

Sodium intake in South Africa: an analysis of food supply, 24-hour excretion and blood pressure in a tri-ethnic population

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M.Sc. Nutrition

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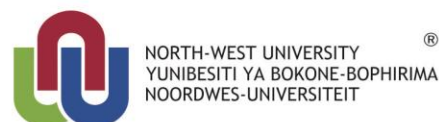
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“Today is the day to start living your best life, to accept only the best, to only spend energy on the things that make you the best, and to create the best possible world around you. Life is short. Create the absolute best!”

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Strength to finish what I started and thank you for placing people in my life to support
and carry me! Your grace was and is always sufficient!

ABSTRACT

Introduction: Currently, 1.13 billion people in the world have increased blood pressure. Low and middle income countries, including South Africa, contribute significantly to this number. The burden caused by hypertension is to a large extent preventable and therefore, serious efforts need to be made by all to address this. Excess dietary sodium intake is associated with increased blood pressure and the reduction of sodium is considered one of the best investments in public health. The South African government has recently implemented a mandatory regulation (R.214) pertaining to the reduction of sodium in foodstuffs as part of a wider sodium reduction strategy. Monitoring of such a strategy is crucial.

Objectives: The main aim of this research was to provide insight into the current sodium and potassium intake of South Africans. Specific objectives included (i) establishing baseline sodium and potassium intake values; (ii) investigating alternative methodology for sodium intake in South Africans and (iii) evaluating the sodium content in foodstuffs and reporting on the food industry's compliance with the targets set in the regulation.

Methods: For the population's sodium intake, 24-hour urine samples and spot urine samples were collected from three different population groups i.e. White, Black and Indian. Sodium, potassium and iodine were analysed using appropriate methods. Three different formulas were used to estimate sodium excretion i.e. Kawasaki, Tanaka and INTERSALT. To evaluate the sodium content of foodstuffs we randomly selected ten food products from each of the 13 food categories and measured the sodium content by means of an atomic absorption spectrometer.

Results: In total, 692 successful 24-hour urine collections and 681 spot urine samples were collected. The median sodium and potassium excretion was 122.9 and 33.5mmol/day, respectively and the median calculated salt intake was 7.2g/day. The majority (92.8%) of the population did not meet the recommended potassium intake per day and 65.6% consumed more than 6g of salt per day. The median sodium-to-potassium ratio was 3.5. Individuals in the lowest salt intake category still had significant iodine levels. The Kawasaki and the Tanaka formulas showed significantly higher estimated sodium values than the measured 24-hour excretion in the whole population (5677.79mg/d and 4235.05mg/d vs. 3279.19mg/d) whereas the INTERSALT formula did not differ. The Kawasaki formula also showed the highest degree of bias (-2242mg/d, 95% CI: -10659 – 6175) in comparison with the INTERSALT, which had the lowest (161mg/d, -4038 – 4360). In terms of the sodium content of the foodstuffs, 72% of the food products tested comply with the targets for 2016 and 42% of the products with the 2019 targets. All of the food categories, except for "*flavoured potato crisp*" and "*flavoured salt-and-vinegar snacks*", complied with the 2016 target.

Conclusion: These findings support the South African government's motivation for a sodium reduction strategy. The sodium excretion estimations of the three formulas should be used with caution when reporting on sodium intake levels. More research is needed to validate and develop a specific formula for South Africans. The sodium content in foodstuffs can serve as a baseline for monitoring compliance over the next few years.

Keywords: sodium; potassium; 24-hour urine; spot urine; salt; South Africa; blood pressure

OPSOMMING

Die natrium inname in Suid Afrika: 'n analise van die voedel sisteem, 24-uur uitskeiding en bloed druk in drie populasie groepe

Inleiding: Daar is tans 1.13 biljoen mense met verhoogde bloed druk in die wêreld. Lae en middel inkomste lande, insluitend Suid Afrika, dra betekenisvol by tot hierdie getal. Die las wat deur hipertensie veroorsaak word, is voorkombaar en dus moet alle pogings moontlik aangewend moet word om dit aantespreek. Oortollige natrium inname word geassosieer met verhoogde bloed druk en die verlaging daarvan word gesien as een van die beste beleggings in publieke gesondheid. Die Suid Afrikaanse regering het onlangs 'n Regulasie (R.214) geïmplimenteer wat te doen het met die verlaging van natrium in voedselsoorte as deel van 'n groter natrium-verlagingstrategie. Monitering en versekering van implementasie van so 'n strategie is van kardinale belang.

Doelstellings: Die hoof doel van hierdie navorsing was om insig te kry oor wat die huidige natrium en kalium inname van Suid-Afrikaners is. Spesifieke doelwitte het ingesluit (i) die vasstel van 'n basislyn vir natrium en kalium inname; (ii) om alternatiewe metodes te ondersoek om natrium inname te bepaal in Suid-Afrika en (iii) om die natrium inhoud van sekere voedselsoorte te bepaal en te rapporteer op die voedselindustrie se nakoming van die Regulasie

Metode: Vir die populasie se natrium inname, is 24-uur en spot urine-monsters versamel in drie verskillende populasie-groepe (Blank, Swart en Indiërs). Natrium, kalium en jodium is geanaliseer volgens die korrekte protokol. Drie verskillende formules was gebruik om die natrium uitskeiding te skat (Kawasaki, Tanaka en INTERSALT). Om die natrium-inhoud van die verskillende voedselsoorte te bepaal was tien produkte lukraak gekies vanuit elk van die 13 voedsel kategorië in die regulasie. Natrium was dan gemeet in die voedselsoorte met behulp van die atomiese absorpsie spektrometer.

Resultate: In totaal was 692 en 681 suksesvolle 24-uur en spot urine-monsters versamel. Die mediaan van die natrium en kalium waardes was 122,9 en 33,5mmol/dag, en die mediaan sout inname was 7,2g/dag. Die meederheid (92,8%) van die populasie het nie aanbevole kalium ingeneem nie en 65,6% het meer as 6g sout ingeneem per dag. Die mediaan natrium-tot-kalium ratio was 3.5. Die Kawasaki en Tanaka formule het aansienlik hoër natrium waardes geskat in vergelyking met die 24-uur urine waardes (5677,79mg/d en 4235,05mg/d vs. 3279,19mg/d) waar die INTERSALT formule nie verskil het nie. Die Kawasaki formule het die hoogste vooroordeel gewys (-2242mg/d, 95% CI: -10659 – 6175) teenoor die INTERSALT wat die laagste was (161mg/d, -4038 – 4360). In terme van natrium in die voedselsoorte het 72% van

die produkte aan die regulasie se 2016 teiken voldoen en 42% reeds aan die 2019 teiken waarde. Al die voedsel kategorieë behalwe vir “gegeurde aartappel skyfies” en “gegeurde sout-en-asyn happies” het aan die teiken waardes van die regulasie voldoen.

Gevolgtrekking: Hierdie bevindinge ondersteun die motivering van die Suid Afrikaanse regering vir ‘n natrium-verlagende strategie. Geskatte natrium inname deur middel van een van die drie formules moet met versigtigheid gebruik word wanneer natrium waardes gerapporteer word. Meer navorsing is nodig om ‘n spesifieke formule te ontwikkel en dan te bevestig binne die Suid Afrikaanse konteks. Die natrium inhoud van voedselsoorte kan dien as ‘n basislyn vir toekomstige monitering.

Sleutel woorde: natrium; kalium; 24-uur urien; spot urien; sout; Suid Afrika; bloed druk

TABLE OF CONTENTS

ACKNOWLEDGEMENTS	III
ABSTRACT	V
OPSOMMING	VII
CHAPTER ONE: INTRODUCTION	1
1.1 Introduction	1
1.2 Aim and objectives	4
1.3 Ethics	4
1.4 Financial support.....	5
1.5 Team.....	5
1.6 Outline of the thesis	6
CHAPTER TWO: LITERATURE REVIEW	8
2.1 Cardiovascular disease as contributor to the burden of disease	8
2.1.1 Burden of cardiovascular disease globally	8
2.1.2 Burden of cardiovascular disease in South Africa	13
2.2 Global and local trends of hypertension.....	14
2.2.1 Risk factors contributing to hypertension	15
2.2.2 The pathophysiological development of hypertension.....	18
2.3 Nutritional factors in blood pressure management	19
2.3.1 The holistic diet.....	20
2.3.2 Potassium.....	21
2.3.3 Sodium-to-potassium ratio	22

2.3.4	Sodium	22
2.3.4.1	Role of sodium in the body	22
2.3.4.2	Contribution of sodium overconsumption to hypertension.....	23
2.3.4.3	Differences in sodium excretion in population groups	24
2.3.4.4	Methods of determining sodium intake in a population.....	25
2.3.4.5	Role of sodium in food	29
2.3.5	Measurement of sodium content in food	29
2.4	Sodium reduction strategies	31
2.4.1	Global sodium reduction initiatives.....	32
2.4.2	South Africa's sodium reduction strategy	33
2.4.3	Contribution of foods to total sodium intake	35
2.4.4	Monitoring.....	35
2.4.5	Cost-effectiveness and long term impact	36
2.5	Summary of the literature	37
	CHAPTER THREE: SODIUM AND POTASSIUM INTAKE IN SOUTH AFRICA: AN EVALUATION OF 24-HOUR URINE COLLECTIONS IN A WHITE, BLACK AND INDIAN POPULATION	39
	CHAPTER FOUR: MONITORING THE SOUTH AFRICAN POPULATION'S SALT INTAKE: SPOT URINE VERSUS 24-HOUR URINE	59
	CHAPTER FIVE: DOES THE FOOD INDUSTRY COMPLY WITH THE UPDATED SODIUM CONTENT OF FOOD REGULATION IN SOUTH AFRICA?	78
	CHAPTER SIX: GENERAL DISCUSSION AND CONCLUSION.....	92
6.1	General discussion.....	92

6.2	Strengths and limitations of the study	93
6.2.1	Limitations:	93
6.2.2	Strengths:	94
6.3	Way forward	95
6.4	Policy implications	95
6.5	Conclusion	95
CHAPTER SEVEN: REFERENCE LIST		97

LIST OF TABLES

Table 2-1: Observed and counterfactual changes in Global deaths due to cardiovascular diseases, 1990 – 2013 9

Table 2-2: Patterns of demographic and epidemiological change in cardiovascular mortality 11

Table 2-3: Underlining factors that increase or are associated with high blood pressure..... 16

Table 2-4: Methods for estimating sodium intake on a population level 27

Table 2-5: Sampling method of the different food categories included in R.214 regulation 30

Table 2-6: Food categories included in the regulation R.214..... 34

LIST OF FIGURES

Figure 1-1: Voluntary global targets for prevention and control of NCDs to be attained by 2025 (adapted from WHO)..... 2

Figure 2-1: Causes of death in South Africa in all age groups including both genders.... 14

Figure 2-2: Factors affecting arterial pressure 18

Figure 2-3: The classic renin-angiotensin vasoconstrictor mechanism for renal retention of sodium and water 19

LIST OF ADDENDA

ADDENDUM A: ETHICS CERTIFICATE 108

ADDENDUM B: PUBLISHED MANUSCRIPT..... 109

LIST OF ABBREVIATIONS

AAS	atomic absorption spectrometry
African-PREDICT	<i>African <u>P</u>rospective study on the <u>E</u>arly <u>D</u>etection and <u>I</u>dentification of <u>C</u>ardiovascular disease and hyper<u>T</u>ension</i>
BMI	body mass index
CVD	cardiovascular diseases
CHD	coronary heart disease
DALYs	disability-adjusted life-years
DASH	dietary approach to stop hypertension
GBD	global burden of disease
HREC	health research ethics committee
ICP	inductively coupled plasma
IHD	ischaemic heart disease
K	potassium
LMIC	low- and middle income countries
LDL	low density lipoprotein
Na	sodium
NaCl	sodium chloride
Na:K	sodium-to-potassium ratio
NCD	non-communicable disease
NRF	National Research Foundation
SAMRC	South African medical research council
SARChI	South African research chairs initiative
WHO	World Health Organization

CHAPTER ONE: INTRODUCTION

“It always seems impossible, until it is done” ~ Nelson Mandela

1.1 Introduction

Despite the well-known contribution of hypertension to the global burden of disease, the prevalence of high blood pressure has increased globally from 594 million individuals in 1975 to 1.13 billion in 2015 (NCD RiskC, 2017), accounting for a 90% increase in the past four decades. The increase was also due to population growth over the time period and was mostly observed in middle- and lower-income countries (South Asia and sub-Saharan Africa) (NCD Risk factor collaboration, 2016). There has also been a significant increase in hypertension in South Africa from 1998 to 2008 which predicts a further increase in stroke and heart attacks in future (Bradshaw *et al.*, 2010). Recently a hypertension prevalence of as high as 78% was observed in a black South African population, aged 50 years and older (Lloyd-Sherlock *et al.*, 2014).

Looking at the burden of cardiovascular disease (CVD) in South Africa, van Wyk and co-workers reported that CVD was the second most common cause of death (17.6%) in South Africa (van Wyk *et al.*, 2013). Recent estimates by Maredza and co-workers suggest that at least 30,000 strokes occur annually in rural South Africa. High blood pressure and excess weight, which both have effective interventions, are responsible for a significant proportion of the stroke burden currently observed in South Africa (Maredza *et al.*, 2015).

Sodium intake above the recommendation (2000mg/d) is linked to increased blood pressure as demonstrated by numerous studies using different types of study designs (Graudal *et al.*, 2012; He *et al.*, 2013; Steyn *et al.*, 2013). The reduction of sodium has been identified as one of the “best buys” for preventing and management of hypertension (Zarocostas, 2011) on a national level because of the cost-effectiveness of such an intervention (Barton *et al.*, 2011). In a recent analysis of cost-effectiveness (in 183 countries) Webb and co-workers (Webb *et al.*, 2017) concluded that a combined strategy of targeted industry agreements to reduce salt in food products and a population education campaign to reduce discretionary salt use is highly cost-effective, even if potential health care savings are excluded.

The World Health Organization (WHO) has recognised the burden of non-communicable diseases (NCDs) on the world population and in 2011 an extensive global focus on NCDs culminated in a United Nations General Assembly high-level meeting (WHO, 2015). A political declaration was adopted by the General Assembly and all 193 member countries and states showed their commitment to this declaration. In the declaration nine voluntary targets were set for the prevention and control of NCDs (Figure 1.1) to be achieved by the year 2025.

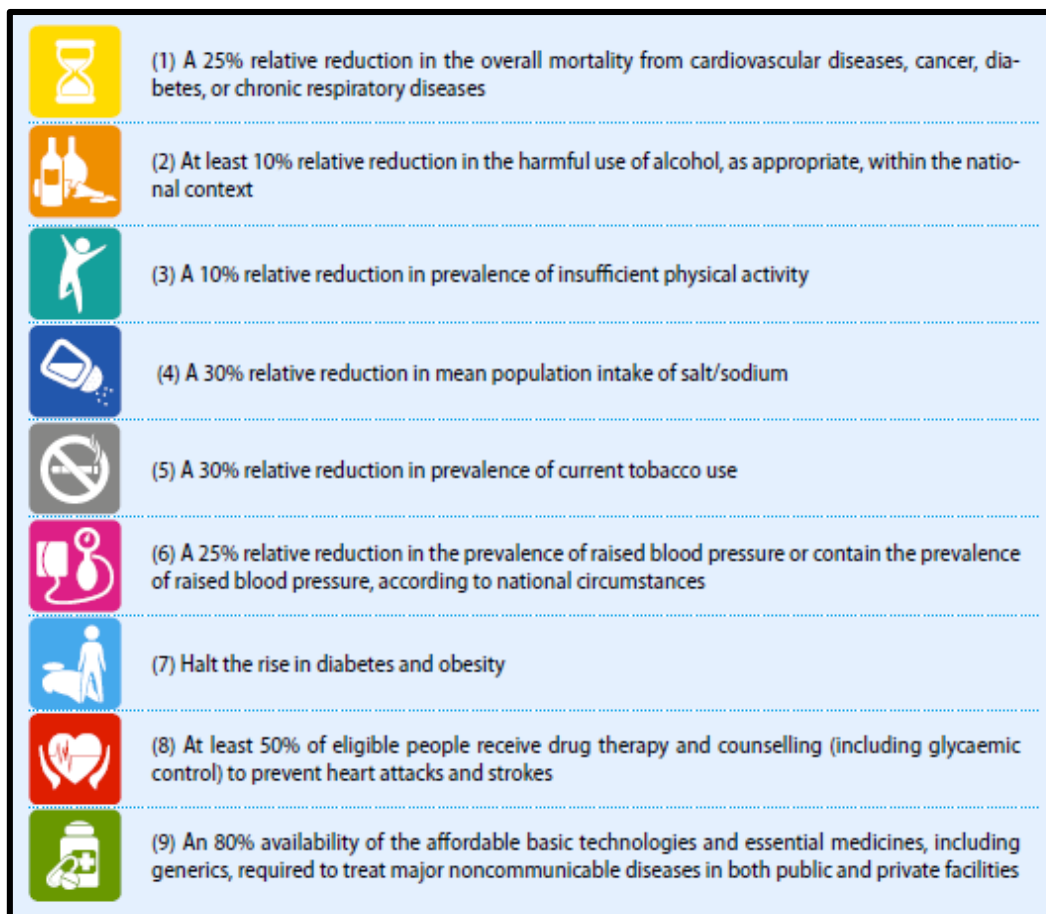


Figure 1-1: Voluntary global targets for prevention and control of NCDs to be attained by 2025 (adapted from WHO)

South Africa, a WHO member state, became one of the first countries to commit itself to the targets on the prevention and control of NCDs. Leading up to the high-level meeting mentioned above, and considering all the evidence, a national summit was hosted by the South African minister and deputy minister of health. The summit adopted a National Declaration and set 10 targets to be reached by 2020, all to do with prevention and control of NCDs. In addition, a strategic plan was then developed to achieve these targets.

From the strategic plan of the Department of Health, only the targets which are related to reducing blood pressure in the South African population are listed below:

- Reduce by at least 25% the relatively premature mortality (<60 years) from NCDs by 2020;
- Reduce the mean population intake of salt to <5 grams per day by 2020;
- Reduce the prevalence of people with raised blood pressure by 20% by 2020 (through lifestyle and medication);

- Increase the percentage of people controlled for hypertension, diabetes and asthma by 30% by 2020 in sentinel sites (DoH, 2013).

The targets set out by the WHO and the South African Department of Health show commitment on all levels to reduce sodium intake in populations. They also reflect the importance and relevance of the current research in the South African context.

For the monitoring of a sodium reduction strategy, it is vital to use accurate and reliable methods to determine sodium intake in the population as well as sodium content in the food supply chain. In terms of sodium intake, the 24-hour urine collection method (one or more) is considered to be the “gold standard” in determining sodium intake in individuals as well as in population groups (WHO, 2013). However, alternative methods have been explored because of several logistical challenges in collecting these samples in large population-based studies. A spot urine sample is a popular alternative to estimate sodium excretion but there is a need for validation studies relevant to the context of the specific population (Ji *et al.*, 2012). Together with the monitoring of the sodium intake, it is important to note that measurement of iodine also needs to be included in the monitoring strategy. In South Africa it is mandatory that salt be iodised, and it needs to be shown that a recommended lower salt intake will still supply sufficient iodine intake.

As one of the first steps in achieving the set targets and to reduce sodium intake in South Africa, the National Department of Health, Directorate: Food Control, published regulations relating to the reduction of sodium in certain foodstuffs (R.214:20 March 2013, amended in 2016). The two targets included in the regulation are June 2016 and June 2019. South Africa was the first country to legislate the reduction of sodium in a number of food products. This legislation forms part of the larger sodium reduction strategy that includes monitoring (sodium intake and sodium in the food supply), public awareness and education campaigns. In summary, we identified three main gaps in terms of measuring the effectiveness of South Africa’s sodium reduction strategy. The first would be that there is limited and outdated data regarding the sodium intake of South Africans (especially in different population groups). The second gap identified has to do with the validation of alternative methods (use of a spot urine versus a 24-hour urine sample) to determine and monitor sodium intakes in South Africa. Then lastly, monitoring of sodium content in foodstuffs requires accurate and robust methodology as well as baseline values to evaluate compliance to set out targets. This is not available in South Africa. It is important to note that the focus of this thesis will be on these identified gaps in an effort to contribute towards reducing the public health burden of hypertension in South Africa and will not focus on blood pressure per se. The importance of this research in relation to the main health outcome i.e. blood pressure will become evident through the thesis. The following aim and objectives were then specified in an attempt to answer these gaps and contribute to a

successful implementation of a sodium reduction strategy and ultimately reduce the number of South Africans suffering from hypertension.

1.2 Aim and objectives

The main aim of this research project is to provide insight into the current sodium and potassium intake of South Africans. The following objectives support this aim:

- 1) To determine the sodium and potassium intake in three different population groups (black, white and Indian) in South Africa before commencing the implementation of the sodium reduction regulations and programmes, by means of 24-hour urinary sodium and potassium excretion measurement.
- 2) To determine the urinary sodium-to-potassium (Na:K) ratio of South Africans and to assess the relationship between the Na:K ratio, as well as 24-hour urinary sodium excretion, and blood pressure, in the black, white and Indian population groups;
- 3) To determine the iodine intake by means of a 24-hour urine excretion sample as part of the monitoring aspect of the sodium reduction regulations and programmes in South Africa in the black, white and Indian population groups;
- 4) To estimate sodium and potassium excretion measured in a spot urine sample and compare it with the same measurement in a 24-hour urine sample, using three different formulas (Kawasaki formula, INTERSALT formula and Tanaka formula) in the black, white and Indian population groups in South Africa;
- 5) To determine the sodium content in different food products in each of the 13 food categories within the R214 sodium reduction regulation before the June 2016 deadline, when the new sodium reduction regulations will have been implemented.

1.3 Ethics

The projects in this thesis as well as the thesis in totality obtained ethical clearance from the Health Research Ethics Committee (HREC) of the North-West University, South Africa, with the following number: NWU-00085-15-A1 (Addendum A). All studies included were conducted according to the guidelines laid down in the Declaration of Helsinki. Written informed consent was obtained from each participant before commencing with the research.

1.4 Financial support

The African-PREDICT study was financially supported by the South African medical research council (SAMRC) with funds from National Treasury under its Economic Competitiveness and Support Package, the South African Research Chairs Initiative (SARChI) of the Department of Science and Technology and the National Research Foundation of South Africa, as well as corporate social investment grants from Pfizer (South Africa), Boehringer Ingelheim (South Africa), Novartis (South Africa), the Mediclinic Hospital Group (South Africa) and contributions in kind from Roche Diagnostics (SA).

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1.5 Team

The research team that contributed to this thesis is highlighted in the table below:

Team member	Affiliation	Contribution
Miss B Swanepoel	Centre of Excellence for Nutrition, North-West University	PhD student of the study. Conceptualised and obtained funding for the research. Collected a significant portion of data used in this thesis and analysed urine samples for sodium and potassium. Conducted sodium analyses in food products as well as developing the protocol. Wrote all three manuscripts and did the statistical analysis.
Prof. E Wentzel-Viljoen	Centre of Excellence for Nutrition, North West University	Promotor of the PhD study. Formulated all the research questions, conceptualised and critically reviewed all the manuscripts
Prof. A E Schutte	Hypertension in Africa Research Team (HART), Medical Research Council Unit for Hypertension and Cardiovascular Disease, North-West University	Co-promotor of the PhD study. Formulated all the research questions, conceptualised and critically reviewed all the manuscripts and assisted with the statistical analysis. Designed the African-PREDICT study

Prof. K Steyn	Chronic Disease Initiative for Africa (CDIA), Department of Medicine, Faculty of Health Sciences, University of Cape Town	Co-promotor of the PhD study. Formulated all the research questions, conceptualised and critically reviewed all the manuscripts
Mr P H Myburgh	Centre of Excellence for Nutrition, North West University	Co-author of the third manuscript. Assisted with all sodium analysis (food) and statistical analyses and critically reviewed manuscript three
Dr L Malan	Centre of Excellence for Nutrition, North West University	Co-author of the third manuscript. Assisted with all sodium analysis (food) and statistical analyses and critically reviewed manuscript three
Mrs M Cochrane	Statistical Consultation Services, North-West University	Supervised and assisted the researcher in the all statistical analysis for manuscripts one and two.

1.6 Outline of the thesis

The structure of this thesis is in article format and it is divided into seven chapters. The format and referencing style of the three articles (Chapters 3-5) are according to the respective journals' guidelines, but to ensure uniformity throughout the thesis the font type and size are the same.

Chapter 1 – Situation analyses, aim and objectives of the study

Chapter 2 – Literature review

Chapter 3 – First article relating to baseline data (sodium, potassium, iodine and Na:K ratio) prior to the sodium reduction regulations in three different population groups (Objectives one, two and three). This article was published in the *Journal of the American Society of Hypertension* 2016 [10(11): 829–837] with the title “Sodium and potassium intake in South Africa: an evaluation of 24-hour urine collections in a white, black, and Indian population.” (Addendum B)

Chapter 4 – Second article relating to the validation of a spot urine sample against a 24-hour urine sample in three different population groups (Objective four). This article was prepared according to the guidelines of the journal, *Public Health Nutrition*, and was submitted with the title “Monitoring the South African population’s salt intake: spot urine *versus* 24-hour urine.”

Chapter 5 – Third article relating to measurement of the sodium content of food products included in the sodium reduction regulation before the June 2016 deadline (Objective five). This article was prepared according to the guidelines of the journal “*Food composition and analysis*”

and was submitted with the title “Does the food industry comply with the updated sodium content of food regulation in South Africa?”

Chapter 6 – Conclusion and recommendations for future research

Chapter 7 – Bibliography of Chapters 1, 2 and 6. The references used in Chapters 3, 4 and 5 are included at the end of the chapters as part of the manuscripts.

CHAPTER TWO: LITERATURE REVIEW

“I have been impressed with the urgency of doing. Knowing is not enough; we must apply. Being willing is not enough; we must do” ~ Leonardo Da Vinci

2.1 Cardiovascular disease as contributor to the burden of disease

The mortality and morbidity burden caused by CVDs is to a large extent preventable and therefore serious efforts need to be made by all to curb this burden. A number of high-level strategic and action plans have been developed in order to address this public health problem. In 2004, member states of the WHO requested the Director-General to develop a global strategy on diet, physical activity and health in a call to recognise the growing burden of NCDs (WHO, 2004). The overall goal is to promote and protect health, which will lead to reduced rates of disease and death related to unhealthy diet and physical inactivity. More recently, the *Global action plan for the prevention and control of NCDs (2013-2020)* was released by the WHO. This action plan focuses on providing member states (of which South Africa is one) with guidance and a variety of policy options which will assist in achieving the nine voluntary global targets, one of which includes a 25% relative reduction in premature mortality from NCDs by 2025 (WHO, 2013).

CVD can be categorised as coronary heart disease (CHD), cerebrovascular disease, peripheral arterial disease and hypertension (WHO, 2016). The focus of this thesis will be hypertension or high blood pressure and stroke and therefore more emphasis will be placed on these diseases.

2.1.1 Burden of cardiovascular disease globally

CVD accounts for more than 17.5 million deaths in the world, which makes it the number one cause of death on a global scale (WHO, 2016). In the recent Global Burden of Disease (GBD) study it was reported that CVD deaths increased by 41.7% in the period between 1990 and 2013 (Roth *et al.*, 2015). Roth and co-workers further calculated that an ageing population contributed an increase of 52.5% to these deaths, while the growth in the population contributed a 23.6% increase. As seen in Table 2.1, ischaemic stroke and hypertensive heart diseases increased by 50.2% and 74.1% respectively in the period between 1990 and 2013. In both of these diseases, the ageing population contributed significantly to the increases seen.

Table 2-1: Observed and counterfactual changes in Global deaths due to cardiovascular diseases, 1990 – 2013

Disease	Deaths in 1990	Deaths in 2013	% change, 1990 – 2013	% change from 1990 due to population growth	% change from 1990 due to population ageing
Ischaemic heart disease	5,737,483	8,139,852	41.7	23.6	52.5
Ischaemic stroke	2,182,865	3,272,924	50.2	21.6	62.1
Haemorrhagic stroke	2,401,931	3,173,951	30.7	26.8	59.5
Hypertensive heart disease	622,148	1,068,585	74.1	29.5	63.6
Other cardiovascular and circulatory diseases	478,261	554,588	15.2	33.7	44.9
Total	12,279,565	17,297,480	40.8	25.1	55.0

(Adapted from Roth *et al.*, 2015)

The changes observed in the number of CVD deaths between 1990 and 2013 also differed rather significantly in the different regions in the world. South Asia and East Asia had the greatest increase (1.7 million and 1.2 million respectively) in absolute number of deaths. The African regions (Western, Central and Southern Sub-Saharan) also showed increases of between 40 000 to 160 000 in mortality (caused by CVD) in the timeframe mentioned. Central and Western Europe were the only regions that showed a decrease in the number of deaths caused by CVD (Roth *et al.*, 2015). These distinct trends, which can be seen in the different regions of the world, can be ascribed to a combination of growing populations and changes in age-specific death rates, as well as an increase in population ageing. The epidemiological transition can clearly be seen in the different regions. As first described by Omran, the epidemiological transition refers to a shift from a pattern of high prevalence of infectious disease to one with a high prevalence of chronic and degenerative disease, associated with urbanised and industrial lifestyles (Omran, 1971). More relevant to this research, Popkin (1998) further described the nutritional transition which is a combination of the demographic transition and the epidemiological transition, with a focus on the shift in diet patterns. The interaction between a growing and ageing population and changes in age-specific deaths is complex. Roth and co-workers summarised these complex interactions, which can also be observed in the epidemiological transition. They categorised the different regions into six general demographic and epidemiologic patterns (Table 2.2). Looking at Table 2.2 one can see that the first three

categories represent regions in which population ageing and growth drive the increases in CVD deaths. The last three categories represent regions in which advances in CVD health, represented by declines in the age-specific CVD death rate, appear to have partially or completely negated the increase in CVD deaths due to population growth and ageing.

Table 2-2: Patterns of demographic and epidemiological change in cardiovascular mortality

Category	Change in CVD death, 1990–2013	Effect of population growth	Effect of population aging	Effect of age-specific CVD death rate	Regions
Category 1 — Population growth and ageing: Regions with large and continuous increases in the number of cardiovascular deaths due to population growth or aging but little change in age-specific rates of death	Increase	Large (≥20%)	Large (>30%)	Small (decline <30%)	Oceania, South Asia, Southeast Asia, Caribbean
Category 2 — Population growth: Regions with increases in deaths due mostly to population growth	Increase	Large (>80%)	Small (<10%)	Small (decline <30%)	Central sub-Saharan Africa, Western sub-Saharan Africa, Eastern sub-Saharan Africa
Category 3 — Population ageing: Regions in which cardiovascular deaths rose and then fell during the preceding 20 years, resulting in a net increase in deaths due to population aging and only a small decrease in age-specific rates of cardiovascular death	Increase then decrease	Very small (<20%)	Moderate (>20%)	Very small (decline <15%)	Eastern Europe, Central Asia
Category 4 — Improved health moderating effect of population ageing: Regions in which large increases in the number of cardiovascular deaths due to population aging were moderated by a fall in age-specific rates of death	Increase	Small (<30%)	Very large (>70%)	Large (decline >30%)	High-income Asia–Pacific, East Asia

Category	Change in CVD death, 1990–2013	Effect of population growth	Effect of population aging	Effect of age-specific CVD death rate	Regions
<p>Category 5 — Improved health moderating effect of population growth and aging:</p> <p>Regions with large relative increases in the number of cardiovascular deaths due to both population growth and aging that were moderated by a fall in age-specific rates of death</p>	Increase	Large (>30%)	Large (>30%)	Large (decline >30%)	Central Latin America, Tropical Latin America, Andean Latin America, Southern sub-Saharan Africa, North Africa and Middle East
<p>Category 6 — Improved health exceeding effect of population growth and aging:</p> <p>Regions in which large declines in age-specific cardiovascular death rates have led to only small increases or even a decline in the number of cardiovascular deaths despite the large effects of an aging population</p>	Small increase or decrease	Small (<40%)	Large (>30%)	Large (decline >30%)	Southern Latin America, Australasia, high income North America, Central Europe, Western Europe

(Adapted from Roth *et al* 2015)

It is emerging that it is not only affluent countries that contribute to the rate of CVD deaths; there is enough evidence to suggest that low- and middle-income countries (LMIC) contribute a large portion to this burden (approximately 80%) facing the world at the moment (Bovet & Paccaud, 2012). The WHO has reported that three quarters of the world's deaths caused by CVD occur in LMICs, affecting men and women equally, and mainly individuals in the working-age group (WHO, 2016).

Looking specifically at stroke incidence, the GBD study further reported that stroke is ranked second as cause of death (Lozano *et al.*, 2013) and third in relation to cause of disability-adjusted life years (DALYs) (Murray *et al.*, 2013). The GBD study reported that, although stroke mortality rates and mortality-to-incidence ratios have decreased in the past two decades, the global burden of stroke in terms of the absolute number of people affected every year, the numbers of stroke survivors and DALYs lost are large and increasing, with most of the burden in low-income countries. If these trends in stroke incidence continue, by 2030 there will be almost 12 million stroke deaths, 70 million stroke survivors and more than 200 million DALYs lost globally. Stroke was traditionally thought of as a disease of elderly people (Feigin *et al.*, 2009); however, data from the recent GBD (Roth *et al.*, 2015) study showed that the proportion of the stroke burden is greater overall in individuals younger than 75 years, especially in low-income countries. The number of young people (aged <20 years) as well as adults (aged 20-64 years) affected by stroke increased from 1990 to 2010. These findings would suggest that stroke can no longer be regarded as a disease of old age.

It is clear that not enough has been done to curb the CVD burden that we are facing both globally and in Africa. CVD causes the most deaths in the world and because of the complexity of CVD, the different aspects should be investigated individually as well as holistically to enable us to find the most appropriate solution to reduce the burden of CVD on a global level.

2.1.2 Burden of cardiovascular disease in South Africa

South Africa is one of the countries that has had a complex and unique health transition (Kahn, 2011). The 2016 mid-year estimations indicated that the South African population is at 55.9 million, with slightly more women (51%) than men (49%) (STATS SA, 2016). Looking at the burden of CVD in South Africa, the most recent report (Wyk *et al.*, 2013) stated that in South Africa CVD was the second most common cause of death (17.6%). This was again reported in the GBD study, as can be seen in Figure 2.1, which indicates that ischaemic heart disease is

the second largest contributor to death in South Africa across all age groups in both genders (in 2015). Recent estimates by Maredza and co-workers suggest that at least 30,000 strokes occur yearly in rural South Africa (Maredza *et al.*, 2015).

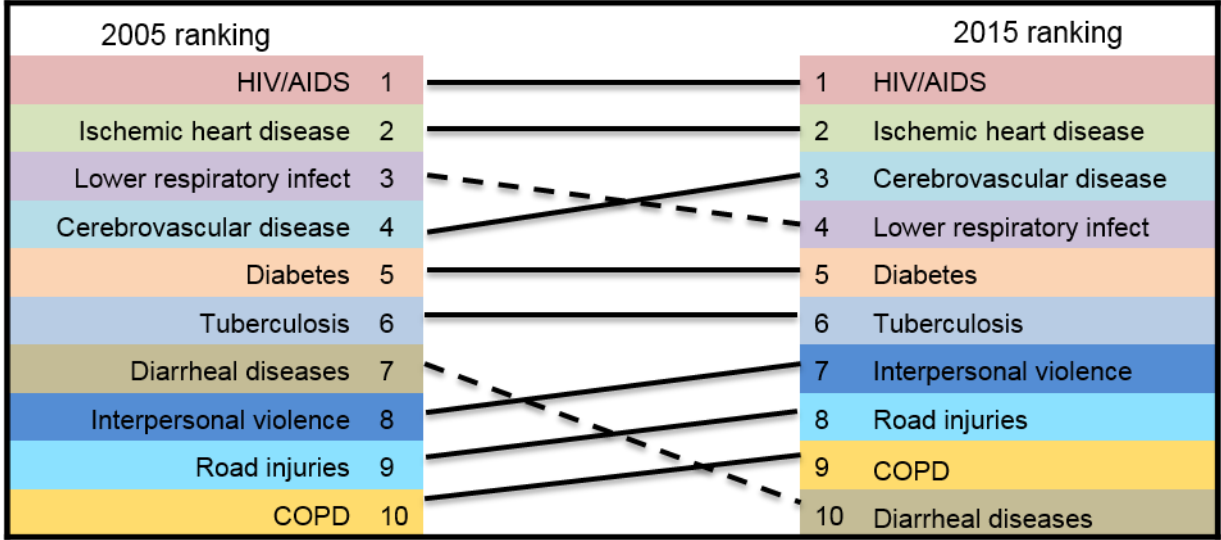


Figure 2-1: Causes of death in South Africa in all age groups including both genders
(Adapted from GBD 2015)

Two-thirds of all strokes can be ascribed to hypertension which, therefore, can be regarded as one of the most important risk factors (Perkovic *et al.*, 2007). In rural South Africa, a recent study concluded that high blood pressure and excess body weight are responsible for a significant proportion of the stroke burden (Maredza *et al.*, 2015).

2.2 Global and local trends of hypertension

The WHO and its member states have adopted targets pertaining to the combating of NCDs (WHO, 2013). One of these targets included lowering the prevalence of raised blood pressure by 25% by the year 2025. Hypertension is defined as a disorder in which the pressure exerted by the circulating volume of blood on the walls of the arteries and veins on the chambers of the heart is persistently high, which in turn causes strain on the heart. A person is considered to be hypertensive if the office systolic blood pressure is equal to or above 140 mmHg and/or the diastolic blood pressure is equal to or above 90 mmHg, or the individual is taking medication to reduce blood pressure (Tran & Giang, 2014).

According to the most recent pooled analysis, globally, an increase from 594 million in 1975 to 1.13 billion in 2015 was reported for the number of adults with increased blood pressure (NCD

RisC, 2017). This observation was more prevalently observed in LMICs (South Asia and sub-Saharan Africa) than in high-income countries. These countries are the ones that can least afford the social and economic consequences of ill health like hypertension. Over the past four decades, raised blood pressure has increased by a staggering 90% and this has been driven mainly by the increases in LMICs, as well as by the growth and ageing of the population (NCD RisC, 2017). The lowest prevalence of high blood pressure (in 2015) was observed in South Korea, Canada, the USA, Peru, the UK, Singapore and Australia, for both genders, with an age standardised prevalence of less than 19% in men and 13% in women. A high prevalence (above 35%) of raised blood pressure was reported in men from Central and Eastern Europe and in women (above 33%) from countries in West Africa. Men had higher systolic and diastolic blood pressure than women in 2015, except in sub-Saharan Africa, where the gender pattern was reversed. The findings of these global trends in hypertension prevalence are generally similar to those of other large-scale studies (Danaei *et al.*, 2011; Evans *et al.*, 2001; Tunstall-Pedoe *et al.*, 2006).

In a systematic review (pooled data of over 110 414 participants) by Ataklte and co-workers regarding the burden of hypertension in sub-Saharan Africa, a hypertension prevalence of 15 – 70% was reported (Ataklte *et al.*, 2015). The South African studies included in this review reported hypertension prevalence of 14.7% (Steyn *et al.*, 2001), 49.8% (Basu & Millett, 2013) and 46.2% (Maseko *et al.*, 2011). Bradshaw also reported a significant increase in hypertension from 1998 to 2008, which predicts a further increase in strokes and heart attacks in future (Bradshaw *et al.*, 2010).

2.2.1 Risk factors contributing to hypertension

Risk factors can be of genetic, behavioural, or environmental origin or the result of a medical disorder. Some of these risk factors are summarised in Table 2.3 (Ibrahim & Damasceno, 2012). These risk factors can be reversible or irreversible.

Table 2-3: Underlining factors that increase or are associated with high blood pressure

Non-modifiable factors	<ul style="list-style-type: none"> • Age • Genetic predisposition • Family history • Susceptible ethnic origin • Low birth weight
Modifiable factors (environmental or lifestyle)	<ul style="list-style-type: none"> • Overweight and obesity • Excess salt intake • Low potassium intake • Unhealthy diet, particularly excess calories, fats, and fructose • Excess alcohol • Physically inactivity • Psychological stress • Urban living • Smoking • Low fruit and vegetable intake • Excess sucrose intake
Other factors	<ul style="list-style-type: none"> • Dyslipidaemia • Hyperuricaemia • High gross national product per head • Increased arterial stiffness • Systemic pro-inflammatory state • Undernutrition in childhood • Sleep deprivation • Prescription drugs (e.g., non-steroidal anti-inflammatory drugs) • Long-term exposure to noise

(Adapted from Ibrahim & Damasceno, 2012)

Harding and co-workers reported a stronger correlation between blood pressure and environmental factors or an interaction between environmental and genetic factors than genetic factors alone (Harding *et al.*, 2006).

High blood pressure prevalence increases with age, and is a treatable risk factor for the most common causes of morbidity and mortality in older age: stroke, ischaemic heart disease, renal insufficiency and dementia (Steyn *et al.*, 2005 and Ferri *et al.*, 2011). Recently this has been demonstrated by Lloyd-Sherlock and co-workers (2014) where they reported a high prevalence of hypertension among older adults in South Africa and Ghana. The majority of the modifiable risk factors that ultimately contribute to the hypertension burden in South Africa are caused and can be ascribed to the country going through a demographic transition which is accompanied by an epidemiological transition. The demographic transition arises when a country experience improved socioeconomic development, whereas an epidemiological transition occurs when a change in disease profile from that of infectious diseases to a pattern of chronic degenerative diseases takes place. The nutrition transition accompanies these demographic and epidemiologic shifts toward nutrition-related NCDs, including hypertension (Amuna & Zotor, 2008).

Firstly looking at obesity, in the past decade (2003–2012) the obesity rates in South Africans have increased among men by 2 % from 9 to 11 % and among women by 12 % from 27 to 39 % making South Africa the country with the highest obesity prevalence in Africa (Shisana *et al.*, 2014). This very prominent risk factor cannot be ignored in terms of its contribution to the hypertension problem we are facing in South Africa. In the large Nurses' Health Study II (Forman *et al.*, 2009), body mass index (BMI) was reported as the strongest predictor of hypertension, showing a linear relationship between adiposity and blood pressure (correcting for age and body-fat distribution). In a South African study (Schutte *et al.*, 2003), similar correlations with blood pressure and BMI were observed. Urbanisation is another risk factor that is very relevant to the South African population and is strongly correlated with blood pressure (Steyn *et al.*, 2008). The researchers from this study also reported that individuals who lived in urban areas were more likely to have hypertension than individuals from rural areas. Overall, urbanisation (as a result of demographic and epidemiological transition) affects food consumption patterns and has been shown to include a diet that is high in fats and animal-based foods. This in turn increases BMI, which is a strong predictor of hypertension, and therefore indirectly causes hypertension. A research study in South Africa by van Rooyen and co-workers (2000) reported that blood pressure positively correlated with age, urbanisation, waist:hip ratio and smoking (van Rooyen *et al.*, 2000). Additional analyses revealed clusters of risk factors that correlated with blood pressure: the first cluster included malnutrition (high intake of saturated fats, animal protein and sodium), the second cluster had characteristics of metabolic syndrome and the third cluster consisted of hypercholesterolaemic and obesity factors, which included age, total and low density lipoprotein (LDL) cholesterol, high BMI and inactivity.

It is therefore clear from the literature that hypertension is not caused by one single risk factor, and that although sodium and potassium intake has a strong correlation with hypertension and is the focus of the current research, it does not lead to high blood pressure in a vacuum. All these modifiable risk factors forms part of the NCD cycle and cannot be ignored when investigating the hypertension epidemic of a country.

2.2.2 The pathophysiological development of hypertension

As discussed in the previous section, blood pressure is influenced by a number of physiological factors. Blood pressure (Figure 2.2) is dependent on the volume of blood pumped by the heart (cardiac output), as well as by the resistance the blood encounters in the arterioles (peripheral resistance) (Rolfes *et al.*, 2014). Cardiac output is raised when heart rate or blood volume increases and peripheral resistance is affected mostly by the diameters of the arterioles and blood viscosity. Blood pressure is therefore influenced by the nervous system, which regulates heart muscle contractions and arteriole diameters, as well as hormonal signals which may cause fluid retention or blood vessel constriction (Guyton & Hall, 2016). The kidneys also play a role in regulating blood pressure by controlling the secretion of the hormones involved in vasoconstriction and retention of sodium and water (Rolfes *et al.*, 2014).

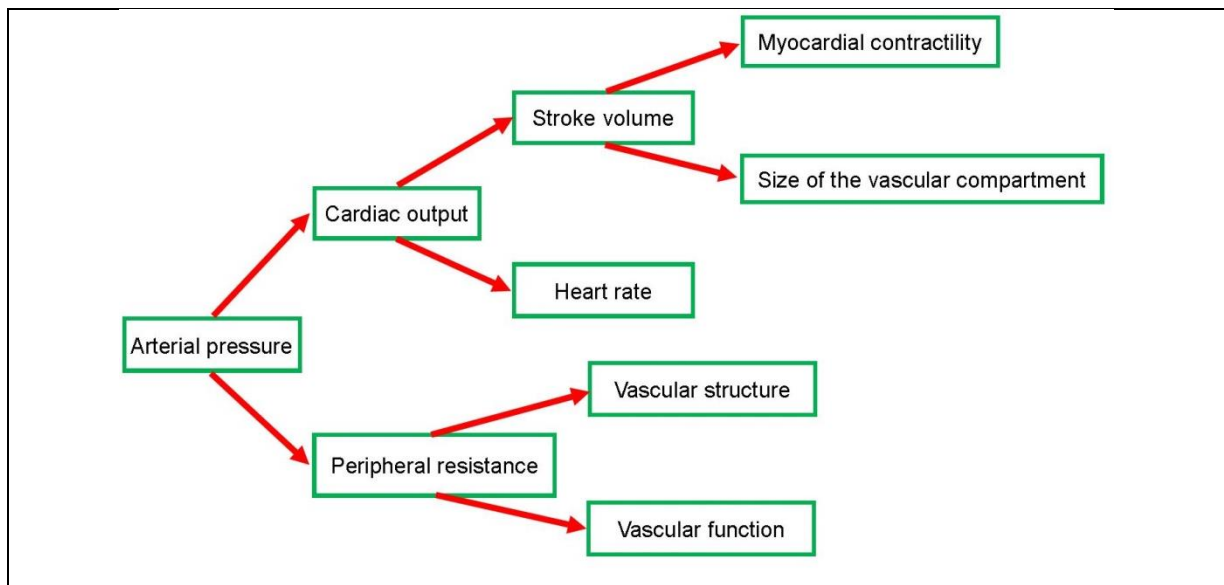


Figure 2-2: Factors affecting arterial pressure

(Adapted from Guyton and Hall, 2016)

In most people with established primary hypertension, an increase in peripheral resistance will account for the high pressure while the cardiac output will remain normal (Guyton & Hall, 2016). Many mechanisms have been proposed to account for the rise in peripheral resistance in hypertension. Structural narrowing of small arteries and arterioles (caused by lifestyle factors) is suggested as the main cause of increased peripheral resistance (Zieman *et al.*, 2005), while most evidence proposes either disturbances in renal salt and water handling [particularly abnormalities in the intrarenal renin-angiotensin system (Figure 2.3)] and/or abnormalities of the sympathetic nervous system (Guyton & Hall, 2016). These mechanisms are not mutually exclusive and it is likely that both contribute to some extent in most cases of essential hypertension. It has also been suggested that endothelial dysfunction and vascular inflammation may contribute to increased peripheral resistance and vascular damage in primary hypertension (Marchesi *et al.*, 2008; Versari *et al.*, 2009).

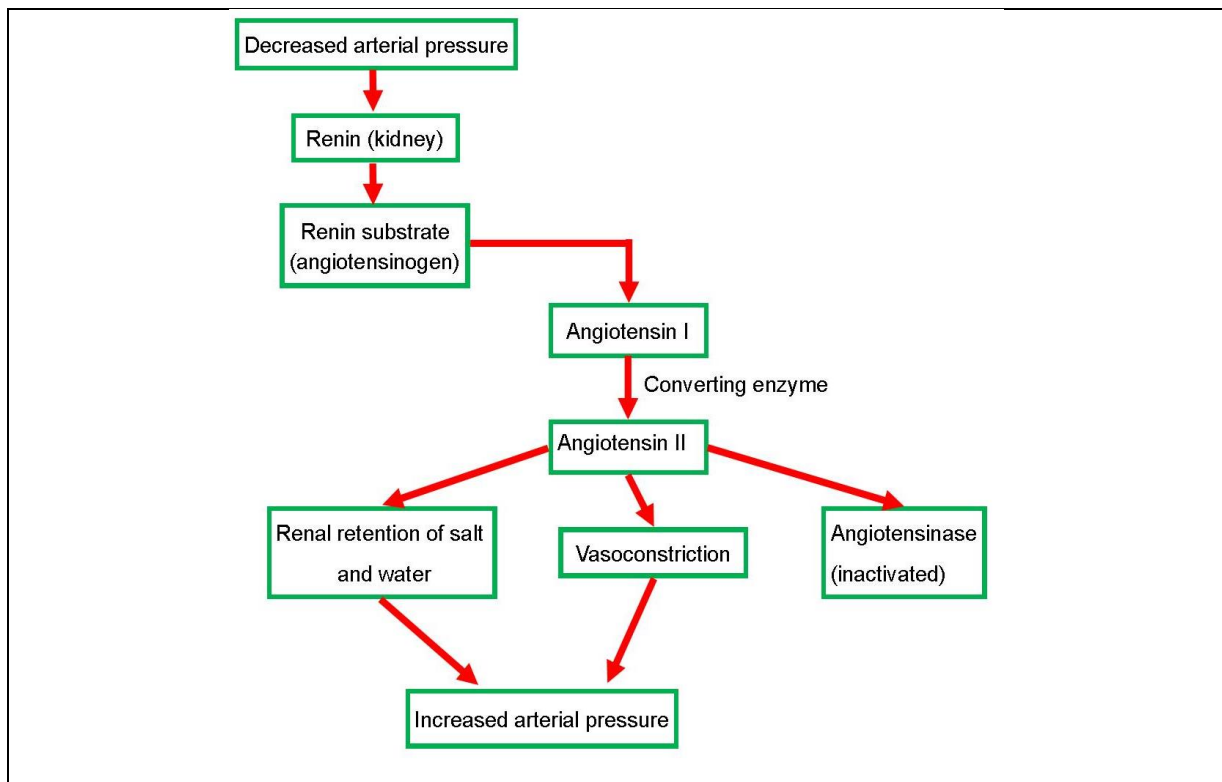


Figure 2-3: The classic renin-angiotensin vasoconstrictor mechanism for renal retention of sodium and water

(Adapted from Guyton and Hall, 2016)

2.3 Nutritional factors in blood pressure management

As already established, there are a number of factors that affect blood pressure development, and diet is one of them. After reporting on the diet as a whole, I will place more emphasis on

sodium and potassium, as these minerals are the focus of this research. In a recent meta-analysis, Ndanuko and co-workers, rather than focusing on one specific mineral, investigated dietary patterns and their effect on blood pressure (Ndanuko *et al.*, 2016). The dietary patterns investigated included the dietary approach to stop hypertension (DASH) diet, the Nordic diet and the Mediterranean diet.

2.3.1 The holistic diet

The DASH diet is a well-known and well-researched diet for combating high blood pressure and several research studies have shown that a significant reduction in blood pressure can be achieved following a diet high in fruits, vegetables and low-fat dairy products, as well as whole grains, poultry, fish and nuts, (Appel *et al.*, 1997; Bray *et al.*, 2004; Sacks *et al.*, 2001). The initial DASH trial by Apple and co-workers (1997) included 459 participants with prehypertension and stage 1 hypertension (participants were untreated). The participants were randomly assigned to one of three groups *i.e.* control group (typical American diet), diet rich in fruits and vegetables, and the DASH diet. After the trial the blood pressure of the participants in the fruit and vegetable group as well as the DASH diet group decreased by 5.5/3.0mmHg and 2.8/1.1mmHg in comparison with the control group. Numerous studies followed after this trial and tested the DASH diet in various settings (Bray *et al.*, 2004; Mitka, 2007; Sacks *et al.*, 2001).

Specific minerals within a holistic diet are also investigated by many researchers. With regard to calcium intake and its association with blood pressure, results are inconclusive and complex largely because of the interaction with other nutrients in the diet. Nevertheless, two meta-analyses (Allender *et al.*, 1996; Bucher *et al.*, 1996) assessing the relationship between dietary calcium supplementation and blood pressure reported small reductions in blood pressure (both systolic and diastolic). In another Cochrane review (Dickinson *et al.*, 2006b), significant reduction in systolic blood pressure was reported, but not in diastolic pressure. The conclusion by the researchers was that the evidence was inconclusive. Once again, on looking at whole foods and diets, De Goede and co-workers illustrated an inverse relationship between milk consumption and incidence of stroke (De Goede *et al.*, 2016). Research also suggests that dietary calcium can alleviate sodium's effect on high blood pressure (McCarron, 1997; Saito *et al.*, 1989).

Magnesium is also a mineral of interest when it comes to blood pressure control. Single studies published in the 1980s and 1990s have reported higher blood pressure in individuals who are magnesium deficient (Altura *et al.*, 1984; Ma *et al.*, 1995); however, the causal relationship was weak, as reported in a review published in 2006 (Dickinson *et al.*, 2006). A possible explanation

for the anti-hypertensive effect of magnesium is the fact that it is a vasodilator when infused into veins and arteries (Teragawa *et al.*, 2001) and can cause a small but significant reduction in blood pressure in the short term. Adebamowo and co-workers reported that, in two US cohorts, high intakes of magnesium were associated with a reduced risk of stroke. However, a combined mineral score of magnesium, calcium and potassium was even more inversely associated (Adebamowo *et al.*, 2015). Again, it seems that, with regard to blood pressure, magnesium as part of a holistic diet has more advantages than magnesium on its own.

Fibre intake is also associated with blood pressure and is included as part of the DASH diet (Appel *et al.*, 1997). In a study conducted in French adults, total and insoluble fibre were associated with a lower risk of hypertension, whereas soluble fibre was not (Lairon *et al.*, 2005). In a more recent cross-sectional study, the INTERMAP study, the researchers also reported a linear association between total dietary fibre and blood pressure (Aljuraiban *et al.*, 2015). Larger, prospective studies are needed, however, to investigate this further.

As mentioned in the introductory paragraph, sodium and potassium will be the focus of this research and will be discussed separately in the following sections.

2.3.2 Potassium

Potassium can be seen as the opposing mineral of sodium. It is the body's principal intracellular cation and plays a major role in maintaining fluid balance, nerve impulse transmission, muscle contractions and cell integrity (Young, 2001). Fruit and vegetables are the main dietary sources of potassium and, on the opposite end of the spectrum, processing of any of these foods reduces the potassium level and is often seen in individuals who consume a diet high in processed foods (Webster *et al.*, 2010). Diets low in potassium play an important role in the development of high blood pressure, especially when combined with a high sodium intake (D'Elia *et al.*, 2011; Geleijnse *et al.*, 2003; Whelton *et al.*, 1997). Epidemiologic observations in animal and human studies also concluded that potassium deficiency increases the negative impact of a high sodium intake on the development of hypertension and other CVD (Adrogué & Madias, 2007, Adrogué & Madias, 2014; He & Macgregor, 2001; He & MacGregor, 2008). Potassium intakes in populations are generally low owing to their high intakes of processed foods (He & MacGregor, 2008), as is confirmed in a South African study where potassium levels were seen to differ between different population groups and where very few of the participants met the optimal dietary intake (Charlton *et al.*, 2005).

Potassium and sodium function are closely related and have to be in a balance. The ratio of sodium to potassium (Na:K) can be regarded as an important factor in CVD development (Oberleithner *et al.*, 2009; Young, 2001).

2.3.3 Sodium-to-potassium ratio

A high ratio of Na:K has been linked to high blood pressure, heart disease and stroke (Maillot *et al.*, 2013). Evidence suggests that the interaction between sodium and potassium plays the main role in development of hypertension, and a number of mechanisms for this exist (Adrogué & Madias, 2007). The modern-day diet, which is high in sodium and low in potassium, creates a biological interaction with the kidneys and causes the human body to have excess sodium and insufficient potassium levels (Adrogué & Madias, 2014). This will then cause vascular smooth muscle cells to contract and the peripheral resistance to increase, which ultimately results in high blood pressure (Adrogué & Madias, 2014). It has been suggested that lowering the dietary Na:K ratio by increasing the consumption of potassium-rich foods can be very useful dietary advice (Grimes *et al.*, 2011; Mozaffarian *et al.*, 2011) which may have a greater impact on public health. There have also been recommendations that the absolute potassium and sodium intake levels be replaced with recommended Na:K ratios (Meneton *et al.*, 2009; Yang *et al.*, 2011). It is clear from the literature that both potassium and sodium play an important role in blood pressure. The focus will now move to sodium and its role in hypertension.

2.3.4 Sodium

Sodium is a chemical element with the symbol Na and atomic number 11. Throughout history, people have held salt (sodium) in high regard. We describe someone we admire as “the salt of the earth” and people we don’t admire as much as “not worth their salt”. The importance of sodium is illustrated in the fact that one taste quality (saltiness) is devoted to identifying sodium in foods (Mattes, 1997). In humans, sodium is also an essential mineral that regulates blood volume, blood pressure and pH. Sodium chloride (NaCl) is commonly referred to as salt and is the principal source of sodium in the diet (Rolfes *et al.*, 2014).

2.3.4.1 Role of sodium in the body

Sodium is the principal cation of the extracellular fluid and the primary regulator of its volume; it maintains acid-base balance and is essential to neural transmission and muscle contraction (Dötsch *et al.* 2009). Sodium is absorbed by the intestinal tract and transported to the kidneys, which will filter all the sodium out of the circulation. The kidneys then return the exact amount of sodium required by the body back into the circulation for use by the human body. Usually, the

amount of sodium excreted is equal to the amount ingested. When a blood sodium concentration is high, a person's thirst signal will be triggered to restore the sodium-to-water ratio. The kidney will in this case then excrete the excess sodium and water together (Guyton & Hall, 2016; Rolfes *et al.*, 2014).

2.3.4.2 Contribution of sodium overconsumption to hypertension

Evidence supporting the direct relationship between hypertension and sodium consumption is overwhelming, with numerous types of study designs indicating this relationship (Graudal *et al.*, 2012; He *et al.*, 2013; Steyn *et al.*, 2013). In a meta-analysis it was also reported that a direct association between high dietary sodium intake and risk of stroke exists (Strazzullo *et al.*, 2009). Furthermore, it was concluded from the meta-analysis that a dose-dependent association can be seen between increasing sodium intake and the incidence of strokes, in particular, and total cardiovascular events. A review by He and MacGregor (2008) pointed out that animal studies (Denton *et al.*, 1995; Elliott *et al.*, 2007), human genetic studies (Lifton, 1996; Lifton *et al.*, 2001), epidemiological studies (Elliott & Stamler, 2002; Elliott *et al.*, 1996; Khaw *et al.*, 2004; Uzodike, 1993; Zhou *et al.*, 2003), population-based intervention studies (Forte *et al.*, 1989; Takahashi *et al.*, 2006) and treatment studies (Hooper *et al.*, 2002; Sacks *et al.*, 2001) all indicated a relationship between high sodium consumption and the risk of hypertension. The relationship between high sodium intake and hypertension is therefore supported by ample different types of evidence and studies. On the other hand, studies also reported no associations between sodium intake and blood pressure (Ruppert *et al.*, 1993 and Watt *et al.*, 1985). He and co-workers (2013) concluded that there would be heterogeneity in the relation of sodium intake to health outcomes because of environmental, genetic and behavioural factors. Meta-analyses published on the topic of sodium restriction and the effect it might have on various hormones have also received some attention (Gradual & Jurgens, 2011 and Gradual & Jurgens, 2012). The authors concluded that the lowering of blood pressure in normotensive individuals holds no public health benefit. Looking at salt intake more closely from a public health viewpoint, He and co-workers (2013) conducted a follow-up meta-analysis to determine the effects of a longer-term modest reduction in salt intake. They argued that the two meta-analyses conducted by Gradual and Jurgens (2011) looked at studies from short-term trials with a large change in salt intake, which is not relevant to the current public health situation. He and co-workers (2013) concluded that a longer-term step-wise reduction in salt intake caused significant and important decreases in blood pressure and had no adverse effects on plasma hormones. With regard to the pathophysiology and how sodium is regulated, the renin-angiotensin system is mainly responsible. This system controls the volume of fluid and sodium in the body. When blood pressure is about to fall and the sodium concentration in the kidneys is low, renin will be produced and will then trigger the release of angiotensin and

aldosterone, which collectively retains sodium in the urine. If sodium increases again, the production of renin will decrease (Guyton & Hall, 2016). In the long term, a diet that is constantly high in sodium would disrupt the natural sodium balance in the body, which will in turn cause fluid retention, increasing the pressure exerted by the blood against the blood vessel walls (Blaustein *et al.*, 2006).

Sodium intakes of different populations around the world may vary markedly, but consistently exceed the WHO's recommended 2000mg/day. In a review conducted by Powells and co-workers (2013), it was reported that in 2010 the mean worldwide sodium consumption was 4000mg/day (equivalent to 10 g of salt per day) and that, overall, 99.2% of the world's adult population exceeded the recommendation of the WHO. There was little variation in sodium intakes in the different age groups, aged 25-29 years (3780mg/d) and 40-44 years (4040mg/d). The Asian regions had the highest sodium intake, with East Asia reporting 4800mg/d and Central Asia 5510mg/day (12.2 and 14.0 g of salt per day, respectively). Very high sodium intakes were also reported in Eastern Europe (4180mg/d), Central Europe (3920mg/day and the Middle East and North Africa (3920mg/d). Sub-Saharan Africa, Latin America and the Caribbean reported the lowest sodium intake but results were based on very few data sources. Brown *et al.* (2009) reported similar findings with regard to sodium intake in the world population.

A limited number of studies have been conducted in the South African population, where it has been estimated that the average South African consumes 6 – 11 g of salt per day. The studies on which this estimation is based are summarised elsewhere (Wentzel-Viljoen *et al.*, 2013) and the data are relatively outdated. More recent sodium intake data are needed in South Africa for monitoring and other purposes.

2.3.4.3 Differences in sodium excretion in population groups

As previously mentioned, Harding and co-workers (2006) suggested that there is a stronger correlation between blood pressure and environmental factors, or an interaction between environmental and genetic factors, than genetic factors alone. Nevertheless, genetic factors, often observed in black people, seem to play a part in salt sensitivity, (Kotchen *et al.*, 2013; Meneton *et al.*, 2005). Some mechanisms suggest that single gene mutations promote salt retention through a defect in renal sodium handling and then increase blood pressure (Sanders, 2009). It is estimated that about 30 – 50% of people that have hypertension have salt sensitivity (Weinberger *et al.*, 1996). Black ethnic groups tend to have higher blood pressure than their white counterparts; however, the mechanisms involved are poorly understood (Bankir *et al.*,

2007). Weber and co-workers reported that black individuals are often diagnosed at a younger age with hypertension, which is sometimes also more severe than in their white counterparts (Weber *et al.*, 2014). These researchers also stated that black individuals are more sensitive to sodium's raising effect on blood pressure (Weber *et al.*, 2014). The mechanism of salt sensitivity is poorly understood, but involves changes in renal function, fluid hormones, the vasculature, the heart, and/or central sympathetic outflow (Farquhar *et al.*, 2015). According to some researchers (Harshfield *et al.*, 1991; Luft *et al.*, 1977), a possible explanation could be that, on average, black individuals excrete sodium less efficiently than white individuals. This renal dysfunction *i.e.* reduced capacity of the kidneys to excrete sodium, results in more sodium and fluid retention (Luft *et al.*, 1977). In other words, there is a greater drop or rise in blood pressure in response to sodium restriction or excess, respectively, and this is more common in people of African ethnicity (Weinberger, 1996). It has been suggested that the difference in handling of renal potassium by whites and blacks can also be involved in the fractional reabsorption of sodium in specific renal tubular segments (Aviv *et al.*, 2004). Plasma renin activity as well as aldosterone concentrations are indirect measurements of salt sensitivity (Rayner *et al.*, 2011). It has been reported (Rayner *et al.*, 2001) that, under comparable intakes of sodium, black South African individuals have lower renin and aldosterone concentrations in comparison with white individuals. In a recent Cochrane review by Gradual and co-workers, it was concluded that studies regarding the sensitivity of sodium restriction in a black population are required as different populations react differently to lower sodium diets (Graudal *et al.*, 2012).

2.3.4.4 Methods of determining sodium intake in a population

Accurate estimation of population-wide sodium intake is crucial in obtaining relevant and correct data for monitoring and evaluation purposes. Sodium intake can be determined either by the collection of dietary intake data or by measuring the amount of sodium excreted in the urine. Table 2.5 is a summary of the different tools (adapted from Elliot and Brown, 2007) that can be used to estimate sodium intake in a population, as well as their limitations and strengths.

The use of dietary recalls to estimate sodium intake was reported to be an inadequate research tool because of underreporting of food intake as well as incomplete food databases (Espeland *et al.*, 2001). The kidneys handle most of the sodium consumed under normal circumstances. Up to 95% of the sodium consumed is excreted in the urine within a 24-hour period, while the other 5% is excreted through saliva, sweat and gastrointestinal secretions. Twenty-four hours is the minimum time required to characterise the pattern of urinary excretion for a given individual

(Elliott & Brown, 2007). The 24-hour urine collection method (one or more) is considered to be the “gold standard” in determining sodium intake in individuals as well as in population groups (WHO, 2013). In a salt balance study conducted by Lerchl and co-workers (2015), the researchers concluded that collecting three and even seven consecutive 24-hour urine samples improved the accuracy of sodium intake to 75% and 92%, respectively. They concluded that a single 24-hour urine collection at intakes from 6 to 12 g salt per day would probably not be able to detect a 3 g difference in individual salt intake. In a reproducibility study, Sun *et al.* (2017) concluded that three 24-hour urine samples were adequate for the measurement of long-term exposure in epidemiological studies.

However, alternative methods have been explored because of the high burden placed by a 24-hour urine collection period on a participant and because of several logistical challenges in collecting these samples in large population-based studies. As reported in a recent systematic review (Ji *et al.*, 2012), initiatives for finding a replacement method for the 24-hour urine collection method, without compromising the accuracy of the data, are high on the agenda. The review concluded that the reliability of alternative methods is still unclear and that more research is required with suitable study designs, as well as statistical testing, to determine the true usefulness of these alternative methods. The need for validation studies relevant to the context of the specific population was further highlighted by the researchers (Ji *et al.*, 2012). Some studies suggested that spot urine samples may be representative of the sodium intake of the group despite the fluctuations in values for individuals (Mente *et al.*, 2014; Tanaka *et al.*, 2002). As spot urine samples are readily obtained at low cost, they may prove to be of value in monitoring sodium intakes, particularly in resource-poor settings or where 24-hour urine collections are not deemed feasible. However, spot urine samples have not been extensively tested in epidemiological surveys and further validation is required (Elliott & Brown, 2007; Ji *et al.*, 2012).

Table 2-4: Methods for estimating sodium intake on a population level

Method	Key reference	Description	Strengths	Limitations
Food table approach (i.e. 24-hour dietary recall, food frequency questionnaire)	Clark & Mossholder, 1986	Food and beverage consumption is recorded in detail and Na is estimated from standard tables of nutrient data of these foods	<ul style="list-style-type: none"> Data are collected regularly Food data tables are widely available 	<ul style="list-style-type: none"> Moderate to high participant burden Difficult to establish how much salt is added while cooking or at the table Different manufacturers of the same food product can have different Na contents Subject to reporting errors
Duplicate portions	Clark & Mossholder, 1986	Duplicate samples of everything eaten are collected for a specified period. Samples are transported to the laboratory, where they are homogenized and analysed for Na content	<ul style="list-style-type: none"> Accounts for salt added during cooking. Direct analysis of Na content 	<ul style="list-style-type: none"> High participant burden. Cook must prepare extra portions. May not account for salt added at the table
24-hour urine collection (single and more than 1)	Bingham <i>et al.</i> , 2002	All urine is collected for a 24-hour period. The volume in this period is recorded and the Na is analysed in a laboratory	<ul style="list-style-type: none"> Urinary excretion of Na is nearly equal to intake, Biological marker not subject to reporting or observer bias; difficulties in assessing dietary intake avoided 	<ul style="list-style-type: none"> High participant burden; Excretion may be biased by incomplete collection. Self-reported completeness subject to misreporting

Method	Key reference	Description	Strengths	Limitations
Overnight urine collection	Liu <i>et al.</i> , 1977	Urine voided overnight is collected for a timed period (usually 8 or 12 h). The volume collected & Na concentration are calculated so that excretion may be estimated	<ul style="list-style-type: none"> • Moderate participant burden, • Overnight collection interferes less with daily routine. • True overnight excretion correlates well with true 24-h excretion in healthy individuals 	<ul style="list-style-type: none"> • Collection must be complete and accurately timed. • Requires the assumption that the ratio of daytime to overnight excretion is constant
Single spot urine collection	Watson & Langford, 1970	A single voiding is collected & Na concentration is measured in the laboratory. If time since last voiding & volume are known, then excretion rate may be calculated	<ul style="list-style-type: none"> • Low participant burden • Voiding can be made at a clinic, where other data may be collected simultaneously 	<ul style="list-style-type: none"> • Concentration is dependent not only on Na consumed, but also on fluid ingested • Depends on time of day. • Highest concentrations are with first void in the morning

(Adapted from Elliot & Brown, 2007).

2.3.4.5 Role of sodium in food

Sodium in the form of salt is used in a variety of foods to improve flavour and increase palatability (Dötsh *et al.*, 2009). Besides taste, sodium has two other important functions, i.e. processing and preservation. The oldest use of sodium (in the form of salt) is as a preservative in that the salt that was added to the product lowered the water activity and prevented microbial growth (Kilcast and Angus, 2007). In addition to that, it also has a specific processing function for different food categories. In most bakery products, gluten development and the regulation of fermentation is regulated by salt and in meat products the water binding capacity of proteins is enhanced by salt (Desmond 2006, and Taormina, 2010). Another technological property of salt influences the activity of micro-organisms and enzymes needed for cheese maturation (Kilcast and Angus, 2007). Therefore, maintaining microbiological stability and structure are important aspects that need to be taken into account. However, there are multiple strategies that industry can follow to reduce the sodium without compromising the above-mentioned properties. These include adaptation (reducing sodium gradually), flavours (multisensory principles), salt substitutes (use of mineral salts) and salt boosters (Dötsch *et al.*, 2009).

2.3.5 Measurement of sodium content in food

There are a number of different techniques that can be used when measuring the sodium content in food. These include using flame atomic absorption spectrometry (AAS), flame atomic emission spectrometry, inductively coupled plasma (ICP) atomic emission spectrometry, ICP mass spectrometry, and photometric and ion-selective detection (de Brätter *et al.*, 1995; Dolan & Capar, 2002). In order to prepare these samples for sodium analysis, the sample matrices must be sampled correctly and digested. The sampling methods for the different food matrices are summarised in Table 2.4 (Greenfield & Southgate, 2003). The foodstuffs included for reduction of sodium are also set out in the regulation R.214. Microwave digestion has been shown to be a rapid technique for preparing complex food matrix for sodium analysis (Dolan & Capar, 2002). However, the Minister of Health in South Africa, under section 15(1) of the foodstuffs, cosmetics, and disinfectants Act, 1972 (act 54 of 1972), gazetted the regulations relating to the reduction of sodium in certain foodstuffs (R.214). In the regulation the specific method for sodium determination is stipulated as “suitable sodium potentiometric method or elemental analysis, with either flame AAS or ICP, for determining typical total sodium content which shall be applied for monitoring”. The permitted tolerance for nutrient declaration in the labelling of sodium cannot be more than 20% in excess of the target sodium value.

Table 2-5: Sampling method of the different food categories included in R.214 regulation

Foodstuffs category	Sampling method
Bread	Take every fourth slice and one end slice and crumb thoroughly to form composite sample
All breakfast cereals and porridges, whether ready-to-eat, instant or cook up, hot or cold	Quartered then crushed with a pestle to form composite sample
All fat spreads and butter spreads	Units will be softened over a warm water bath and then blended together gently to form the composite sample.
Ready-to-eat savoury snacks, excluding salt and vinegar flavoured snacks	Quartered then crushed with a pestle to form composite sample
Flavoured potato crisps, excluding salt and vinegar flavoured potato crisps	Quartered then crushed with a pestle to form composite sample
Flavoured, ready-to-eat, savoury snacks and potato crisps-salt-and-vinegar only	Quartered then crushed with a pestle to form composite sample
Processed meats – uncured	The edible portion is chopped coarsely with knife and mixed thoroughly to form the composite sample.
Processed meat – cured	The edible portion is chopped coarsely with knife and mixed thoroughly to form the composite sample.
Raw processed meat sausages (all types) and similar products	The edible portion is chopped coarsely with knife and mixed thoroughly to form the composite sample.
Dry soup powders (not instant type)	Unit will be mixed thoroughly and the combined mass quartered.
Dry gravy powders and dry instant savoury sauces	Unit will be mixed thoroughly and the combined mass quartered.
Dry savoury powders with dry instant noodles to be mixed with a liquid	Unit will be mixed thoroughly and the combined mass quartered.
Stock cubes, stock powders, stock granules, stock emulsions, stock pastes or stock jellies	Unit will be mixed thoroughly and the combined mass quartered.

2.4 Sodium reduction strategies

A number of guidelines and documents have been published to summarise the characteristics of a national sodium reduction strategy in order to provide guidance to countries when embarking on or implementing such a strategy (WHO, 2013). It has been recommended that the WHO's three-pillar approach be used for successful sodium reduction. The three pillars include:

- i) **product reformulation** – this is focussed mainly on engagement with the food industry and is particularly effective in countries where processed foods are the major source of sodium;
- ii) **consumer awareness and education campaigns** – this includes informing the public of the harmful effects of sodium as well as reading of nutritional labels;
- iii) **environmental changes** – this includes elements such as pricing strategies as well as the development of a clear labelling system.

Many countries are in the early stages of implementing a sodium reduction strategy and, in order to create a tailor-made strategy, the WHO recommends a further eight steps for success:

Step 1: Organising support to mobilise change

Step 2: Environmental scan of the country

Step 3: Setting the target (national dietary guideline on salt)

Step 4: Planning the campaign and engaging partners for implementation

Step 5: Consumer awareness campaigns

Step 6: The use of labelling to highlight the salt content of foods

Step 7: Negotiating agreements with the food industry as a whole to lower salt in a wide range of products

Step 8: Monitoring progress, continuous revision and evaluation

Some countries have already successfully implemented a sodium reduction strategy by following these steps. Other countries, however, have a different focus, which may involve changing consumer behaviour or labelling regulations or setting targets for industry.

2.4.1 Global sodium reduction initiatives

Since the announcement by the United Nations at a General Assembly in 2011 that the prevention and control of non-communicable diseases should be addressed, member states have adopted the global target of reducing salt intake by 30% in 2025 (WHO, 2013).

In 2010, 32 countries implemented (Webster *et al.*, 2010) some sort of sodium reduction strategy in their countries and this number doubled in 2014, 75 countries now having sodium reduction strategies in place (Trieu *et al.*, 2015). In 2010, the majority of these countries were in Europe (Webster *et al.*, 2010) compared with the study done in 2014, where countries of all income levels had a strategy (Trieu *et al.*, 2015). Within the 75 countries there were five implementation strategies for sodium reduction, which included food reformulation, consumer education, front-of-pack labelling, interventions in public institution settings and taxation.

Trieu and co-workers (2015) reported that, in general, 12 countries showed a reduction in population salt intake, which is an increase from the four reported in 2010 (Webster *et al.*, 2011). Four of the 12 countries used 24-hour urine samples to show this reduction and included Finland (reduction of 36%); Slovenia (reduction of 8.9%), Turkey (reduction of 16.7%) and the United Kingdom (reduction of 14.7%). Nineteen countries reported a change in the sodium content of foods. All these countries except for Malaysia showed a decline in sodium in bread at least, with reductions ranging from 6% to 38% (Trieu *et al.*, 2015). Consumer knowledge as a result of a sodium reduction strategy also improved in seven countries in 2014. Finland (Pietinen *et al.*, 2010) and the United Kingdom (He *et al.*, 2014) are considered the world leaders in salt reduction on a country level, in that both of these countries have reported reductions not only in salt intake but also in blood pressure and stroke deaths. Finland's success can be ascribed to the mandatory labelling law that states that a "high salt content" must be labelled, if the salt content is more than 1.3% in bread, 1.8% in sausages, 1.4% in cheese, 2.0% in butter, and 1.7% in breakfast cereals or crisp bread. Looking at the United Kingdom, He and co-workers (2014) reported a fall in blood pressure of 2.7/1.1 mmHg as a result of the 15% reduction in salt intake from 2003 to 2011. They also showed a 40% reduction in stroke incidence in the same time period as mentioned above. All eyes are now focussed on South Africa, which is the one of the few countries to legislate the reduction of sodium in a large number of processed foods in order to curb the high hypertension prevalence.

2.4.2 South Africa's sodium reduction strategy

South Africa's sodium reduction strategy was initiated as a result of the national Department of Health setting up a strategic plan to scale up efforts to prevent and control NCDs (based on recommendations of the WHO). In the strategic plan of the Department of Health, the targets which are related to reducing blood pressure in the South African population are listed in Chapter 1.

These national targets, context-specific data (Charlton *et al.*, 2005; Wentzel-Viljoen *et al.*, 2013) and cost-effectiveness analyses (Bertham *et al.*, 2012) were the driving forces for the passing of this regulation by the Minister of Health. The Minister of Health, under section 15(1) of the foodstuffs, cosmetics, and disinfectants Act, 1972 (act 54 of 1972), gazetted the regulations (R.214) relating to the reduction of sodium in certain foodstuffs in March 2013. The food categories, as well as the two target dates included in the regulation, are summarised in Table 2.6. The regulation was amended on the 6th of September 2016, and therefore the amended target dates are included in the table.

Table 2-6: Food categories included in the regulation R.214.

Food category	2016 target (Na/100mg)	2019 target (Na/100mg)
Bread	400	380
All breakfast cereals	500	400
All fat and butter spreads	550	450
Savoury snacks, excluding salt-and-vinegar flavoured	800	700
Flavoured potato crisp, excluding salt-and-vinegar	650	550
Flavoured ready-to-eat savoury snack and potato crisp, salt-and-vinegar only	1000	850
Processed meat – uncured	1300	1150
Processed meat – cured	850	650
Raw-processed meat sausages	800	600
Dry soup powder (not instant type)	5500	3500
Dry gravy powders and dry instant savoury sauces	3500	1500
Dry savoury powders with dry instant noodles to be mixed with a liquid	1500	800
Stock cubes, -powder, -granules, -emulsions, -pastes or -jellies	18000	13000

As already mentioned, regulating the sodium content in foods is only one pillar (product reformulation) of the sodium reduction strategy. A consumer education and awareness campaign on salt intake, named Salt Watch, was launched in 2014, (Heart and Stroke Foundation, 2016).

Research with regard to the third pillar, environmental changes, is ongoing or still needs to be conducted in the South African context. Research includes the individual's understanding of sodium content on a label as well as the use of a logo to indicate a product with high salt.

2.4.3 Contribution of foods to total sodium intake

According to Trieu *et al.*, 2015, the majority (81%) of national sodium reduction strategies included industry engagement to reduce the sodium in certain foodstuffs. Globally, bread is the most targeted food product for reducing salt content, followed by bakery products, processed meats, sauces and convenience meals. Anderson and co-workers (2010) investigated the main dietary sources of sodium in China, Japan, United Kingdom and America. For Japan, the top three food sources contributing most to sodium intake were soy sauce (20%), soups (16.4%) and salted fish (15%). In China, most of the sodium came from adding salt while cooking or at the table (75.8%). In the United Kingdom, bread, cereals and grains contributed the most (34.6%), followed by processed red meats, poultry and eggs (20.4%). The same food products were responsible in America, with bread, cereals and grains contributing 19.5% and processed meats 12%.

In South Africa, dietary data indicate that the main food products that contribute to the country's sodium intake are white and brown bread (5 – 35%), hard or block margarine contributed up to 13% and soup and gravy powder up to 17% (Wentzel-Viljoen *et al.*, unpublished). Thirteen different food categories were identified as contributing most to sodium intake and were included in the Regulation R.214.

2.4.4 Monitoring

Monitoring sodium consumption at population level is a vital part of the reduction strategy and provides information on the effectiveness of the programme as well as the accountability of all involved. According to the WHO (2010), there are four different aspects to the monitoring process:

- Monitoring of sodium intake at population level.
- Monitoring the main sources of sodium intake in the diet.
- Consumer knowledge, attitudes and behaviours regarding sodium and health.
- Monitoring the actual impact and results of the sodium reduction intervention.

Looking at monitoring of sodium intake in a population, Trieu *et al.* (2015) reported that over half of the countries with a sodium reduction strategy monitored change in sodium intake by the use of dietary surveys. Although this method is prone to underestimate the sodium intake, it can be useful in indicating change if the same method and survey are used pre- and post-intervention. As mentioned in section 4.1.3, the 24-hour urine collection method is still considered the gold standard in determining sodium intake in populations although it is costly and has a high participant burden. The use of a spot urine sample for monitoring purposes is widely used, and

if this method is used, it is recommended that a sub-sample of 24-hour urine collections must be analysed (WHO, 2012). However, the need for validation of a spot urine sample against a 24-hour urine sample relevant to the context of the specific population is highlighted by Ji and co-workers (Ji *et al.*, 2012). Therefore more research is needed in South Africa in terms of validation of the estimation of sodium intake by means of spot urine versus 24-hour urine samples in different population groups.

Monitoring of sodium levels in food is also vital in establishing the effectiveness of a national strategy. Trieu and co-workers reported that, in 2014, two thirds of the countries that monitored sodium levels in food used laboratory analysis. This method provides accurate results but usually covers a limited range of food products. Large-scale surveys of sodium levels in food, based on label information, should be conducted in parallel with laboratory analysis to ensure that progress can be tracked across all food products, as surveys are not as labour-and cost-intensive as laboratory analysis.

An additional aspect in monitoring sodium intake and sodium levels in foods is whether iodine deficiency occurs once sodium reduction is established. The prevention of iodine deficiency by means of iodisation of salt is a very effective and a sustainable long-term public health measure (Andersson *et al.*, 2005). To comply with the international goal of universal salt iodisation, compulsory iodisation of all table salt was introduced in South Africa on 1 December 1995 (Jooste *et al.*, 2001). The monitoring of iodine levels is therefore an important aspect in light of the sodium reduction regulations in order to ensure that the recommended low-salt diets will provide sufficient iodine intake.

2.4.5 Cost-effectiveness and long term impact

Over the past few years a number of cost-effective analyses have been conducted to establish the health and financial effects of reducing a population's sodium consumption. All of these analyses found that reducing the sodium consumption of a population is very cost-effective (He & MacGregor, 2008). Collins and co-workers conducted a cost-effectiveness analysis of four public health policies that aim to reduce salt intake in England. All four policies resulted in reducing CVD events and increasing life years in the population. This translates into reducing health care cost spend, thus resulting in cost saving. In England the biggest estimated savings came from mandatory reformulation, which suggests that implementing legislation to reduce the sodium content in processed foods will reduce spending on health care for CVD (Collins *et al.*

2014). Similar cost-effectiveness analysis was done by Wilcox and co-workers (2015) in Syria. They found that a combination of sodium reduction strategies, i.e. health promotion campaign, labelling and reformulation, resulted in the largest gain in life years. Reformulation and labelling was the most cost-effective, non-cost-saving policy in Syria. In a recent health and economic impact study the researchers aimed to compare the impact of eight sodium reduction interventions (Nghiem *et al.*, 2015). The use of mandatory controls on sodium in the food supply chain led to the greatest health gain as well as major cost savings. This intervention also had the greatest effect in reducing ethnic inequalities in health. Bibbins-Domingo and co-workers (2010), reported in their study that a national effort in the US to decrease salt consumption by 3 g per day would result in an estimated annual gain of 194,000 to 392,000 QALYs and could save \$10 billion to \$24 billion in health care costs. In South Africa, the sodium reduction strategy is expected to have the same cost-effectiveness as seen in other countries. Sodium reduction in South Africa (only in bread, margarine, gravy and soup) is also expected to result in 7 400 fewer CVD deaths and 4 300 fewer non-fatal strokes per year, leading to cost savings of up to R300 million (Bertram *et al.*, 2012). Watkins *et al.* (2015) conducted further economic evaluations, called the extended cost-effectiveness analysis, which assess the effect of public policies on the broader public health system. The results of these analyses showed that, in a cohort of 1 million South Africans, the sodium reduction policy would prevent 403 deaths and 1 680 cases of CVD per year. When broken down, 39% of stroke deaths would be avoided, as well as 23% of deaths caused by ischaemic heart disease (IHD). They concluded that in the whole South African population 5 600 deaths and 23 000 cases of CVD would be averted through the sodium reduction policy. This demonstrates substantial cost-saving for a country that already subsidises health care. Looking at the economic implications, they reported that a sum total of US\$51.25 million could be saved on hypertension and CVD subsidies annually. It is therefore clear that a national salt reduction programme not only holds health benefits for a population but is also cost-effective. Monitoring of the strategies will be crucial to verify these predictions.

2.5 Summary of the literature

Studying the literature, one can clearly see that high blood pressure places a huge burden on the health of global populations and also on the health care system. South Africa faces a massive problem if something is not done to curb the rates of high blood pressure in the country. In addition to this, a limited number of studies have been conducted in the South African population to estimate sodium consumption. Following on the successful implementation of sodium reduction strategies in other countries, as well as the literature supporting the association between sodium intake and high blood pressure, South Africa has developed a sodium reduction strategy that is focussed mainly on mandatory food reformulation. Although

the strategy is in the beginning phases, a few gaps have been identified through this literature review. The first gap is that no recent sodium intake data are available for South Africa to form a baseline from which the effectiveness of the sodium reduction strategy can be determined and monitored. Secondly, monitoring of sodium intake in South Africans in terms of the use of a spot urine sample vs 24-hour samples is still under discussion as validation of the spot sample in different population groups in South Africa has not yet been conducted. As mentioned, collecting a 24-hour urine sample has a high participant burden and validating a spot urine sample will ensure that monitoring can be done more frequently and on a larger scale. Baseline data (through laboratory analysis) of the sodium content of the different foodstuffs included in the R.214 regulation have also not yet been established. This will be crucial in establishing the effectiveness of R.214 and charting the way forward.

CHAPTER THREE: MANUSCRIPT ONE

“Look closely at the present you are constructing. It should look like the future you are dreaming” ~ Alice Walker

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Research Article

Sodium and potassium intake in South Africa: an evaluation of 24-hour urine collections in a white, black, and Indian population



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Sodium and potassium intake in South Africa: an evaluation of 24-hour urine collections in a White, Black and Indian population

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Abstract:

Limited number of studies on salt intake studies has been conducted in South Africans. The present study established the sodium and potassium excretion (24-hour urine collection) of three different South African populations. In total, 692 successful 24-hour urine collections were analyzed for sodium, potassium and iodine levels. The median sodium and potassium excretion was 122.9 and 33.5mmol/day, respectively and the median calculated salt intake was 7.2g/day. The majority (92.8%) of the population did not meet the recommended potassium intake per day and 65.6% consumed more than 6g of salt per day. Potassium excretion showed a linear relationship with calculated salt intake (p-trend ≤ 0.001). The median sodium-to-potassium ratio was 3.5. These findings support the South African government's sodium reduction legislation, as well as global initiatives. More consideration should be given to promoting the intake of potassium-rich foods, as this may have a greater public health impact than focusing only on dietary sodium reduction.

Keywords: Salt; South Africa; Sodium; Potassium; 24-hour urine; Hypertension

Introduction:

It is widely reported that cardiovascular disease (CVD), and specifically hypertension, contributes significantly to the disease burden, not only globally but also in sub-Saharan Africa [1; 2; 3]. The modification of lifestyle behaviors, including dietary salt intake, is currently an area of profound interest.

In a review by He and MacGregor [4] it was pointed out that animal studies [5; 6], human genetic studies [7; 8], epidemiological studies [9; 10; 11; 12], population-based intervention studies [13; 14] and treatment studies [15; 16] all indicate a relationship between high sodium (salt) consumption and the risk of high blood pressure. The role of low potassium intake in the development of high blood pressure is also essential since epidemiologic observational studies have concluded that potassium deficiency increases the negative impact of a high sodium (salt) intake on the development of high blood pressure [17; 18; 19]. Simultaneously meeting the recommended intake of both sodium and potassium poses a major nutritional challenge. The World Health Organization (WHO) recommends a sodium:potassium ratio of 1:1 (86mmol/day:90mmol/day) (Na:K) [20].

According to the WHO, the average salt intake per person in most countries is too high, usually being between 9 and 12g/day [21]. Although a limited number of studies have been conducted in the South African population, it has been estimated that the average South African consumes between 6 and 11g of salt per day [22]. These studies were all conducted at least 10 years ago, but with rapid urbanization the dietary environment has changed. Because of the high prevalence of hypertension in South Africa [1; 2; 3], the Department of Health has implemented a nationwide sodium reduction strategy enforcing mandatory reduction in the sodium content of certain processed foods, which comes into effect in June 2016 [23]. For monitoring, it is not only the sodium excretion data that are needed, but also pre-regulation iodine intake levels. Because South Africa has a mandatory national salt iodization programme, there are concerns that the reduction of salt in foods could interfere with the purpose of the iodization programme.

The purpose of this paper is to establish the current 24-hour sodium (as a marker of salt intake) and potassium excretion, of three different South African populations from different geographical regions. This will set a comparative benchmark for future investigations post-legislation to establish the effectiveness of the policy of sodium reduction.

Experimental methods:

Study participants

We obtained data from three ongoing studies, two based in the North West province and one in KwaZulu-Natal, South Africa. Relevant data for the different studies were collected in the period from 2013 to 2015. This study was cross-sectional in nature.

We obtained data firstly from the baseline sample of the *African **P**rospective study on the **E**arly **D**etection and **I**dentification of **C**ardiovascular disease and hyper**T**ension* (African-PREDICT), which is a longitudinal study that commenced in 2013 and is expected to continue for at least 10 years. The participants were comprised of apparently healthy black and white men and women (aged 20-30 years) who were normotensive, had no known CVD and were not taking any blood pressure medication. The detailed inclusion criteria are summarized in Thompson *et al* [24]. To date we have collected 24-hour urine samples from 509 participants.

Secondly, we collected 24-hour urine samples from the Thusa-Bothle study. We randomly selected apparently healthy black women aged between 35 and 65 years from the urban community of Ikageng in the North West province of South Africa. Another inclusion criteria was also that the women could have had hypertension, but the person must have received antihypertensive treatment. Women with any other diagnosed acute- or non-communicable chronic diseases were excluded. We successfully collected 24-hour urine samples from 73 women.

Lastly, data were collected from an urban area of Umkomaas in the KwaZulu-Natal province, South Africa. The women were also healthy with no diagnosed chronic diseases including hypertension. Successful 24-hour urine samples were collected from 111 Indian women between the ages of 18 and 50 years.

In total, 692 complete 24-hour urine samples were collected. All the studies included were conducted according to the guidelines laid down in the Declaration of Helsinki and all the procedures involving human participants were approved by the various ethics committees [NWU-0001-12-A1, NWU-00060-14-A1 and IREC 035/14]. Written informed consent was obtained from each of the participants. The three studies to determine sodium and potassium intake were also ethically approved [NWU-00085-15-S1].

24-hour urine collection

Trained field staff members explained the collection protocol of the 24-hour urine sample and provided all the equipment according to WHO standards [25]. Instructions were given to collect a 24-hour urine sample on a day that was convenient for the participant, which was noted. The “first-pass urine” was discarded and all urine passed thereafter was collected in the container provided, including the first urine of the following morning. The participants recorded the start and finish times of the collection period.

Urinary sodium, potassium and chloride were measured by means of ion-selective electrode potentiometry on the Cobas Integra® 400 plus (Roche, Basel, Switzerland) and creatinine concentrations were measured using the Creatinine Jaffé Gen.2 reagent (Roche, Basel, Switzerland). Urinary iodine concentration was determined using the Pino modification of the

Sandell-Kolthoff reaction with spectrophotometric detection [26]. We calculated sodium and potassium excretion as follows:

Multiplying the sodium, potassium and creatinine concentrations (mmol/l) by the total volume of urine (in liters) resulted in the sodium, potassium and creatinine in mmol/day. Salt was calculated by multiplying the mmol sodium by 58.9 (combined molecular weight of sodium and chloride).

To check for completeness of the 24-hour urine samples, the following cut-off points were used: volume of the 24-hour urine collections <500 ml and urinary creatinine <4.0 mmol/day for women or <6.0 mmol/day for men [27].

Blood pressure and anthropometric measurements

We used standard methodology to measure blood pressure, height, weight and waist circumference in the African-PREDICT study [24]. Blood pressure of the Black and Indian women was measured on a semi-automatic blood pressure device (M3W-HEM7202, OMRON Healthcare, Kyoto, Japan), respectively, using the participants' right arms after a 5-minute rest in the sitting position with legs uncrossed. Readings were done in duplicate with a 3-minute interval between the two readings. The blood pressure device used in the African-PREDICT study (DINAMAP, GE Healthcare, Buckinghamshire, UK) [28; 29] and the Omron device (M3W-HEM7202, OMRON Healthcare, Kyoto, Japan) [30] used in the other two studies are both validated. Trained field staff members with experience in blood pressure measurements, conducted the blood pressure measurements. Appropriate cuff sizes were used for all participants and the arm circumferences printed on the cuffs fitted the standard guideline for the actual bladders in the cuffs. Both of the blood pressure devices used are validated and in all three studies, the blood pressure measurements were reasonably close together with the average difference between systolic blood pressure readings being between 3 and 5 mmHg and diastolic blood pressure between 3.5 and 4 mmHg (for the same individual). Therefore the same device reads more or less the same blood pressure for the same individual.

Body mass index (BMI) was calculated as weight (kg)/height (m)². The participants' weight was measured to the nearest 0.01kg (in duplicate) with a digital scale (Seca, Hamburg, Germany) and height to the nearest 0.1cm using a stadiometer (Seca 264, Hamburg, Germany). The waist circumference of both the Black and Indian women was measured in triplicate to the nearest 0.1cm at the midpoint between the lowest rib and the top of the iliac crest, using a steel tape (Lufkin, Apex, NC, USA).

Statistical analysis

We used IBM SPSS version 23 (SAGE publications Ltd, London, UK) for statistical analyses. Normality was established by using the Shapiro-Wilk test, examining the histogram and Q-Q plot for each variable. Data are reported as mean and standard deviation (SD) or median and interquartile ranges (25-75th percentile), depending on the normality. The population was stratified according to the different studies, ethnicity (four groups) and gender. Parametric and non-parametric ANOVAs were performed to determine the differences between the population groups (within the different studies) and a Bonferroni post-hoc test to determine where the differences were. An independent T-test and the Mann-Whitney U test were used to determine difference between genders. We plotted age, BMI and potassium excretion against calculated salt intake cut-offs ($\leq 4\text{g/d}$; $4.1\text{-}5.9\text{g/d}$; $6\text{-}9.9\text{g/d}$; $\geq 10\text{g/d}$) for the different study populations. The Jonckheere Trend test was used to calculate the p-trend for each of these plots.

To illustrate the percentage of the population within recommended sodium ($<86\text{mmol/day}$ OR 2000mg/day) and potassium ($>90\text{mmol/day}$ OR 4300mg/day) intakes, pie charts are presented. A p-value of <0.05 was considered statistically significant.

Results:

From 1022 participants, a total of 692 successful 24-hour urine sample collections (based on the cut-offs for completeness of 24-hour urine sample) were included for final analysis. The population's characteristics, as well as results from the 24-hour urine collections, are summarized in Table 1. Sodium excretion was significantly ($p<0.001$) lower in the older Indian women than in their Black counterparts. Whites had the highest potassium excretion ($p=0.001$). The median sodium and potassium excretion of the populations were 122.9mmol/day and 33.5mmol/day , respectively. Iodine levels differed significantly between the ethnic groups and the median of the populations was $152.6\mu\text{g/L}$. The Indian women had the lowest ($p<0.001$) calculated salt intake, the median for this population being 7.1g/day . Men had higher sodium ($p<0.001$) and potassium ($p<0.001$) excretions and calculated salt intake than women, except for iodine, which was significantly higher ($p<0.001$) in the women. Women had significantly ($p<0.001$) higher BMI's than the men. The women from the ThusaBothle study, had higher ($p<0.001$) blood pressure values than the younger black women from the African-PREDICT study as well as the Indian women ($p<0.001$).

Table 1: Demographic and 24-hour excretion data of the study population

	African-PREDICT study		Thusa-Bothle study	KwaZulu-Natal study	Total		
	White (n=277)	Black (n=234)	Black (n=70)	Indian (n=111)	Men (n=220)	Women (n=472)	All (n=692)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Age (years)	25.5 ±2.8	24.6±3.2	52.7±8.2	39.8±11.5	25.1±3.0	32.7±12.4	30.3±11.0
BW (kg)	76.7±17.9	67.0±15.4	78.1±19.2	68.2±14.6	76.5±18.3	70.2±16.6	72.2±17.4
BH (cm)	172.7±8.3	163.4±8.3	157.2±6.0	156.6±5.6	174.8±7.6	161.0±7.9	165.4±10.1
BMI (kg/m ²)	25.6±5.2	25.2±6.3	31.7±7.7	27.8±5.6	24.9±5.1	27.2±6.6	26.4±6.2
SBP (mmHg)	117.6±12.3	119.5±11.7	139.7±20.4	124.7±19.2	125.0±10.7	120.1±17.5	121.6±15.8
DBP (mmHg)	77.2±7.6	79.5±7.8	85.6±11.7	82.1±11.8	80.2±7.6	79.3±9.9	79.6±9.3
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
24 h urine vol. (ml)	1205.6 (857.0 - 1657.0)	1210.1 (857.0-1757.0)	1290.8 (978.5-1688.6)	851.2 (631.9-1316.9)	1357.0 (895.5-1757.0)	1057.0 (742.5-1557.0)	1145.3 (757.0-1654.2)
Na excr. (mmol/day)	133.1 (93.5 - 193.8)	132.4 (92.8-192.2)	135.1 (76.3-212.9)	101.7 (72.1-143.2)	143.1 (102.1-212.2)	112.7 (81.7-164.3)	122.9 (87.8-180.2)
K excr. (mmol/day)	45.3 (31.3-65.3)	37.8 (24.8-59.5)	31.8 (18.9-49.1)	28.9 (18.6-35.6)	48.7 (30.6-68.3)	33.9 (23.9-51.6)	37.6 (24.8-56.7)
Cr excr. (mmol/day)	11.1 (7.5-15.6)	10.2 (7.7-13.5)	12.9 (8.4-19.0)	7.1 (5.8-9.9)	13.7 (9.1-17.4)	8.5 (6.4-11.2)	9.7 (7.0-13.9)
Iodine (µg/L)	135.0 (85.1-193.0)	146.7 (95.1-214.3)	-	253.5 (163.6-372.5)	142.4 (94.5-208.4)	158.8 (99.9-257.6)	152.6 (97.5-233.0)
Na:K ratio *	3.1 (2.2-3.9)	3.6 (2.5-5.0)	4.0 (3.2-5.5)	3.7 (2.9-4.7)	3.3 (2.3-4.7)	3.5 (2.6-4.6)	3.5 (2.5-4.6)
NaCl (g/day)	7.7 (5.4-11.1)	7.6 (5.3-11.1)	7.8 (4.4-12.2)	5.8 (4.1-8.2)	8.2 (5.9-12.2)	6.5 (4.7-9.4)	7.1 (5.0-10.4)

n, number of individuals; SD, standard deviation; BW, body weight; BH, body height; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; IQR, interquartile range (25th - 75th); Na, sodium; excr., excretion; K, potassium; Cr, creatinine; NaCl, sodium chloride (salt); *, ratio of sodium (mmol/day) to potassium (mmol/day)

No significant differences were found between the four salt categories in terms of age and BMI (Figure 1). Potassium excretion had a linear relationship with calculated salt intake and differed between the categories (p for trend ≤ 0.001).

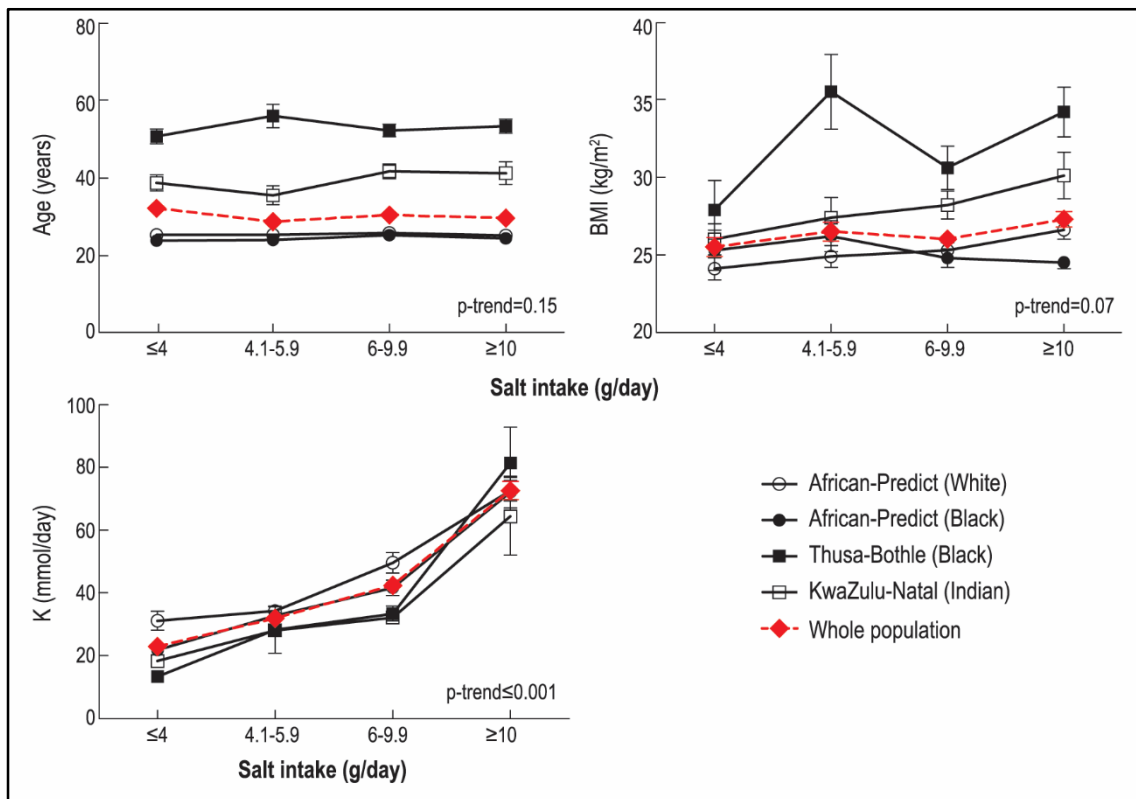


Figure 1: Age, BMI and potassium excretion according to salt categories

BMI, body mass index; K, potassium. Non-parametric ANOVA was conducted to determine the differences between the calculated salt intake (≤ 4 g/d; 4.1-5.9g/d; 6-9.9g/d; ≥ 10 g/d) groups and age, BMI and potassium excretion. The Jonckheere Trend test was used to calculate the p-trend for these plots. A p-trend value of < 0.05 was considered statistically significant.

Within this population, 92.8% did not meet the recommended potassium intake of 90mmol per day (Figure 2). The median of the individuals above and below the recommended potassium intake was 130.5mmol/day and 39.5mmol/day, respectively. The median sodium-to-potassium ratio was 3.5, which is three times the recommended ratio.

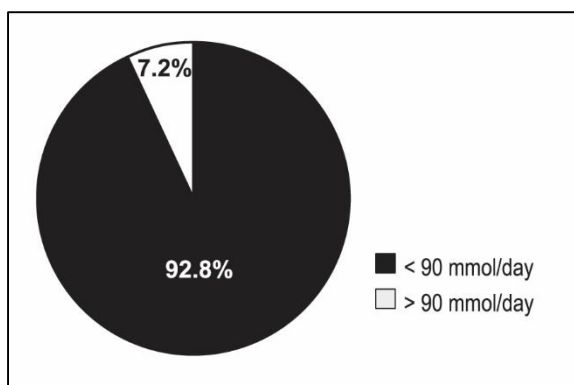


Figure 2: Percentage of the population reaching the recommended potassium intake per day

Figure 3 and Table 2 represent the proportion of the population which falls in the different calculated salt intake categories. The majority (65.6%) consumed more than 6g of salt per day, while 15.6% consume less or equal than 4g/day. The median of the individuals in the lowest ($\leq 4\text{g/day}$) and highest ($\geq 10\text{g/day}$) category is 2.8g and 15.6g of salt per day, respectively.

Table 2: Percentage of the population in different salt intake and potassium excretion categories

Study (Ethnicity)	Salt intake per day				Potassium excretion	
	$\leq 4\text{g/day}$ (%)	4.1-5.9g/day (%)	6-9.9g/day (%)	$\geq 10\text{g/day}$ (%)	<90mmol/day (%)	>90mmol/day (%)
African predict (White)	13.4	17.5	35.3	33.8	92.7	7.2
African predict (Black)	12.6	20.2	36.8	30.5	91.7	8.3
Thusa-Bothle (Black)	23.2	10.1	30.4	36.2	87.1	12.9
KwaZulu-Natal (Indian)	23.3	27.2	35.0	14.6	98.1	1.9
Whole population	15.6	18.9	35.7	29.9	92.8	7.2

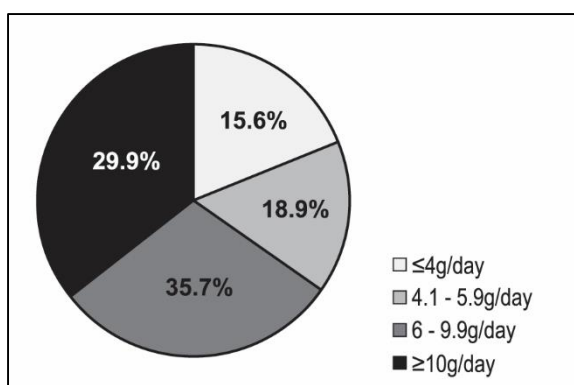


Figure 3: Percentage of the population in the different salt categories

In all the study and ethnicity groups, the distribution looked similar to that of the whole population in terms of calculated salt intake and potassium excretion (Table 2). Most of the

Black, White and Indian population consumed between 6 and 9.9g of salt per day. A majority of the older Black (36.2%) women and a minority of the Indian women (14.6%) consumed more or equal than 10g of salt per day, compared with the other salt categories.

Discussion:

We found that 77% of the South African population consumes >5 grams of salt/day, which is more than the WHO's recommendation. This includes Black, White, and Indian populations from different gender and ethnic groups. What is perhaps of greater importance is that, as our study highlights, only 7% adhered to the required potassium intake of 90mmol/day, which may be one of the main reasons we observe such high numbers of hypertension cases in South Africa, as a diet deficient in potassium increases the negative impact that high sodium intake has on the development of hypertension [17].

A recent systematic analysis of global, regional and national salt intakes reported that, overall, the mean sodium intake in adults was 9.9g of salt per day (calculated as 171.7mmol/day sodium), which is higher than the WHO's recommended 5g/day (86mmol/day) [21]. The Asian regions reported the highest intakes, with Central Asia having salt intakes of 13.8g/day (239.6mmol/day sodium). Intakes of 10.5g/day (181.7mmol/day sodium) and 9.8g/day (170.4mmol/day sodium) were reported for Eastern Europe and North Africa, respectively [31]. This analysis also reported a mean salt intake of 6.2g/day (107.8mmol/day sodium) within the South African populations included in this study in 2010. Previous studies conducted on normotensive individuals in South Africa reported mean salt intakes (measured by 24-hour urine collection) of 8.6g/day (146.8mmol/day sodium) (Johannesburg, 1982, n=105) [32] and 8.7g/day (148.6mmol/day sodium) (Cape Town, 2002, n=96) [33]. The median sodium excretion of the current study is measured as 122mmol/day (7.1g/day salt). This is more than the recommended intake of 86mmol/day (5g/day salt) and could indicate that the sodium consumption of South Africans may have started to decline, but it is still well above the recommended intake. This is further established by looking at the 25th and 75th percentiles of the population which, in terms of sodium excretion, is 87.8 – 180.2mmol/day. The lowest percentile of the population has a sodium excretion of just above the recommended intake, and the highest percentile has twice the recommended sodium excretion value. Figure 3 illustrates this more clearly, indicating that the majority (35.7%) of the population consumes between 6 and 9.9g of salt per day, and that 29.9% consumes more than 10g of salt per day, which is of even greater concern. Only 15.6% consumes less than 4g of salt per day, therefore supporting the sodium reduction regulation. In the specific studies and ethnicities, older Black women from the Thusa-Bothle study had the highest sodium excretion and Indian women had the lowest. In the present study, young men had significantly higher sodium levels than women (who were older) (143.1 vs 112.7mmol/day),

probably because of their generally higher food intake and different energy requirements [34; 35].

A linear increase between BMI and salt intake, although not significant, is observed, as has been previously reported [35; 36]. A possible explanation is that obese and overweight individuals tend to have a great intake of food calories and follow a more unhealthy diet high in processed foods (generally high in salt). It is well reported that South African women have higher BMI's than men, therefore our observation is expected [37; 38].

The higher blood pressure values observed in the older ThusaBothle women were previously reported in a similar South African population, where the authors stated blood pressure measurements ranging from 135-138/87-90mmHg in the women [39]. This is therefore not an unexpected observation within the ThusaBothle women.

The median potassium excretion in this population is 37.6mmol/day, which is lower than the excretion found in other South African studies done on normotensive individuals (55.2 and 45.1mmol/day) [32; 33]. The recommended intake by the WHO is at least 90mmol/day. As previously mentioned, almost 93% of this South African population does not reach the recommended potassium intake. Although the task is very challenging, public health efforts should also be directed towards increasing potassium intakes together with decreasing the sodium intake in the population, through educational campaigns focusing on diets rich in fruits and vegetables and limiting processed foods high in sodium. We found a significant linear relationship (p -trend ≥ 0.001) between potassium excretion and salt intake. A possible explanation for this could be that the individual that consumes high amounts of salt (in the form of processed foods) generally consumes more food, therefore might have higher intakes of potassium rich food. The challenge, therefore, is to decrease the sodium intake while increasing the potassium intake even further, *i.e.* making sure the population reaches the recommended Na:K ratio. The median Na:K in this study is 3.5, which is more than three times the recommended 1:1 by the WHO. It is important to note that not a single person from this population reached their Na:K ratio. This further supports the fact that more value should be placed on reaching the recommended potassium intake in this population together with the reduction in sodium intake. In a review article by Adrogué and Madias [18], the authors summarize the pathogenesis of both sodium and potassium on hypertension. This review provides strong evidence of a number of population studies [40; 41; 42], which reported an inverse relationship of potassium with blood pressure. Results from the INTERSALT study also reported an inverse relationship between urinary Na:K ratio and blood pressure, and further reported that the ratio had a stronger statistical relationship with blood pressure than either sodium or potassium alone [43].

As mentioned, it is important to monitor the iodine levels of the population pre-legislation. Iodine levels in the lowest salt category ($\leq 4\text{g/day}$) still showed compliance to the recommended intake

of iodine (152.6ug/L). Charlton and colleagues [44] reported that the iodine levels of consumers within the recommended less than 5g of salt per day were sufficient and within the recommended intake, and that the median iodine level did not differ across the salt intake categories, as was also the case in the current study. It is also not mandatory to use iodized salt in the manufacturing of processed foods as well as salt packed in bags of at least 20kg, therefore, the reduction of sodium in processed foods should not have an effect on the iodine levels.

There are a few limitations in the current study that should be noted. Firstly, it would have been better to measure 24-hour sodium excretion in a large, nationally representative population sample, but despite limitations in funding to undertake such a study, the sampling frame used in the present study does capture both sexes, different age ranges and ethnicities from different geographic regions of South Africa. Future sodium excretion data within these regional areas will be ideal for evaluating post-legislation salt intakes and the impact on public health. Only one 24-hour urine collection was taken from each participant. The ideal number of 24-hour urine collections depends on whether or not sodium is being estimated at individual or population level. As many as fourteen 24-hour urine collections may be needed for the accurate estimation of sodium intake at individual level because of the day-to-day variation [45; 46]. In a more recent balance study conducted by Lerchl and co-workers [47] they conclude that single 24-hour urine collections at intakes ranging from 6 to 12 g salt per day were not suitable to detect a 3-g difference in individual salt intake and that repeated measurements of 24-hour urine collections will improve precision with regards to the sodium intake. By including a sufficient number of people, a single 24-hour urine collection should be adequate in estimating the mean sodium excretion for a population, with little error of the mean [48]. However, more than one 24-hour collection would give a more accurate representation of the sodium excretion of the population. Future research should also include balance studies in specifically this population group with regards to sodium and potassium excretion and the accuracy thereof. In a recent article from Bochud and co-workers (2009) [49] looking at the differences in the segmental handling of sodium along the proximal and distal nephron in black South Africans and white Belgians, they concluded that there are significant differences and that more research should be conducted on the accuracy to estimate sodium intake through 24-hour urine collections. Even though there is evidence suggesting that 24-hour urine collections has many limitations and needs further research. However, it is still regarded as the gold standard and until a more accurate and “variation-free” methods is established, this is the method that is recommended by the World Health Organization to estimate population sodium intake. Monitoring of sodium intake in a population is crucial and alternative methods (to the collection of 24-hour urine collection) have been investigated. One of these methods includes the collection of an “overnight” urine sample. This method is easier to collect, and according to Luft *et al.* provided

accurate results in terms of the sodium intake of a population. A home chloride strip can be used to estimate the urinary sodium excretion, which makes it a quick and easy alternative to the 24-hour urine collection [50]. However, this need to be tested in the South African population in future studies before suggesting it as an alternative to 24-hour urine collections.

Possible reasons for not observing strong correlations in this population could be because of the population being apparently healthy and the population sample relatively small. As mentioned, the study design was never intended to establish these correlations.

Longitudinal data is needed to investigate the role of age on the relationship between sodium and blood pressure. Future follow-up of the African-PREDICT participants would shed some light on the role of age on the relationship between sodium intake and blood pressure. Another limitation of the current study is that no data was collected on the climate in the different areas, which could possibly have an effect on the excretion of sodium and potassium. Future studies should also be conducted that does not truncate the blood pressure values of the population, therefore including hypertensive and normotensive individuals.

The strength of this study lies in the providing of valuable and essential information regarding the current sodium and potassium intake in a sample of South Africans from different age groups and ethnicities. This information contributes not only to the much-needed local database, but also to the global body of knowledge and to a better understanding of the sodium and potassium consumption patterns around the world. More data is crucial in establishing effectiveness of the sodium reduction policy for future investigation.

Conclusion:

The results presented in this study support the national sodium reduction intake strategy, including the regulation of the sodium content of 13 categories of foodstuffs, due to take effect in June 2016. The majority of the population studied consumes more than the recommended 5g of salt per day. However, more consideration should be given to promoting an increase in potassium intake in South Africa. This, together with the sodium reduction regulation, may have a greater impact on public health than only focusing on sodium reduction.

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Authorship:

BS: Formulated the research questions, collected and analyzed all data used in this article, assisted with the statistical analysis of data and wrote the manuscript

AS: Critically reviewed manuscript, assisted in formulating the research question as well as the statistical analysis. Designed the African-PREDICT study

MC: Conducted all statistical analysis for the manuscript

KS: Formulated the research question, critically reviewed the manuscript

EWV: Formulated the research question, conceptualized the article, critically reviewed the manuscript

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CHAPTER FOUR: MANUSCRIPT TWO

“All that man achieves and all that he fails to achieve is the direct result of his own thoughts” ~ James Allen



Manuscript two will be submitted to Public Health Nutrition

JOURNAL DETAILS	
Title:	Public Health Nutrition
Impact factor:	2.433
Publisher:	Cambridge University Press
Aim and scope:	<ul style="list-style-type: none"> • Address monitoring and surveillance of nutritional status and nutritional environments in communities or populations at risk • Identify and analyse behavioral, sociocultural, economic, political, and environmental determinants of nutrition-related public health • Develop methodology needed for assessment and monitoring • Inform efforts to improve communication of nutrition-related information • Build workforce capacity for effective public health nutrition action • Evaluate or discuss the effectiveness of food and nutrition policies • Describe the development, implementation, and evaluation of innovative interventions and programs to address nutrition-related problems • Relate diet and nutrition to sustainability of the environment and food systems
Author guidelines:	https://www.cambridge.org/core/journals/public-health-nutrition

Monitoring the South African population's salt intake: spot urine *versus* 24-hour urine

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Shortened version of the title: Monitoring of sodium intake in South Africa

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Conflict of interest: none.

Authorship:

BS: Formulated the research questions, collected and analysed all data used in this article, assisted with the statistical analysis of data and wrote the manuscript

AS: Critically reviewed manuscript, assisted in formulating the research question as well as the statistical analysis. Designed the African-PREDICT study

MC: Conducted all statistical analysis for the manuscript

KS: Critically reviewed manuscript

EWV: Formulated the research question, conceptualised the article, critically reviewed manuscript

Ethical standards: All the included studies were conducted according to the guidelines laid down in the Declaration of Helsinki and all the procedures involving human participants were approved by the various ethics committees [NWU-0001-12-A1, NWU-00060-14-A1 and IREC 035/14]. Written informed consent was obtained from each of the participants. Additional approval from the Health Research Ethics Committee was obtained to perform analyses on sodium and potassium intake [NWU-00085-15-S1].

Abstract:

Objective: This study set out to determine whether morning spot urine samples can be used to monitor sodium (and potassium) intake levels in South Africa, instead of the “gold standard” 24-hour urine sample.

Design: Participants collected one 24-hour and one spot urine sample for sodium and potassium analysis after which estimations using three different formulas (Kawasaki, Tanaka and INTERSALT) were calculated.

Setting: Between 2013 and 2015, urine samples were collected from different population groups in South Africa

Subjects: A total of 681 spot and 24-hour urine sample were collected from a white (n=259), black (n=315) and Indian (n=107) population, mostly women.

Results: The Kawasaki and the Tanaka formula showed significantly higher ($p \leq 0.001$) estimated sodium values than the measured 24-hour excretion in the whole population (5677.79mg/d and 4235.05mg/d vs. 3279.19mg/d). The INTERSALT formula did not differ from the measured 24-hour excretion, for the whole population. The Kawasaki formula seems to overestimate sodium excretion in all the sub-groups tested and also showed the highest degree of bias (-2242mg/d, 95% CI: -10659 – 6175), compared to the INTERSALT, who had the lowest (161mg/d, -4038 – 4360).

Conclusion: Estimations of sodium excretion by the three formulas should be used with caution when reporting on sodium intake levels. More research is needed to validate and develop a specific formula for the South African context with its different population groups. The WHO's recommendation of using the 24-hour urine collection until more studies are carried out is still supported.

Keywords: spot urine; 24-hour urine; sodium; potassium; salt; South Africa

Introduction:

Hypertension is an important contributor to the burden of disease in South Africa. There is convincing evidence that a high sodium intake contributes to the development of hypertension ^(1,2). Accurate estimation of population sodium intake is crucial for monitoring trends in sodium intake. Estimating sodium intake by means of dietary questionnaires does not accurately reflect actual sodium intake ⁽³⁻⁵⁾. The amount of sodium excreted in the urine is, however, a more acceptable method.

Twenty-four hours is the minimum time required to characterise the pattern of urinary excretion for a given individual ⁽⁶⁾. The 24-hour urine collection method (one or more) is considered to be the 'gold standard' in determining sodium intake in individuals as well as in population groups ⁽⁷⁾. However, alternative methods have been proposed due to the high methodological burden of a 24-hour urine collection in large population based studies. As reported in a recent systematic review, initiatives for finding a replacement for 24-hour urinary collection, that does not compromise data accuracy, are high on the agenda ⁽⁸⁾.

A paper by Mente *et al.* in 2014 indicated that spot urine samples from the Prospective Urban and Rural Epidemiological (PURE) study may be representative of the sodium intake of the group despite the fluctuations in values for individuals⁽⁹⁾. This was also shown earlier by Tanaka *et al.* ⁽¹⁰⁾. However, this methodology was greatly criticised ^(11,12) when spot urine samples were used by the PURE-authors to indicate the potentially harmful effects of very low salt intake on cardiovascular health and mortality ^(2,13).

As spot urine samples are affordable and easy to obtain, they would be valuable in monitoring sodium intake particularly in resource-poor settings or where 24-hour urine collections are not deemed feasible. Validity is also needed in terms of estimating a population's sodium intake above a specific threshold, *i.e.* classifying what percentage of the population is above and below the recommended 2000mg of sodium or 5g of salt per day ⁽¹⁴⁾. However, the validity of spot urine samples is still inconclusive ^(6,8) and, specific ethnic sub-group analyses are also needed to determine whether certain equations are better suited for a specific population, particularly in black populations known for renal sodium retention ⁽¹⁵⁾. Recently, South Africa developed a national strategy to reduce the sodium intake of the population ⁽¹⁶⁾ and has implemented a national sodium reduction regulation (R214) to regulate the sodium content in certain processed foods ⁽¹⁷⁾. Therefore, reliable, ongoing population-wide data on sodium intake are necessary to monitor the progress and the effectiveness of public health efforts to curb the high hypertension rates.

For this reason, the aim of this paper is to compare single morning spot urine samples with 24-hour urine samples in three ethnic populations in South Africa to assess whether spot urine collections can be used to monitor sodium intake levels in this country.

Methods:

Participants:

Participants were recruited from three on-going studies *i.e.* two in the North West province and one in KwaZulu-Natal and included individuals of different age categories, ethnicity and gender. All relevant data were collected between 2013 and 2015. In all the studies the data were cross-sectional in nature. Details concerning the studies are summarised elsewhere (Swanepoel et al., 2016).

Firstly, we collected data from the *African PRospective study on the Early Detection and Identification of Cardiovascular disease and hyperTension* (African-PREDICT) study. The participants included black and white men and women (aged between 20 and 30 years) who were apparently healthy and normotensive, and not using chronic medication.

The Thusa-Bothle study included older black women (35 – 65 years) that were apparently healthy, from an urban community in the North West province of South Africa. Lastly, data were collected in an urban area in the KwaZulu-Natal province of South Africa. The study included apparently healthy Indian women between the ages of 18 and 50 years.

Urine collection:

Participants from all three studies were given the same collection instructions by a trained field researcher. Each participant was provided with the necessary equipment (collection kit) to collect both a 24-hour urine and a spot urine sample. On a day that was convenient for the participant, they were instructed to discard the “first pass urine” on the morning of the start of their collection and collect all the urine passed thereafter, ending with the first urine of the following morning. This first urine collection of the following morning was collected and divided into a spot urine sample (collected in a separate container), and the rest of the urine, which was added to the larger container (with the rest of the 24-hour urine). The start and end times were also recorded. After an aliquot was taken from the spot urine sample, the remaining urine in the spot urine sample was also added to the large container before aliquoting of the 24-hour urine sample.

To check for completeness of the 24-hour urine samples, the following cut-off points were used: volume of the 24-hour urine collections >500 ml and urinary creatinine >4.0 mmol/day for women or >6.0 mmol/day for men ⁽¹⁹⁾.

Biochemical analysis, blood pressure and anthropometric measurements:

After careful aliquoting of the 24-hour and spot urine samples, the samples were stored at -20 degrees Celsius, until analysis. For 24-hour and spot urine samples, sodium, potassium and creatinine were measured as described in Swanepoel *et al.* ⁽¹⁸⁾.

The measurements of blood pressure, height and weight in the African-PREDICT study were performed using appropriate methods, and are described elsewhere ⁽²⁰⁾. Blood pressure of the Black and Indian women was measured on a semi-automatic blood pressure device (M3W-HEM7202, OMRON Healthcare, Kyoto, Japan) ⁽¹⁸⁾.

Body mass index (BMI) was calculated as weight (kg)/height (m)². The participants' weight was measured to the nearest 0.01kg (in duplicate) with a digital scale (Seca, Hamburg, Germany) and height to the nearest 0.1cm using a stadiometer (Seca 264, Hamburg, Germany). The waist circumference of both the Black and Indian women was measured in triplicate to the nearest 0.1cm at the midpoint between the lowest rib and the top of the iliac crest, using a steel tape (Lufkin, Apex, NC, USA).

Calculated formulas used:

Sodium and potassium from the 24-hour urine collections were converted from mmol/day to mg/day by multiplying by 23 and 39, respectively. Salt was calculated by multiplying the mmol sodium by 58.9 (combined molecular weight of sodium and chloride).

To estimate 24-hour urinary sodium from spot urine the following three formulas were used; *Kawasaki formula* ⁽²¹⁾: **Estimated 24-hour sodium (mmol/day):** $16.3 \times \sqrt{[\text{spot Na (mmol/L)} / (\text{spot Cr (mg/dl)} \times 10)]} \times [\text{predicted 24-h urinary Cr (mg/day)}]$;

where **predicted Cr (mg/day) for women** = $-4.72 \times \text{age (years)} + 8.58 \times \text{weight (kg)} + 5.09 \times \text{height (cm)} - 74.5$;

and for **men** = $-12.63 \times \text{age (years)} + 15.12 \times \text{weight (kg)} + 7.39 \times \text{height (cm)} - 79.9$

INTERSALT formula ⁽²²⁾: **Estimated 24-hour sodium for men (mg/day):** $23 \times (25.46 + [0.46 \times \text{spot Na (mmol/L)}] - [2.75 \times \text{spot Cr (mmol/L)}] - [0.13 \times \text{spot K (mmol/L)}] + [4.10 \times \text{BMI (kg/m}^2\text{)}] + [0.26 \times \text{age (years)}])$;

Estimated 24-hour sodium for women (mg/day): $23 \times (5.07 + [0.34 \times \text{spot Na (mmol/L)}] - [2.16 \times \text{spot Cr (mmol/L)}] - [0.09 \times \text{spot K (mmol/L)}] + [2.39 \times \text{BMI (kg/m}^2\text{)}] + [2.35 \times \text{age (years)}] - [0.03 \times \text{age}^2 \text{ (years)}])$;

Tanaka formula ⁽¹⁰⁾: **Estimated 24-hour sodium (mmol/day):** $21.98 \times \text{XNa}^{0.392}$; **Where XNa** = $[\text{spot Na (mmol/L)} / (\text{spot Cr (mg/dl)} \times 10)] \times [\text{predicted 24-h urinary Cr (mg/day)}]$; **Where predicted Cr** = $[-2.04 \times \text{age (years)}] + [14.89 \times \text{weight (kg)}] + [16.14 \times \text{height (cm)}] - 2244.45$.

To estimate 24-hour potassium excretion, the Kawasaki and Tanaka formulas were used. The INTERSALT formula is not designed to estimate potassium excretion, and was therefore not used.

Kawasaki formula (Kawasaki et al., 1993): **Estimated 24-hour potassium (mg/day):** $7.2 \times \sqrt{[\text{spot K (mmol/L)} / [\text{spot Cr (mg/dl)} \times 10] \times \text{predicted 24-h urinary Cr (mg/day)}]}$;

where **predicted Cr (mg/day) for women** = $-4.72 \times \text{age (years)} + 8.58 \times \text{weight (kg)} + 5.09 \times \text{height (cm)} - 74.5$;

and for **men** = $-12.63 \times \text{age (years)} + 15.12 \times \text{weight (kg)} + 7.39 \times \text{height (cm)} - 79.9$

Tanaka formula (Tanaka et al., 2002): **Estimated 24-hour potassium (mg/day):** $(7.59 \times \text{XK})^{0.431}$;

Where XNK = $[\text{spot K (mmol/L)} / (\text{spot Cr (mg/dl)} \times 10)] \times [\text{predicted 24-h urinary Cr (mg/day)}]$;

Where predicted Cr = $[-2.04 \times \text{age (years)}] + [14.89 \times \text{weight (kg)}] + [16.14 \times \text{height (cm)}] - 2244.45$.

Statistical analyses:

The population was stratified according to the different studies, ethnicity and gender. To analyse agreement between the measured sodium (and potassium) excretion (24-hour urine sample) and the estimated sodium (and potassium) excretion (spot urine samples, for all three formulas), Bland-Altman plots were used ⁽²³⁾. The degree of bias was also calculated with the 95% confidence interval. The bias of each individual is the measured sodium or potassium intake (24-hour urine sample) minus the predicted (using Kawasaki, Tanaka and INTERSALT formulas) sodium or potassium intake divided by the mean of the predicted and measured 24-h urinary sodium excretion. We further calculated the possibility of proportional bias by conducting a linear regression with the difference (between the measured and predicted sodium excretion) and the mean (between the predicted and measured sodium intake). The beta value of the regression should be as close to zero as possible with an insignificant p-value to indicate no proportional bias. Correlations between estimated sodium and potassium excretion from a spot urine sample (using the three different formulS) and the measured 24-hour urine sample were calculated using Interclass Correlation Coefficients (ICCs).

Sensitivity and specificity of the estimated sodium excretion (based on spot urine samples) to correctly classify the mean sodium intake of this population as above or below the WHO's recommended 2000mg of sodium per day was also assessed by using the following equations:

$$\text{Sensitivity} = \frac{\text{Sodium spot} > 2000\text{mg/day} \times \text{Sodium 24-hour} > 2000\text{mg/day}}{\text{Sodium}_{24\text{-hour}} > 2000\text{mg/day}}$$

$$\text{Specificity} = \frac{\text{Sodium spot} < 2000\text{mg/day} \times \text{Sodium 24-hour} < 2000\text{mg/day}}{\text{Sodium}_{24\text{-hour}} < 2000\text{mg/day}}$$

Results:

We collected 24-hour urine as well spot urine samples from 470, 104 and 107 participants from the African-PREDICT, ThusaBothle and KwaZulu Natal study, respectively. The basic characteristics of the three populations studied are summarised in Table 1. The average age and BMI of this population was 35.5years and 27.8kg/m². More women (476) than men (205) were included in this study. Further details of the characteristics of this population and the differences between sub-groups are described elsewhere ⁽¹⁸⁾.

Table 1: Characteristics of the population

	African-PREDICT study		Thusa-Bothle study		KwaZulu-Natal study		Total							
	White (n=259)		Black (n=211)		Black (n=104)		Indian (n=107)		Men (n=205)		Women (n=476)		All (n=681)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	25.5	2.9	24.5	3.2	50.2	9.0	40.2	11.6	25.0	3.1	38.6	13.9	35.5	13.6
Weight (kg)	76.4	18.0	66.1	14.9	76.0	21.8	68.7	14.8	73.4	18.3	72.7	19.2	72.9	19.0
Height(cm)	172.4	8.4	163.4	8.3	156.7	5.6	155.4	13.6	171.7	9.1	159.4	9.9	161.9	10.9
BMI (kg/m ²)	25.6	5.3	24.9	6.1	30.9	8.7	28.1	5.8	24.8	5.4	28.6	7.7	27.8	7.4
WC (cm)	82.0	14.0	77.4	11.9	87.9	15.2	91.8	14.2	81.4	13.5	85.6	15.2	84.8	14.9
SBP (mmHg)	117.6	12.4	119.3	11.7	135.5	17.7	123.4	19.9	122.5	11.4	126.4	18.8	125.6	17.6
DBP (mmHg)	77.2	7.7	79.4	7.7	83.2	11.2	81.8	12.2	79.5	7.9	80.9	10.7	80.6	10.2

n, number; SD, standard deviation; BW, body weight; BH, body height; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure

In Table 2 we compared sodium excretion obtained from 24-hour collections with estimated sodium values from spot samples, based on the three formulas described. The Kawasaki and the Tanaka formulas showed significantly higher ($p \leq 0.001$) estimated sodium values than the measured 24-hour excretion in the whole population (5677.79mg/d and 4235.05mg/d vs. 3279.19mg/d). In the younger white (3547.81mg/d vs 3352.27mg/d) and black individuals (3560.6mg/d vs 3417.57mg/d), the Tanaka formula did not differ from the 24-hour measurement. The INTERSALT formula also did not differ from the measured 24-hour excretion, for the whole population. In all the population groups, except for the Indian population (2683.08mg/d vs 3523.12mg/d), the INTERSALT formula underestimated the sodium excretion. The Kawasaki formula seems to overestimate sodium excretion in all the sub-groups tested and also showed the highest degree of bias (-2242mg/d, 95% CI: -10659 – 6175), whereas the INTERSALT, had the lowest (161mg/d, -4038 – 4360).

The beta values of the linear regression were above zero and significant in the INTERSALT formula, but not in the Kawasaki and Tanaka formulas. There were no significant and strong correlations (ICC) observed, except for the INTERSALT (0.2, 95%CI: 0.5 – 0.3) formula in the whole population.

Sensitivity and specificity analysis showed more or less the same pattern in all three formulas when estimating sodium excretion, with a high sensitivity (>90%) and a very low specificity (<10%).

Potassium excretion was estimated only by the Kawasaki and Tanaka formulas (Table 3). The Kawasaki overestimated the potassium excretion but was this not significant in the young White (1884.47mg/d vs. 1722.71mg/d) and Black (1865.17mg/d vs. 1632.59mg/d) population. The Tanaka underestimated the potassium value in all the population groups. The degree of bias was the lowest in the Kawasaki formula (-483mg/d, 95%CI: -4425 – 3458). There were also no significant correlations observed in either of the two formulas. Both sensitivity (8.11%) and specificity (7.35%) analysis showed low values when estimating potassium excretion with the Kawasaki formula, and showed 0.0% and 0.2% with the Tanaka formula, respectively.

Bland–Altman plots (Figure a) showed inconsistent sodium estimations across low and high levels of 24-hour sodium excretion. The mean difference of the Kawasaki and Tanaka formula is -2221mg/d and -836.8mg/d, respectively, with a wide limit of agreement. The INTERSALT formula overestimated 24-hour sodium excretion between 0 and 5000mg/d and underestimated sodium excretion of above 5000mg/d. For the 24-hour potassium excretion the Kawasaki formula both overestimated and underestimated the potassium intake and the Tanaka formula overestimated the potassium at high levels.

Table 2: Summary of the comparison between the different methods of estimated 24-hour sodium excretion vs. measured excretion

		24-h measured excretion	Kawasaki method	Tanaka method	INTERSALT method
Na excretion (mg/d) Mean (SD)	All	3279.19 (2077.00)	5677.79 (2936.41)#	4235.05 (1777.15)#	3140.32 (730.86)
	AP White	3352.27 (1762.0)	4551.75 (2026.56)#	3547.81 (3241.26)	2887.85 (742.43)*
	AP Black	3417.57 (1919.49)	4828.74 (2216.12)#	3560.60 (1216.75)	3047.35 (710.47)*
	TB Black	3477.39 (3308.26)	7485.42 (3256.53)#	5487.03 (1993.68)#	3254.33 (585.98)
	K Indian	2683.08 (1459.46)	6446.32 (3344.56)#	4754.03 (1926.46)#	3523.12 (714.73)#
Range of excretion		271.3 – 21568.6	1248.5 – 19795.6	1292.9 – 11226.9	868.1 – 5175.5
Degree of bias (mg/d) (95% CI)		Reference	-2242 (-10659–6175)\$	-837 (-6476–4802)\$	161 (-4038–4360)
Linear regression (95% CI)		Reference	0.11 (-0.04 – 0.06)	0.03 (-0.06 – -0.11)	0.48 (0.25 – 0.70)¥
Validation (ICC) – Na	All		0.03 (-0.14 – 0.18)	0.05 (-0.12–0.19)	0.20 (-0.50–0.31)β
	AP White		0.17 (-0.09 – 0.37)	0.14 (-0.14–0.34)	0.29 (0.06–0.46)
	AP Black	Reference	0.24 (-0.02 – 0.43)	0.12 (-0.08–0.39)	0.26 (0.03–0.44)
	TB Black		0.04 (-0.43 – 0.36)	0.06 (-0.40–0.37)	0.15 (-0.26–0.43)
	K Indian		-0.07 (-0.60 – 0.29)	-0.13 (-0.69–0.25)	0.03 (-0.48–0.35)
Sensitivity (%)		Reference	99.30	98.59	95.44
Specificity (%)		Reference	2.60	3.90	11.39

Na, sodium; AP, African-PREDICT; TB, Thusa-Bothle; KZN, KwaZulu Natal; ICC, intra class correlations

significantly higher than 24-h measured excretion

* significantly lower than 24-h measured excretion

\$ Greater bias than INTERSALT

β, p-value = 0.005

¥, significant (p≤0.001), indicating proportional bias

Table 3: Summary of the comparison between the different methods of estimated 24-hour potassium excretion vs measured excretion

		24-h measured excretion	Kawasaki method	Tanaka method
K excretion (mg/d)	Mean (SD)			
	All	1594.18 (1181.04)	2422.45 (2719.72)#	587.54 (478.69)*
	AP White	1722.71 (1117.72)	2355.28 (3362.51)#	562.84 (576.32)*
	AP Black	1632.59 (1037.17)	2290.24 (2765.96)#	527.09 (479.18)*
	TB Black	1502.40 (1521.71)	2450.87 (1009.57)#	635.04 (236.10)*
	KZN Indian	1271.14 (946.15)	2671.37 (2942.31)#	653.52 (517.18)*
Range of excretion		206.1 – 11341.55	418.9 – 36087.9	133.6 – 5809.6
Degree of bias (mg/d)		Reference	-782 (-6930 – 5366)	1039 (-1577 – 3657)†
				(95% CI)
Linear regression (95% CI)			-1.34 (-1.48 – -1.24) ¥	1.41 (1.30 – 1.53) ¥
Validation (ICC) – K	All		0.07 (-0.05 – 0.12)	0.08 (-0.09 – 0.22)
	AP White		0.06 (-0.24 – 0.29)	0.10 (-0.19 – 0.32)
	AP Black	Reference	0.00 (-0.33 – 0.26)	0.02 (-0.32 – 0.26)
	TB Black		0.20 (-0.20 – 0.46)	0.07 (-0.38 – 0.38)
	KZN Indian		-0.03 (-0.55 – 0.31)	-0.06 (-0.59 – 0.29)
Sensitivity (%)		Reference	8.11	0.00
Specificity (%)		Reference	7.35	0.2

K, potassium; AP, African-PREDICT; TB, Thusa-Bothle; KZN, KwaZulu Natal; ICC, intra class correlations

significantly higher than 24-h measured excretion

* significantly lower than 24-h measured excretion

† Greater bias than Kawasaki

¥, significant (p≤0.001), indicating proportional bias

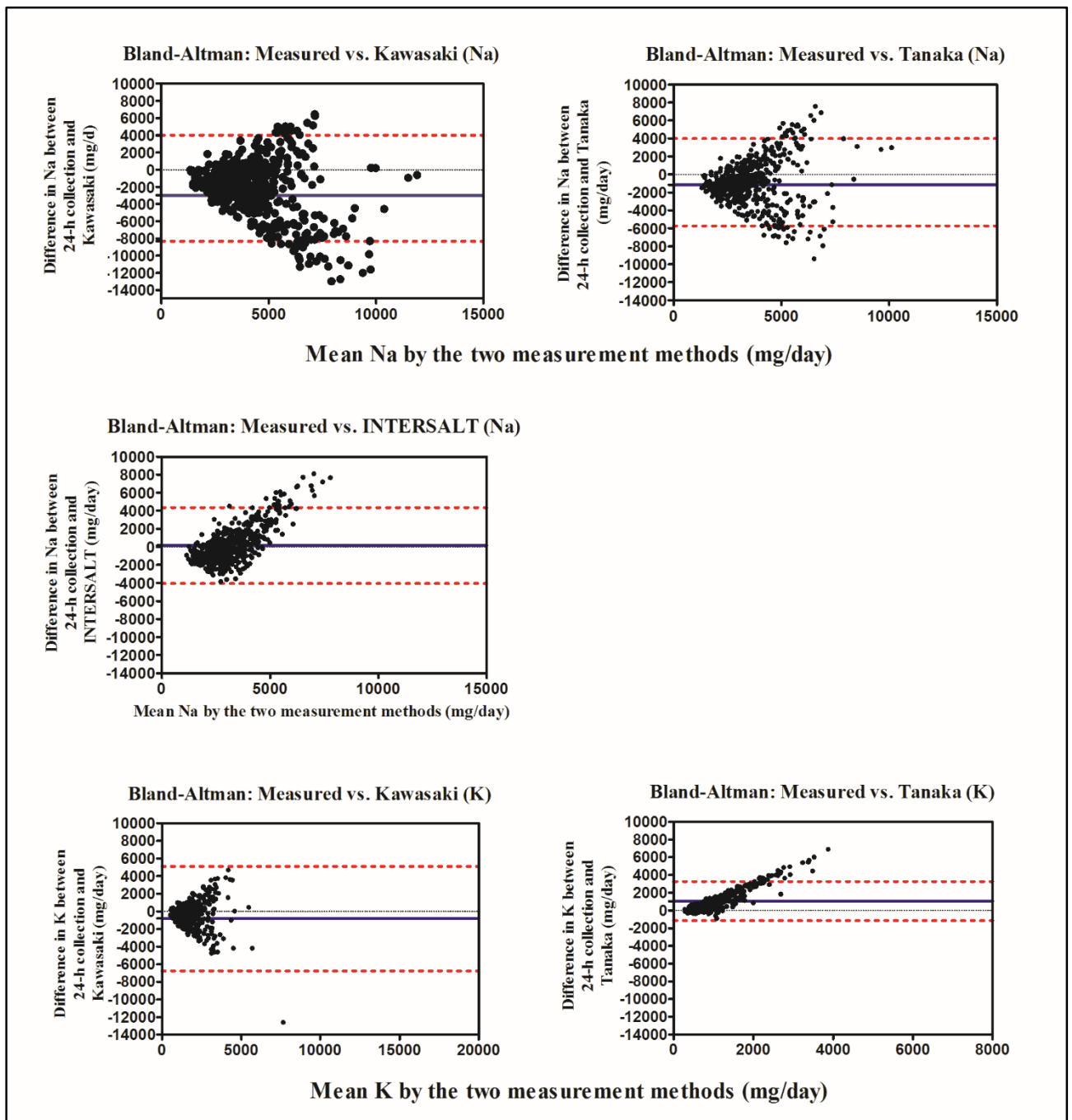


Figure 1: Bland-Altman plots comparing measured vs. estimated 24-hour sodium and potassium using the different formulas

The upper and lower limits of agreement are calculated as the mean difference $\pm 1.96 \times \text{SD}$ and are indicated by the dashed lines. The solid line represents the mean of the difference between the measured and predicted intake

Discussion:

This study set out to determine whether morning spot urine samples, instead of the “gold standard” 24-hour urine sample can be used to monitor sodium (and potassium) intake levels in South Africa.

Of the three prediction formulas, the INTERSALT provided the least biased information about group mean 24-hour sodium excretion in the population studies as a whole. The younger white and black groups, showed no difference between the Tanaka formula and the 24-hour sodium excretion but there was a significant underestimation when using the INTERSALT formula. The Kawasaki formula showed overestimation in the whole group as well as in each of the different population groups, but to a lesser extent in the younger black and white groups.

In terms of the correlations of the three formulas, the INTERSALT had a weak but significant correlation in the whole group. This formula also had the lowest degree of bias when compared with the Kawasaki and Tanaka formula. Kawasaki and co-workers ⁽²¹⁾ reported a correlation of 0.53 and Tanaka ⁽¹⁰⁾ and colleagues a correlation of 0.54 between the predicted and actual 24-hour excretion. Our study report much weaker correlations (Kawasaki = 0.03 and Tanaka = 0.05). The hypothesis, on which the Kawasaki and Tanaka formula is based, does not seem to relate to the South African population and could be a possible reason for not observing the same correlations. Creatinine values are highly influenced by weight (and BMI) and are used to form the hypothesis of these two formulas. The Kawasaki and Tanaka formulas were developed and tested in a Japanese population with a mean BMI (in women) of 21.4 and 22.1kg/m², respectively. The mean BMI of the women included in this population was 28.6kg/m², therefore a population that was overweight versus a population of normal weight population. The younger white and black groups studied had a normal BMI and showed a smaller although still significant estimated Kawasaki value compared to the other groups. The Tanaka formula also did not differ significantly from the 24-hour sodium excretion in these two groups. It seems that the formulas could be used in a young, healthy South African population, although still with caution. Both the Tanaka and INTERSALT formula were developed and validated in young populations ^(10,22), whereas the Kawasaki ⁽²¹⁾ was validated in a wider age group. Looking specifically at the Indian women, a possible reason why the INTERSALT formula did not underestimate the sodium excretion could be because they did not contribute the full volume of urine (even after cut off values for completeness of sample were applied) and hence their excretions would be lower.

Sensitivity is the proportion of true positives that are correctly identified by the estimation formulas ⁽²⁴⁾. In other words 95.44%, 99.30% and 98.59% of the sodium estimation from Kawasaki, Tanaka and INTERSALT formula correctly classified individuals that had a sodium intake of above 2000mg/day. Specificity, on the other hand, is the proportion of true negatives that are correctly identified by the estimation formulas ⁽²⁴⁾. Only 11.39%, 2.60% and 3.90% of the Kawasaki, Tanaka and INTERSALT formulas correctly identified individuals with having a sodium excretion of less than 2000mg/d. Therefore, the different formulas have the ability to identify true positives (sensitivity) but struggles to identify true negative (specificity) individuals. This will translate in the formulas overestimating the sodium excretion and classifying

individuals with low sodium intake as having high sodium intake, in other words low specificity. This should be kept in mind when using these formulas in estimating sodium excretion in a population setting.

According to a systematic review done by Ji *et al.* ⁽⁸⁾, the INTERSALT study produced the most convincing evidence with regard to feasibility and usefulness. This study was conducted in 52 different populations. The method of Tanaka ⁽¹⁰⁾, and Kawasaki ⁽²¹⁾ is population specific (Japanese individuals) and requires internal calibration with age, weight, and creatinine. It also has been reported to overestimate low intakes and underestimate high intakes ⁽²⁵⁾.

Our results are different from those reported by Mente and co-workers ⁽⁹⁾ where the researchers found that the Kawasaki formula showed the best agreement and the least bias when compared with the other two formulas. The INTERSALT had the highest degree of bias and the weakest correlation compared with the Kawasaki and Tanaka formulas ⁽⁹⁾. Cogswell and co-workers ⁽²⁶⁾ conducted a cross-sectional study to evaluate the validity of these three formulas with a 24-hour urine sample in young Americans. As in our findings, they reported that the INTERSALT formula provided the least bias when compared with Kawasaki and Tanaka formulas and would be recommended in America for the monitoring of sodium intake.

Because the INTERSALT formula showed the least bias and did not differ from the measured sodium intake, research on developing a formula based on the INTERSALT but more specific to the South African population should continue. As suggested by Cogswell *et al.*, designing a study to standardize mean estimated sodium intake from spot urine samples among a small group within the larger population may better inform monitoring at a population level and could be viable in South Africa. Furthermore, research should investigate differences of the predictions of spot urine samples that were collected at different times in the day within this population. Kawasaki and colleagues ⁽²¹⁾ reported an even stronger correlation when participants collected three 24-hour urine samples, and this should also be considered for future research.

With regards to the potassium intake estimations, the Kawasaki formula overestimated and the Tanaka formulas underestimated the potassium intake compared with the 24-hour excretion. No correlation was found for either of these formulas, however, the Kawasaki reported the lowest degree of bias. These formulas are also based on the same hypothesis as explained earlier and were developed for a population with a much lower BMI than the current population (which means the creatinine values will differ significantly). A formula should be developed for estimating potassium accurately in the South African, or similar population, as potassium is crucial in monitoring health in a country. The sensitivity and specificity of the formulas to

correctly identify true positive and negatives was very low, and therefore it is not advised to use these two formulas in estimating potassium excretion.

Our study had some limitations. Our sample was not representative of the whole of South African population and we collected only one 24-hour urine sample from each participant.

The importance of establishing reliable and accurate monitoring tools for the estimation of population sodium consumption is important in the light of the public health concern with regards to hypertension in South Africa. This research therefore contributes indirectly to this public health problem facing South Africa.

To conclude, our findings suggest that the INTERSALT formula performed the best in estimating sodium intake in three different South African populations, yielding more reliable results in young healthy adults. But spot urine samples should be used with caution when estimating sodium intake, especially when using the Kawasaki and Tanaka formulas. As also suggested by other authors ^(2,22,26), estimated sodium excretion from spot urine samples may possibly be used to monitor trends in the population, but the WHO's statement of "*until more studies are carried out to assess simpler but reliable methods of urine collection for the purpose of estimating daily excretions [of sodium], 24-hour urine collections are recommended*" is still supported until more conclusive evidence is produced with regard to the use of spot urine in sodium intake monitoring.

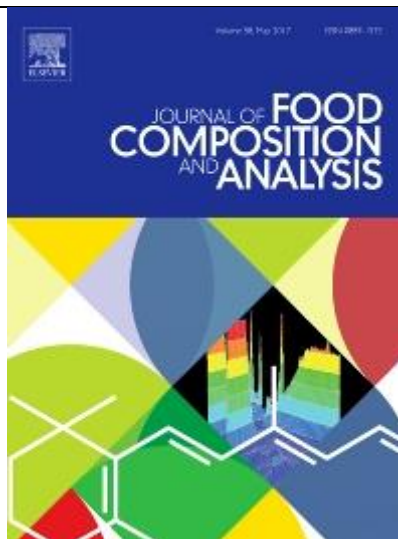
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CHAPTER FIVE: MANUSCRIPT THREE

*“One person with belief is equal to a force of ninety-nine who have only interest”
~ John Stuart Mill*



Manuscript three was submitted to Journal of food composition and analysis

JOURNAL DETAILS	
Title:	Journal of food composition and analysis
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Does the food industry comply with the updated sodium content of food regulation in South Africa?

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Abstract: As a first step in combating the high hypertension rate in South Africa, the Government has recently implemented a mandatory regulation (R.214) pertaining to the sodium content of foodstuffs with targets for 2016 and 2019. We aimed to establish whether or not industry is complying with the targets set in Regulation R.214.

Ten food products which were randomly selected from each of the 13 food categories were measured by means of an atomic absorption spectrometer. The majority of the food products tested comply with the targets for 2016 (72%) and almost half of the products with the 2019 targets (42%). The highest variation was observed in the “*all fat and butter spread*” (31.99%) category, as well as the “*raw-processed meat sausages*” (31.75%). All of the food categories, except for “*flavoured potato crisp, excluding salt-and-vinegar*” and “*flavoured ready-to-eat savoury snack and potato crisp, salt-and-vinegar only*”, complied with the 2016 target.

South Africa is at the forefront of countries implementing mandatory legislation for the reduction of sodium levels in food. These data provide valuable information with regard to monitoring and evaluation and can serve as a baseline for monitoring product compliance over the next few years.

Keywords: Sodium, Regulation, salt, industry, South Africa

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Introduction

High salt (sodium) intake has been linked to increased prevalence of hypertension (Kotchen et al., 2013), stomach cancer (D'Elia et al., 2012) and kidney disease (Deckers et al., 2014). Worldwide, mean sodium intake exceeds 2000mg/day (5g salt per day), which is the daily recommended allowance by the World Health Organization (WHO) (WHO, 2012). In South Africa, individuals are currently consuming an average of 7.8g of salt per day (Swanepoel et al., 2016). One of the leading causes of death in South Africa is hypertensive heart disease, with the number increasing each year (Nojilana et al., 2016). In response to this public health problem and the overwhelming evidence that supports population-wide sodium reduction strategies, South Africa was one of the 75 countries to develop sodium reduction strategies in order to reach the targeted 2000mg/day recommended by the WHO before 2025 (WHO, 2012). One of the steps taken by the South African National Department of Health was to reduce non-discretionary sodium intake by passing a regulation in 2013, limiting the sodium content of certain processed foods (Table 1) (South African Government., 2013) (R.214:March 2013, amended in 2016). South Africa was the first country to implement mandatory sodium reduction targets for certain foods.

The first targeted reduction in sodium came into effect in June 2016. Monitoring of sodium in the 13 food categories is not only important to evaluate regulation compliance but is also essential in determining the success of the National sodium reduction strategy of South Africa. The monitoring will provide valuable information that can improve the strategy in South Africa and globally. Regulation and monitoring of sodium in food also requires standardisation of the methodology in terms of the protocol followed as well as in the preparation of the different food samples. Within the Regulation R.214, the following methodology is recommended: *“For all foodstuff categories, suitable sodium potentiometric method or elemental analysis, with either flame atomic absorption spectroscopy or inductively coupled plasma, for determining typical total sodium content which shall be applied for monitoring and law-enforcement purposes; provided that these methods may also be used for routine testing or for the purpose of nutritional information labelling of the typical total sodium content by manufacturers.”*

The aims of this research were therefore to describe sodium measurement methodology in detail and establish whether industry is complying with the targets set in Regulation R.214. In addition, we compared the sodium as analysed with the sodium values given on the food labels at the time of testing.

Materials and Methods

Samples and preparation

Where possible, ten random food samples were identified from each of the 13 food categories (see Table 1) included in Regulation R.214. Different brands were collected for each food category and included all the major food companies in South Africa. The collection period was from March to May 2016. Three food samples (primary samples) with identical batch numbers and expiry dates were used to form the composite sample for each food product (Figure 1). Sampling of the food products to form the composite sample was conducted according to the guidelines of Greenfield and Southgate (Greenfield et al., 2003). Each food category had a different method of preparation before analysis (because of the different matrices), as is also indicated in Greenfield and Southgate (Greenfield et al., 2003). To ensure homogeneity within the composite sample, all the primary samples were blended after sampling. The composite samples of each food product were divided into three analytical samples, weighing approximately 0.5 g each. Each of these analytical samples was weighed in duplicate. All the food products were purchased at a major chain supermarket in Potchefstroom, South Africa. The homogeneous analytical samples were kept in air-tight containers until analysis.



Figure 1: Sampling protocol followed to reach the analytical sample for sodium analysis

With each food category, certified reference material from the National Institute of Standards and Technology (NIST, Gaithersburg, MD, USA) was analysed to ensure accuracy (a total of 13 measured NIST samples). The NIST standard used was Peanut Butter (SRM2387), with a certified sodium content of $4890 \pm 140 \text{ mg/kg}$.

Sodium analysis

In line with the methods prescribed by Regulation R.214 we performed the sodium analysis as follows. After appropriate sampling of each food category the analytical samples were accurately weighed to the nearest 0.5g with a Boeco scale (Boeco, Hamburg, Germany). The analytical samples were directly weighed in the Teflon vessels of the microwave digester (Milestone, ETHOS Easy, Shelton, USA). A combination of 65% HNO_3 (UltraSpec SupraPURE, De Bruyn Spectroscopic Solutions, Bryanston, South Africa) and 30% H_2O_2 (SupraPURE, Merck, Darmstadt, Germany) was added (to make up a total of 10ml) to each Teflon vessel containing the analytical sample. Each digestion series contained one reagent blank *i.e.* HNO_3 without sample material. The vessels were then transferred to the microwave digester for

digestion. Each food category was digested according to the programme that suited the matrix of the food category. The digested samples were transferred into 500ml volumetric flasks and filled up to exactly 500ml with double distilled (dd)H₂O, after which dilutions were made so that the final concentration of sodium was within the linear range of the atomic absorption spectrometer (AAS, Agilent, 240 FS, USA). The standard curve on the AAS was between 1 and 5ppm. Measurements were performed in duplicate. Standard solutions of sodium concentrations of 1.0, 2.0, 3.0, 4.0 and 5.0ppm were prepared each day before measurements. The wavelength and slit width was set at 303.3nm and 0.2nm, respectively.

Statistical analysis

After normality was determined, the mean and standard deviation of six (three analytical samples measured in duplicate) measurements were calculated for each food product in a food category. The mean of each food category was also calculated. The measured sodium content was evaluated against the sodium content allowed according to Regulation R.214 (both the 2016 and 2019 targets) and expressed as a percentage of food products complying. The percentage difference between the measured sodium and the sodium content stated on the label was also calculated. The average coefficient of variation (CV) was also calculated for each food category.

Results

We analysed all 13 food categories stated in regulation R.214, which amounted to 110 different food products (of different brands). The average r-value of the sodium calibration curve of the AAS analyses across all measurements was 0.9996. The NIST sample was analysed 13 times on different days and gave an accuracy and coefficient of analytical variation of 98.1% and 5.7%, respectively. The targeted concentration was 2.445 ppm and the average measured concentration was 2.398±0.136 ppm. Within the different food samples, the variation between measurements ranged from 12.36% to 31.75% and the average CV (the analytical samples in a food category) was calculated for each food category (Table 1). The highest variation was observed in the “*all fat and butter spread*” (25.16%) category as well as the “*raw-processed meat sausages*” (31.75%).

Table 1: Summary of the sodium content of the food categories included in Regulation R.214¹

Food category	Measured sodium (mean±SD)	CV (%)	2016 target	2019 target
Bread	306.13±0.32	17.57	400	380
Raw-processed meat sausages	514.28±0.34	31.75	800	600
Processed meat – uncured	585.99±0.22	14.30	1300	1150
Processed meat – cured	811.22±0.26	15.01	850	650
All fat and butter spreads	440.28±0.32	25.16	550	450
All breakfast cereals	329.17±0.26	14.86	500	400
Savoury snacks, excluding salt-and-vinegar flavoured	685.80±0.24	15.93	800	700
Flavoured ready-to-eat savoury snack and potato crisp, salt-and-vinegar only	1104.14±0.21	12.36	1000	850
Dry savoury powders with dry instant noodles to be mixed with a liquid	1197.11±0.65	19.71	1500	800
Flavoured potato crisp, excluding salt-and-vinegar	1648.19±0.23	16.98	650	550
Stock cubes / powder / granules / emulsions / pastes / jellies	13906.49±0.35	13.78	18000	13000
Dry gravy powders and dry instant savoury sauces	3433.01±0.52	16.43	3500	1500
Dry soup powder (not instant type)	5078.66±0.49	14.49	5500	3500

¹Values given as mg/100g

All of the food categories, except for “*flavoured potato crisp, excluding salt-and-vinegar*” and “*flavoured ready-to-eat savoury snack and potato crisp, salt-and-vinegar only*”, complied with the 2016 target as stipulated in the R.214 regulation.

Figure 2 (A and B) gives an overall indication of the proportion of all the foods (collected and analysed in 2016) within the 13 food categories that comply with the 2016 and 2019 targets. The majority of the food products tested comply with the targets for 2016 (72%) and almost half of the products with the 2019 targets (42%).

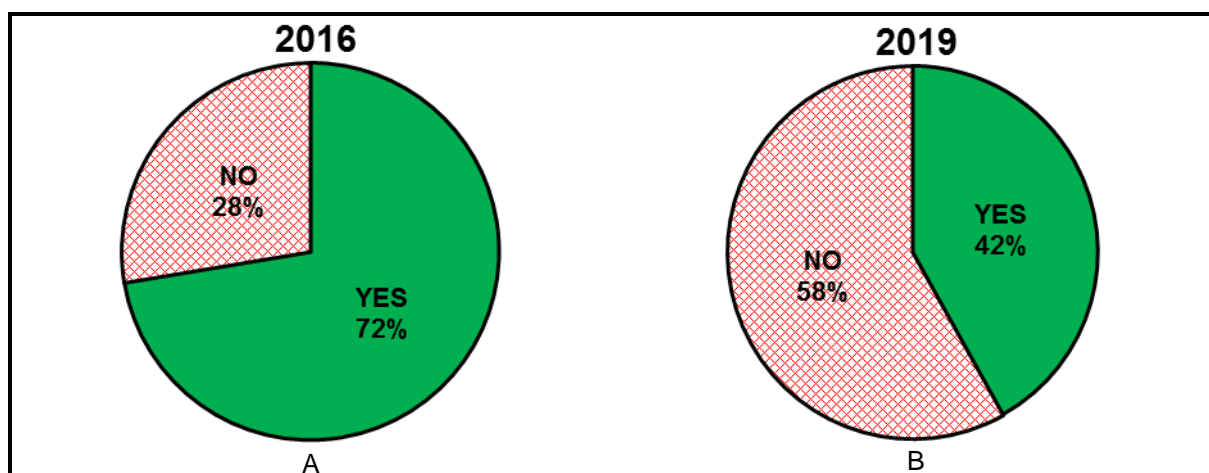


Figure 2: Proportion of food products meeting and exceeding the targets set out by the R.214 regulation

Focusing on each of the food categories, figure 3 summarise the percentage of the food products within each category that complied with the R.214 regulation targets for 2016 and

2019. As seen in figure 3, 100% of the food products tested in the “dry savoury powders with dry instant noodles”, “all breakfast cereals”, and “raw-processed meat sausages” categories, complied with the 2016 targets. Ninety percent of the breads tested complied with the 2016 target and 80% with the 2019 target. Seventy percent of the “flavoured potato crisp, excluding salt-and-vinegar” category did not comply with any of the targets.

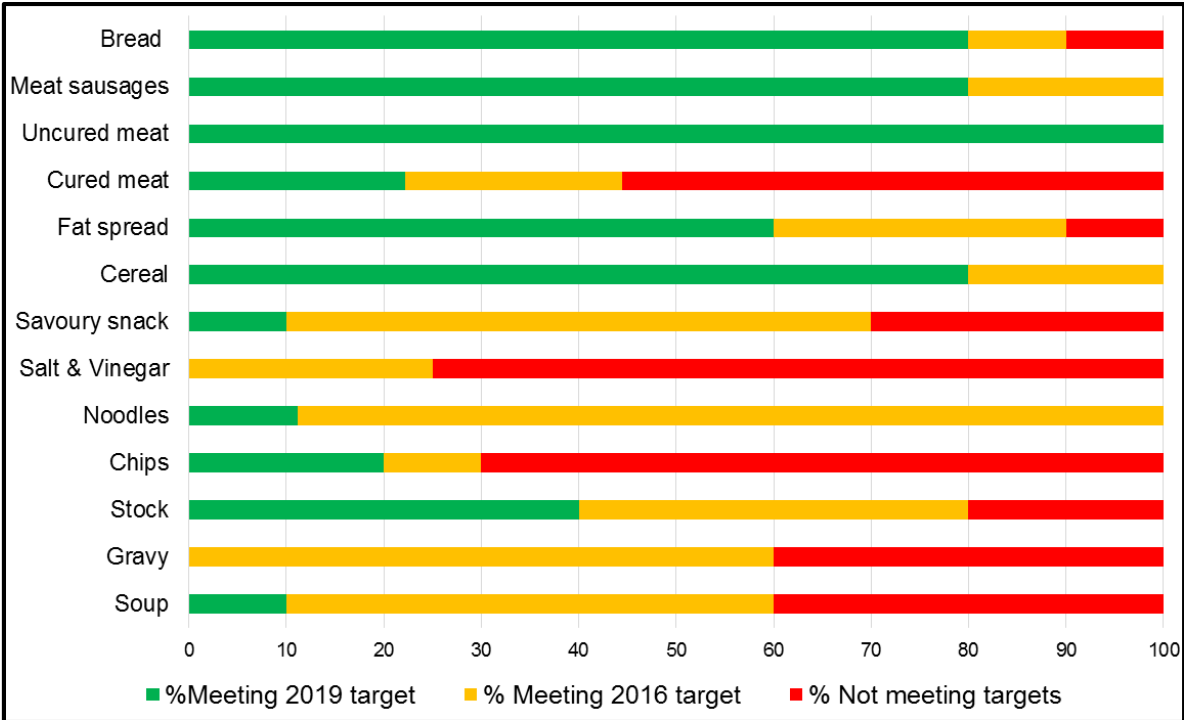


Figure 3: Food categories’ compliance with the 2016 and 2019 targets

In the following figures the sodium content of individual food samples is compared with the sodium content indicated on the labels. In addition, the 2016 and 2019 targets are indicated, as well as the average sodium content of the food category as analysed. “Bread”, “all fat and butter spreads” and “dry soup powder (not instant type)” are the food categories that contribute the most to South Africans’ sodium intake (Wentzel-Viljoen et al., 2013), and are summarised in Figure 4, 5 and 6.

Within the “bread” category, sodium on all the labels overestimated actual sodium content when compared with the AAS analysis (Figure 4). The 2016 target for sodium in bread was sufficiently met when considering the category average (306.13mg/100g vs the target of 400 mg/100g).

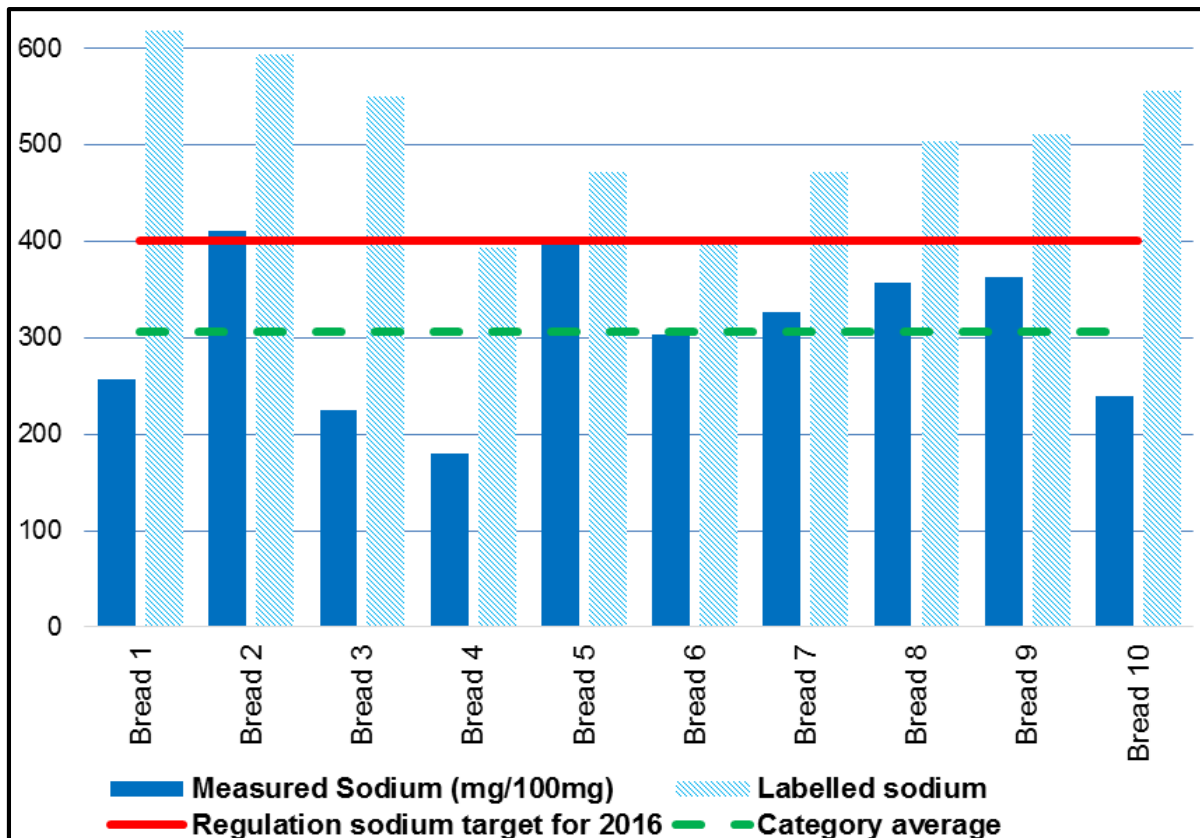


Figure 4: Analysis of the sodium content within the “bread” category

The mean sodium content of both the “dry soup powder (not instant type)” (Figure 5) (5078.66 mg/100g vs the target of 5500mg/100g) and “All fat and butter spreads” (Figure 6) (440.28mg/100g vs the target of 550mg/100g) were under the 2016 target set out in the regulation. Although the mean of these food categories were under the 2016 target, it is important to note that certain food companies did not comply, for example “bread 2”, “soup 1”, “soup 4”, “soup 5” as well as “fat spread 10”.

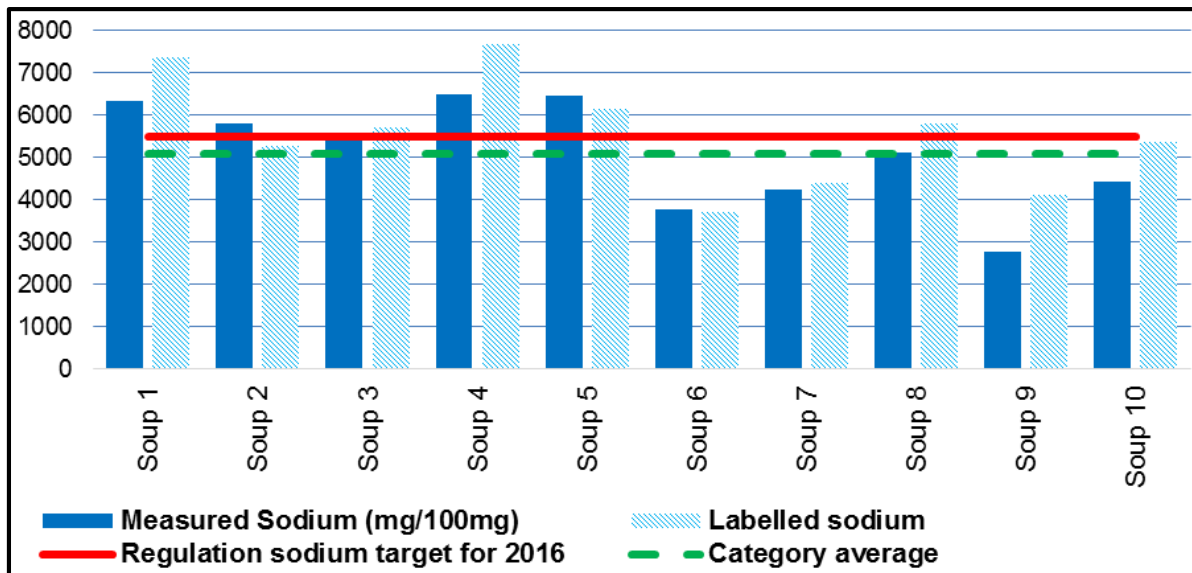


Figure 5: Analysis of the sodium content within the “*Dry soup powder (not instant type)*” category

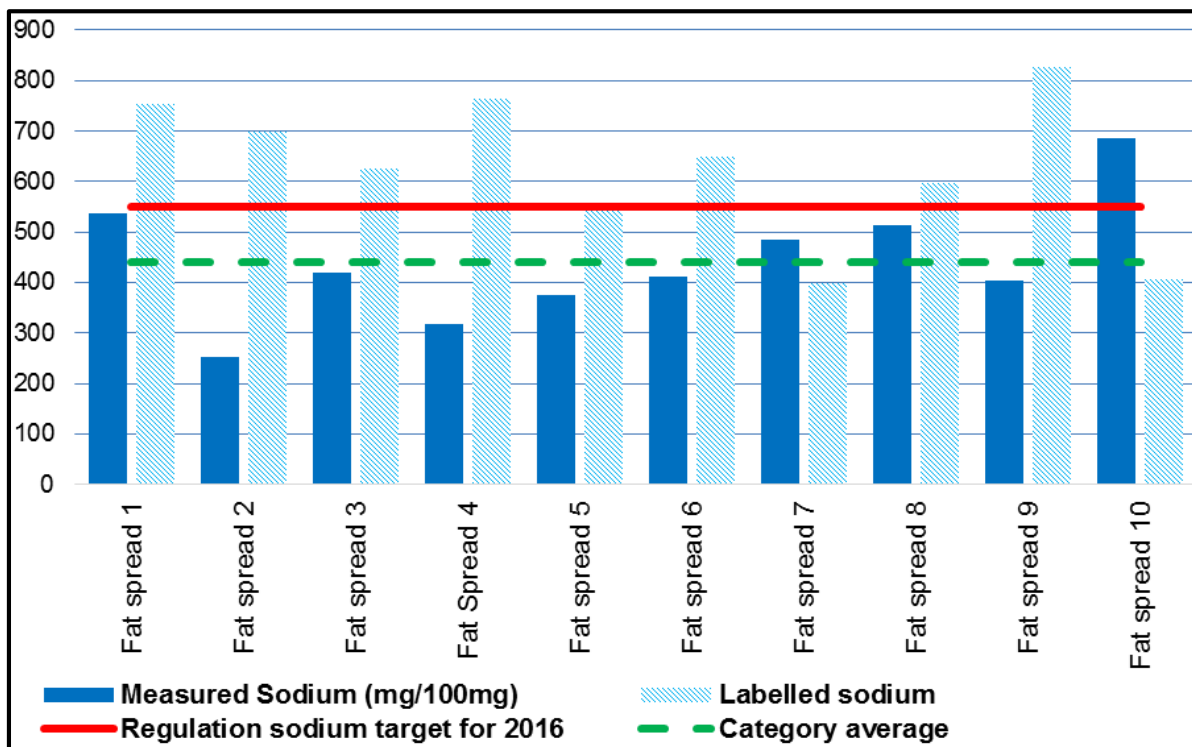


Figure 6: Analysis of the sodium content within the “*All fat and butter spreads*” category

In most of the food products analysed, the label overreported the sodium content (Figure 7). Within the “*Flavoured potato crisp, excluding salt-and-vinegar*” category, a difference of up to 240% was observed in some of the food products and was excluded from the graph in Figure 7. Most of the labels of the food products in the “*Dry gravy powders and dry instant savoury sauces*” category underreported the sodium content of their products. According to the R.214 regulation, the permitted tolerance for nutrient declaration in the labelling of sodium cannot be more than 20% in excess of the targeted sodium value. Some of the food products in the “*Dry*”

as a baseline for monitoring product compliance over the next few years. According to the results of this study, 72% of food products tested complied with the 2016 sodium target and almost half with the 2019 target. It should be borne in mind that food sampling was done between March and May 2016, thus before the target date. Food categories that had 100% compliance included “*Raw-processed meat sausages*”, “*all breakfast cereals*” and “*dry savoury powders with dry instant noodles to be mixed with a liquid*”. Bread, fat spreads and soup powders are the food products that contribute the most to South African sodium intake (Wentzel-Viljoen et al., 2013) and these food categories had good compliance (bread = 90%, fat spreads = 90% and soup powders = 60 %) with the 2016 targets set out in the regulation.

“*Flavoured potato crisp, excluding salt-and-vinegar*” as well as “*Flavoured ready-to-eat savoury snack and potato crisp, salt-and-vinegar only*” had the weakest compliance of 30% and 25%, respectively. These two categories had the weakest compliance and should be carefully monitored after the regulation’s target date for 2016.

In most of the food products, the sodium reported on the label and the measured sodium in the food product did not correspond. Differences of more than 20% can be seen across the categories. A possible reason for this could be that re-printing of labels can take time, or that product development and adaptation were not finalised at the time of the sampling.

While this research is vital for monitoring aspects, it has some limitations. The first is the sampling of the food products in that these were not sampled from different areas in the country; however, we did ensure that the batch number and expiry date were the same. The second limitation is that funding permitted the measurement of only 10 food products in each category. The bread samples were all those with a label providing the sodium content per 100g of the food. Therefore we cannot report on the sodium content of ‘regular’ bread (baked in-house in the supermarket) consumed by the majority of the population since it is cheaper than packaged and labelled bread.

In a recent review (Webster et al., 2014) investigating which types of programme are more likely to have an impact on sodium reduction, it was reported that 35 countries decided to implement voluntary targets for industry. Nine countries had established mandatory sodium targets, all of which had a target for bread and only two countries (South Africa and Argentina) had mandatory targets for a range of food products. The majority of these countries did report a reduction of sodium in the targeted food products and, as already mentioned, these were mostly voluntary. The implementation of mandatory targets in some countries is relatively new and therefore the impact will be determined only at a later stage. The United Kingdom, which is often used as the success story in terms of sodium reduction, implemented voluntary targets in 2006 and in 2011 reported an overall reduction of 7% in the sodium content of their identified food categories (Eyles et al., 2013). Another two countries with voluntary targets (Australia and New Zealand) reported an increase from 29% (2007) to 50% (2010) and 49% (2007) to 90%

(2010) in the number of bread products meeting the set targets, respectively (Dunford et al., 2011). It is therefore crucial for South Africa to monitor the sodium in the food supply chain, in order to compare the efficiency of mandatory versus voluntary sodium targets between countries.

In summary, South Africa was the first country in the world to legislate the sodium content of certain food products as part of the strategy to reduce the sodium intake of the population in order to manage the high incidence of hypertension. Reduction in salt intake has a health, health systems and financial impact on South Africa. This study is the first to look comprehensively at the compliance of food products with the R.214 regulation as well as a detailed methodology. This data are vital to the monitoring aspect of the regulation to measure success and eventually contribute to a reduction in the burden of disease due to hypertension and related cardiovascular diseases.

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CHAPTER SIX: GENERAL DISCUSSION AND CONCLUSION

*“Life is a journey to be experienced, not a problem to be solved” ~
Winnie the Pooh*

6.1 General discussion

This research endeavour was undertaken after realising the gap in information with regards to certain aspects of the sodium reduction strategy in South Africa. It is widely accepted that South Africa plays a leading role in sodium reduction globally. This together with the cost and health benefits of a successful sodium reduction strategy highlights the importance of executing all the elements included in such a strategy. As deduced from the literature in Chapter 2 high blood pressure is an important risk factor for CVD mortality and morbidity (Perkovic *et al.*, 2007). Globally, the incidence of high blood pressure has increased by 90% in the past four decades an increase driven mainly by its expansion in low and middle income countries (NCD-RisC, 2017), including South Africa (Bradshaw *et al.*, 2010). Different types of evidence in terms of the linear relationship between sodium intake and blood pressure (He & MacGregor, 2008) have been established, as formerly stated.

Considering all the relevant evidence, South Africa has also embarked on a national sodium reduction strategy following the call from high level WHO meetings to reduce the sodium intake to less than 2000mg sodium per day (WHO, 2012). This strategy has however not been without shortcomings. The gaps identified relating to the sodium reduction strategy include (i) the availability of recent sodium intake data to use as baseline from which the effectiveness of the sodium reduction strategy could be monitored, is absent; (ii) whether the assessment and monitoring of sodium intake in South Africans is accurate when using more convenient spot urine samples coupled with estimation formulae, instead of the gold standard method of using 24-hour urine samples; (iii) a lack in the availability of baseline data (through independent laboratory analysis) of the sodium content of the different food stuffs included in the R.214 regulation for monitoring purposes.

Considering the abovementioned shortcomings, the main aim of this research was therefore, to provide insights into some of these shortcomings with these specific objectives and related findings:

Chapter three of this thesis: Objective one, two and three set out to determine the sodium, potassium, Na:K ratio and iodine intake in three different population groups (black, white and Indian) in South Africa. The results obtained included that almost 30% of the population consumed more than 10g of salt per day and that even more alarmingly only 7% of the

population consumed the recommended potassium intake of above 3510mg per day. The median Na:K ratio was 3.5 which is more than three times higher than the recommended 1:1 (WHO, 2012). The findings indicated that not a single participant in this study reached this 1:1 recommendation. This emphasised the need to strengthen efforts to increase the potassium intake while decreasing the sodium intake. In terms of the iodine levels in our population, individuals in the lowest salt intake category ($\leq 4\text{g/d}$), still showed compliance with the recommended intake of iodine. This should nevertheless, be frequently monitored in South Africa in order to ensure that the recommended iodine intake of $150\mu\text{g/day}$ is met.

Chapter four: Objective four was formulated to estimate sodium and potassium excretion measured in a spot urine sample and compares it with a 24-hour urine sample using three different formulas (Kawasaki formula, INTERSALT formula and Tanaka formula) in the different population groups. Chapter 4 concluded that spot urine samples should be used with caution when estimating sodium intake for monitoring purposes, especially when using the Kawasaki and Tanaka formulas. No correlation was found between 24-hour sodium (and potassium) excretion and the predicted excretion by any one of the three formulas. The INTERSALT formula was the only formula that did not differ significantly from the measured 24-hour sodium excretion. Therefore until more conclusive evidence is generated in this specific population, 24-hour urine collections still remain the recommended method of determining sodium and potassium intake.

Lastly, in Chapter five we reported on a detailed protocol for measuring sodium in different matrixes of food. We also determined the sodium content in different food products in each of the 13 food categories within the R.214 Regulation, before the June 2016 deadline for implementation of the new sodium reduction regulation. The majority of the food products tested complied with the targets for 2016 (72%) and almost half of the products with the 2019 targets (42%). Although there were some food categories that had a weak compliance, overall the industry should be commended for the effort made to ensure that the standards are met. These data are vital to the monitoring aspect of the regulation to measure success and eventually contribute to a reduction in the burden of disease due to hypertension and related CVDs.

6.2 Strengths and limitations of the study

6.2.1 Limitations:

Firstly, it would have been ideal to measure 24-hour sodium (and potassium) excretion in a large, nationally representative population sample, including both adults and children. Individuals from only two (North-West and KwaZulu-Natal) of the nine provinces were included

in this research. Secondly, the fact that only one 24-hour urine sample was collected in this population can also be seen as a limitation. As many as fourteen 24-hour urine collections are suggested by some researchers for accurate estimation of sodium intake at individual level because of the day-to-day variation (Lui *et al.*, 1979). For population estimates, however, most studies still use one to two 24-hour urine collections. Until more research can establish the “ideal” number of 24-hour urine collections or more effective and accurate methods to determine sodium and potassium intake in a population, the WHO’s recommendation still stands that one 24-hour urine collection should be adequate if a sufficient number of individuals is included in the sample (Elliot and Brown, 2007). Another factor that can be seen as a limitation is the fact that only one cut off value for completeness of samples for all the population groups were used. Although this was not the focus of the articles, it could be investigated in the future to establish specific cut off values for each population groups according to its unique compilation.

In terms of the sodium analyses of the different foodstuffs, a limitation is the fact that the food samples were not sampled from different areas in the country and that only ten food products in each food category were analysed.

6.2.2 Strengths:

As mentioned, the collection of a 24-hour urine samples is labour intensive and places a huge burden on the participants. The fact that we nevertheless managed to collect 24-hour urine samples in different age, gender and ethnic groups with a relatively large sample size is valuable in the light of South Africa’s sodium reduction strategy and the monitoring thereof.

Quality assessment of food stuffs prior to legislation is also seen as a strength pertaining to this research. Laboratory analysis of sodium in food products is time consuming and requires very specific skills and equipment to conduct these analyses correctly. It is also seen as the most accurate way of determining the sodium content in food and therefore contributes significantly to the data on which the monitoring of foodstuffs in South Africa will be based. Publication of the sodium content of these food products will also act as a motivation for the food industry to make sure that all of their food products comply with the regulation and also provides them with an independent sodium measurement in their sodium containing products. In addition to this we also compared the sodium declared on the label with what is truly in the product.

All the gaps that have been identified and addressed in this thesis are related and contribute towards the bigger public health problem of addressing hypertension in South Africa.

6.3 Way forward

In a recent consultative meeting about the progress made and challenges faced in South Africa's sodium reduction strategy and the way forward, 25 members from government, non-governmental organisations and universities, including the researcher, and research societies attended (Webster *et al.*, 2017). Priority areas for the way forward were identified and are also the recommendations for future research from this research project. Firstly, it was recommended that the monitoring process should be reinforced and industry actively engaged, and that informal food production sectors be communicated with to ensure compliance by all relevant stakeholders. Secondly, the members at the consultative meeting proposed that there is a need to investigate the contribution of foods (including fast-foods) eaten outside the home to the sodium intake of South Africans and subsequently to establish whether intervention may also be needed in this industry. The implementation of a more extensive education campaign, in terms of the dangers of high salt use, is also a priority and should be incorporated into a broader health message communication strategy. This will ensure that the "increase-of-potassium" message is also communicated to the public. Lastly, the monitoring of sodium intake could be integrated into national surveys to make sure that a representative picture of the sodium intake of South Africans is painted. Sodium intake in South African children can then also be determined and monitored.

6.4 Policy implications

If the sodium reduction strategy in South Africa is a success and all the elements are implemented and monitored effectively, around 5600 death and 23 000 cases of CVD may be prevented, which translates into an 11% reduction in deaths from heart diseases (Watkins *et al.*, 2015). Taking into consideration the health benefits of a strategy such as this, a total cost saving of ZAR713 million per year is also estimated for the country (Watkins *et al.*, 2015). The public health impact of reducing sodium intake in South Africans is immense and all efforts should be undertaken by all stakeholders involved to see that this strategy is successfully implemented

6.5 Conclusion

Through this research, we have demonstrated that the sodium intake of South Africans is too high and that the majority (65%) of the population studied consumed more than 5g of salt per day, confirming the need for an active sodium reduction strategy in South Africa. In terms of validating the use of a spot urine sample (with different formulas) against a 24-hour urine sample to estimated sodium and potassium excretion, our research revealed that the use of a spot urine sample with estimation formulas should be used with caution, and that a 24-hour

urine sample should be advised to determine the sodium and potassium excretion in our population. Lastly, we have shown that the role players in the food supply chain can be commended on their progress and overall good compliance (72%) with regard to the sodium content stipulated in the regulation's first target in the identified food categories.

Although much has been achieved in terms of South Africa's sodium reduction strategy, the continuation of research within this field is vital to show-case to the world what can be achieved and what public health impact such a strategy can have in a country like South Africa.

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ADDENDUM A: ETHICS CERTIFICATE



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ETHICS APPROVAL CERTIFICATE OF PROJECT

Based on approval by Health Research Ethics Committee (HREC), the North-West University Institutional Research Ethics Regulatory Committee (NWU-IRERC) hereby approves your project as indicated below. This implies that the NWU-IRERC grants its permission that, provided the special conditions specified below are met and pending any other authorisation that may be necessary, the project may be initiated, using the ethics number below.

Project title: An analysis of the sodium intake and blood pressure dilemma in South Africa															
Project Leader: Prof E Wentzel-Viljoen															
Ethics number:	N	W	U	-	0	0	0	8	5	-	1	5	-	A	1
	<small>Institution</small>	<small>Project Number</small>	<small>Year</small>	<small>Status</small>											
	<small>Status: S = Submission; R = Re-Submission; P = Provisional Authorisation; A = Authorisation</small>														
Approval date: 2015-11-18	Expiry date: 2016-11-30	Risk	Minimal												

Special conditions of the approval (if any): None

<p>General conditions:</p> <p>While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, please note the following:</p> <ul style="list-style-type: none">The project leader (principle investigator) must report in the prescribed format to the NWU-IRERC:<ul style="list-style-type: none">annually (or as otherwise requested) on the progress of the project,without any delay in case of any adverse event (or any matter that interrupts sound ethical principles) during the course of the project.The approval applies strictly to the protocol as stipulated in the application form. Would any changes to the protocol be deemed necessary during the course of the project, the project leader must apply for approval of these changes at the NWU-IRERC. Would there be deviations from the project protocol without the necessary approval of such changes, the ethics approval is immediately and automatically forfeited.The date of approval indicates the first date that the project may be started. Would the project have to continue after the expiry date, a new application must be made to the NWU-IRERC and new approval received before or on the expiry date.In the interest of ethical responsibility the NWU-IRERC retains the right to:<ul style="list-style-type: none">request access to any information or data at any time during the course or after completion of the project;withdraw or postpone approval if:<ul style="list-style-type: none">any unethical principles or practices of the project are revealed or suspected,it becomes apparent that any relevant information was withheld from the NWU-IRERC or that information has been false or misrepresented,the required annual report and reporting of adverse events was not done timely and accurately,new institutional rules, national legislation or international conventions deem it necessary.
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The IRERC would like to remain at your service as scientist and researcher, and wishes you well with your project. Please do not hesitate to contact the IRERC for any further enquiries or requests for assistance.

Yours sincerely

Linda du Plessis
Digitally signed by Linda du Plessis, o=NWU, ou=Faculty of Health Sciences, email=linda.duplessis@nwu.ac.za, c=ZA
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Prof Linda du Plessis
Chair NWU Institutional Research Ethics Regulatory Committee (IRERC)

Research Article

Sodium and potassium intake in South Africa: an evaluation of 24-hour urine collections in a white, black, and Indian population



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Abstract

Limited number of studies on salt intake has been conducted in the South Africa. The present study established the sodium and potassium excretion (24-hour urine collection) of three different South African populations. In total, 692 successful 24-hour urine collections were analyzed for sodium, potassium, and iodine levels. The median sodium and potassium excretion was 122.9 and 33.5 mmol/d, respectively, and the median salt intake was 7.2 g/d. The majority (92.8%) of the population did not meet the recommended potassium intake/d, and 65.6% consumed more than 6 g of salt/d. Potassium excretion showed a linear relationship with salt intake (P -trend $\leq .001$). The median sodium-to-potassium ratio was 3.5. These findings support the South African government's sodium reduction legislation, as well as global initiatives. More consideration should be given to promoting the intake of potassium-rich foods, as this may have a greater public health impact than focusing only on dietary sodium reduction. *J Am Soc Hypertens* 2016;10(11):829-837. © 2016 American Society of Hypertension. All rights reserved.

Keywords: Hypertension; potassium; salt; sodium; South Africa.

Introduction

It is widely reported that cardiovascular disease, and specifically hypertension, contributes significantly to the disease burden, not only globally but also in sub-Saharan Africa.¹⁻³ The modification of lifestyle behaviors, including dietary salt intake, is currently an area of profound interest.

In a review by He and MacGregor,⁴ it was pointed out that animal studies,^{5,6} human genetic studies,^{7,8} epidemiological studies,⁹⁻¹² population-based intervention studies,^{13,14} and treatment studies^{15,16} all indicate a relationship between high sodium (salt) consumption and the risk of high blood pressure. The role of low potassium intake in the development of high blood pressure is also essential since epidemiologic

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Any opinion, findings, and conclusions or recommendations expressed in this material are those of the authors, and the NRF, therefore, does not accept any liability in this regard.

Conflict of interest: none.

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observational studies have concluded that potassium deficiency increases the negative impact of a high sodium (salt) intake on the development of high blood pressure.^{17–19} Simultaneously, meeting the recommended intake of both sodium and potassium poses a major nutritional challenge. The World Health Organization (WHO) recommends a sodium:potassium ratio of 1:1 (86 mmol/d:90 mmol/d) (Na:K).²⁰

According to the WHO, the average salt intake per person in most countries is too high, usually being between 9 and 12 g/d.²¹ Although a limited number of studies have been conducted in the South African population, it has been estimated that the average South African consumes between 6 and 11g of salt/d.²² These studies were all conducted at least 10 years ago, but with rapid urbanization, the dietary environment has changed. Because of the high prevalence of hypertension in South Africa,^{1–3} the Department of Health has implemented a nationwide sodium reduction strategy enforcing mandatory reduction in the sodium content of certain processed foods, which comes into effect in June 2016.²³ For monitoring, it is not only the sodium excretion data that are needed, but also preregulation iodine intake levels. Because South Africa has a mandatory national salt iodization program, there are concerns that the reduction of salt in foods could interfere with the purpose of the iodization program.

The purpose of this paper is to establish the current 24-hour sodium (as a marker of salt intake) and potassium excretion, of three different South African populations from different geographical regions. This will set a comparative benchmark for future investigations postlegislation to establish the effectiveness of the policy of sodium reduction.

Experimental Methods

Study Participants

We obtained data from three ongoing studies, two based in the North West province and one in KwaZulu-Natal, South Africa. Relevant data for the different studies were collected in the period from 2013 to 2015. This study was cross-sectional in nature.

We obtained data first from the baseline sample of the African Prospective study on the Early Detection and Identification of Cardiovascular disease and Hypertension (African-PREDICT), which is a longitudinal study that commenced in 2013 and is expected to continue for at least 10 years. The participants were comprised of apparently healthy black and white men and women (aged 20–30 years) who were normotensive, had no known cardiovascular disease, and were not taking any blood pressure medication. The detailed inclusion criteria are summarized in Thompson et al.²⁴ To date, we have collected 24-hour urine samples from 509 participants.

Second, we collected 24-hour urine samples from the Thusa-Bothle study. We randomly selected apparently

healthy black women aged between 35 and 65 years from the urban community of Ikageng in the North West province of South Africa. Another inclusion criteria were also that the women could have had hypertension, but the person must have received antihypertensive treatment. Women with any other diagnosed acute or noncommunicable chronic diseases were excluded. We successfully collected 24-hour urine samples from 73 women.

Finally, data were collected from an urban area of Umkomaas in the KwaZulu-Natal province, South Africa. The women were also healthy with no diagnosed chronic diseases including hypertension. Successful 24-hour urine samples were collected from 111 Indian women between the ages of 18 and 50 years.

In total, 692 complete 24-hour urine samples were collected. All the studies included were conducted according to the guidelines laid down in the Declaration of Helsinki, and all the procedures involving human participants were approved by the various ethics committees [NWU-0001-12-A1, NWU-00060-14-A1 and IREC 035/14]. Written informed consent was obtained from each of the participants. The three studies to determine sodium and potassium intake were also ethically approved [NWU-00085-15-S1].

24-Hour Urine Collection

Trained field staff members explained the collection protocol of the 24-hour urine sample and provided all the equipment according to WHO standards.²⁵ Instructions were given to collect a 24-hour urine sample on a day that was convenient for the participant, which was noted. The “first-pass urine” was discarded, and all urine passed thereafter was collected in the container provided, including the first urine of the following morning. The participants recorded the start and finish times of the collection period.

Urinary sodium, potassium, and chloride were measured by means of ion-selective electrode potentiometry on the Cobas Integra 400 plus (Roche, Basel, Switzerland), and creatinine concentrations were measured using the Creatinine Jaffé Gen.2 reagent (Roche, Basel, Switzerland). Urinary iodine concentration was determined using the Pino modification of the Sandell-Kolthoff reaction with spectrophotometric detection.²⁶ We calculated sodium and potassium excretion as follows:

Multiplying the sodium, potassium, and creatinine concentrations (mmol/l) by the total volume of urine (in liters) resulted in the sodium, potassium, and creatinine in mmol/d. Salt was calculated by multiplying the mmol sodium by 58.9 (combined molecular weight of sodium and chloride).

To check for completeness of the 24-hour urine samples, the following cutoff points were used: volume of the 24-hour urine collections <500 mL and urinary creatinine <4.0 mmol/d for women or <6.0 mmol/d for men.²⁷

Blood Pressure and Anthropometric Measurements

We used standard methodology to measure blood pressure, height, weight, and waist circumference in the African-PREDICT study.²⁴ Blood pressure of the black and Indian women was measured on a semiautomatic blood pressure device (M3W-HEM7202, OMRON Healthcare, Kyoto, Japan), respectively, using the participants' right arms after a 5-minute rest in the sitting position with legs uncrossed. Readings were done in duplicate with a 3-minute interval between the two readings. The blood pressure device used in the African-PREDICT study (DINAMAP, GE Healthcare, Buckinghamshire, UK)^{28,30} and the Omron device (M3W-HEM7202, OMRON Healthcare, Kyoto, Japan)³⁰ used in the other two studies are both validated. Trained field staff members with experience in blood pressure measurements conducted the blood pressure measurements. Appropriate cuff sizes were used for all participants and the arm circumferences printed on the cuffs fitted the standard guideline for the actual bladders in the cuffs. Both of the blood pressure devices used are validated, and in all three studies, the blood pressure measurements were reasonably close together with the average difference between systolic blood pressure readings being between 3 and 5 mm Hg and diastolic blood pressure between 3.5 and 4 mm Hg (for the same individual). Therefore, the same device reads more or less the same blood pressure for the same individual.

Body mass index (BMI) was calculated as weight (kg)/height (m)². The participants' weight was measured to the nearest 0.01 kg (in duplicate) with a digital scale (Seca, Hamburg, Germany) and height to the nearest 0.1 cm using a stadiometer (Seca 264, Hamburg, Germany). The waist circumference of both the black and Indian women was measured in triplicate to the nearest 0.1 cm at the midpoint between the lowest rib and the top of the iliac crest, using a steel tape (Lufkin, Apex, NC, USA).

Statistical Analysis

We used IBM SPSS version 23 (SAGE publications Ltd, London, UK) for statistical analyses. Normality was established by using the Shapiro–Wilk test, examining the histogram and Q-Q plot for each variable. Data are reported as mean and standard deviation or median and interquartile ranges (25–75th percentile), depending on the normality. The population was stratified according to the different studies, ethnicity (four groups), and gender. Parametric and nonparametric analysis of variance were performed to determine the differences between the population groups (within the different studies) and a Bonferroni post hoc test to determine where the differences were. An independent *t*-test and the Mann-Whitney U test were used to determine difference between genders. We plotted age, BMI,

and potassium excretion against salt intake cutoffs (≤ 4 g/d; 4.1–5.9 g/d; 6–9.9 g/d; ≥ 10 g/d) for the different study populations. The Jonckheere Trend test was used to calculate the *P*-trend for each of these plots.

To illustrate the percentage of the population within recommended sodium (<86 mmol/d or 2000 mg/d) and potassium (>90 mmol/d or 4300 mg/d) intakes, pie charts are presented. A *P*-value of $<.05$ was considered statistically significant.

Results

From 1022 participants, a total of 692 successful 24-hour urine sample collections (based on the cutoffs for completeness of 24-hour urine sample) were included for final analysis. The population's characteristics, as well as results from the 24-hour urine collections, are summarized in Table 1. Sodium excretion was significantly ($P < .001$) lower in the older Indian women than in their black counterparts. Whites had the highest potassium excretion ($P = .001$). The median sodium and potassium excretion of the populations were 122.9 mmol/d and 33.5 mmol/d, respectively. Iodine levels differed significantly between the ethnic groups, and the median of the populations was 152.6 $\mu\text{g/L}$. The Indian women had the lowest ($P < .001$) calculated salt intake, the median for this population being 7.1 g/d. Men had higher sodium ($P < .001$) and potassium ($P < .001$) excretions and salt intake than women, except for iodine, which was significantly higher ($P < .001$) in the women. Women had significantly ($P < .001$) higher BMIs than the men. The women from the Thusa-Bohle study had higher ($P < .001$) blood pressure values than the younger black women from the African-PREDICT study as well as the Indian women ($P < .001$).

No significant differences were found between the four salt categories in terms of age and BMI (Figure 1). Potassium excretion had a linear relationship with salt intake and differed between the categories (P -trend $\leq .001$).

Within this population, 92.8% did not meet the recommended potassium intake of 90 mmol/d (Figure 2). The median of the individuals above and below the recommended potassium intake was 130.5 mmol/d and 39.5 mmol/d, respectively. The median sodium-to-potassium ratio was 3.5, which is three times the recommended ratio.

Figure 3 and Table 2 represent the proportion of the population which falls in the different salt intake categories. The majority (65.6%) consumed more than 6 g of salt/d, while 15.6% consume less or equal than 4 g/d. The median of the individuals in the lowest (≤ 4 g/d) and highest (≥ 10 g/d) category is 2.8 g and 15.6 g of salt/d, respectively.

In all the study and ethnicity groups, the distribution looked similar to that of the whole population in terms of salt intake and potassium excretion (Table 2). Most of the black, white and Indian population consumed between 6 and 9.9 g of salt/d. A majority of the older black (36.2%)

Table 1
Demographic and 24-hour excretion data of the study population

	African-PREDICT Study		Thusa-Bohle Study	KwaZulu-Natal Study	Total		
	White (n = 277)	Black (n = 234)	Black (n = 70)	Indian (n = 111)	Men (n = 220)	Women (n = 472)	All (n = 692)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Age (y)	25.5 ± 2.8	24.6 ± 3.2	52.7 ± 8.2	39.8 ± 11.5	25.1 ± 3.0	32.7 ± 12.4	30.3 ± 11.0
BW (kg)	76.7 ± 17.9	67.0 ± 15.4	78.1 ± 19.2	68.2 ± 14.6	76.5 ± 18.3	70.2 ± 16.6	72.2 ± 17.4
BH (cm)	172.7 ± 8.3	163.4 ± 8.3	157.2 ± 6.0	156.6 ± 5.6	174.8 ± 7.6	161.0 ± 7.9	165.4 ± 10.1
BMI (kg/m ²)	25.6 ± 5.2	25.2 ± 6.3	31.7 ± 7.7	27.8 ± 5.6	24.9 ± 5.1	27.2 ± 6.6	26.4 ± 6.2
WC (cm)	82.2 ± 13.8	78.1 ± 12.2	89.7 ± 13.4	91.1 ± 13.9	83.2 ± 13.3	82.9 ± 14.5	83.0 ± 14.1
SBP (mm Hg)	117.6 ± 12.3	119.5 ± 11.7	139.7 ± 20.4	124.7 ± 19.2	125.0 ± 10.7	120.1 ± 17.5	121.6 ± 15.8
DBP (mm Hg)	77.2 ± 7.6	79.5 ± 7.8	85.6 ± 11.7	82.1 ± 11.8	80.2 ± 7.6	79.3 ± 9.9	79.6 ± 9.3
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
24-h urine vol (ml)	1205.6 (857.0–1657.0)	1210.1 (857.0–1757.0)	1290.8 (978.5–1688.6)	851.2 (631.9–1316.9)	1357.0 (895.5–1757.0)	1057.0 (742.5–1557.0)	1145.3 (757.0–1654.2)
Na excr. (mmol/d)	133.1 (93.5–193.8)	132.4 (92.8–192.2)	135.1 (76.3–212.9)	101.7 (72.1–143.2)	143.1 (102.1–212.2)	112.7 (81.7–164.3)	122.9 (87.8–180.2)
K excr. (mmol/d)	45.3 (31.3–65.3)	37.8 (24.8–59.5)	31.8 (18.9–49.1)	28.9 (18.6–35.6)	48.7 (30.6–68.3)	33.9 (23.9–51.6)	37.6 (24.8–56.7)
Cr excr. (mmol/d)	11.1 (7.5–15.6)	10.2 (7.7–13.5)	12.9 (8.4–19.0)	7.1 (5.8–9.9)	13.7 (9.1–17.4)	8.5 (6.4–11.2)	9.7 (7.0–13.9)
Iodine (µg/L)	135.0 (85.1–193.0)	146.7 (95.1–214.3)	—	253.5 (163.6–372.5)	142.4 (94.5–208.4)	158.8 (99.9–257.6)	152.6 (97.5–233.0)
Na:K ratio ^a	3.1 (2.2–3.9)	3.6 (2.5–5.0)	4.0 (3.2–5.5)	3.7 (2.9–4.7)	3.3 (2.3–4.7)	3.5 (2.6–4.6)	3.5 (2.5–4.6)
NaCl (g/d)	7.7 (5.4–11.1)	7.6 (5.3–11.1)	7.8 (4.4–12.2)	5.8 (4.1–8.2)	8.2 (5.9–12.2)	6.5 (4.7–9.4)	7.1 (5.0–10.4)

BH, body height; BMI, body mass index; BW, body weight; Cr, creatinine; DBP, diastolic blood pressure; excr., excretion; IQR, interquartile range (25th–75th); K, potassium; n, number of individuals; Na, sodium; NaCl, sodium chloride (salt); PREDICT, the African Prospective study on the Early Detection and Identification of Cardiovascular disease and Hypertension; SBP, systolic blood pressure; SD, standard deviation; WC, waist circumference.

^a Ratio of sodium (mmol/d) to potassium (mmol/d).

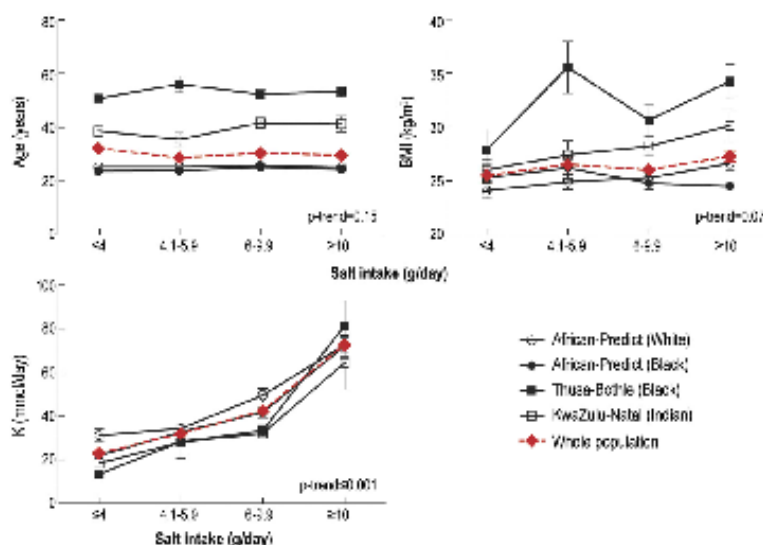


Figure 1. Age, BMI, and potassium excretion according to salt categories. Nonparametric analysis of variance was conducted to determine the differences between the salt intake (≤ 4 g/d; 4.1–5.9 g/d; 6–9.9 g/d; ≥ 10 g/d) groups and age, BMI, and potassium excretion. The Jonckheere Trend test was used to calculate the *P*-trend for these plots. A *P*-trend value of $<.05$ was considered statistically significant. BMI, body mass index; K, potassium.

women and a minority of the Indian women (14.6%) consumed more or equal than 10g of salt/d, compared with the other salt categories.

Discussion

We found that 77% of the South African population consumes >5 grams of salt/d, which is more than the WHO's recommendation. This includes black, white, and Indian populations from different gender and ethnic groups. What is perhaps of greater importance is that, as our study

highlights, only 7% adhered to the required potassium intake of 90 mmol/d, which may be one of the main reasons we observe such high numbers of hypertension cases in South Africa, as a diet deficient in potassium increases the negative impact that high sodium intake has on the development of hypertension.¹⁷

A recent systematic analysis of global, regional, and national salt intakes reported that, overall, the mean sodium intake in adults was 9.9 g of salt/d (calculated as 171.7 mmol/d sodium), which is higher than the WHO's recommended 5 g/d (86 mmol/d).²¹ The Asian regions reported the highest intakes, with Central Asia having salt intakes of 13.8 g/d (239.6 mmol/d sodium). Intakes of 10.5 g/d (181.7 mmol/d sodium) and 9.8 g/d (170.4 mmol/d sodium) were reported for Eastern Europe and North Africa, respectively.²¹ This analysis also reported a mean salt intake of 6.2 g/d (107.8 mmol/d sodium) within the South African populations included in this study in 2010. Previous studies conducted on normotensive individuals in South Africa reported mean salt intakes (measured by 24-hour urine collection) of 8.6 g/d (146.8 mmol/d sodium) (Johannesburg, 1982, $n = 105$)³² and 8.7 g/d (148.6 mmol/d sodium) (Cape Town, 2002, $n = 96$).³³ The median sodium excretion of the current study is measured as 122 mmol/d (7.1 g/d salt). This is more than the recommended intake of 86 mmol/d (5 g/d salt) and could indicate that the sodium consumption of South Africans may have started to decline, but it is still well above the recommended intake. This is further established by looking at the

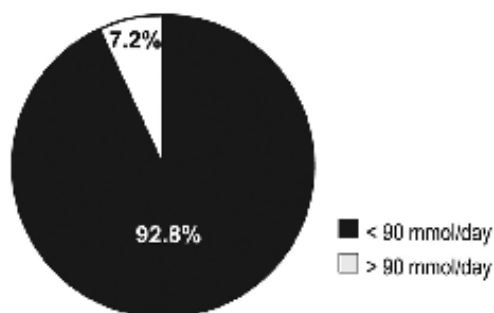


Figure 2. Percentage of the population reaching the recommended potassium intake/d.

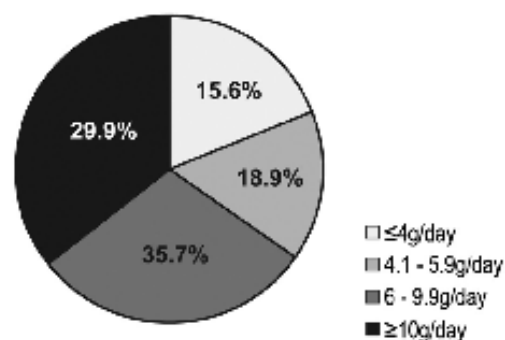


Figure 3. Percentage of the population in the different salt categories.

25th and 75th percentiles of the population which, in terms of sodium excretion, is 87.8–180.2 mmol/d. The lowest percentile of the population has a sodium excretion of just above the recommended intake, and the highest percentile has twice the recommended sodium excretion value. Figure 3 illustrates this more clearly, indicating that the majority (35.7%) of the population consumes between 6 and 9.9 g of salt/d, and that 29.9% consumes more than 10 g of salt/d, which is of even greater concern. Only 15.6% consumes less than 4 g of salt/d, therefore supporting the sodium reduction regulation. In the specific studies and ethnicities, older black women from the Thusa-Bothle study had the highest sodium excretion and Indian women had the lowest. In the present study, young men had significantly higher sodium levels than women (who were older) (143.1 vs 112.7 mmol/d), probably because of their generally higher food intake and different energy requirements.^{34,35}

A linear increase between BMI and salt intake, although not significant, is observed, as has been previously reported.^{35,36} A possible explanation is that obese and overweight individuals tending to have a great intake of food calories and follow a more unhealthy diet high in processed foods (generally high in salt). It is well reported that South African women have higher BMIs than men; therefore, our observation is expected.^{37,38}

The higher blood pressure values observed in the older Thusa-Bothle women were previously reported in a similar South African population, where the authors stated blood pressure measurements ranging from 135 to 138/87 to 90 mm Hg in the women.³⁹ This is therefore not an unexpected observation within the Thusa-Bothle women.

The median potassium excretion in this population is 37.6 mmol/d, which is lower than the excretion found in other South African studies done on normotensive individuals (55.2 and 45.1 mmol/d).^{32,33} The recommended intake by the WHO is at least 90 mmol/d. As previously mentioned, almost 93% of this South African population does not reach the recommended potassium intake. Although the task is very challenging, public health efforts should also be directed toward increasing potassium intakes together with decreasing the sodium intake in the population, through educational campaigns focusing on diets rich in fruits and vegetables and limiting processed foods high in sodium. We found a significant linear relationship (P -trend $\geq .001$) between potassium excretion and salt intake. A possible explanation for this could be that the individual who consumes high amounts of salt (in the form of processed foods) generally consumes more food, therefore might have higher intakes of potassium-rich food. The challenge, therefore, is to decrease the sodium intake while increasing the potassium intake even further, that is, making sure the population reaches the recommended Na:K ratio. The median Na:K in this study is 3.5, which is more than three times the recommended 1:1 by the WHO. It is important to note that not a single person from this population reached their Na:K ratio. This further supports the fact that more value should be placed on reaching the recommended potassium intake in this population together with the reduction in sodium intake. In a review article by Adrogué and Madias,¹⁸ the authors summarize the pathogenesis of both sodium and potassium on hypertension. This review provides strong evidence of a number of population studies,^{40–42} which reported an inverse relationship of potassium with blood pressure. Results from the INTERSALT study also reported an inverse relationship between urinary Na:K ratio and blood pressure, and further reported that the ratio had a stronger statistical relationship with blood pressure than either sodium or potassium alone.⁴³

Table 2

Percentage of the population in different salt intake and potassium excretion categories

Study (Ethnicity)	Salt Intake/d				Potassium Excretion	
	≤4 g/d (%)	4.1–5.9 g/d (%)	6–9.9 g/d (%)	≥10 g/d (%)	<90 mmol/d (%)	>90 mmol/d (%)
African-PREDICT (white)	13.4	17.5	35.3	33.8	92.7	7.2
African-PREDICT (black)	12.6	20.2	36.8	30.5	91.7	8.3
Thusa-Bothle (black)	23.2	10.1	30.4	36.2	87.1	12.9
KwaZulu-Natal (Indian)	23.3	27.2	35.0	14.6	98.1	1.9
Whole population	15.6	18.9	35.7	29.9	92.8	7.2

PREDICT, the African Prospective study on the Early Detection and Identification of Cardiovascular disease and Hypertension.

As mentioned, it is important to monitor the iodine levels of the population prelegislation. Iodine levels in the lowest salt category (≤ 4 g/d) still showed compliance to the recommended intake of iodine (152.6 $\mu\text{g/L}$). Charlton et al.⁴⁴ reported that the iodine levels of consumers within the recommended less than 5 g of salt/d were sufficient and within the recommended intake and that the median iodine level did not differ across the salt intake categories, as was also the case in the current study. It is also not mandatory to use iodized salt in the manufacturing of processed foods as well as salt packed in bags of at least 20 kg; therefore, the reduction of sodium in processed foods should not have an effect on the iodine levels.

There are a few limitations in the current study that should be noted. First, it would have been better to measure 24-hour sodium excretion in a large, nationally representative population sample, but despite limitations in funding to undertake such a study, the sampling frame used in the present study does capture both sexes, different age ranges, and ethnicities from different geographic regions of South Africa. Future sodium excretion data within these regional areas will be ideal for evaluating postlegislation salt intakes and the impact on public health. Only one 24-hour urine collection was taken from each participant. The ideal number of 24-hour urine collections depends on whether or not sodium is being estimated at individual or population level. As many as fourteen 24-hour urine collections may be needed for the accurate estimation of sodium intake at individual level because of the day-to-day variation.^{45,46} In a more recent balance study conducted by Lerchl et al.,⁴⁷ they conclude that single 24-hour urine collections at intakes ranging from 6 to 12 g salt/d were not suitable to detect a 3-g difference in individual salt intake and that repeated measurements of 24-hour urine collections will improve precision with regard to the sodium intake. By including a sufficient number of people, a single 24-hour urine collection should be adequate in estimating the mean sodium excretion for a population, with little error of the mean.⁴⁸ However, more than one 24-hour collection would give a more accurate representation of the sodium excretion of the population. Future research should also include balance studies in specifically this population group with regard to sodium and potassium excretion and the accuracy thereof. In a recent article from Bochud et al.⁴⁹ looking at the differences in the segmental handling of sodium along the proximal and distal nephron in black South Africans and white Belgians, they concluded that there are significant differences and that more research should be conducted on the accuracy to estimate sodium intake through 24-hour urine collections. Even though there is evidence suggesting that 24-hour urine collections has many limitations and needs further research. However, it is still regarded as the gold standard, and until a more accurate and “variation-free” method is established, this is the method that is recommended by the WHO to estimate population sodium intake. Monitoring of sodium intake in a

population is crucial, and alternative methods (to the collection of 24-hour urine collection) have been investigated. One of these methods includes the collection of an “overnight” urine sample. This method is easier to collect, and according to Luft et al provided, accurate results in terms of the sodium intake of a population. A home chloride strip can be used to estimate the urinary sodium excretion, which makes it a quick and easy alternative to the 24-hour urine collection.⁵⁰ However, this needs to be tested in the South African population in future studies before suggesting it as an alternative to 24-hour urine collections.

Possible reasons for not observing strong correlations in this population could be because of the population being apparently healthy and the population sample relatively small. As mentioned, the study design was never intended to establish these correlations.

Longitudinal data are needed to investigate the role of age on the relationship between sodium and blood pressure. Future follow-up of the African-PREDICT participants would shed some light on the role of age on the relationship between sodium intake and blood pressure. Another limitation of the current study is that no data were collected on the climate in the different areas, which could possibly have an effect on the excretion of sodium and potassium. Future studies should also be conducted that does not truncate the blood pressure values of the population, therefore including hypertensive and normotensive individuals.

The strength of this study lies in the providing of valuable and essential information regarding the current sodium and potassium intake in a sample of South Africans from different age groups and ethnicities. This information contributes not only to the much-needed local database, but also to the global body of knowledge and to a better understanding of the sodium and potassium consumption patterns around the world. More data are crucial in establishing effectiveness of the sodium reduction policy for future investigation.

Conclusion

The results presented in this study support the national sodium reduction intake strategy, including the regulation of the sodium content of 13 categories of foodstuffs, due to take effect in June 2016. The majority of the population studied consume more than the recommended 5 g of salt/d. However, more consideration should be given to promote an increase in potassium intake in South Africa. This, together with the sodium reduction regulation, may have a greater impact on public health than only focusing on sodium reduction.

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Authorship

BS formulated the research questions, collected and analyzed all data used in this article, assisted with the statistical analysis of data, and wrote the manuscript. AS critically reviewed manuscript, assisted in formulating the research question as well as the statistical analysis, and designed the African-PREDICT study. MC conducted all statistical analysis for the manuscript. KS formulated the research question and critically reviewed the manuscript. EWV formulated the research question, conceptualized the article, and critically reviewed the manuscript.

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