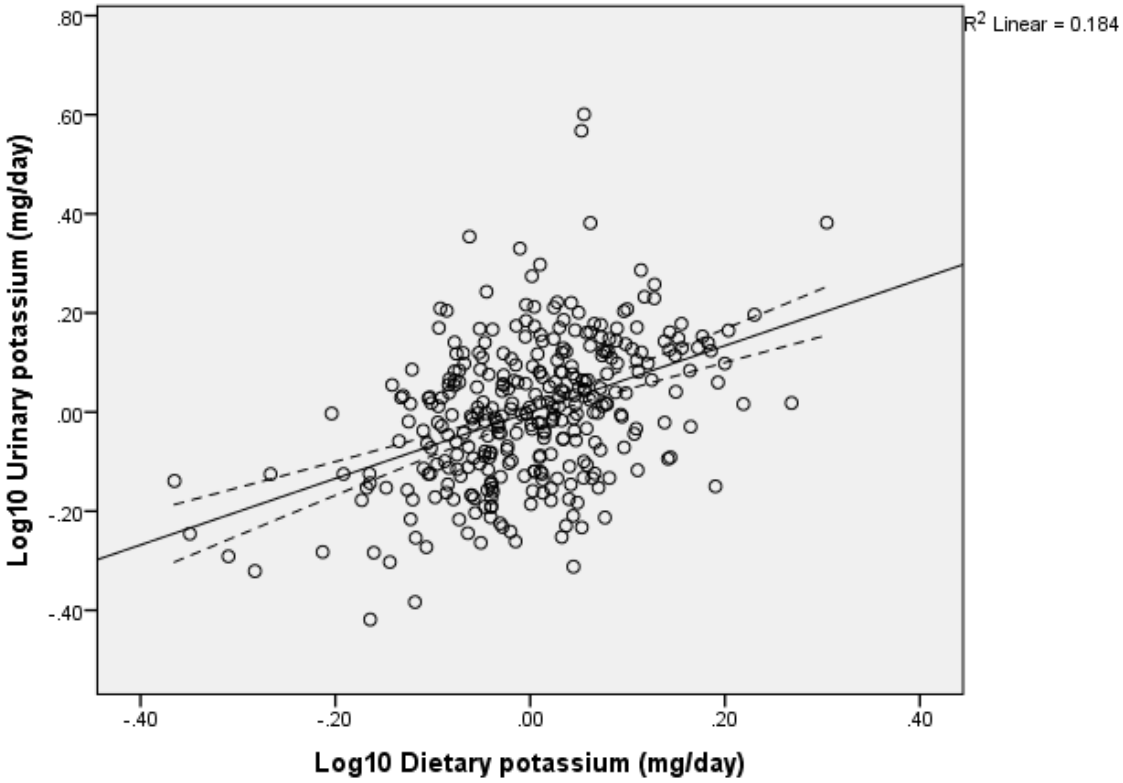

Figure 4.2 Relationship between dietary potassium and urinary potassium excretion. The solid line represents the regression best of line of fit while the dotted lines indicate the 95% confidence limits for mean predicted values.

4.3.4 Relationship between sodium, potassium and sodium-potassium-ratio and blood pressure

Urinary sodium was positively correlated with SBP (r = 0.176, P = 0.001) and DBP (r = 0.150, P = 0.003). Sodium-to-potassium ratio was positively correlated with SBP (r = 0.1, P = 0.035). In multiple linear stepwise regression, urinary sodium [(F (4,323) = 20.381, P < 0.0005; adjusted R^2 = 0.231)] and sodium-to-potassium ratio [(F (4,323) = 25.008, P < 0.0005; adjusted R^2 = 0.227)] were identified as significant predictors of SBP after controlling for age, sex, BMI and hypertension medication use. Likewise, dietary potassium was a significant predictor of DBP [(F (4,323) =

28.059, $P < 0.0005$; adjusted $R^2 = 0.249$)] (Table 4.3). No statistically significant associations were observed between urinary potassium and SBP, urinary sodium and sodium-to-potassium ratio and DBP, dietary sodium and dietary potassium and SBP, and dietary sodium and DBP.

Table 4.3 Stepwise regression analyses using SBP and DBP as the dependent variables and age, sex, BMI, urinary sodium, dietary potassium and Na:K ratio as independent variables

Variable	***B***[1]	**SE *B***	**Standardized *B***	***P* value**
SBP:				
Age	0.002	0.0003	0.367	<0.001
BMI	0.003	0.001	0.242	<0.001
Urinary sodium	0.037	0.014	0.118	0.02
Na:K ratio	0.033	0.014	0.118	0.02
DBP:				
Age	0.003	0.0004	0.358	<0.001
Sex	-0.031	0.006	-0.232	<0.001
BMI	0.003	0.001	0.230	<0.001
Dietary potassium	-0.051	0.024	-0.104	0.035

[1]Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; Na:K, sodium-to-potassium ratio; SBP, systolic blood pressure; B, β standardized coefficient. Only statistically significant variables are shown; variables excluded include urinary potassium and dietary sodium.

4.4 Discussion

This secondary analysis of baseline data from a weight loss clinical trial confirmed that the relationship between dietary sodium intake and sodium-to-potassium ratio as analysed using the 24h sodium excretion, and SBP can be observed within an overweight clinical sample. In addition, age and BMI significantly predicted SBP, while age, sex and BMI significantly predicted DBP. Dietary potassium as measured using food records was also significantly associated with DBP. There was a marked difference between urinary and dietary sodium and potassium intakes. It has been shown that there is a tendency for subjects with a higher BMI to under-report their dietary sodium intake and over-report dietary potassium intake [151]. Moreover, the discrepancy between estimations of reported dietary intake and urinary excretion of sodium in our sample may be an indication of discretionary salt intake.

This study focused on a clinical obese population that was participating in a weight loss trial. About 26% of the participants were hypertensive with more than half taking anti-hypertensive medication. Lifestyle interventions such as consuming a healthy diet (such as the DASH diet and reduced sodium intake), weight loss and regular physical activity, are some of the strategies recommended for blood pressure management [10]. In the present study, we observed a significant association between sodium intake, sodium-to-potassium ratio and SBP. This is in line with findings from a previous Australian study whereby sodium intake (3567 mg/d) and sodium-to-potassium ratio (1.99) were both positively associated with SBP [211] though the sample population was older (mean age: 64 y) and less overweight (mean BMI: 28 kg/m^2) in comparison to our relatively young study population. Although dietary potassium was significantly associated with DBP in the present study, no

association was found with urinary potassium. The higher dietary potassium could have been due to over-reporting of fruit and vegetable intake which has been observed in epidemiological studies [212]. In this study, the sodium-to-potassium ratio (1.9) exceeded the World Health Organization recommendation of a sodium-to-potassium molar ratio of 1:1 [65]. A recent review demonstrated that in various randomised controlled trials the sodium-to-potassium ratio had a stronger association with BP than sodium or potassium alone [63]. In the development of hypertension, excessive sodium and insufficient potassium intake are both shown to play a role since they result in vascular smooth muscle cell contraction which leads to increased peripheral vascular resistance thus causing high BP [62].

The major food sources of sodium that were identified in this study included cereal-based products and dishes; cereal and cereal products; meat, poultry and game products and dishes; and milk products and dishes. These four food groups provided more than 60% of the total sodium intake. This is comparable to the recent 2011-2012 population based cross-sectional Australian Health Survey (AHS) which found that cereal-based products and dishes (25%), cereal and cereal products (18%) and meat and poultry (18%) were the major sources of sodium [213]. Similar results have been found in other studies in Finland [162] and South Africa [214]. In contrast, sources of sodium may vary in other countries depending on the major foods consumed and cultural context. For instance, in Japan, most of the dietary sodium is derived from soy sauce, salted soups, processed fish/ seafood and preserved vegetables [210]. While meal patterns and their sodium contribution to the total daily intake were not analysed, a previous Australian study found that lunch had the highest sodium density compared to dinner and breakfast [215]. This study did not assess the use of discretionary salt, but in low and low-middle income countries,

this has been found to be a significant source of sodium which may account for up to 76% of total intake in China [210]. Commercially processed foods are a major source of sodium in most high income countries. In Australia, 54% of processed food products have been reported to exceed maximum sodium level voluntary targets recommended by the UK Food Standards Agency (FSA) [216]. Similarly, in the US more than half of the commercially packaged food products exceed maximum upper limits recommended by the Food and Drug Administration [217].

There are a limited number of studies that have assessed food sources of potassium. In this study, vegetable products and dishes; meat, poultry and game products and dishes; and milk products and dishes were identified as major contributors, accounting for half of total potassium intake. These results are similar to the nationally representative Australian Health Survey whereby vegetable products and dishes accounted for 17.5% of total potassium intake [213].

Nutrient intakes, including sodium and potassium, are contributed from combinations of food groups that are consumed within the context of dietary patterns and cuisines. In a recent meta-analysis as described in Chapter 3, it was demonstrated that consumption of diets that are rich in fruit, vegetables, wholegrains, legumes, seeds, nuts, fish and dairy, and that are low in meat, sweets and alcohol, significantly lowered SBP and DBP by 4.26 mm Hg and 2.38 mm Hg, respectively [218]. In addition, specific dietary patterns that are related to blood pressure in another clinical trial datasets were identified in an entirely different population of obese adults attending for weight loss. Dietary patterns that included larger amounts of fruits & nuts and/or seafood were associated with lower blood pressure at baseline, while patterns that were characterised by yeast extract & seasonings were associated with higher blood pressure [166]. Hence, diets that are high in potassium

and low in sodium are shown to be beneficial in lowering blood pressure in clinical populations.

While large cohort studies have provided in principle evidence of the relationship between dietary sodium and potassium with blood pressure [219], the current analysis of data from a clinical trial provides a novel confirmation that the relationship between dietary sodium and SBP can still be observed in a relatively small sample of an at risk group. Importantly, the analysis identifies the food sources of sodium and potassium that would form the basis of dietary counselling in these settings.

The major strength of this study includes the use of 24-hour urine excretion to estimate sodium and potassium intake given the recognised problems with underreporting and over-reporting of sodium and potassium respectively [151]. Dietary assessment remains important as it assists in identifying food sources of sodium and potassium which may be useful in making recommendations in health education [154]. A limitation of this study is that the dataset was not large enough to group participants according to their level of sodium and potassium intake, though the number of participants meeting the sodium and potassium targets is reported.

4.5 Conclusions

This study has confirmed that the relationship between dietary sodium and sodium-to-potassium ratio and SBP can be observed in a clinical sample of overweight adults. In addition, dietary potassium as measured through food records was associated with DBP. While much of the evidence for this relationship is translated into population health messages, the analysis suggests there is good reason to translate this advice to clinical practice for patient groups such as overweight adults.

Importantly, the identification of food sources of sodium and potassium in the usual diet enables a direct pathway to practice, with food based dietary advice specifically targeting changes for improved blood pressure regulation.

In addition to individual nutrients, consideration of the combinations of foods which can influence blood pressure in the context of a clinical sample is required. The association between dietary patterns and blood pressure in the HealthTrack study clinical sample will be investigated in the next chapter, utilising dietary pattern analysis methodology discussed in Chapter 2.

CHAPTER 5 – ASSOCIATIONS BETWEEN DIETARY PATTERNS AND BLOOD PRESSURE IN A CLINICAL SAMPLE OF OVERWEIGHT ADULTS

The majority of this chapter is the substantative content of the published work: Ndanuko, R.N., Tapsell, L. C., Charlton, K. E., Neale, E. P., Batterham, M. J. Associations between dietary patterns and blood pressure in a clinical sample of overweight adults. *Journal of Academy of Nutrition and Dietetics*. 2017;117:228-239: doi:10.1016/j.jand.2016.07.019.

The findings of this section were also presented in poster presentations:

Ndanuko, R.N., Tapsell, L. C., Charlton, E. K., Neale, E. P., Batterham, M. J. Dietary patterns associated with blood pressure in a clinical sample of overweight adults volunteering for a weight loss trial. International Congress of Dietetics, Granada, Spain. 7th – 9th September 2016.

5.1 Introduction

As discussed in Chapter 1, research on dietary management of hypertension has mainly focussed on single nutrients such as sodium and potassium or single foods. Also highlighted previously is the fact that diets are complex and may result in multiple nutrient interactions thus making it difficult to isolate the role of individual foods or nutrients in relation to specific health and disease outcomes [103]. Inconsistencies in the findings for single foods, and possible differences in population sub-groups suggest a need for more research to better understand diet-blood pressure associations, particularly in at risk groups such as obese and overweight adults.

Dietary pattern analysis has been recommended in nutritional epidemiology as an additional method to better understand relationships between diet and chronic diseases [104]. Various beneficial dietary patterns for blood pressure regulation as identified in Chapter 3 include the DASH diet [24], the Nordic diet [108] and the Mediterranean diet [113]. These dietary patterns are characterized by a diet that is high in fruit and vegetables, whole grains, legumes, seeds and nuts, fish and dairy and has a low consumption of meat and sweets and moderate alcohol intake. In dietary pattern analysis, two different approaches are commonly used to derive specific dietary patterns; a priori or hypothesis-oriented approaches, for example diet quality scores; and exploratory or posteriori methods that derive dietary patterns from the data at hand, such as principal component analysis, exploratory factor analysis, or cluster analysis [165].

Previously, the principal component analysis method has been demonstrated that it can reveal dietary patterns associated with blood pressure in clinical cohorts

participating in weight loss trials [166]. In these food based dietary trials, significant associations were found between blood pressure and dietary patterns, namely those characterised by fruit and nuts (inversely associated with SBP), seafood (inversely associated with DBP), or a yeast extract and seasonings (positively associated with both SBP and DBP). These results need to be confirmed by further studies in broader lifestyle interventions with at risk populations to add to the evidence base. The aim of this study was to examine the association between dietary patterns and blood pressure in a sample of overweight adults volunteering for a lifestyle intervention trial targeting weight loss. A secondary aim was to identify the association between dietary patterns and 24-hour sodium and potassium excretion.

5.2 Methods

The current study is an analysis of baseline data from the 12-month HealthTrack randomised controlled trial which has been described in detail in Chapter 2. Estimation of sodium and potassium excretion was done through 24-hour urine. Dietary intake was estimated via 4-day food records taken over 4 consecutive days, including 1 weekend day.

5.2.1 Statistical analysis

To derive dietary patterns, principal component analysis was performed based on consumption of the 24 AUSNUT 2011-13 major food groups (grams/day) estimated from the 4-day food records data. The suitability of principal component analysis was assessed prior to analysis. Sampling adequacy was supported by a Kaiser-Meyer-Olkin (KMO) measure of 0.55 and Bartlett's test of sphericity < 0.0005, indicating that the data was likely factorizable. Inspection of the Anti-image Matrices was performed in order to determine the food groups to retain for principal

component analysis. To determine the number of components to retain, eigenvalues > 1.0 were considered along with examination of the Scree Plot [220]. To simplify the structure and improve interpretability, an orthogonal (varimax) rotation was applied. Calculation of the factor scores for each component was performed using the regression method. Food groups with positive loadings signify direct relationship with that pattern while those with negative loadings indicate an inverse relationship. Multiple regression analysis was performed to assess the association between the extracted dietary patterns and blood pressure, controlling for age, sex, BMI, blood pressure medication, energy intake and physical activity in the model. As alcohol intake was collected in the four day food records and included in the principal component analysis as a food group, it was not included as a covariate in the analysis. Similarly due to the low number of smokers in the sample (4%), smoking was also not included as a covariate. The difference in macronutrient and micronutrient intakes between individuals adhering or not adhering with specific dietary patterns was analysed using independent t-test. Chi square test was performed to determine the association between the dietary patterns and hypertension status. All statistical analyses were performed using the Statistical Package for the Social Sciences (Version 21, 2012, IBM Corp. New York, USA). Statistical significance was considered at $P < 0.05$.

5.3 Results

5.3.1 Baseline characteristics

A total of 377 participants were randomised to the HealthTrack study. For the present analysis, data was included from 328 participants (89 men and 239 women)

who had complete dietary intake, blood pressure and 24-hour urine collections data. The main characteristics of the participants are presented in Chapter 4, Table 4.1.

5.3.2 Dietary pattern analysis

Due to a lack of participants consuming foods from the AUSNUT 2011-13 categories labelled *Infant formulae and foods, Reptiles, amphibia and insects,* and *Dietary supplements*, these food groups were excluded, leaving n = 21 AUSNUT 2011-13 food groups categorized for this analysis (Appendix H).

Six principal components (dietary patterns) were derived, explaining 46% of the total variance (Appendix I). Food groups with factor loadings of more than 0.4 were considered as significant contributors to the dietary pattern. The "nuts, seeds, fruit and fish" dietary pattern was characterized by the consumption of seeds/nuts, fruit, fish and seafood products, and confectionery (including cereal/nut/fruit/seed bars); "milk and meat" dietary pattern by consumption of non-alcoholic beverages, milk products and dishes, and meat, poultry and game products and dishes; "breads, cereals and snacks", dietary pattern by intake of cereal based products and dishes, confectionery and snack foods; "cereal based products, fats and oils" dietary pattern by intake of cereals and cereal products, fats and oils; "alcohol, eggs and legumes" dietary pattern by consumption of alcoholic beverages, eggs products and dishes, and legumes; and "savoury sauces, condiments and meat" dietary pattern by intake of savoury sauces and condiments and meat.

After adjusting for age, sex, BMI, hypertension medication, physical activity and energy intake, multiple linear regression found the "nuts, seeds, fruit and fish" dietary pattern was significantly and inversely associated with SBP (F (7,320) = 15.248, $P < 0.0005$; adjusted $R^2 = 0.234$), DBP (F (7,320) = 17.351, $P < 0.0005$;

adjusted R^2 = 0.259) and sodium-to-potassium ratio (F (7,320) = 6.210, P < 0.0005; adjusted R^2 = 0.100). On the other hand, the association between SBP and DBP with the other dietary patterns was not significant. The "alcohol, eggs and legumes" and "savoury sauces, condiments and meat" dietary patterns were significantly and positively associated with sodium excretion while the, "milk and meat", and "breads, cereals and snacks" dietary patterns were significantly and positively associated with potassium excretion. The "savoury sauces, condiments and meat" dietary pattern was significantly and positively associated with urinary sodium-to-potassium ratio (Table 5.1).

Table 5.1 Regression coefficients (confidence intervals) showing associations between the six dietary patterns with blood pressure, urinary sodium, urinary potassium and sodium-to-potassium ratio among participants of the HealthTrack study (n=328)

	Nuts, seeds, fruit and fish	**Milk and meat**	**Breads, cereals and snacks**	**Cereal based products, fats and oils**	**Alcohol, eggs and legumes**	**Savoury sauces, condiments and meat**
SBP[b]	-0.005 (-0.010, -0.000)*	-0.001(-0.005, 0.004)	-0.003 (-0.008, 0.002)	0.003 (-0.002, 0.008)	0.005 (0.000, 0.010)	0.003 (-0.002, 0.008)
DBP[c]	-0.007 (-0.013, -0.001)*	-0.003 (-0.009, 0.002)	0.001 (-0.005, 0.007)	0.006 (0.000, 0.012)	0.004 (-0.002, 0.010)	0.003 (-0.003, 0.009)
Urinary sodium	-4.001 (-10.543, 2.540)	1.541 (-4.767, 7.850)	-4.652 (-11.418, 2.14)	-0.438 (-7.175, 6.300)	9.575 (3.161, 15.989)**	9.865 (3.485, 16.245)**
Urinary Potassium	2.165 (-1.169,5.499)	3.589 (0.390, 6.789)*	-4.960 (-8.377, -1.544)**	0.297 (-3.137, 3.732)	3.269 (-0.031, 6.570)	-0.903 (-4.199, 2.393)
Sodium-to-potassium ratio	-0.128 (-0.215, -0.040)**	-0.076 (-0.161, 0.010)	0.057 (-0.035, 0.149)	0.014 (-0.077, 0.106)	0.014 (-0.074, 0.103)	0.123 (0.036, 0.209)**

Model adjusted for age, sex, BMI, antihypertensive medication, energy intake and physical activity; [b]SBP, systolic blood pressure; [c]DBP, diastolic blood pressure; *$P < 0.05$, **$P < 0.01$.

Mean energy intake between participants whose diet aligned and those not aligned with “milk and meat”, “breads, cereals and snacks”, “cereal based products, fats and oils”, “alcohol, eggs and legumes” and “savoury sauces, condiments and meat” dietary patterns were significantly different ($P < 0.05$) (Appendix J). There was a significant difference in percentage protein intake between participants that aligned to the “milk and meat”, “breads, cereals and snacks”, “cereal based products, fats and oils” and “savoury sauces, condiments and meat” dietary patterns and those not aligned to the specific dietary patterns. Dietary sodium intake was not significantly different in participants aligned with “nuts, seeds, fruit and fish” dietary pattern compared to those not aligned with this pattern. Dietary potassium between participants whose diets aligned and those not aligned to all the dietary patterns was significantly different ($P < 0.05$). There was no association between hypertension status and whether participants were aligned or not aligned with a dietary pattern in all patterns identified ($P > 0.05$) (data not shown).

5.4 Discussion

Findings from this study reveal dietary patterns associated with blood pressure in a defined clinical cohort. In this study, a dietary pattern characterised by a high intake of nuts and seeds, fruit, and fish was inversely associated with both SBP and DBP. Whilst this pattern also included confectionery items but as that also meant muesli bars and snack bars, some of which contain seeds and nuts, the inclusion was not considered noteworthy. This combination of foods provides nutrients and food components that have been shown to be protective for blood pressure such as potassium [55], magnesium [74], polyphenols [221], and long chain omega-3 fatty acids [222]. The pattern is consistent with a previous analysis from a different

clinical cohort that found dietary patterns characterised by fruit and nuts or by seafood were inversely associated with SBP and DBP, respectively [166]. The larger sample size in the study reported here (n=328 vs n=118) may account for the stronger ability to cluster all these foods and to show associations with both SBP and DBP. In addition, the present study included younger participants (mean age = 43.6 vs 45.1 years) that had higher BMI (32.4 vs 31.2 kg/m^2) compared to the previous cohort and also did not exclude participants with diabetes and chronic disease risk factors such as elevated LDL (low density lipoproteins) and low HDL (high density lipoproteins) cholesterol.

The association between dietary patterns and blood pressure has been investigated in large population-based cohort studies in different countries. In middle-aged Chinese men, a dietary pattern characterized by fruits and milk was inversely associated with SBP and DBP ($P < 0.001$) [223]. In the Netherlands, a "cosmopolitan" dietary pattern that was high in vegetables and vegetable oil, pasta, rice, fish, chicken and wine was significantly associated with lower SBP while a "traditional" dietary pattern that was higher in intake of red meat, coffee, potatoes, beer and high saturated added fat and low in fruit, tea, breakfast cereals and low-fat dairy was associated with higher SBP in adults aged 20-65 years [224]. Likewise, in Japan, a high intake of the "vegetable" pattern in women was significantly associated with lower SBP and DBP [225]. There is however a paucity of data on the association between dietary patterns and blood pressure in clinical populations.

The dietary patterns inversely associated with blood pressure emphasise plant based foods. Plant-based diets that include consumption of fruit, vegetables, nuts, and whole grains have been associated with lower risk of cardiovascular disease [226]. In the Framingham Study, an inverse association was observed between fruit and

vegetable intake and development of stoke in middle-aged men after 20 years of follow-up [227]. Likewise, consumption of nuts was significantly inversely associated with hypertension (RR: 0.66; 95% CI: 0.44, 1.00; $P = 0.049$) in a recent meta-analysis of four prospective studies [87]. Dietary patterns such as the DASH diet [24], the Mediterranean diet [113] and the Nordic diet [115] have been shown to reduce blood pressure. In addition, a dietary pattern that was rich in fruits, vegetables, wholegrains, legumes, nuts, seeds, dairy and fish and low in processed foods and red meat was shown to reduce blood pressure in Chapter 3. In the current study, a diet that was high in nuts, seeds, fruit and fish was associated with lower blood pressure and therefore these findings are consistent with previous research.

In the analysis reported here, there was no significant difference between the reported dietary sodium intakes in participants who aligned and those not aligned with the "nuts, seeds, fruit and fish" dietary pattern which was significantly associated with blood pressure. However, the "nuts, seeds, fruit and fish" and the "savoury sauces, condiments and meat" dietary patterns were associated with the urinary sodium-to-potassium ratio. Previous studies have reported a positive correlation between sodium-to-potassium ratio and high blood pressure [228] with the ratio showing a stronger association with blood pressure compared to sodium or potassium alone [229]. Many blood pressure-lowering intervention studies focus on reduction of dietary sodium, with or without an increase in potassium intake [207] [230]. This approach may not be useful for translation of dietary advice into practice, where consideration of the whole of diet within the context of the population cuisine appears to be more important.

There are a number of potential synergistic mechanisms at play between sodium and potassium that could explain the findings of this study as outlined in Chapter 1. In

addition, other dietary constituents and diets that have been found to improve endothelial function include polyunsaturated fats [231], polyphenols [232], de-alcoholized red wine [233] and the Mediterranean diet [234]. Vegetables are a rich source of nitric oxide [235] and ingestion of dietary nitrate load has been shown to reduce blood pressure in acute studies [236]. This highlights that blood pressure regulation may be achieved via a combination of various dietary constituents present in different foods.

A major strength of this study is the use of 24-hour urinary sodium and potassium excretion which is considered as the "gold standard" [154] to assess dietary sodium and potassium intake, given that under-reporting of energy intake has been shown to occur in overweight and obese participants [237]. This is therefore a novel approach in dietary patterns research as it allows for the evaluation of the relationship between dietary patterns and urinary sodium, potassium and sodium-to-potassium ratio.

There are limitations to this study including the subjective nature of the PCA method to extract dietary components. Some subjective but crucial decisions include the number of factors to extract and description of the components for each of the dietary patterns identified. However, the use of eigenvalues and examination of the scree plots guided determination of the best number of components to extract. The food grouping classifications used were done a priori by Australian Bureau of Statistics and Food Standards Australia and New Zealand to group similar foods together and to examine trends in food consumption and not necessarily to investigate food-health relationships. However, these groupings have been designed to classify similar foods together in order to reflect the current food supply in Australia, thus warranting their use in this study. Information on the use of dietary supplements was not collected in this study and this could be a potential study

limitation. The use of discretionary salt was included in the 4-day food records although it has been shown to be poorly reported [154].

5.5 Conclusions

This analysis demonstrated that for participants in a weight loss clinical trial, consumption of a dietary pattern rich in nuts, seeds, fruit and fish was inversely associated with blood pressure and with urinary sodium-to-potassium ratio. Other dietary patterns shown to be associated with either urinary sodium or potassium excretion or sodium-to-potassium ratio were not predictive of blood pressure. In clinical weight loss settings, these findings could be integrated with other well-studied dietary patterns that have been shown to reduce blood pressure such as the DASH diet, the Nordic diet and the Mediterranean diet for blood pressure regulation. The findings also align with current dietary guidelines and highlight the importance of considering the whole dietary pattern when exploring the diet-disease relationship.

As highlighted in this and previous chapters, it is important to consider the role of nutrients, foods and dietary patterns in blood pressure management. While the role of nutrients is well established, nutrients are consumed in foods, and in different food combinations or dietary patterns. The types of foods that individuals consume can be influenced by various interventions in clinical care settings. In the following chapter, the effect of individualised dietary advice in the context of a randomised clinical trial will be explored. The change in nutrients and food intake and dietary patterns after 3 months will be investigated.

CHAPTER 6 – MORE SPECIFIC DIETARY ADVICE FOR WEIGHT LOSS SUPPLEMENTED WITH WALNUTS PRODUCED GREATER REDUCTIONS IN BLOOD PRESSURE THAN GENERAL ADVICE

The majority of this chapter is the substantative content of the published work:

Ndanuko, R.N., Tapsell, L. C., Charlton, K. E., Neale, E. P., Batterham, M. J. Effect of individualised dietary advice for weight loss supplemented with walnuts on blood pressure: The HealthTrack study. *European Journal of Clinical Nutrition*. (under review).

The findings of this chapter have also been presented as conference poster presentations:

Ndanuko, R.N., Tapsell, L. C., Charlton, E. K., Neale, E. P. Changes in blood pressure, urinary sodium and sodium-to-potassium ratio in a clinical sample of overweight adults. Nutrition Society of Australia. Annual Scientific Meeting, Melbourne, Australia. 29th November – 2nd December 2016.

Ndanuko, R.N., Tapsell, L. C., Charlton, E. K., Neale, E. P., Batterham, M. J. Effect of specific dietary advice on change in blood pressure, dietary patterns, food and nutrients in the HealthTrack study. Australian Society for Medical Research. NSW scientific meeting, Sydney, Australia. 2nd June 2017.

6.1 Introduction

As discussed in Chapter 1, dietary trials for blood pressure-lowering have primarily focused on interventions that result in reductions in sodium intake, either with or without a concomitant increase in potassium intake [45] [81]. However, Chapters 3 and 4 of this thesis have identified dietary patterns that influence blood pressure, especially in the context of a clinical sample of overweight adults.

Given that weight loss itself helps to reduce blood pressure [238], adding knowledge of healthful food patterns over and above the benefits of energy restriction alone may be beneficial in managing obesity and its related disorders such as hypertension. The relationship between obesity and hypertension is well established [239]. As a result, weight loss is recommended as a strategy to lower blood pressure in overweight and obese individuals [71]. An average of 5 kg weight loss resulted in blood pressure reduction of 4.4 mm Hg and 3.6 mm Hg in SBP and DBP respectively in a meta-analysis of 25 randomised controlled trials [238].

While weight loss is dependent on total food intake, investigations into the effects of individual foods on blood pressure have been conducted through randomised clinical trials and observational studies as discussed in Chapter 1. Research that focuses on individual nutrients or single foods may not consider the complexity of the interactions between nutrients and foods and their relationship with disease outcomes [103]. In nutritional epidemiology, research on dietary patterns may present a broader view of the impact of nutrient and food intakes and enable a better understanding of the association between diet and chronic disease risk [104]. Given that improved dietary choices is a goal of dietary advice in practice, the aim of this

study was to examine the impact of more specific dietary advice, on blood pressure during a weight loss trial.

6.2 Methods

The current study is a secondary analysis using baseline and 3 month data from the 12 month HealthTrack randomised controlled trial. The 3 months data was utilised since this was the intensive period of the trial. The HealthTrack study has been discussed in detail in Chapter 3. Participants were randomised to one of three groups: intervention [(I) (interdisciplinary intervention with individualised dietary advice], intervention + walnut [(IW) (interdisciplinary intervention with individualised dietary advice plus a supplement of 30 grams of walnuts per day], or control [(C) (usual care].

For the analysis in this chapter, dietary intake data from self-reported diet history interviews was utilised. Specifically, intakes of the AUSNUT 2011-13 major food groups *seed and nut products and dishes*, *fruit products and dishes*, and *seafood products and dishes* were determined. These food groups were selected as they were significantly associated with blood pressure in a previous baseline analysis in this sample in Chapter 5. For the analysis reported here, SBP and DBP were the outcomes of interest.

6.2.1 Statistical analysis

In this secondary analysis of the HealthTrack study data, baseline characteristics were presented as means and standard deviation for normally distributed data and median and interquartile range for data that was not normally distributed. To assess differences between study groups at baseline, one-way analysis of variance was conducted for normally distributed data such as age, height, weight, BMI and waist

circumference. Kruskal-Wallis H test was conducted for data that was not normally distributed such as dietary intake, and urinary excretion. A chi square test was performed to compare difference in the proportion of participants with hypertension (participants were categorised as hypertensive if blood pressure was ≥140/90 mm Hg and/or taking antihypertensives) between study groups. To determine change from baseline to 3 months in blood pressure, urinary excretion and intake of key food groups (*seed and nut products and dishes, fruit products and dishes,* and *seafood products and dishes)*, the Wilcoxon signed-rank test was used to assess the difference between baseline and 3 months in each study group. The Kruskal-Wallis H test was used to determine the difference between groups at each time point, and significant results were explored via post-hoc Mann Whitney U tests with Bonferroni adjustment. These analyses were repeated after excluding participants who were taking diuretics at baseline and/ or 3 months, as diuretics have been shown to increase sodium and potassium excretion [240]. Multiple linear regression was performed to assess the association between change in blood pressure from baseline and (1) change in urinary excretion and (2) consumption of key food groups, while controlling for age, sex, blood pressure medication, weight loss, change in physical activity, and smoking. All analyses were performed in accordance with an as-treated analysis approach. Statistical analysis was performed using the Statistical Package for the Social Sciences (IBM Corp., SPSS for Windows Version 21, Armonk, New York, USA). Significance level was considered at P value <0.05.

6.3 Results

6.3.1 Baseline characteristics

A total of 377 participants were randomised to one of the 3 groups; intervention + walnut (IW), intervention (I) or control (C). For this study, data were analysed from 211 participants (60 men and 151 women) who had complete blood pressure, urinary excretion data and dietary intake data at baseline and 3 months. Appendix K shows the baseline characteristics of the 3 groups.

6.3.2 Change from baseline to 3 months

SBP reduced significantly in all the three groups from baseline to 3 months *(P* < 0.001 in IW and I groups, *P* = 0.002 in C group). The greatest reduction in SBP was observed in the IW group (Appendix L). The change in SBP was significantly greater in the IW and I groups compared to the control group (*P* = 0.022 and *P* = 0.041, respectively). There was no significant difference in change in SBP between IW and I groups (P = 0.692). DBP significantly reduced in both IW and I groups (*P* < 0.001). The decrease in urinary sodium excretion was larger in the IW and C group compared to the I group (*P* = 0.007 and *P* = 0.018 respectively). The decrease in urinary sodium-to-potassium ratio was larger in the IW group compared to the I group (*P* = 0.012). At 3 months there was greater consumption of *seed and nut products and dishes* by the IW group compared to the I group (*P* < 0.001), and C group (*P* = 0.024). From baseline to 3 months the IW group increased intakes of *seed and nut products and dishes* more than the I group (*P* < 0.001) and the C group (*P* < 0.001). Intake of *fruit products and dishes* also increased from baseline to 3 months in both the IW (*P* < 0.001) and I (*P* = 0.005) groups. Results were similar when participants on diuretics were excluded from the analysis (data not shown).

In multiple linear regression, an increase in urinary potassium and decrease in urinary sodium-to-potassium ratio was significantly associated with SBP reduction in the IW group (Appendix M). On the other hand, a reduction in urinary sodium was significantly associated with a reduction in DBP in the C group. In the IW group, an increase in the consumption of *seed and nut products and dishes* was significantly associated with a reduction in SBP while increased intake of *seafood products and dishes* was significantly associated with decreased DBP. The results did not change after excluding participants who were taking diuretics at baseline and 3 months (data not shown).

6.4 Discussion

This secondary analysis of data from a weight loss trial provided further insights into the impact of changes in dietary patterns, foods and nutrients on blood pressure. Dietary patterns [24], key foods such as nuts [88] and dietary levels of nutrients such as sodium [45] and potassium [81] can all affect blood pressure, but these effects are also inter-related [40]. The present analysis showed that highly specified dietary advice, strengthened by a daily supplement of a healthy food (30 g walnuts) resulted in a greater reduction in SBP than general advice referencing the dietary guidelines. The effect was supported by a greater decrease in urinary sodium-to-potassium ratio, a parameter associated with lower blood pressure [63]. After adjusting for weight loss, the study found the decrease in sodium-to-potassium ratio and concomitant increase in intakes of the “nuts and seeds” and “seafood” food categories were significantly associated with blood pressure reduction, confirming the effect of diet composition.

The first observation was a greater significant reduction in sodium-to-potassium ratio in the IW group compared to the other groups. Diets with a lower sodium-to-potassium ratio have been negatively associated with hypertension in epidemiological studies [219] and have been found to reduce blood pressure in randomised controlled trials [200]. Sodium and potassium play an interdependent role in affecting blood pressure, whereby consumption of excessive sodium and insufficient potassium cause the vascular smooth muscle cell to contract and as a result lead to an increase in the peripheral vascular resistance which increases blood pressure [62].

The results of the current study build on the analysis from Chapter 5 that identified an inverse association between blood pressure and a dietary pattern that was rich in "nuts, seeds, fruit and fish". In addition, significant inverse associations between SBP and dietary patterns characterized by fruit and nuts, and between DBP and dietary patterns characterized by seafood were found in previously conducted analyses of food-based dietary trials [166]. Previously reported randomised controlled trials show beneficial effects of walnut consumption on blood pressure. In a 2-year study investigating the effect of a Mediterranean-style diet on endothelial function and inflammation markers in 180 patients with metabolic syndrome, a Mediterranean-style diet that included consumption of 25-50 g of walnuts per day significantly reduced SBP by 3 mm Hg and DBP by 2 mm Hg compared to a control prudent diet [114]. Likewise, in the PREDIMED study, the group following a Mediterranean diet which contained a daily supplement of 30 g mixed nuts including 15 g of walnuts showed greater reductions in ambulatory SBP and DBP (-2.4 mm Hg and -1.0 mm Hg respectively) after one year compared to the control diet [206]. In a recent meta-analysis of 21 randomised controlled trials, total nut consumption was

shown to lower SBP by 1.29 mm Hg in participants without type 2 diabetes [88]. Nuts contain high amounts of mono- and polyunsaturated fats, magnesium, potassium and fibre and are low in sodium and saturated fats and thus may elicit a blood pressure lowering response [86]. Consumption of nuts may also be associated with improved diet quality [241] which in turn may lead to adoption of healthier dietary patterns.

In this study, we found that an increase in seafood consumption was associated with a decrease in DBP in the IW group. The effect of fish consumption on blood pressure has also been assessed in previous studies. For example, moderate consumption of fatty fish (150 g of salmon three times per week) led to greater reductions in DBP in an 8 week weight-loss study compared to lean fish, fish oil capsules or placebo capsules [242]. While various studies have shown a blood pressure lowering effect through supplementation with omega-3 polyunsaturated fatty acids [243], conclusive evidence on the effect of dietary fish intake on blood pressure is lacking. This is possibly due to other factors that may attenuate the protective effects such as the method of preparation, consumption of salted fish or presence of other contaminants such as mercury and pesticides [244].

Compared to individual foods, however, dietary pattern analysis may better demonstrate diet- blood pressure relationships since foods are not consumed in isolation but as part of a total diet. In addition, the concept of food synergy proposes that investigation of patterns of food consumption may be more informative than focussing on individual food components such as nutrients or single foods [39]. This study has demonstrated that under weight-loss conditions, an increase in nuts, seeds and seafood was associated with reductions in blood pressure. Further investigations

are warranted on the effect of change in dietary patterns on change in BP especially in different cultural contexts and cuisines.

6.5 Conclusions

This secondary analysis from a weight-loss trial found greater reductions in SBP for the group provided with individualised dietary advice supplemented with walnuts and this was associated with increased intake of seeds and nuts, and seafood, and reduced Na and sodium-to-potassium excretion. Identification of a dietary pattern that includes these foods could be helpful in the development of food based dietary recommendations in clinical practice that not only address weight loss but also blood pressure.

CHAPTER 7 – CONCLUSIONS AND RECOMMENDATIONS

In the context of a lifestyle intervention trial targeting weight loss, this thesis has confirmed the central hypothesis that dietary patterns characterised in terms of nutrients and foods significantly influence blood pressure in adults, as confirmed by associations at baseline and changes in the proposed direction with dietary intervention in a clinical setting.

7.1 Introduction

While much of the diet-blood pressure research has been conducted in larger populations, the implications for dietetic practice in smaller clinical cohorts are not known. In addition, people are more likely to present for dietetic management for conditions such as weight loss rather than blood pressure alone [245]. This thesis addressed the question of how dietary factors might influence blood pressure in the context of an overweight adult clinical population by providing novel evidence for the relationship between consumption of nutrients, foods, and dietary patterns, and blood pressure in this setting. The results from the analyses conducted in this thesis have implications for clinical practice, where dietary advice is a central strategy.

Furthermore, it is important to investigate dietary interventions in a pragmatic way because patients with high blood pressure present with other risk factors for chronic disease such as obesity, unhealthy diet, physical inactivity and risky alcohol consumption [16]. In terms of total cardiovascular disease risk, the absolute cardiovascular disease risk scores used by general practitioners in primary care setting assist in the management of multiple individual risk factors [17]. The modifiable risk factors that are considered include blood pressure, diet, smoking, physical activity level, alcohol consumption, lipids, waist circumference and BMI.

Blood pressure control is therefore seen in the context of total cardiovascular disease risk.

7.2 Diet and blood pressure

As highlighted in Chapter 1, the problem of high blood pressure (hypertension) is of major public health concern globally [7] and is a major risk factor for developing cardiovascular disease, stroke and kidney disease [5]. Lowering blood pressure would therefore result in numerous health benefits such as reduced risk of stroke, coronary heart disease and cardiovascular events [21] [22]. Previously, research to address the problem of high blood pressure has mainly focussed on the nutrient level specifically on dietary intake of sodium (high intake associated with increased blood pressure) [45] and potassium (high intake associated with lower blood pressure) [55] [56]. In addition, the sodium-to-potassium ratio has been implicated in influencing blood pressure [63] [64] as opposed to sodium and potassium alone. However, from a translation perspective, it is well known that humans do not consume single nutrients in isolation, but rather as whole foods. Additionally, as sodium and potassium come from distinct foods, the ratio may be a reflection of certain food choices or dietary patterns. Investigations on the effect of single foods on blood pressure have nevertheless yielded conflicting results. Moreover, single foods go to make up whole diets or dietary patterns. As these dietary patterns may also be characterised by nutrient composition, the ability to truly separate out effects of nutrients, foods and whole diets remain problematic [40] [41]. Indeed, an understanding of the interdependence between nutrients, foods and dietary patterns is required to translate dietary advice in clinical practice especially in food-based recommendations for blood pressure reduction.

In the sections ahead, the effect of nutrients, foods and dietary patterns on blood pressure are outlined with respect to the results obtained from this thesis and implications for clinical practice will be highlighted.

7.3 Current level of evidence on dietary patterns and blood pressure

To evaluate the current level of evidence on the effect of dietary patterns on blood pressure, the thesis began with a systematic review and meta-analysis of randomised controlled trials. This published analysis found that a dietary pattern characterised by high consumption of fruit, vegetables, whole grains, legumes, seeds, nuts, fish and low-fat dairy and low consumption of meat, sweets and alcohol resulted in significant reductions in SBP by 4.26 mm Hg and DBP by 2.38 mm Hg compared to comparator or usual diet.

This was the first systematic review and meta-analysis to examine the effect of dietary patterns on blood pressure in adults. The magnitude of blood pressure reduction is of clinical significance. For instance, reducing DBP in the population by 2.0 mm Hg would result in reduction of stroke by 17% and reduction in the risk of coronary heart disease decrease by 6% [246]. In addition, lowering SBP and DBP by 5.0 and 3.0 mm Hg respectively has been shown to result in a 15% reduction in the incidence of coronary heart disease and 27% reduction in stroke incidence [24].

Whether this would still relate to a clinical sample of overweight adults is an important question for practice which was addressed in subsequent secondary analysis of clinical trial data from a 12 month lifestyle intervention trial (the HealthTrack study).

7.4 Sodium and potassium intake and blood pressure

The first stage in the analysis of the trial data started with the nutrient aspects of the diet-blood pressure relationship. The results confirmed that the relationship between sodium intake and sodium-to-potassium ratio and blood pressure seen in large epidemiological studies can still be present in smaller clinical samples of overweight adults. Among the sample from the HealthTrack study, only 15% and 27% of the participants were meeting the World Health Organization recommended targets for sodium and potassium intakes, respectively, based on urinary sodium and potassium excretion values [54]. This data was established using the 'gold standard' biomarker of intake of the 24-hour urine excretion.

The baseline results clearly showed that majority of the participants had high sodium and low potassium dietary intakes, reflective of the general Australian population [211]. The dietary sodium-to-potassium ratio was shown to be positively correlated with SBP while both urinary sodium and sodium-to-potassium ratio were identified as significant predictors of SBP after controlling for age, sex, BMI and hypertension medication use. Again, this may reflect certain food choices or dietary patterns. Establishing the types of foods or dietary patterns consumed by this clinical sample would enable appropriate food based dietary advice especially within the context of clinical practice.

7.5 Food sources of sodium and potassium

Identification of food sources of sodium and potassium then enabled translation from the nutrient level of understanding to that of foods. This is important since it allows food based dietary recommendations to be implemented in clinical practice. The major food sources of sodium that were identified were cereal based products and

dishes; cereal and cereal products; meat, poultry and game products and dishes; and milk products and dishes. On the other hand, vegetable products and dishes; meat, poultry and game products and dishes; and milk products and dishes were the major contributors for dietary potassium intake. Thus, while relationships could be seen with nutrient intakes, the consumption of specific foods was also implicated in this relationship.

The results were comparable to results from the recent Australian Health Survey [213] as well as with results from other countries with similar food supply and hypertension prevalence such as the United States [247] and Finland [162]. Various plant-based foods have been shown to influence blood pressure due to their high potassium content. These foods include fruits and vegetables [77] [75], nuts [87] and pulses [92]. For example, in the PREDIMED randomised controlled trial, supplementation of the Mediterranean diet with mixed nuts or olive oil was shown to significantly reduce blood pressure in comparison to a low-fat diet [113]. When analysing data from the HealthTrack study, the research in this thesis confirmed the influence of food supplementation reported in other research [248].

7.6 Dietary patterns and blood pressure

The regular consumption of specific foods constitutes a dietary pattern, so dietary patterns drove the next level of analysis for the thesis. This analysis of data from the HealthTrack study investigated the association between dietary patterns and blood pressure. Six dietary patterns were derived using the principal component analysis from 21 food groups. These include; the “nuts, seeds, fruit and fish”; “milk and meat”; “breads, cereals and snacks”; “cereal based products, fats and oils”; “alcohol, eggs and legumes”; and “savoury sauces, condiments and meat” dietary patterns.

Multiple regression analysis showed that a dietary pattern characterised by nuts, seeds, fruit and fish was significantly and inversely associated with SBP and sodium-to-potassium ratio. In addition, there was no difference in mean energy intake between participants whose diet aligned with the nuts, seeds, fruit and fish pattern and those not aligned with this pattern. Thus a dietary pattern that is dominated by specific foods: nuts, seeds, fruit and fish appeared protective. These foods are naturally low in sodium and the plant foods are all high in potassium. In addition, these foods have been associated with reduced blood pressure in previous randomised controlled trials [88] [166] and prospective studies [77] [87]. In the "nuts, seeds, fruit and fish" dietary pattern, the aspect of food synergy – whereby the combination of nutrients provided through different food matrices may have greater benefits compared to individual nutrients in individual foods themselves, seems to play a role in its protective nature [39].

It is important to determine the effect of change in consumption of nutrients, foods and dietary patterns over time especially in clinical populations undergoing lifestyle intervention. Furthermore, interventions are higher level of evidence than observational (baseline analyses) studies. As a result, this led to the second stage in the analysis of the HealthTrack trial data. After 3 months it was found that participants who received individualised dietary advice that was strengthened by a daily supplement of a heathy food, (30 g walnuts) had greater reduction in SBP than those receiving generalized advice that referenced the Australian dietary guidelines. In addition, the effect was supported by a greater decrease in urinary sodium-to-potassium ratio, a biological parameter associated with lower blood pressure [63]. This clearly shows that in addition to the effects seen with nutrients, reductions in blood pressure can also be seen with consumption of whole foods. After adjusting

for weight loss, an increase in intakes of the *seed and nut products and dishes* and *seafood products and dishes* food categories were significantly associated with blood pressure reduction, confirming the effect of diet composition, namely combination of different foods which forms dietary patterns. These greater effects on blood pressure were observed in participants receiving specific individualised dietary advice as opposed to those receiving general advice based on dietary guidelines and it highlights the importance of such advice being offered in clinical practice to overweight patients with high blood pressure. On the other hand, no significant associations were observed between change in intakes of *fruit products and dishes* or *seafood products and dishes* and blood pressure.

7.7 Limitations of this thesis

The major limitations in this thesis relate to the secondary analysis of HealthTrack study data. Firstly, the HealthTrack study being a randomised controlled trial testing the effects of forms of intervention on weight loss, there is a likelihood the analysis would be underpowered, particularly in relation to the analysis of changes in dietary patterns which carry a high degree of variability. The participants were an overweight clinical population from a regional area of New South Wales, Australia, who had volunteered to participate in the 12-month weight loss trial. The results may therefore not be generalizable to the wider adult population. In addition, the study participants were about 70% female. It has been shown that females are more likely to seek primary care services compared to males especially in the age group between 20 and 44 years [249].

In terms of dietary intake, participants may have under-reported dietary sodium intake and over-reported dietary potassium intake, especially since it has been shown

to occur in individuals with higher BMI [151]. However, a strength of the study was the assessment of sodium and potassium intake by the gold standard of 24-hour urine excretion [154], with completeness of urine samples being determined by the use of urinary creatinine concentrations. However due to the large day-to-day variability of sodium and potassium intake, repeated 24-hour urinary collections would have provided greater accuracy [163].

In terms of potential bias, about a quarter of the participants were already hypertensive and may have made dietary changes as a result of receiving previous dietary advice from a health professional [250]. The use of office blood pressure is another potential source of bias. Ambulatory blood pressure has been shown to eliminate “white coat hypertension” and has increased precision over office blood pressure [251]. Repeated measurements of ambulatory blood pressure provide an even more accurate indication of usual blood pressure than a single 24-hour measurement [206]. However, automated office blood pressure measurement is recommended for use in primary care settings as it has been shown to be comparable with awake ambulatory blood pressure [252], and was thus deemed appropriate in this research context.

7.8 Conclusions

The combination of studies conducted for this thesis has confirmed the central hypothesis that dietary patterns characterised in terms of nutrients, foods and dietary patterns significantly influence blood pressure in adults. It was also confirmed that in the context of clinical practice for weight loss, specific food choices and nutrient intakes that align with beneficial dietary patterns may also assist in reducing blood pressure. Despite this thesis utilising a secondary analysis of trial data, the results

demonstrated that blood pressure effects can nonetheless be seen in small clinical samples and where weight loss is the primary outcome. This has important translational implications for the delivery of dietary advice for blood pressure management. In clinical practice, dietary advice based on specific food choices and attention to sodium and potassium intakes could be helpful in not only addressing weight loss but also high blood pressure associated with being overweight. Further trials to test this hypothesis in practice would strengthen these findings.

7.9 Future research and recommendations

Based on the findings of this thesis, the following recommendations are proposed:

1. Clinical settings:

   In clinical settings, in addition to messages on salt (sodium) reduction or increased potassium intake, providing food based dietary advice for the management of high blood pressure would also be beneficial and especially in patients undergoing weight loss. This includes advice on increased consumption of foods that were found to be associated with lower blood pressure in this thesis such as nuts, seeds, fruit and fish; and also foods associated with a lower sodium-to-potassium ratio such as increased fruit and vegetables. Apart from health practitioners, the management and administration of clinical settings also needs to be aware of these data and be champions to advocate for diet interventions in clinical settings.

2. Public health programs:

   In public health programs, the messages that are provided to the population for lowering blood pressure should not only address salt reduction but also include food based strategies. This includes promoting consumption of

healthy dietary patterns that consist of foods that are high in potassium such as fruit, vegetables, nuts, seeds and legumes. In addition, consumption of seafood should be encouraged since it was identified to be significantly associated with reduced blood pressure.

3. Energy intake:

   The energy value of food is an important factor that needs to be addressed through dietary advice both in the public health and clinical settings, since weight loss is one of the strategies recommended for lowering blood pressure.

4. Healthcare service delivery and clinical level relevance:

   In the healthcare setting, dietitians are the health professionals trained and qualified to deliver nutrition education and counselling as was demonstrated in the HealthTrack study. They play a major role in the delivery of healthcare interventions in clinical settings. However, in primary healthcare, the first contact for most patients with a clinician is with a general practitioner. Ensuring general practitioners are aware of the value of dietary intervention would therefore enable them to plan more effective nutrition management strategies for hypertension especially in at risk populations such as overweight individuals.

Further randomised controlled trials on the effects of dietary patterns on blood pressure would strengthen the findings for this thesis. These can be carried out in the context of primary health care and for a longer duration to establish the role of nutrients, foods and dietary patterns especially in overweight populations.

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APPENDIX A

ANZCTRN summary

ANZCTR
Australian New Zealand Clinical Trials Registry

Questions in **bold** text are mandatory. **(*)**

Request Number:	
Current Page:	Review

Trial from ANZCTR

Trial ID	ACTRN12614000581662
Trial Status:	Registered
Date Submitted:	23/05/2014
Date Registered:	30/05/2014
	Prospectively registered

Page 1

Public title	HealthTrack : a healthy lifestyle intervention for overweight adults
Study title in 'Participant-Intervention-Comparator- Outcome (PICO)' format	Is a novel lifestyle intervention more effective than usual care in achieving weight loss in overweight/obese adults ?
Secondary ID [1]	Nil
UTN	U1111-1157-2562
Trial acronym	

Page 2

Health condition(s) or problem(s) studied:	
overweight and obesity	
Condition category:	**Condition code:**
Diet and Nutrition	Obesity
Mental Health	Studies of normal psychology, cognitive function and behaviour
Public Health	Epidemiology

Page 3

Descriptions of intervention(s) / exposure	This is a 12 month single blinded parallel randomised controlled trial with 3 arms: control (usual care), intervention (multidisciplinary lifestyle support) and intervention (multidisciplinary lifestyle support) + a food supplement. Participants will be randomised into a control or one of the intervention groups testing the effect of a novel versus conventional form of individualised health care targeting diet, exercise and health behaviour. Both control and intervention arms will attend the clinic at baseline, 1,2,3,6,9,12 mo for a face to face session with a health practitioner (nurse/control or dietitian supported by an ExercisePhysiologist(EP)/intervention) for 40-60 mins. Participants will be encouraged to set diet and physical activity goals based on either information sheets devised for the control or intervention strategy. A client centred approach will be used, with cognitive behavioural enhancement strategies in the intervention group. A phone call will be made between visits by the nurse/control or a health coach (supervised by psychologists)/intervention. Adherence will be monitored by repeat 4 day food records and paedomoters. A subset will be given accelerometers. The food supplement is 30g snack packs of walnuts /day for 12 months.
Intervention Code:	Lifestyle
Intervention Code:	Treatment: Other
Intervention Code:	Behaviour
Comparator / control treatment	Control: usual care involving client centred support and general advice on diet and physical activity using national guidelines Comparator: novel approach to lifestyle counselling with diet, physical activity and health coaching
Control group	Active

Page 4

Primary Outcome:	Body weight (kg) will be measured in an upright position in minimal clothing and without shoes using scales with a bio-electrical impedance

	component to also estimate body fat (%) (Tanita TBF-662).
Timepoint:	Baseline, 1mo, 2mo, 3, 6,9,12 months
Secondary Outcome:	Diet intake will be assessed using diet history interview at clinic visits and 4 day food records (including one weekend day) completed in the periods prior to attending the clinic (to correspond with the timepoints below). Participants record all foods consumed including amounts and recipes.
Timepoint:	Baseline, 3mo , 6mo, 9mo, and 12mo
Secondary Outcome:	Systolic blood pressure (SBP) and diastolic blood pressure (DBP) will be measured using the Omron BP-203RPEIII VP-1000 device (Omron Health Care, Kyoto, Japan). Measurements to be collected at the end of 5 min resting period in supine position. Arterial stiffness (baPWV) and arterial occlusion (ABI) data also collected from device.
Timepoint:	Baseline, 3 mo, 12mo
Secondary Outcome:	Physical activity will be assesed using the International Physical Activity Questionnaire (IPAQ) short form survey questions, along with a set of questions regarding the participants' peroeptions on how much physical activity is necessary for a healthy lifestyle. A scientific grade pedometer will be used that is accurate and reliable for counting steps and can be used to explain physical activity levels and sedentary time (cut-points) In a subsample participants will be assigned an accelerometer and trained in its use (placement on wrist, record keeping). They will be asked to wear the accelerometer on two week days and one weekend (to coincide with the 4 day food record). Total number of counts will be recorded for each day.
Timepoint:	Baseline , 3mo , 12 mo
Secondary Outcome:	A composite psychological assessment will be conducted at 0,3,12 months using items from validated questionnaires to test for psychological flexibility, diet flexibility, and exercise motivation. This assessment will include include items relating to Physical and mental health Sf-12 (12 questions) , Acceptance and action (11 questions), AAQ-II, Positive Emotional Well-being (3 questions), Depression anxiety stress short form (DASS – 21; 21 questions), Emotional eating (3 questions), Rigid control of diet (R16; 16 questions), and Motivation for exercise (24 questions)
Timepoint:	Baseline , 3 mo , 12 mo
Secondary Outcome:	Fasting blood lipids (cholesterol, LDL, HDL, Trig), Blood samples collected at a registered Pathology service (Southern Pathology)
Timepoint:	Baseline 3,6,9,12mo
Secondary Outcome:	Urinary sodium Participants will be asked to collect a 24 hour urine sample (at 0, 3 and 12 months) prior to their pathology visit and deliver the sample to nursing staff at Southern Pathology. A container and instruction sheet will be provided to participants at the same time as they are provided with the pathology forms. A protocol of contact will be undertaken to remind participants to complete the 24 hour urine collection. This urine sample will test urinary sodium, potassium and creatinine excretion as the gold standard for sodium intake.
Timepoint:	0,3,12 months
Secondary Outcome:	Fasting blood glucose Blood samples collected at a registered Pathology service (Southern Pathology)
Timepoint:	Baseline, 3,6,9,12 mo
Secondary Outcome:	Serum HBA1c
Timepoint:	Baseline, 3,6,9,12 months

Page 5

Key inclusion criteria	men and women from the Illawarra community (adults aged 25-54 years, permanent resident, community dwelling), at higher risk of lifestyle related disease (defined by BMI range 25-40kg/m2
Minimum age	25 Years
Maximum age	54 Years
Gender	Both males and females
Healthy volunteers?	No
Key exclusion criteria	Unable to communicate in English; severe medical conditions impairing ability to participate in study; other medical conditions thought to limit survival to 1 year; immunodeficiency; reported illegal drug use or regular alcohol intake associated with alcoholism (>50g/day); difficulties or major impediments to participating in the components of the study

Page 6

Study type	Interventional
Purpose of the study	Treatment
Allocation to intervention	Randomised controlled trial
Describe the procedure for enrolling a subject and allocating the	Recruitment is via advertising to the general media and completion of a

treatment (allocation concealment procedures)	screening questionnaire
Describe the methods used to generate the sequence in which subjects will be randomised (sequence generation)	A researcher independent of the participant interface will undertake the randomisation of subjects into diet groups (stratified by sex and BMI, block randomised STATA (V12 Cary NC)
Masking / blinding	Blinded (masking used)
Who is / are masked / blinded (choose all that apply)	The people receiving the treatment/s The people assessing the outcomes The people analysing the results/data
Assignment	Parallel
Other design features	
Type of endpoint (s)	Efficacy
Statistical Methods/Analysis	Several power calculations were conducted using SAS PROC POWER using a range standard deviations from 3.5 to 5. One hundred subjects per group were considered sufficient to detect a minimum between group weight loss difference of 2.7kg as significant with 90% power and a two tailed a of 0.025 and 0.017 (adjusted for planned contrast between control and each treatment group and a between treatments comparison). This assumes up to ~25% post randomization dropout rate and a within group weight loss standard deviation of 3.5-5kg (using available literature and our own experience) The analysis will be conducted using a linear mixed model. The use of the mixed model allows partial datasets incorporating all available data regardless of whether or not the subject completes the study. The planned contrasts are between the control and the intervention groups.

Page 7

Phase	Not Applicable
Anticipated date of first participant enrolment	9/06/2014
Date of first participant enrolment	
Anticipated date last participant recruited/enrolled	28/11/2014
Actual date last participant recruited/enrolled	
Target sample size	300
Recruitment status	Not yet recruiting

Recruitment in Australia

Recruitment state(s)	NSW
Postcode:	2522 - University Of Wollongong

Recruitment outside Australia

Page 8

Funding Source:	Other Collaborative groups
Name:	Illawarra Health and Medical Research Institute
Address:	University of Wollongong Wollongong NSW 2522
Country:	Australia
Funding Source:	Other Collaborative groups
Name:	California Walnut Commission
Address:	101 Parkshore Drive, Suite 250 Folsom CA 95630-4726 USA
Country:	United States of America
Primary Sponsor	Other Collaborative groups
Name:	Illawarra Health and Medical Research Institute
Address:	University of Wollongong Wollongong NSW 2522
Country:	Australia
Secondary Sponsor:	University
Name:	University of Wollongong

Address:	Wollongong NSW 2522
Country:	Australia
Secondary Sponsor:	Hospital
Name:	Illawarra Shoalhaven Local Health District
Address:	Wollongong Hospital Locked Bag 8808 South Coast Mail Centre NSW 2521
Country:	Australia

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Has the study received approval from at least one Ethics Committee?	Yes
Ethics Committee name:	Human Research Ethics Committee
Address:	University of Wollongong Wollongong NSW 2522
Country:	Australia
Approval Date:	21/06/2013
Submitted Date:	22/04/2013
HREC:	HE13/189
Brief summary	This is a 12 month single blinded parallel randomised controlled trial with 3 arms: control (usual care), intervention (multidisciplinary lifestyle support). A 3rd arm comprises intervention + a food supplement . Participants will be randomised into a control or one of the intervention groups testing the effect of a novel versus conventional form of individualised health care targeting diet, exercise and health behaviour
Trial website	http://www.ihmri.uow.edu.au/healthtrackstudy
Trial related presentations / publications	
Public Notes	The research is focused on healthy lifestyle which also includes physical activity

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Principal Investigator

Title:	Prof
Name:	Linda Tapsell
Address:	Smart Foods Centre University of Wollongong Wollongong NSW 2522
Country:	Australia
Tel:	+61 2 4221 3152
Fax:	+61 2 4221 4844
Email:	ltapsell@uow.edu.au

Contact person for public queries

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Email:	beck@uow.edu.au

Contact person for scientific queries

Title:	Prof
Name:	Linda Tapsell
Address:	Smart Foods Centre University of Wollongong Wollongong NSW 2522
Country:	Australia
Tel:	+61 2 4221 3152
Fax:	+61 2 4221 4844
Email:	ltapsell@uow.edu.au

Contact person responsible for updating information

Title:	Prof

Name:	Linda Tapsell
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Country:	Australia
Tel:	+61 2 4221 3152
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Email:	ltapsell@uow.edu.au

APPENDIX B

Ethics approval letter for the HealthTrack study (Chapter 4, 5 and 6)

UNIVERSITY OF WOLLONGONG

APPROVAL
In reply please quote: HE13/189; HE V13/189
Further Enquiries Ph: 4221 3386

1 July 2013

Professor Linda Tapsell
IHMRI Building 32
University of Wollongong
Wollongong NSW 2522

Dear Professor Tapsell,

Thank you for your response to the HREC letter regarding the ethics application below. I am pleased to advise that the application and the Pilot Study application have been approved. Before you can proceed with the project you must first have authorisation from the relevant NSW Ministry of Health Local Health District.

Ethics Number:	HE13/189; HE V13/189
AuRED Number:	HREC/13/WGONG/65
Project Title:	Health Track: Illawarra Shoalhaven Healthy Lifestyle Study Health Track: Illawarra Shoalhaven Healthy Lifestyle - Pilot Study (Formerly: The IHMRI Flagship Study)
Researchers:	Professor Linda Tapsell, Professor Maureen Lonergan, Dr Kim Alexander, Professor Joseph Ciarrochi, A/Professor Victoria Flood, Dr Bridget Kelly, Dr Gregory Peoples, Ms Marianna Milosavljevic, Dr Jan Potter, Ms Catherine Zelinsky, Professor David Steel

Sites/CIs approved:

Site	Principal Investigator for site
University of Wollongong	Professor Linda Tapsell

Documents Reviewed/Approved:

1. Initial Application HE13/189 received 22 April 2013
2. Additional Information dated 21 June 2013
3. Appendix 1: Health Track Study: General Information v.12 dated 21 June2013

Ethics Unit, Research Services Office
University of Wollongong NSW 2522 Australia
Telephone (02) 4221 3386 Facsimile (02) 4221 4338
Email: rso-ethics@uow.edu.au Web: www.uow.edu.au

4. Appendix 2: Health Track Script for Recruiters: Cohort Survey v.12 dated 21 June2013

5. Appendix 3: Health Track Lead Letter: Cohort Study v.12 dated 21 June2013

6. Appendix 4: Health Track Brochure: Cohort Study v. 12 dated 21 June 2013

7. Appendix 5: Participant Information Sheet: Cohort Survey v.12 dated 21 June 2013

8. Appendix 6: Participant Consent Form: Cohort Study v.12 dated 21 June 2013

9. Appendix 7: Participant Consent Form: Blood and Urine Sample v.12 dated 21 June 2013

10. Appendix 8: Cohort Survey v.12 dated 21 June 2013

11. Appendix 9: Thank you Letter to Cohort Participant v.12 dated 21 June 2013

12. Appendix 10: Thank You Letter to GP for Cohort Participant v.12 dated 21 June 2013

13. Appendix 11: Health Track Brochure: RCT v.12 dated 21 June 2013

14. Appendix 12: Participant Information Form: RCT v.12 dated 21 June 2013

15. Appendix 13: Participant Consent Form: RCT v.12 dated 21 June 2013

16. Appendix 14: Letter to Potential RCT Participant v.12 dated 21 June 2013 **(To be amended as per wording of Appendix 9: Pilot RCT Letter to Successful Participants v. dated 25 June 2013)**

17. Appendix 15: Letter to Participant who did not meet RCT eligibility requirements v. 12

18. Appendix 16: RCT Behavioural Survey v. 12 dated 21 June 2013

19. Appendix 17: Thank you letter to RCT Participant v.12 dated 21 June 2013

20. Appendix 18: GP Thank you letter to RCT Participant v. 12 dated 21 June 2013

21. Appendix 19: GP Screening and Pathology v.12 dated 21 June 2013

22. Appendix 20: Individual Case Report v. 12 dated 21 June 2013

23. Appendix 21 Cohort Health Report v.12 dated 21 June 2013

24. Initial Application HE V13/189 v8 dated 21 June 2013

UNIVERSITY OF WOLLONGONG

25. Appendix 1: Pilot RCT Advertisement v.8 dated 21 June 2013

26. Appendix 2: Pilot RCT Brochure v 8 dated 21 June 2013

27. Appendix 3: Pilot RCT Participant Information Form v. 8 dated 21 June 2013

28. Appendix 4: Pilot RCT Participant Consent Form v. 8 dated 21 June 2013

29. Appendix 5: Pilot RCT Participant Blood and Urine Consent Form v.8 dated 21 June 2013

30. Appendix 6: Pilot Email response to interested Volunteers via Advertisement v.8 dated 21 June 2013

31. Appendix 7: Pilot RCT Medical Screening Survey v.8 dated 21 June 2013

32. Appendix 8: Pilot RCT Behavioural Survey v. 8 dated 21 June 2013

33. Appendix 9: Pilot RCT Letter to Successful Participant v. dated 25 June 2013

34. Appendix 10: Pilot letter to Participant who did not meet Eligibility Requirements v.8 dated 21 June 2013

35. Appendix 11: Pilot RCT Thank You Letter v.8 dated 21 June 2013

36. Appendix 12: Pilot RCT GP Thank You Letter v.8 dated 21 June 2013

37. Appendix 13: Pilot RCT GP Screening and Pathology v.8 dated 21 June 2013

38. Appendix 14: Pilot RCT Individual Case Report v.8 dated 21 June 2013

Approval Date:	25 June 2013
Expiry Date:	24 June 2014

The University of Wollongong/ISLHD Health and Medical HREC is constituted and functions in accordance with the NHMRC *National Statement on Ethical Conduct in Human Research.* The HREC has reviewed the research proposal for compliance with the *National Statement* and approval of this project is conditional upon your continuing compliance with this document.

A condition of approval by the HREC is the submission of a progress report annually and a final report on completion of your project. The progress report template is available at http://www.uow.edu.au/research/rso/ethics/UOW009385.html. This report must be completed, signed by the appropriate Head of School and returned to the Research Services Office prior to the expiry date.

Ethics Unit, Research Services Office
University of Wollongong NSW 2522 Australia
Telephone (02) 4221 3386 Facsimile (02) 4221 4338
Email: rso-ethics@uow.edu.au Web: www.uow.edu.au

As evidence of continuing compliance, the Human Research Ethics Committee also requires that researchers immediately report:

- proposed changes to the protocol including changes to investigators involved
- serious or unexpected adverse effects on participants
- unforseen events that might affect continued ethical acceptability of the project.

Please note that approvals are granted for a twelve month period. Further extension will be considered on receipt of a progress report prior to expiry date.

Please note that Governance approval is required for research within NSW Ministry of Health.

Refer to: https://ethicsform.org/Au/SignIn.aspx

For further information regarding the SSA in the ISLHD, contact:

Research Governance Officer
Illawarra Shoalhaven Local Health District
Research Directorate
Wollongong Hospital
Block C, Level 8
P: 02 4253 4876
E: Kristy.Pierce@SESIAHS.HEALTH.NSW.GOV.AU

A copy of this letter has been forwarded to the ISLHD Research Governance Officer.

If you have any queries regarding the HREC review process, please contact the Ethics Unit on phone 4221 3386 or email rso-ethics@uow.edu.au.

Yours sincerely,

Associate Professor Sarah Ferber
Chair, UOW & ISLHD Health and Medical
Human Research Ethics Committee

cc: Governance Officer, Research Directorate, ISLHD

APPENDIX C

Hypertension guidelines and recommendations

Guideline	**Management guidelines for different populations and BP goals (mm Hg)**
ESH/ESC, 2013 [8]	General non-elderly: • SBP 130-139 or DBP 85-89: no BP intervention • SBP ≥140 or DBP ≥90: lifestyle changes and BP drugs with goal BP of <140/90 General elderly <80 years: • Goal BP of <150/90 General elderly >80 years: • Goal SBP of <150 if in good mental and physical condition Diabetes: • Goal BP of <140/85 CKD and no proteinuria: • Goal BP of <140/90 CKD and proteinuria: • Goal BP of <130/90
JNC 8, 2014 [5]	General population:

(includes JNC 7 recommendations [10])	• SBP<120 and DBP<80: Encourage lifestyle modification • SBP 120-139 or DBP 80-89: Lifestyle changes, no hypertensive drugs indicated • In adults aged <60 years, SBP≥ 140/90: Lifestyle changes and initiate antihypertensive drugs with goal BP of <140/90 • In adults ≥60 years, SBP≥150/90: Lifestyle changes and initiate antihypertensive drugs with goal BP of <150/90 CKD and diabetes: • Lifestyle changes and goal BP of <140/90
CHEP, 2015 [12]	Lifestyle changes for all hypertensive individuals including: • 30-40 minutes of moderate physical activity on most days of the week • Reduce weight if overweight or obese • Reduce alcohol intake to less than 2 standard drinks per day, not exceeding 14 and 9 standard drinks for men and women per week respectively (1 standard drink = 13.6 g Ethanol, 44 mL of 80-proof spirits, 355 mL of 5% beer or 148 mL of 12% wine) • Consume a diet rich in fruits, vegetables, whole grains, low fat dairy, dietary fibre, plant protein, reduced saturated fat and low cholesterol • Reduce sodium intake to 2000 mg/day (5.2 g salt per day) • Stress management using appropriate relaxation techniques

	BP targets: • General population <80 years with no other risk factors: Goal BP <140/90 • General population >80 years with no other risk factors: Goal SBP <150 • Diabetes: Goal BP <130/80 • Cardiovascular disease and nondiabetic CKD: Goal BP <140/90

Abbreviations: BP, blood pressure; ESH, European Society of Hypertension; ESC, European Society of Cardiology; CKD, chronic kidney disease; JNC, Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8); AHA, American Heart Association; ACC, American College of cardiology; CHEP, Canadian Hypertension Education Program.

APPENDIX D

Completed PRISMA checklist for the systematic review and meta-analysis publication (Chapter 3)

Section/topic	#	Checklist item	Reported on page #
TITLE: Dietary patterns and blood pressure in adults: A systematic review and meta-analysis of randomized controlled trials			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			

Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097.

APPENDIX E

Characteristics of the randomised controlled trials on dietary patterns and blood pressure

Author, country, duration	**Subjects, inclusion and exclusion criteria**	**Intervention[2]**	**Control[2]**	**Nature of intervention (Sodium restriction/ weight loss/ exercise)**	**Office or 24-h ABP**	**Change in SBP, mm Hg**	**Change in DBP, mm Hg**	**Sodium/ potassium excretion**
Moore et al 1999 [187] United States 8 wk	354 Adults Inclusion: >22y, not taking BP[1] medication, BP < 160/80 to 95 mm Hg , BMI<35 kg/m^2 Exclusion: Serious health problems, conditions that may affect nutrient metabolism	Fruit and vegetable (F&V) diet: fruit~5 servings/d, vegetables~3 servings/d, whole grains~7 servings/d, low fat dairy~0, nuts, seeds and legumes~1 serving/d, snacks and sweets~1 serving/d, fats/oils~5 servings/d, sodium~ 3000mg/d	Typical American diet: fruit~2 servings/d, vegetables~2 servings/d, refined grains~8 servings/d, low fat dairy~0, meat~1.5 servings, nuts, seeds, legumes~0, snacks and sweets~4	All kept constant	24-h ABP	DASH diet: -4.5 (-6.2, -2.8)[3] *P*=0.0001 F&V diet: -3.1 (-4.8 to -1.4) *P*=0.001	DASH diet: -2.7 (-4.0, -1.4) *P*=0.0001 F&V diet: -2.0 (-3.3, -0.8) *P*=0.002	24h urine sodium change: DASH diet -73±1499 mg F&V -232±1365 mg Control +142±1427 mg 24 hr potassium change:

	or BP	DASH diet: fruit~5 servings/d, vegetable~4 servings/d, whole grains~8 servings/d, low fat dairy~2 servings/d, nuts, seeds and legumes~1 serving/d, snacks and sweets~1 serving/d, reduced fat/oils~3 servings/d, sodium~ 3000mg/d	servings/d, fats/oils~6 servings/d, sodium~ 3000mg/d					DASH diet +1500±1105 mg F&V +1298±1104 mg Control +146 ±608 mg
Sacks et al. 2001 [105] United States	412 adults Inclusion: >22yrs BP 120-159/ 80-95 mmHg	DASH diet with 3 sodium amounts for both intervention and control: High: 150 mmol/d	Typical American diet	Sodium restriction	Office BP	High sodium: -5.9 (-8.0, -3.7) P<0.001 Intermediat	High sodium: -2.9 (4.3, -1.5) P<0.001) Intermediate sodium:	24hr urine sodium: High Na level ~142 mmol/d Intermediate Na level

90 days	Exclusion: heart disease, renal disease, poorly controlled diabetes or hyperlipidaemia, insulin dependent diabetes mellitus, special dietary requirements, >14 alcoholic drinks/week, use of anti-hypertensives or other medication affecting BP	(3500mg Na) Intermediate: 100 mmol/d (2300 mg Na) Low: 50 mmol/d (1150 mg Na)				e sodium: -5.0 (-7.6, -2.5) P<0.001 Low sodium: -2.2 (-4.4, -0.1) P<0.05	-2.5 (-4.1, -0.8) P<0.01	~105 mmol/d Low Na level ~65 mmol/d
Appel et al. 2003 [122] United	810 Adults Inclusion: >25 years	Established behavioural intervention: weight loss, reduced sodium intake ~ 2300mg/day,	Advised on factors affecting BP such as weight, sodium reduction,	Weight loss, exercise, sodium restriction	Office BP	Established vs advice: -3.7 (-5.3, -2.1)	Established vs advice 1.7 (-2.8, -0.6)	Established vs advice: Significant change in Na excretion after 6 months. -11mEq/24h

States 6 mo	BMI 18.5-45.0 Kg/m^2 BP 120-159/ 80-95 mmHg Not on BP medication Exclusion: Diabetes, drugs that affect BP, weight loss medication, prior cardiovascular disease event, congestive heart failure, angina, cancer in the past 2 years, >21 alcoholic drinks/week, pregnancy/ lactation	increased exercise, limited alcohol intake, no goal for fruit, vegetable or dairy Established plus DASH diet: Above goals plus fruit and vegetables ~9-12 servings/d, low fat dairy ~2-3 servings/d	physical activity and DASH diet. No behaviour change counselling			(P<0.001 Established plus DASH vs advice -4.3 (-5.9, -2.8) P<0.001	P=0.002 Established plus DASH vs advice -2.6 (-3.7, -1.5) P<0.001	(P=0.01) Established plus DASH vs advice: Sign change in K excretion +20.6mEq/24h (P<0.001) Established plus DASH vs Established: K excretion +18.4mEq/24h (P<0.001)
Blumenthal et al. 2010	144 Adults	DASH diet alone (DASH-A) and DASH diet plus weight	Usual care (Typical American diet)	Weight loss, exercise	Office BP and 24-h ABP	DASH-WM vs usual care	DASH-WM vs usual care	Urinary sodium excretion:

[123] United States 4 months	Inclusion: >35 years, BMI 25-40 kg/m^2 BP 130-159/85-99 mmHg, not on BP medication, sedentary Exclusion: Diabetes, CKD, serious medical condition, use of medications that would affect cardiovascular disease system	management (DASH-WM) Both interventions: -DASH diet -reduced total fat~27% -saturated fat~6% -protein ~18% -high fibre -Na 2400mg/d/2000Kcal DASH-WM -500 calories less -exercise sessions 3 times /week	-no exercise recommended			-12.7±4.5[4] P<0.001 DASH-A vs usual care -7.8±4.5 P<0.001 DASH-WM vs DASH-A -4.9±4.3 P=0.02	-6.1±2.2 P<0.001 DASH-A vs usual care -3.7±2.4 P<0.001 DASH-WM vs DASH-A -2.4±2.4 P<0.048	DASH-WM 114 mmol/L (95% CI: 97,130) DASH-A 125 mmol/L (95% CI: 108,142) Control 145 mmol/l (95% CI: 129,161) Change in both interventions vs control: P=0.01 Urinary potassium excretion: DASH-WM 71.1mmol/L (95% CI: 64,79)

								DASH-A 74.9 mmol/L (95% CI: 67,83) Control 52.9 mmol/l (95% CI: 46,60) Change in both interventions vs control: P=0.001
Svetkey et al. 2009 [41] United States 6 months	574 Adults Inclusion: ≥25 years Receiving primary care from participating physicians, hypertensive and on	Physician intervention (MDI): On-line training modules on management of BP Patient intervention (PI): weight loss, DASH diet, increased	Physician control (MDC) Usual care Patient control (PC): usual care ~ written	Weight loss, exercise, sodium restriction	Office BP	MDI/PI -9.7±12.7 P=0.0006 compared to MDI/PC	MDI/PI -5.4 ±4.6 P<0.05 compared to MDI/PC	No significant differences between groups in the urinary sodium and potassium excretion

	BP medications Exclusion: Chronic kidney disease, cardiovascular disease event last 6 months, pregnant, lactating	physical activity, reduced sodium intake, moderate alcohol intake, adherence to BP medication	materials on lifestyle modification according to guidelines					
Lima et al. 2013 [106] Brazil 6 months	206 Adults Inclusion: >20 years, BP>140/ >90 mmHg, all on BP medication Exclusion: Diabetes, chronic renal disease, cancer, pregnancy	Intervention: Low glycaemic index Brazilian diet incorporating DASH-Na principles: reduced salt, low fat dairy~3 servings/d, fruit~3-5 servings/d, vegetable~4-5 servings/d, legumes~1 serving/d, grains, roots and tubers~5-9 servings/d, meat mainly fish~1-2 servings/d	Usual care**:** salt reduction, BP control	Sodium restriction	Office BP	-9.2 (SD not provided) P=0.02	-6.2 (SD not provided) P=0.04	Urinary sodium: Intervention: Reduced by 43.4 mmol/L (1000 mg) (P<0.01) No significant change in the control group

Brader et al. 2014 [108] Iceland, Sweden, Denmark and Finland 12 weeks	37 adults Inclusion: 30-65 years, metabolic syndrome, BP <160/100 mm Hg with or without BP medications, BMI 27-38 kg/m^2 Exclusion: Poor compliance, chronic liver, kidney or thyroid disease, diabetes	Nordic diet: whole grains (rye, barley, oats), nuts, rapeseed oil, fruits/ berries ≥150g/d, vegetables ≥500g/day, fish≥300g/week, low-fat dairy 2 servings/d, salt intake <7g/d men, <6g/d women	Control diet (Mean nutrient intake in Nordic countries): wheat products, dairy fat-based spreads, fruit, vegetables ≤250g/d, fish ≤100g/week, salt intake <10g/d	Sodium restriction	24-h ABP	No significant change	-4.4 (-6.9, -2.0) P=0.001	No difference in urinary sodium and potassium excretion between groups
Nowson et al. 2005 [191] Australia	63 men Inclusion: >25 years, BMI 25-35 kg/m^2, BP ≥120/≥80 mm Hg	DASH diet: fruit ≥4 servings/d, vegetables ≥4 servings/d, low-fat dairy ≥3 servings/d, fish ≥3 serves/week, legumes~1 cup /	Low fat diet Advised to reduce high energy food and drinks, choose plant based foods, choose low fat	Weight loss, exercise, sodium restriction	Home BP	-5.2 ± 1.8 (P=0.006)	-4.8 ± 1.3 (P=0.001)	Urinary sodium analysis not done

12 weeks	Exclusion: cardiovascular disease event in the past 6mo, insulin dependent diabetes mellitus, medication such as warfarin or phenytoin, consumed meals outside home >twice/week, >30 standard drinks/ week, use of dietary supplements	week, unsalted nuts and seeds~30g 4 times/week, red meat ≤2 serves/week, fat~ 4 servings/d 30 minutes moderate physical activity on most days	dairy, limit cheese and ice cream to twice per week, use lean meat, avoid frying foods in fat 30 minutes moderate physical activity on most days					
Burke et al. 2005 [192] Australia 4 and 12 months	241 adults Inclusion: 40-70 years, BMI >25 kg/m^2,could be on blood pressure medication Exclusion: BP >160/90 mmHg,	Lifestyle programme (4 months): DASH diet: high in fruits and vegetables, low salt and sugar, 4 fish meals/ week, alcohol < 2 standard drinks/ day for both men	Usual care: Provided with information from the National Heart Foundation and Health Department of Western Australia, no behaviour change	Weight loss, exercise, sodium restriction	24-h ABP	-3.0 (-6.3, 0.1) P=0.02	-1.8 (-3.4, -0.2) P=0.006	Intervention group reduced 24h urinary sodium by 4.9 mmol/24h compared to control group at 4 months (P=0.007) but no significant difference at 12 months

	intake of >2 fish meals per week or 4 fish oil capsules per week, alcohol intake >4 standard drinks/d for women, >6 standard drinks/d for men, drug or insulin treated diabetes, chronic renal failure, symptomatic cardiovascular disease of less than 3 months duration, other chronic debilitating disease	and women 30 minutes moderate intensity physical activity on most days, advice on cessation of smoking, social support from partners encouraged 12 month follow-up period: telephone contact, 6 sessions for measurements and group workshops	information					
Nowson et al. 2009 [193] Australia	111 women Inclusion: 45-75 years, BMI 18-35 kg/m^2,	Vitality diet (low acid load, low sodium DASH diet): lean red meat 6	Reference healthy diet (high acid load, high carbohydrate, low fat diet):	Sodium restriction	Home BP	Significant reduction only in those taking antihypertensives:	Significant reduction only in those taking antihypertensives:	Vitality diet group reduced 24h urinary sodium excretion: -38.6±6.9 mmol/d (P<0.001)

14 weeks	menopausal or postmenopausal not on HRT Office BP: 120-160/80-95 mmHg Home BP: SBP ≥116/ ≥78 mmHg Exclusion criteria: Menopause before 43 years, taking warfarin, diphenylhydantoin, medications for osteoporosis treatment, treated for cancer in the past 3 years, cardiovascular	servings/ week (600g/wk), low fat dairy ≥3 servings/d, fruit ≥4 servings/d, vegetables ≥4 servings/d, fats/ oils ≥4 tsp/d, whole grain breads/ cereals ≤4 servings/d, caffeine drinks ≤4 servings/d, alcoholic drinks ≤2 servings/d Sodium intake = 69 mmol/d (1590 mg/d)	lean red meat ≤2 servings/ week (200g/wk), low fat dairy ≥3 servings/d, fruit 2 servings/d, vegetables 2-3 servings/d, fats/ oils ≥8 tsp/d, whole grain or white breads/ cereals ≥4 servings/d, caffeine drinks ≤4 servings/d, alcoholic drinks ≤2 servings/d			-5.5 (-11.0, 0.02) P=0.05	-3.6 (-6.9, -0.3) P=0.04	

	disease event in the last 6 mo, insulin dependent diabetes, intake of >30 standard drinks/ week, consumed meals outside the home >2 times/ week							
Miller et al. 2002 [188] United States 9 weeks	45 adults Inclusion: 22-70 years, on a single antihypertensive medication, BP 130-170/80-100 mmHg, BMI>25 kg/m^2 Exclusion: Active or prior cardiovascular disease, medication treated diabetes, random glucose of >180 mg/dL, renal insufficiency, fasting	Comprehensive lifestyle intervention: DASH diet, alcohol ~2 drinks/day, caffeinated beverages~3 per day, reduced sodium intake: 100 mmol/d (2300 mg/d), supervised moderate aerobic exercise 3 times/ week, weight loss of 0.6 kg/ week	Control No intervention	Weight loss, exercise, sodium restriction	24-h ABP	-9.5 (-14.5, -4.5) P<0.001	-5.3 (-8.5, -2.1) P<0.002	24-h urinary potassium excretion significantly increased in intervention group by 20 mmol/L (95% CI: 5,35, P=0.009) No significant change in urinary sodium excretion

	cholesterol >260 mg/dL, pregnancy or lactation, consumption of >14 alcoholic drinks/ week, unwillingness to stop supplements intake							
Toobert et al. 2003 [189] United States 6 months	279 women Inclusion: Post-menopausal with type 2 diabetes, living independently, has a telephone and able to read, not developmentally disabled, living within 30miles Exclusion: >75 years, planning to move from study area	Mediterranean Lifestyle Program: Increased amounts of bread, vegetables, fruits, legumes, fish, less red meat, avoid cream and butter, use of olive/ canola oil or margarines	Usual care	Weight loss, exercise	Office BP	No significant change	No significant change	Urinary sodium and potassium analysis not done

Esposito et al. 2004 [114] Italy 24 months	180 adults Inclusion: -three or more features of metabolic syndrome Exclusion: cardiovascular disease disease, psychiatric problems, history of alcohol abuse, smoking, taking any medication	Mediterranean diet: Increased consumption of whole rains (400 g/d), fruits (250-300g/d), vegetables (120-150g/d), walnuts (25-30g /d), olive oil (8g/d) Exercise for 30 minutes per day	Prudent diet General information on healthy food choices, no individualized plan Exercise for 30 minutes per day	Exercise	Office BP	-3.0 (-5.0, -1.0), P=0.01	-2.0 (-3.5, -0.5), P=0.03	Urinary sodium and potassium analysis not done
Esposito et al. 2003 [190] Italy	120 women Inclusion: 20-46 years, BMI ≥30 kg/m^2, sedentary	Mediterranean diet Information on calorie restriction to achieve weight loss of 10% or more, use of food	Control diet Information about healthy food choices and exercise	Weight loss, exercise	Office BP	-2.0 (-3.5, -0.5), P=0.009	-1.7 (-3.0 - 0.4) P<0.001	Urinary sodium and potassium analysis not done

24 months	Exclusion: Diabetes or impaired glucose tolerance, hypertension, cardiovascular disease, psychiatric problems, history of alcohol abuse (≥500g/week), smoking, any medication use	diaries, behavioural and psychological counselling						
Vincent-Baudry et al. 2005 [194] France 3 months	212 adults Inclusion: 18-70 years One of the following: -BP 140-190/90-105 mmHg -cholesterol 6.5-7.7 mmol/L -glucose 6.1-6.9 mmol/L	Mediterranean diet recommended: Nuts, whole meal bread and cereals, fresh or dried fruit, vegetables, legumes, olive oil, fish 4 times/week, red meat once per week, sheep and poultry as main source of meat, cheese from sheep and goats, red	Low fat diet recommended foods: Consume more poultry, avoid offal and saturated fat rich animal products, fish 2-3 times per week, fruit and vegetables, low fat dairy products, use	All kept constant	Office BP	No significant change	No significant change	Urinary sodium and potassium analysis not done

	-BMI>27 kg/m^2 -smoking -sedentary -family history of cardiovascular disease Exclusion: Treatment with hypolipemic or hypoglycemic drugs	wine: 2 glasses/d men, 1 glass/d women	of vegetable oils					
Domenech et al. 2014 [206] Spain 1 year	284 adults Inclusion: Men 55-80 years, women 60-80 years, type 2 diabetes or with ≥3 cardiovascular	Interventions: Mediterranean diet and extra virgin olive oil (provided 1 litre/week) Mediterranean diet	Control: Low fat diet	All kept constant	ABP	Mediterranean diet and extra virgin olive oil: -4.0 (-6.4, -1.6) P<0.001 Mediterran	Mediterranean diet and extra virgin olive oil -1.9 (-3.4, -0.4) P<0.001	Urinary sodium and potassium analysis not done

	disease risk factors Exclusion: History of cardiovascular disease, severe chronic illness, immunodeficiency or HIV, illegal drug or alcohol misuse, allergy to nuts or olive oil, unwilling to change dietary habits	and mixed nuts ~ provided 30g/d (15g walnuts, 7.5g almonds, 7.5g hazelnuts) Mediterranean diet amounts used to assess adherence: olive oil consumption ≥4tbs/d, vegetables ≥2 servings/d, fruit ≥3 servings/d, red meat, hamburger or meat products e.g. ham, sausage <1 serving/d, butter, margarine, cream <1 serving/d (1 serving=12g), sweet and carbonated drinks <1/d, wine ≥7 glasses/week, legumes ≥3 servings/week, fish				ean diet and nuts -4.3 (-6.7, -1.9) P<0.001	Mediterranean diet and nuts -1.9 (-3.4, -0.4) P<0.001	

		≥3 servings/week, commercial sweets/ pastries < 3times /week, nuts ≥30g/week, vegetables, pasta, rice or other dishes seasoned with sofrito (sauce made with tomato and onion, leek or garlic and simmered with olive oil) ≥2 times/ week, consumption of chicken, turkey or rabbit meat instead of veal, pork, hamburger or sausage						
Adamsson et al. 2011 [109] Sweden	88 adults Inclusion: 25-65yrs, BP <145/85 mm Hg, BMI 20-31 kg/m^2	Nordic diet: Foods supplied to participants except beverages: Fruits, berries, vegetables, legumes, low-fat dairy, fatty fish,	Control diet (Usual Western diet) No foods provided	All kept constant	Office BP	-7.2 (-12.3, -1.9) P=0.008	No significant change	Urinary sodium and potassium analysis not done

6 weeks	Hb >120g/L (women), >130g/L (men) LDL-C >3.5mmol/L Exclusion: Use of lipid lowering drugs, Triglycerides >4.5 mmol/L, Allergy to certain foods, weight-loss diets or drugs, special diets eg vegan, pregnancy/ lactation	oats, barley, soy protein, almonds, psyllium seeds Diet provided ad libitum						
Poulsen et al. 2014 [110] Denmark 26 weeks	181 adults Inclusion: 18-65 years, BP > 130/85 mm Hg, waist circumference >80(w), >94(m), BP >130/85 mm Hg, metabolic syndrome	New Nordic diet: Vegetables 400g/d, fruit 300g/d (berries 75g/d), potatoes 150g/d, no limit on fresh herbs, wild plants and	Control - Average Danish diet: Vegetables 180g/d, fruit 200g/d (berries 4g/d), potatoes 100g/d, no	All kept constant	Office BP	-5.2 (-8.0, -2.4) P=0.001	No significant change	No significant difference between 24-h sodium excretion between intervention and control

	Exclusion: Diabetes, food allergies, hypercholesterolemia, pregnant and lactating	mushrooms 5g/d, nuts 30g/d, dairy products 500g milk/d, 25g cheese/d, eggs 25g/d, Foods are organically grown and consumed ad libitum	wild plants and mushrooms, fresh herbs ≤1, nuts ≤1serving/d, refined grains, sweets, imported fruit					
Von Haehling et al. 2013 [196] Germany 12 months	524 adults Inclusion: >18 years, coronary artery disease, any 2 of metabolic syndrome traits, BMI >25 kg/m^2 Exclusion:	Traditional Tibetan diet: Adapted to food availability in the Western world, cooked and warm foods. Barley, wheat, rye, corn, rice, oat, buckwheat, beef, mutton, hare,	Usual care (western diet)**,** guidelines by American heart association and German academy and society of nutritional medicine Cereals; whole	Weight loss, exercise	Office BP	No significant change	No significant change	Urinary sodium and potassium analysis not done

	Pregnancy, end stage renal disease, infectious diseases, malignancy	chicken, venison; Vegetables -onion, garlic, radish, fennel, leek, onion, carrot, soy beans, dried dark beans. Fruit - pomegranate, banana, pineapple, mango, bramble, apricot, nectarine. Eat in a relaxed atmosphere with warm colours, avoid psychological stress, moderate physical activity, sufficient sleep	grain rice and noodles and grains Meat; chicken, turkey, veal, rabbit. All vegetables and fruits Avoid psychological stress, moderate physical activity, obtain sufficient sleep, avoid sudden changes in temperature e.g. sauna and cold water diving					
Azadbakht et al. 2011 [195]	44 adults Inclusion:	DASH diet: Fruit ~5 servings/d,	Usual diabetic diet:	Sodium restriction	Office BP	-10.5 (-19.2, -1.8) P=0.02	-8.8 (-17.1, -0.6) P=0.04	Urinary sodium and potassium analysis not done

Iran 8 weeks	44-70 years, type 2 diabetes Exclusion: Any secondary cause of hyperglycaemia, hepatic or kidney disorders, cancer, oestrogen therapy, untreated hypothyroidism, smoking	vegetables ~6.8 servings/d, dairy~3 servings/d, whole grains~ 4.5 servings/d Sodium = 2300 mg/d	Fruit~3 servings/d, vegetables~ 4 servings/d, dairy~2 servings/d, whole grains~2.5 servings/d Sodium = 3000 mg/d					

[1]Abbreviations: ABP, ambulatory blood pressure; BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension; DBP, diastolic blood pressure; MD, Mediterranean diet; MDC, physician intervention; MDI, physician control; Na, sodium; PC, patient control; PI, patient intervention; wk, week

[2]Serves per day unless otherwise stated, glass in terms of mL, [3]Mean; 95% CI in parenthesis, [4]Mean ± SD (all such values).

APPENDIX F

Characteristics of the observational studies on dietary patterns and blood pressure

Author, country, duration	**Design/ aims**	**Subjects, inclusion and exclusion criteria**	**Dietary assessment/ methods defining dietary pattern**	**Dietary pattern(s) identified**	**Outcomes**	**Statistical analysis/ confounders adjusted for**	**Results**
Dauchet et al. 2007 [77] France 5.4 years (4.4-6.4y)	Longitudinal analysis SU.VI.MAX[1] study - originally a randomised controlled trial of antioxidants from 1994 to 2002 Aim: To investigate the relationship between BP changes and	2341 adults 35-63 years Exclusion criteria: Hypertension, use of hypertensives	Repeated 24-h dietary records every 2 months. Total of 6 records per year. DASH diet characteristics	Fruit and vegetables (excluding potato and legumes) Dairy products including milk, cheese, yoghurt and other dairy products Healthy fat (defined by Keys score)	BP	Specific quartiles calculated and P for linear trend performed with dietary intakes as continuous variables. Confounders: Age, sex, group, total energy intake (excluding alcohol), number of dietary records completed, tobacco use, alcohol, physical activity, educational level, BMI, dietary sodium intake (except table salt), blood pressure at	High fruit and vegetable intake (642g vs 228g) was associated with smaller increase in BP: SBP -2.1 mm Hg (-3.6, -0.7)[2] P<0.004 DBP -0.7 mm Hg (-1.7, 0.3) P<0.03 High DASH score associated with smaller increase in BP: SBP -2.1mm Hg (-3.6, -0.7) P<0.002 DBP -0.6 mm Hg (-1.6, 0.4) P<0.02 No significant associations found with dairy products consumption or

	dietary patterns.					1st clinical examination, magnesium and potassium intakes	healthy fat. Antioxidants intake was found to have no effect on risk of hypertension compared with placebo.
McNaughton et al. 2007 [180] United Kingdom 18 years (1982-1999)	Longitudinal study 1946 Birth cohort study Aim: To determine the association between dietary patterns and risk factors for chronic disease.	1265 adults 36-53 years Included normotensives and hypertensives	5-day food diary Factor analysis	Women: -ethnic foods and alcohol -meat, potatoes and sweet foods -fruit, vegetables and dairy Men: -ethnic foods and alcohol -mixed	BP BMI Waist circumference Red cell folate	Dietary patterns assessed using Mplus factor analysis. Longitudinal analysis conducted using the dietary data obtained in 1982, 1989 and 1999. Confounders: Age, social class, education, region, alcohol, smoking, physical activity, supplement use	Fruit, vegetable and dairy (P=0.02) and ethnic foods and alcohol (P=0.008) dietary patterns were inversely associated with BP in women. Mixed pattern was significantly associated with BP in men (P=0.01).
Umesawa et al.	Longitudinal Prospective	3486 males	Questionnaire containing 19	-dairy products	Incident of hypertensio	Logistic regression models. Odds ratios	Increased risk of developing

2013 [96] Japan Average 4.6 years	study Aim: To determine the association between dietary behaviour and the risk of hypertension.	workers 30-71 years (mean 42.9y) Exclusion: hypertension	items related to dietary behaviour	-meat -eggs -noodle soup	n	(ORs) for risk of hypertension calculated. Confounders: Age, BMI, alcohol intake, job, smoking habits, estimated glomerular filtration rate, SBP at baseline	hypertension in: -those who did not eat meat frequently OR:1.26 (95% CI: 1.00-1.59) -those who did not consume dairy every day OR 1.39 (95% CI: 1.13-1.71) -those who started consuming all noodle soup OR: 1.32 (95% CI: 1.02-1.71) -those not consuming eggs daily OR: 1.33 (95% CI: 1.00-1.75)
Wang et al. 2012 [78] United States 12.9 years	Longitudinal prospective study Women's Health study (WHS) Aim:	28,082 women 39-89 years Exclusion: cardiovascular disease,	131-item semi-quantitative food frequency questionnaire	Fruit and vegetables	Incident of hypertension	Cox models to estimate hazard ratio (HR) of hypertension across levels of fruit and vegetable intake. Confounders: Age, race, total energy intake, BMI, randomised treatment group, smoking status,	Fruit and vegetables: Higher intake of fruits and vegetables was significantly associated with reduced risk of hypertension after adjustment for lifestyle factors; HR: 0.90 (0.82, 0.99), P<0.001 but the association was not significant after adjustment for dietary factors and BMI.

	To assess the association between fruit and vegetables intake and the risk of hypertension.	hypertension or cancer (except non-melanoma cancer)				alcohol use, physical activity, postmenopausal status, postmenopausal hormone use, supplement use, history of diabetes and hypercholesterolemia, dietary risk factors such as whole grains, red meat, low-fat dairy and nuts.	Total fruits: Higher intake of fruits significantly associated with reduced risk of hypertension after adjusting for lifestyle and dietary factors but not BMI. HR: 0.89 (0.81-0.96), p=0.0004 Total vegetables: No significant association with risk of hypertension.
Toledo et al. 2010 [198] Spain 2-6 years (median 4.6	Longitudinal prospective study SUN project (University graduates followed every 2 years beginning December 1999)	10,800 adults Exclusion: hypertension	136-item semi-quantitative food frequency questionnaire	15 priori-defined scores of adherence to healthy food pattern	Incident of hypertension	Cox regression models to assess incidence of hypertension. Confounders: Age, sex, total energy intake, BMI, family history of hypertension, smoking, physical activity	Higher adherence to DASH diet was associated with lower risk of developing hypertension HR: 0.48 (95% CI 0.21-1.09), P=0.02 UMMDS (Updated modified Mediterranean diet score) showed a significant increased risk of development of hypertension HR: 1.34 (95% CI 1.04-1.73),

years)	Aim: To assess the association between adherence to several healthy dietary patterns and the risk of hypertension.						P=0.002 Other dietary scores did not show significant results
Rumawas et al. 2009 [197] United States 7 years mean follow-up	Longitudinal prospective study Framingham Heart Study Offspring Cohort Aim: To assess the association between Mediterranean style dietary	2370 adults Median age: 54 years Exclusion: diabetes, metabolic syndrome	126-item semi-quantitative food frequency questionnaire Mediterranean style dietary pattern score (MSDPS)	Food groups considered: -whole grain cereals -fruit -vegetables -dairy -wine -fish -poultry -olives/ legumes/ nuts	Metabolic syndrome biomarkers including SBP and DBP	ANCOVA to assess relationship between MSDPS and metabolic syndrome traits. Confounders: Age, sex, BMI, energy intake, smoking dose, change in BMI	No association was found between MSDPS score and BP

	pattern and metabolic syndrome.			-potatoes -eggs -sweets -meat -olive oil			
Steffen et al. 2005 [93] United States 15 years	Longitudinal prospective study CARDIA (Coronary artery risk development in young adults) multi-centre study Aim: To determine the association of dietary intake with elevated BP.	4304 adults 18-30 years Exclusion: Diabetes, pregnant, lactating, extreme caloric intakes, elevated BP	Interviewer administered diet history	Food groups considered: Plant – fruit, vegetables, whole and refined grains, nuts, legumes Dairy – milk, yoghurt, cheese, dairy desserts Meat – red and processed meat, poultry, fish, eggs	Elevated BP incidence	Cox proportional hazards regression analysis to assess association between food group consumption with 15-y incidence of BP. Confounders: Age, sex, race, centre, education, BMI, energy intake, smoking, physical activity, alcohol intake, vitamin supplement use, dietary intake, baseline SBP, fasting insulin	Plant food (whole grains, fruit and nuts) intake was inversely associated with elevated BP in the highest compared with lowest quintile. Whole grains: HR 0.83 (95% CI: 0.67, 1.03), P=0.03 Fruit: HR 0.75(95% CI: 0.60, 0.94), P=0.02 Nuts: HR 0.85 (95% CI: 0.72, 0.99), P=0.04 Inverse association with milk, HR 0.87 (95% CI: 0.70, 1.08), P=0.03 and dairy desserts, HR 0.74 (95% CI: 0.60, 0.92), P=0.01.

							Egg intake was inversely associated with elevated BP. HR 0.79 (95% CI: 0.64, 0.98), P=0.05 Red and processed meat intake was significantly positively associated with elevated BP. HR 1.39 (95% CI: 1.05, 1.82), P=0.006
Miura et al. 2004 [178] United States 7 years (1959-1966)	Longitudinal prospective study The Chicago Western Electric Study (study of coronary heart disease and its precursors) Aim: To evaluate the association between food	1710 men 41-57 years (mean 48.5y) Exclusion criteria: Diabetes mellitus, prior myocardial infarction, missing blood		Food groups: -vegetables -fruits -fish -beef/ veal/ lamb -pork/ ham/ bacon -poultry	BP (Measured at the beginning of each yearly medical examination)	Generalized estimating equation method for longitudinal data to assess relationship between baseline dietary factors and average BP change. Confounders: Age, weight, height, education, total energy intake, smoking, alcohol intake, dietary intake (food groups and nutrients – carbohydrate, protein, saturated fatty acid,	Increased vegetable intake at 14-42 cups/month (0.5-1.5cups/day) was associated with smaller BP increase though the association weakened after further adjustment for nutrients. SBP change: -2.8 mm Hg (P=0.008) DBP change: -1.19 mm Hg (P=0.037) Increased fruit intake at 14-42 cups/ months (0.5-1.5cups/day) led to a decrease in BP even after adjusting for nutrients.

	intake and BP change.	pressure or dietary assessment data, fewer than 3 follow-up examinations				polyunsaturated fatty acid, dietary cholesterol, iron, thiamine, riboflavin, niacin, Vitamin C, beta-carotene and retinol)	SBP change: -2.2 mm Hg (P=0.043) DBP change: -1.5 mm Hg (P=0.046) Intake of 8-20 servings/ month and >20 servings/ month of beef, veal and lamb led to a greater rise in SBP by 5.4 mm Hg and 6.0 mm Hg respectively (P<0.05). DBP: >20 servings/ month led to a greater increase by 2.9 mm Hg (P=0.022) compared to <8 servings/month. Pork intake: 4-8 servings/month led to greater rise in SBP by 3.9 mm Hg (P=0.002) Poultry: SBP: >8 servings/ month led to a greater rise by 3.4 mm Hg (P=0.012) DBP: 4-8 servings/month compared to <4 servings/month led to greater

							rise by 1.3 mm Hg (P=0.006), >8 servings/ month led to a greater increase by 1.8 mm Hg (P=0.031)
Nunez-Cordoba et al. 2009 [184] Spain 4.2 median years (1999-2005)	Longitudinal prospective study SUN study Aim: To determine association between adherence to the Mediterranean diet and incidence of hypertension.	9408 adults Exclusion criteria: Hypertension, cardiovascular disease, cancer, diabetes mellitus, extreme caloric intakes	136-item food frequency questionnaire	Mediterranean diet (MD) 9-point MD score. Include : -vegetables -legumes -fruits and nuts -cereals -fish -meat and meat products -dairy products -alcohol -ratio of MUFA:SFA	Incident of hypertension and BP change	Linear regression to assess relationship between MD adherence and relative change in BP in non-hypertensive participants. Cox proportional hazard models to estimate hazard ratios (HR) for hypertension. Confounders: Age, sex, BMI, family history of hypertension, hypercholesterolemia, caffeine intake, total energy intake, smoking, physical activity	MD not associated with incidence of hypertension. Inverse association with intake of legumes. HR:0.84 (95% CI: 0.70-1.00) Direct association between alcohol intake and incidence of hypertension HR: 1.25 (95% CI: 1.03-1.51) MD associated with reduced changes in SBP and DBP in those without hypertension after 6 years. SBP change (P=0.01) in comparison with low adherence score: -3.1mm Hg (-5.4, -0.8) for the high score

							-2.4mm Hg (-4.0, -0.8) for the moderate score DBP change: (P=0.05) -1.9 mm Hg (-3.6, -0.1) for high score -1.3 mm Hg (-2.5, -0.1) for moderate score
Schulze et al. 2003 [179] Germany 2-4 years Baseline examination done between Aug	Longitudinal prospective study EPIC-Potsdam multi-centre cohort study EPIC: European Prospective Investigation into Cancer and nutrition Aim: To determine	8552 women 35-64 years Exclusion criteria: Hypertension, missing data (on dietary intake, anthropometry, physical activity and basal metabolic rate),	148-item self-administered food frequency questionnaire	Dietary patterns identified : Traditional cooking - meat, cooked vegetables, sauce, potatoes, poultry Fruit and vegetables - fruits, raw vegetables, vegetable oil DASH - fruits, vegetables (raw	Incident of hypertension	Cox regression models to estimate relative risks of hypertension. Confounders: BMI, alcohol intake, , smoking status, history of cardiovascular disease or diabetes, physical activity, use of mineral supplement, employment status, education, SBP, DBP, waist to hip ratio, total energy intake, dietary change within the year prior to baseline examination	DASH pattern: 3rd quartile had significant inverse association with incident of hypertension compared to 1st quartile. HR: 0.51 (0.29-0.89) No association was found between the traditional cooking and fruit and vegetable dietary patterns with incident of hypertension.

1994 and Sep 1998	the effect of dietary patterns on incidence of hypertension.	pregnant or lactating, extreme energy intakes		and cooked), milk products (milk, yoghurt, cheese)			

[1]Abbreviations: BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension; DBP, diastolic blood pressure; MD, Mediterranean diet; SBP, systolic blood pressure; SU.VI.MAX, SUpplementation en VItamines et Mine´raux AntioXydants.

[2]Mean; 95% CI in parenthesis.

APPENDIX G

Percentage contribution of major food groups to sodium and potassium intake among clinically overweight adults

Food group[a]	**Sodium**		**Potassium**	
	% Sodium intake	**Median (IQR)**[b] **mg/day**	**% Potassium intake**	**Median (IQR) mg/day**
Cereal based products and dishes (biscuits, cakes, pastries)	**21.61**	**527 (247-878)**	7.37	206(100-343)
Cereal and cereal products (breads, rice, pasta, breakfast cereals)	**14.53**	**384 (251-529)**	7.78	231 (149-326)
Meat, poultry and game products and dishes	**17.57**	**393 (203-709)**	**15.58**	**456 (307-704)**
Milk products and dishes (milk, yoghurt, cheese, custard)	**10.59**	**247 (141-418)**	**12.74**	**356 (181-575)**
Savoury sauces and condiments	8.69	176 (70-333)	1.68	26 (8-76)
Vegetable products and dishes	4.72	100 (46-181)	**22.02**	**682 (426-930)**

Soup	4.27	282 (179-563)	1.93	158 (87-282)
Fish and seafood products and dishes	4.01	134 (77-262)	2.69	128 (65-217)
Non-alcoholic beverages (tea, coffee, soft drinks, juices)	3.11	66 (31-117)	9.51	254 (109-444)
Miscellaneous (yeast, herbs, spices, seasonings)	3.02	76 (23-234)	0.85	16 (3-69)
Snack foods	1.89	76 (38-155)	1.62	58 (22-155)
Legume and pulse products and dishes	1.29	124 (56-201)	0.84	81 (52-129)
Fats and oils	1.13	22 (7-51)	0.04	1 (0.3-2)
Egg products and dishes	0.86	27 (14-54)	0.67	29 (16-50)
Confectionery and cereal/nut/fruit/seed bars	0.75	22(7-41)	1.88	62 (28-123)
Alcoholic beverages	0.65	27 (13-54)	2.08	102 (43-179)
Seed and nut products and dishes	0.60	6 (1-38)	2.00	71(37-147)

Dairy & meat substitutes (soy based beverages and soups)	0.25	22 (3-69)	0.51	62 (26-238)
Special dietary foods	0.17	37 (24-59)	0.23	60(0-133)
Fruit products and dishes	0.15	3 (1-6)	7.74	231 (112-404)
Sugar products and dishes	0.14	1 (0.1-4)	0.24	4 (1-14)

[a]Using AUSNUT 2011-13 major food groups; [b]IQR, interquartile range.

APPENDIX H

AUSNUT 2011-13 major food groups and example foods used in the Principal Component Analysis in the HealthTrack study

Major food group	**Example food items**
Alcoholic beverages	Beers, wines, spirits, cocktails and liqueurs
Cereal and cereal products	Bread, rice, noodles, pasta and breakfast cereals
Cereal based products and dishes	Sweet and savoury biscuits, cakes, sweet and savoury pastry, pizza, sandwiches and burgers
Confectionery and cereal/nut/fruit/seed bars	Chocolate, muesli bars, fruit bars, lollies, chewing gum
Dairy & meat substitutes	Soy beverages, almond milk, tofu, quorn and tofu stirfry
Dietary supplements	Vitamins and mineral supplements, fish oil supplements, fibre supplements
Egg products & dishes	Eggs, omelette, soufflé and frittata
Fats & Oils	Butter, margarine and oils
Fruit products and dishes	Apples, pears, berries, oranges, peaches, bananas, banana split, melons, dried fruit, apple crumble
Infant formulae and foods	Toddler formula, rusks, infant cereals and fruit, infant custards and fruit juices
Legumes and pulse products	Lentils, soy beans, chickpeas, kidney beans, falafel and dhal

and dishes	
Meat, poultry, game product and dishes	Beef, chicken, lamb, pork, veal, kangaroo, ham, dried meats, sausages, casseroles and curries
Milk products and dishes	Milk, yoghurt, cream, cheese, ice cream, dairy desserts, and cheesecake
Miscellaneous	Yeast, salt, intense sweeteners, herbs, stock, essences, gelatine and spreadable yeast extract
Non-alcoholic beverages	Coffee, tea, fruit juice, cordial, soft drink, water and electrolyte drinks
Reptiles, amphibia and insects	Crocodile, turtle, goanna
Savoury sauces and condiments	Tomato sauce, chutney, salad dressings, mayonnaise, vinegar and dips
Seafood products and dishes	Fish, prawns, canned tuna, fish with pasta or rice
Seed and nut products & dishes	Peanuts, walnuts, almonds, peanut butter, pumpkin seeds, coconut milk
Snack foods	Potato crisps, popcorn, corn chips, rice crisps and pretzels
Soup	Canned and homemade soup, dried soup mix
Special dietary foods	Liquid and powdered meal replacements, protein drinks and powders, oral supplement powder and beverages

Sugar products and dishes	Sugar, honey, jam, icing sugar, apple sauce and meringue
Vegetable products and dishes	Potatoes, carrots, beans, tomato, lettuce, cucumber, corn, salads, potato bake

Adapted from:

http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4364.0.55.007Appendix22011-12;

Food groups labelled Infant formulae and foods, Reptiles, amphibia and insects, and Dietary supplements were excluded from analysis due to a lack of participants consuming foods from these categories.

APPENDIX I

Factor loading matrix for the dietary patterns identified by factor analysis among the HealthTrack study participants (n=328)

			Dietary pattern			
Food group	**Nuts, seeds, fruit and fish**	**Milk and meat**	**Breads, cereals and snacks**	**Cereal based products, fats and oils**	**Alcohol, eggs and legumes**	**Savoury sauces and condiments and meat**
Seeds and nut products and dishes	**0.626**[a]	-0.096	-0.053	-0.071	0.024	0.115
Fruit products and dishes	**0.574**	0.146	-0.316	0.117	-0.133	-0.215
Confectionery and cereal/nut/fruit/seed bars	**0.524**	0.062	**0.458**	0.084	-0.064	-0.112
Fish and seafood products and dishes	**0.427**	0.013	0.030	-0.047	0.346	0.138

Non-alcoholic beverages	0.166	**0.693**	-0.013	-0.055	0.155	-0.023
Milk products and dishes (milk, yoghurt, cheese, custard)	0.089	**0.575**	-0.021	0.294	-0.160	-0.159
Dairy and meat substitutes	0.388	**-0.540**	-0.002	0.021	0.072	-0.165
Meat, poultry and game products and dishes	-0.161	**0.482**	-0.121	-0.121	0.145	**0.400**
Snack foods	0.181	0.065	**0.613**	-0.079	-0.050	0.254
Cereal and cereal products (bread, rice, pasta, breakfast cereals)	-0.162	-0.124	**0.612**	0.061	0.134	-0.088
Vegetables products and dishes	0.164	0.064	**-0.548**	0.033	0.364	0.288
Sugar products and dishes	-0.117	0.249	0.262	0.221	0.059	-0.056
Cereal based products and dishes (biscuits, cakes, pastries)	0.047	-0.064	-0.043	**0.669**	-0.040	0.220
Fats and oils	-0.071	0.065	0.100	**0.609**	0.249	0.023
Special dietary foods	-0.010	-0.061	0.008	**-0.535**	0.167	0.043
Alcoholic beverages	-0.090	0.047	0.074	-0.106	**0.673**	0.201
Egg products and dishes	0.040	0.043	-0.033	0.020	**0.584**	-0.097

Legume and pulse products and dishes	0.104	-0.151	-0.143	0.313	**0.438**	-0.364
Savoury sauces and condiments	0.079	-0.049	-0.046	0.262	0.030	**0.784**
Variance explained (%)	9.46	8.69	7.99	7.21	6.71	5.97

[a]Factor loadings represent the magnitude and direction of association with dietary patterns and can range from -1.0 to 1.0. Factor loadings are interpreted similarly to the correlation coefficients. Bold font indicates factor loadings > ± 0.4 that were considered significant for inclusion of a food group in the respective dietary pattern. Two food groups (Miscellaneous and soup) were excluded from analysis due to low Kaiser-Meyer-Olkin measure (< 0.45) after inspection of the Anti-image Matrices.

APPENDIX J

Reported macronutrient and micronutrient intakes per day showing alignment and non-alignment with each of the six dietary patterns among participants of the HealthTrack study (n=328)

	Nuts, seeds, fruit and fish		**Milk and meat**		**Breads, cereals and snacks**		**Cereal based products, fats and oils**		**Alcohol, eggs and legumes**		**Savoury sauces, condiments and meat**	
	Aligned (n=160)	Not aligned (n=168)	Aligned (n=209)	Not aligned (n=119)	Aligned (n=166)	Not aligned (n=162)	Aligned (n=173)	Not aligned (n=155)	Aligned (n=153)	Not aligned (n=175)	Aligned (n=181)	Not aligned (n=147)
Macro Nutrients												
Energy, kcal	2236 (608)	2100 (582)	2224 (618)	2065 (547)*	2299 (661)	2030 (490)***	2328 (597)	1985 (546)***	2303 (640)	2047 (531)***	2267 (635)	2042 (523)***
Protein, g	105.4 (27.9)	103.2 (32.7)	108.6 (28.6)	96.7 (32.1)**	102.6 (30.1)	106.0 (30.6)	107.3 (30.0)	100.8 (30.6)	111.7 (31.4)	97.8 (27.9)**	112.3 (31.8)	94.4 (25.4)***

										*		
Total fat, g	89.7 (30.2)	82.5 (30.2)*	88.1(31.5)	82.3 (28.0)	93.0 (32.9)	78.9 (25.7)***	94.3 (30.3)	76.8 (27.7)***	92.3 (32.6)	80.5 (27.2)***	91.1 (33.0)	79.7 (25.5)***
Saturated fat, g	33.9 (12.8)	34.6 (14.9)	35.5 (14.5)	32.1 (12.6)	38.2 (15.1)	30.2 (11.3)***	38.0 (14.5)	30.1 (12.0)***	36.4 (15.0)	32.4 (12.6)*	35.2 (14.6)	33.1 912.9)
Polyunsaturated fat, g	15.1 (6.2)	11.4 (4.3)***	13.3 (5.6)	13.1 (5.7)	13.7 (5.7)	12.7 (5.3)	14.3 (5.6)	12.0 (5.4)***	14.2 (5.9)	12.3 (5.3)**	14.2 (6.1)	12.0 (4.8)***
Monounsaturated fat, g	34.2 (13.0)	30.6 (11.4)**	33.0 (12.6)	31.2 (11.7)	34.4 (12.9)	30.2 (11.3)**	35.2 (12.6)	29.2 (11.3)***	34.9 (13.2)	30.1 (11.0)***	35.1 (13.6)	28.9 (9.5)***
Cholesterol, mg	309.5 (117.2)	331.4 (142.6)	335.6 (122.8)	294.6 (141.3)**	318.5 (125.0)	323.0 (137.5)	331.4 (131.6)	308.9 (130.0)	372.5 (140.9)	275.5 (102.7)***	339.3 (135.5)	297.9 (122.2)**

Carbohydrate, g	230.1 (73.6)	212.9 (63.8)*	227.0 (73.8)	211.3 (59.1)*	242.2 (75.1)	199.8 (55.0)***	241.2 (70.7)	199.0 (60.3)***	222.1 (76.9)	220.5 (61.8)	223.7 (70.3)	218.3 (67.9)
Sugars, g	105.9 (41.9)	92.8 (39.5)**	106.9 (43.8)	85.8 (32.1)***	107.0 (45.5)	91.2 (34.5)***	106.3 (43.3)	91.3 (37.2)**	94.8 (42.0)	103.1 (40.1)	96.7 (39.8)	102.4 (42.7)
Starch, g	121.0 (44.8)	117.0 (36.3)	117.3 (41.1)	121.9 (39.9)	131.9 (42.2)	105.7 (34.4)***	131.9 (39.1)	104.5 (37.6)***	123.3 (45.1)	115.2 (36.1)	123.5 (41.3)	113.3 (39.3)**
Alcohol, g	6.1 (11.0)	8.5 (13.0)	7.1 (11.7)	7.7 (12.7)	7.1 (11.1)	7.6 (13.0)	6.4 (11.8)	8.4 (12.3)	13.5 (14.6)	1.9 (4.8)***	8.9 (13.2)	5.4 (10.2)**
Dietary fibre, g	27.4 (8.8)	21.8 (7.4)***	24.4 (8.0)	24.7 (9.6)	23.2 (8.5)	25.9 (8.6)**	26.7 (8.6)	22.1 (7.9)***	25.7 (8.4)	23.5 (8.6)*	25.3 (8.5)	23.5 (8.6)
Micronutrients												
Thiamin, mg	1.80 (0.67)	1.69 (0.88)	1.83 (0.83)	1.61 (0.69)*	1.77 (0.82)	1.72 (0.76)	1.94 (0.87)	1.53 (0.62)***	1.74 (0.75)	1.75 (0.82)	1.79 (0.80)	1.70 (0.77)

Riboflavin, mg	2.54 (0.90)	2.40 (1.28)	2.65 (1.19)	2.15 (0.89)**	2.54 (1.15)	2.40 (1.07)	2.68 (1.13)	2.23 (1.04)***	2.38 (1.01)	2.55 (1.20)	2.53 (1.19)	2.40 (1.01)
Vitamin C, mg	110.01 (63.15)	88.84 (61.19)**	100.45 (57.53)	96.91 (71.70)	84.83 (55.05)	113.86 (67.20)***	99.76 (59.65)	98.51 (66.64)	105.97 (52.59)	93.22 (70.40)	100.60 (62.33)	97.41 (63.88)
Vitamin D, µg	3.65 (1.92)	3.14 (1.67)*	3.65 (1.86)	2.93 (1.64)***	3.39 (1.83)	3.40 (1.80)	3.59 (1.77)	3.17 (1.83)*	3.72 (1.86)	3.10 (1.72)**	3.50 (1.94)	3.25 (1.63)
Vitamin E, mg	11.07 (4.31)	8.47 (3.26)***	9.79 (3.90)	9.66 (4.23)	9.62 (3.86)	9.86 (4.18)	10.52 (4.33)	8.87 (3.46)***	10.45 (3.83)	9.11 (4.09)**	10.51 (4.45)	8.79 (3.17)***
Total folate, µg	406.6 (154.1)	366.2 (212.8)	399.6 (194.9)	361.9 (171.4)	378.6 (188.8)	393.4 (186.0)	430.0 (196.6)	336.7 (163.4)***	385.7 (168.6)	386.1 (202.7)	379.2 (190.0)	394.2 (184.2)
Total Vitamin A equivalents, µg	1008.0 (487.2)	923.2 (461.7)	981.2 (446.3)	935.4 (523.6)	877.5 (442.3)	1053.8 (492.9)**	1058.7 (493.1)	859.5 (433.0)***	1049.2 (503.0)	890.6 (438.2)**	992.9 (498.8)	929.7 (444.3)

Retinol, µg	326.7 (161.4)	374.6 (195.7)*	369.3 (183.6)	319.4 (172.7)*	388.2 (200.4)	313.3 (150.3)***	404.8 (192.4)	291.3 (146.3)***	375.6 (186.9)	329.9 (173.6)*	351.5 (179.3)	350.8 (183.8)
Beta-carotene equivalents, µg	4085 (2846)	3291(2357)**	3670 (2405)	3694 (3004)	2935 (2140)	4441 (2870)***	3922 (2728)	3407 (2505)	4040 (2695)	3363 (2545)*	3848 (2719)	3471 (2519)
Sodium, mg	2799 (1129)	2926 (1077)	2953 (1166)	2709 (968)*	3052 (1090)	2671 (1086)**	3073 (1178)	2631 (964)***	3057 (1201)	2696 (982)**	3126 (1202)	2542 (869)***
Potassium, mg	3509 (913)	3064 (875)***	3398 (904)	3077 (915)**	3112 (868)	3454 (941)**	3415 (857)	3132 (966)**	3470 (906)	3116 (902)**	3456 (939)	3067 (850)***
Calcium, mg	986 (385)	908 (316)*	1001 (367)	848 (304)***	966 (362)	925 (343)	1007 (329)	878 (367)**	938 (331)	953 (371)	955 (377)	934 (322)
Magnesium, mg	437 (136)	354 (108)***	405 (129)	375 (125)*	385 (128)	404 (128)	415 (122)	371 (132)**	418 (133)	374 (120)**	420 (133)	363 (115)***

Phosphorus, mg	1763 (424)	1627 (443)**	1763 (433)	1572 (424)***	1689 (453)	1698 (424)	1768 (408)	1610 (457)**	1765 (450)	1631 (420)**	1780 (454)	1587 (396)***
Iron, mg	13.41 (3.75)	11.77 (3.50)***	12.70 (3.51)	12.33 (4.06)	12.24 (3.82)	12.90 (3.58)	13.20 (3.66)	11.86 (3.66)**	13.18 (3.69)	12.04 (3.66)**	13.12 (3.74)	11.89 (3.57)**
Zinc, mg	13.40 (4.19)	12.74 (4.49)	13.67 (4.18)	11.97 (4.45)**	12.65 (4.04)	13.48 (4.62)	13.33 (4.03)	12.75 (4.68)	13.86 (4.52)	12.36 (4.09)**	13.89 (4.578)	12.03 (3.82)***
Iodine, µg	127.60 (43.89)	129.01 (54.14)	138.55 (49.66)	110.38 (43.47)***	131.56 (49.91)	125.02 (48.68)	137.46 (49.84)	118.14 (46.86)***	130.72 (48.92)	126.23 (49.74)	131.18 (51.96)	124.81 (45.83)
% Energy												
Percent of total energy from protein, %	19.5 (3.8)	20.2 (4.3)	20.3(4.1)	19.1 (4.1)*	18.3 (3.1)	21.4 (4.4)***	18.9 (3.3)	21.0 (4.6)***	20.0 (3.9)	19.7 (4.3)	20.4 (3.6)	19.2 (4.6)*
Percent of	35.2	34.2 (5.3)	34.6	34.8	35.4	34.0	35.6	33.7	35.1	34.4	35.1	34.2 (4.8)

total energy from fat, %	(5.2)		(5.3)	(5.2)	(4.9)	(5.6)*	(5.0)	(5.4)**	(5.2)	(5.3)	(5.6)	
Percent of total energy from carbohydrate, %	41.8 (6.3)	41.5 (7.5)	41.4 (6.5)	42.1 (7.7)	43.0 (6.3)	40.3 (7.3)***	42.2 (6.3)	41.1 (7.6)	39.2 (6.9)	43.9 (6.3)***	40.3 (7.1)	43.3(6.4)***

Data presented as mean (standard deviation); *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$; P values represent significant differences between participants who aligned or did not align with a specific dietary pattern.

APPENDIX K

Baseline characteristics of the 211 participants with complete data on blood pressure, urinary sodium and potassium and dietary intake in the HealthTrack study (n=211)

Characteristic	**IW (n=82)**	**I (n=62)**	**C (n=67)**	***P* value for group difference[2]**
Age, years	43.2 (8.7) [1]	45.2 (7.1)	45.1 (7.2)	0.242
Height, m	1.7 (0.1)	1.7 (0.1)	1.7 (0.1)	0.397
Weight, kg	90.0 (14.6)	93.0 (16.1)	89.6 (15.4)	0.400
BMI, kg/m^2	32.0 (4.1)	32.6 (4.4)	32.2 (4.2)	0.784
Waist circumference, cm	102.4 (11.4)	104.7 (11.8)	103.7 (13.3)	0.570
Hypertensives, % (n)[3]	31.7 (26)	32.3 (20)	26.9 (18)	0.755

Dietary intake[d]				
Median energy, kj/day (IQR)	8671 (7309-10350)	8618 (7701-10981)	9486 (8066-11438)	0.165
Median sodium, mg/day (IQR)	2453 (1974-3037)	2260 (1682-3099)	2521 (2003-3065)	0.452
Median potassium, mg/day (IQR)	3694 (3027-4211)	3519 (3044-4452)	3849 (3191-4674)	0.123
Median magnesium, mg/day (IQR)	423 (329-542)	427 (331-522)	449 (349-570)	0.214
Median calcium, mg/day (IQR)	894 (663-1134)	985 (713-1234)	951 (731-1233)	0.334
Urinary excretion[4]				
Volume, mL/d	2114 (962)	2048 (874)	2018 (838)	0.799

Creatinine, mmol/d	13.6 (4.4)	14.2 (4.1)	13.8 (4.7)	0.758
Median sodium, mmol/day (IQR)	137 (108-191)	128 (97-170)	145 (99-181)	0.391
Median potassium, mmol/day (IQR)	72 (54-89)	77 (63-91)	75 (59-98)	0.319
Median sodium-to-potassium ratio (IQR)	1.9 (1.4-2.7)	1.8 (1.3-2.1)	1.9 (1.4-2.1)	0.206

[1]Values are expressed as means (standard deviation) unless otherwise stated; [2]Group comparisons were made using analysis of variance for normally distributed data; [3]Group comparisons were made using Chi square test; [4]Group comparisons were made using Kruskal-Wallis H test for data that was not normally distributed; C, control (usual care); I, interdisciplinary intervention with individualised dietary advice; IQR, interquartile range; IW, interdisciplinary intervention with individualised dietary advice plus a supplement of 30 grams of walnuts per day.

APPENDIX L

Change in blood pressure, 24-hour urinary excretion and key food groups from baseline to 3 months in the HealthTrack study (n=211)

		IW (n=82)	**I (n=62)**	**C (n=67)**	***P* value for group difference**
Blood pressure					
SBP (mmHg)	Baseline	128.5 (114.5-137.5)[1]	127.5 (113.8-133.3)	122.0 (112-131)	0.173
	3 months	119.5 (110-127.3)	121.0 (107.8-130.3)	118.0 (108-130)	0.935
	Change	-7.0 (-12 to 0)[a]	-6.0 (-11 to -1.8)[a]	-3.0 (-9 to 2)[b]	**0.035**
	P value for difference between baseline and 3m	**<0.001**	**<0.001**	**0.002**	
DBP (mmHg)	Baseline	75.0 (66-80)	75.0 (65-83.3)	72.0 (66-78)	0.642
	3 months	70.0 (63-76)	70.0 (60.8-80)	70.0 (64-77)	0.766
	Change	-4.0 (-8 to 0.3)	-4.0 (-9 to 0)	-2.0 (-6 to 3)	0.059

	P value for difference between baseline and 3m	**<0.001**	**<0.001**	0.069	
Urinary excretion					
Urinary sodium (mmol/d)	Baseline	137.0 (108-190.5)	128.0 (96.5-170.3)	145.0 (99-181)	0.396
	3 months	108.0 (83.8-140)	125.5 (89.5-183.5)	111.0 (81-158)	0.078
	Change	-29.5 (-71.3 to 12.3)[a]	-2.5 (-43.3 to 46.5)[b]	-40.0 (-71 to 24)[a]	**0.015**
	P value for difference between baseline and 3m	**<0.001**	0.989	**0.003**	
Urinary potassium (mmol/d)	Baseline	72.0 (54-89.3)	76.5 (62.8-91.3)	75.0 (59-98)	0.398
	3 months	70.0 (50-86)	75.0 (60-90.3)	70.0 (55-88)	0.377
	Change	-3.0 (-24 to 13)	0.5 (-13.5 to 14)	-6.0 (-31 to 8)	0.085
	P value for difference between	0.217	0.986	**0.004**	

	baseline and 3m				
Urinary Na:K ratio (mmol/mmol)	Baseline	1.85 (1.43-2.68)	1.79 (1.26-2.11)	1.86 (1.40-2.14)	0.263
	3 months	1.63 (1.25-2.21)	1.83 (1.15-2.49)	1.68 (1.23-2.23)	0.703
	Change	-0.26 (-0.90 to 0.28)[a]	-0.05 (-0.50 to 0.69)[b]	-0.20 (-0.63 to 0.49)[ab]	**0.050**
	P value for difference between baseline and 3m	**0.008**	0.439	0.355	
Food groups					
Seed and nut products and dishes (g/d)	Baseline	13.4 (5.4-34.4)	16.2 (6.4-30.6)	18.2 (7.1-37.5)	0.560
	3 months	30.0 (27.4-37.3)[a]	10.4 (4.2-19.1)[b]	20.4 (6.9-41.2)[c]	**<0.001**
	Change	20.4 (4.9 to 30)[a]	-1.5 (-13.5 to 5.1)[b]	-1.8 (-18.5 to 11.6)[bc]	**<0.001**

	P value for difference between baseline and 3m	**<0.001**	**0.008**	0.766	
Fruit products and dishes (g/d)	Baseline	113.1 (57.7-224.7)	151.4 (81.0-258.8)	140.8 (69.9-231.6)	0.276
	3 months	212.3 (146.7-270.9)[ab]	241.9 (149.6-301.4)[a]	160.9 (109.9-262.7)[b]	**0.022**
	Change	62.5 (-10.8 to 169.1)	79.2 (-37.6 to 168.9)	37.0 (-51.6 to 107.2)	0.073
	P value for difference between baseline and 3m	**<0.001**	**0.005**	0.096	
Seafood products and dishes (g/d)	Baseline	35.0 (19.8-58.3)	35.4 (14.9-60.6)	32.9 (20.0-67.1)	0.957
	3 months	35.1 (20.3-64.3)	45.4 (21.1-67.5)	40.1 (20.4-57.1)	0.404
	Change	7.8 (-11.0 to 20.1)	2.9 (-15.8 to 29.6)	0.0 (-15.9 to 16.8)	0.641
	P value for difference between baseline and 3m	0.224	0.310	0.716	

[1]Values are median (IQR); [a,b,c]Groups with different superscripts were significantly different after Bonferroni adjustment; change in blood pressure unadjusted for weight loss; C, control (usual care); DBP, diastolic blood pressure; I, interdisciplinary intervention with individualised dietary advice; IW, interdisciplinary intervention with individualised dietary advice plus a supplement of 30 grams of walnuts per day; Na:K. sodium-to-potassium ratio; SBP, systolic blood pressure.

APPENDIX M

Linear regression for association between change in blood pressure and change in urinary markers and key food groups in the HealthTrack study (n=211)

	IW (n=82)		**I (n=62)**		**C (n=67)**	
	B ± SE	***P* value**	**B ± SE**	***P* value**	**B ± SE**	***P* value**
Change in SBP[1]						
Change in urinary Na (mmol/d)	0.009 ± 0.021	0.687	0.010 ± 0.022	0.649	0.019 ± 0.013	0.154
Change in urinary K (mmol/d)	-0.101 ± 0.050	**0.044**	0.057 ± 0.074	0.445	0.022 ± 0.031	0.471
Change in Na:K ratio	2.446 ± 1.171	**0.037**	-1.107 ± 1.976	0.575	0.442 ± 1.041	0.671
Change in consumption of seed and nut products and dishes (g/d)	-0.108 ± 0.051	**0.034**	-0.002 ± 0.061	0.975	-0.011 ± 0.021	0.608
Change in consumption of fruit products and dishes (g/d)	-0.002 ± 0.010	0.867	-0.007 ± 0.010	0.451	0.002 ± 0.006	0.785

Change in consumption of seafood products and dishes (g/d)	-0.072 ± 0.041	0.083	-0.056 ± 0.032	0.077	-0.011 ± 0.030	0.720
Change in DBP						
Change in urinary Na (mmol/d)	0.007 ± 0.015	0.644	0.005 ± 0.017	0.751	0.024 ± 0.011	**0.028**
Change in urinary K (mmol/d)	-0.056 ± 0.034	0.103	0.070 ± 0.056	0.213	0.010 ± 0.025	0.697
Change in Na:K ratio	1.500 ± 0.808	0.063	-1.141 ± 1.497	0.446	0.856 ± 0.851	0.315
Change in seed and nut products and dishes (g/d)	-0.046 ± 0.035	0.195	0.003 ± 0.047	0.946	-0.014 ± 0.017	0.925
Change in fruit products and dishes (g/d)	-0.004 ± 0.007	0.590	-0.003 ± 0.008	0.653	0.001 ± 0.005	0.672
Change in seafood products and dishes (g/d)	-0.063 ± 0.028	**0.024**	0.030 ± 0.025	0.231	-0.0002 ± 0.024	0.994

[1]Controlling for age, sex, BP medication, weight loss, change in physical activity, smoking; C, control (usual care); DBP, diastolic blood pressure; I, interdisciplinary intervention with individualised dietary advice; IW, interdisciplinary intervention with individualised dietary advice plus a supplement of 30 grams of walnuts per day; K, potassium; Na, sodium; Na:K. sodium-to-potassium ratio; SBP, systolic blood pressure.