



**Australian Government**  
**Department of Health**



# **Australian and New Zealand Nutrient Reference Values for Sodium**

**A report prepared for the  
Australian Government Department of Health and the  
New Zealand Ministry of Health**

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## Disclaimer

This is a technical report to the 2017 NRVs for sodium: Suggested Dietary Target and Upper Level of Intake for adults. The recommendations apply to the generally healthy population and may not meet the specific nutritional requirements of all individuals. They are not intended to be clinical practice guidelines used by health professionals treating individuals or assessing diets of individuals. This technical report is based on the best information available at the date of compilation.

## **Council of the National Health and Medical Research Council Approval**



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### **National Health and Medical Research Council**

Updates to the guideline recommendations for sodium for adults were approved by the Chief Executive Officer of the National Health and Medical Research Council (NHMRC) on 13 July 2017, under Section 14A of the National Health and Medical Research Council Act 1992. In approving these guidelines the NHMRC considers that they meet the NHMRC standard for clinical practice guidelines. Approval of the guideline recommendations will be reviewed for currency after five years.

NHMRC is satisfied that the guideline recommendations are systematically derived, based on the identification and synthesis of the best available scientific evidence, and developed for health professionals/practitioners practising in an Australian and New Zealand health care setting.

## **Acknowledgments**

This report was prepared for the Australian Government Department of Health and the New Zealand Ministry of Health, by the Expert Working Group for Sodium: Professor Linda Tapsell, Professor Dorothy Mackerras, Dr Jacqui Webster, Dr Rachael McLean, Dr Barry Fields, Professor Victoria Flood, with Research Assistance from Dr Elizabeth Neale, Dr Deborah Nolan-Clark and Dr Judy Cunningham.

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# 1. Executive Summary

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## Executive Summary

This report addresses the 2014 revision of the Suggested Dietary Target (SDT) and Upper Level of intake (UL) for sodium. It tested the new Methodological Framework for the Review of Nutrient Reference Values (NRVs) and was limited in scope to adults.

Sodium (Na) has an essential role in the maintenance of key physiological activities such as extracellular fluid volume and cellular membrane potential. It is readily available in the food supply. At the population level, the relationship between high sodium intakes and increased systolic blood pressure makes high sodium intake a significant public health issue. The most recent 2013 Australian Dietary Guidelines (ADG) includes a recommendation to limit intakes of foods and drinks containing added salt (sodium chloride; NaCl). The New Zealand Food and Nutrition Guideline Statements for Healthy Adults recommend preparing and choosing foods low in salt [1]. The ADG, New Zealand Food and Nutrition Guideline Statements and this revision of the NRV referred to generally healthy adults in Australia and New Zealand. Given the definitions in the methodological framework, the SDT was considered the NRV which is most directly aligned to these guidelines.

In a general sense, where a NRV has not been reviewed, the value from the 2006 NRVs for Australia and New Zealand stand. Specifically for sodium, the 2006 NRVs for children, the AI for adults, the AI for pregnancy and the AI during lactation still apply. A new NRV, the SDT, has been developed for generally well adults. The new position that no UL value could be set is intended to replace the 2006 UL for adults. The SDT is the most appropriate NRV for preventive health strategies in the population and in relevant cases the SDT may now be referred to in place of the UL.

## Suggested Dietary Target

The SDT is a daily average intake from food and beverages for certain nutrients that will help in the prevention of chronic disease. In this case 'average' refers to the median intake of the population.

In contrast to the UL which is more suited for assessing population health risk, the SDT is more appropriate for guiding preventive health strategies. *The SDT is a target for the median dietary intake of the population.* To achieve this target, most individuals should be aiming to reduce their sodium intake.

The Australian and New Zealand sodium intakes are likely to be within the higher end of the range of intakes of the studies examined, so lowering sodium intake would reduce blood pressure. Therefore an **SDT has been set at 2000 mg/day** for the generally well adult population, based on whole of diet modelling that considered intakes of other nutrients and the current food supply.

## **Upper Level**

The UL is the highest average daily nutrient intake level likely to pose no adverse health effect to almost all individuals. 'Average' intake refers to the usual intake of an individual, typically assessed over several days. The new guidance on the determination of the UL *indicates a level for assessing health risk in the population.*

There is substantial evidence that increasing sodium intake increases blood pressure which is related to adverse health outcomes. Because blood pressure underpins normal physiological functioning, the 'adverse health effect' was defined as the point at which blood pressure increased at a higher rate for a given increase of sodium intake.

This point was not identifiable in the relationship between sodium and blood pressure across the range of sodium intakes in the studies examined. The result followed a systematic review of the scientific literature and a rigorous statistical analysis of available data.

Incremental increases in blood pressure were apparent with increasing sodium intake. Because there was no enhancement of this effect at any point in the range of sodium intakes tested in the studies, by definition a UL could not be determined and a provisional UL (PUL) is not appropriate.

### **Additional considerations**

The SDT applies to the generally well adult population and is not meant to replace clinical practice guidelines used by health professionals treating individuals.

The AI for all ages and the UL for children should be considered as part of a future review.

Communications around these NRVs need to be carefully considered. This exercise confirmed the relationship between sodium intake and blood pressure.

The proposed changes reflect an improvement in methodology and a clear application of the definitions. The SDT is the most appropriate NRV for preventive health strategies in the population.

## 2. Summary of Recommendations

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In a general sense, where a NRV has not been reviewed, the value from the 2006 NRVs for Australia and New Zealand stand. Specifically for sodium, the 2006 NRVs for children, the AI for adults, the AI for pregnancy and the AI during lactation still apply. A new NRV, the SDT, has been developed for generally well adults. The new position that no UL value could be set is intended to replace the 2006 UL for adults. The SDT is the most appropriate NRV for preventive health strategies in the population and in relevant cases the SDT may now be referred to in place of the UL.

- **The Suggested Dietary Target (SDT) for sodium has been determined as 2000 mg for the generally well adult population.**

The SDT is defined in consideration of the contribution of a nutrient intake to chronic disease risk. There is a convincing relationship between increasing sodium intake and increasing blood pressure in the population within the range across which the analysis was done.

The value is a change from the 2006 SDT. The 2006 value was not developed using the new methodological framework which refers to the desirable median intake of the population. The guidance on the determination of the SDT has been applied and the current value reflects the desirable median intake of the population. This is lower than likely current median intakes, so most individuals should be aiming to reduce their sodium intake.

The value for the SDT recognises that sodium intake is one dietary factor that contributes to the prevention of chronic disease, and that the effect of high sodium intakes is also seen in the context of a whole diet.

- **No Upper Level of intake for sodium has been set for the generally well adult population.**

The Upper Level is the highest average daily nutrient intake level likely to pose no adverse health effect to almost all individuals. The evidence on sodium intake and increasing blood pressure in the population appears consistent but it was not possible to define the highest average daily sodium intake where no adverse effects on blood pressure could be observed within the range across which the analysis was done. In other words, while incremental increases in blood pressure were apparent with increasing sodium intake, there was no enhancement of this effect at any point in the range of sodium intakes tested in the studies examined. Thus, applying the definition of a UL in the new methodological framework, a UL could not be determined. For the same reasons, a PUL is also not appropriate.

The recommendation is a change from the 2006 UL, reflecting the new guidance from the methodological framework on the determinants of the UL. Within this framework, there is insufficient evidence to support the determination of a single UL value with confidence. This

does not mean consumption is safe at any level, but rather, using the new methodology, a point estimate for the UL cannot be determined.

### **3. Introduction**

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NRVs are a set of recommended nutrient intakes designed to assist dietitians and other health professionals assess the dietary requirements of population groups or, for some NRVs individuals. Public health nutritionists, researchers, educators, food legislators and the food industry also use the NRVs for dietary modelling and/or food labelling and food formulation.

The current NRVs for Australia and New Zealand were published in 2006 after a comprehensive review process of the Recommended Dietary Intakes (the only type of nutrient reference value that had been produced at the time), commissioned by the Australian Government Department of Health (Health) in conjunction with the New Zealand Ministry of Health (NZ MoH).

The review resulted in a new set of recommendations known as the Nutrient Reference Values (NRVs) for Australia and New Zealand (2006). The National Health and Medical Research Council (NHMRC) carried out the 2006 review and recommended that these guidelines be reviewed every five years to ensure values remain relevant, appropriate and useful.

#### ***3.1 Scoping study***

In 2011 Health, in consultation with the NZ MoH, commissioned a scoping study to determine the need and scope for a review of NRVs. The scoping study considered developments in comparable countries, expert opinions, stakeholder consultation and public submissions. The scoping study concluded there was sufficient justification for conducting a review and as a result, Health and the NZ MoH engaged the Nous Group and a technical team led by Baker IDI to develop a Methodological Framework (the Framework) to guide future NRV reviews.

The scoping study also identified the rationale and triggers for reviewing specific nutrients including changes or developments to NRVs in comparable OECD countries, emergence of new evidence, impact on public health priorities and/or concerns regarding the strength of the underlying methodology or evidence. Fluoride, iodine and sodium were identified in the scoping study as a priority nutrient for review.

#### ***3.2 Methodological Framework***

In 2013, the Nous Group was contracted to develop the Framework to outline the overarching principles, methodologies, and approaches to ensure consistency of application and transparency in the NRV reviews across all nutrients. The Framework was developed

through multiple rounds of consultations with technical experts and relevant stakeholders in Australia and New Zealand.

The Framework is designed for application across a range of nutrients and provides high level guidance that should not be impacted by characteristics unique to specific nutrients.

### *3.3 Review process*

This review is funded by Health and the NZ MoH. The recommendations have been developed by independent experts, and the funding bodies have not influenced the content of the recommendations.

A Steering Group is overseeing the review process and is responsible for all strategic, and funding decisions for the review. It consists of representatives from both funding agencies, Health and the NZ MoH. The Steering Group is also responsible for the ongoing monitoring of triggers for a new review, and ensuring nutrient reviews are conducted in a timely manner.

The Steering Group appointed an Advisory Committee as an expert reference and advisory group that also acts as an independent moderator of nutrient recommendations. The Advisory Committee comprises members with a broad range of expertise, including experts in the areas of micronutrients, toxicology, public health, end user needs, research, chronic disease, nutrition and macronutrients.

The Steering Group, with advice from the Advisory Committee determined that fluoride, iodine and sodium are priority nutrients and first to be reviewed, with the purpose being to pilot the Framework.

The Steering Group (with the advice of the Advisory Committee), established a group of experts to conduct this sodium review. The Sodium Expert Working Group (EWG) was primarily responsible for examining scientific evidence and establishing nutrient values. Membership of the groups involved in the development of the sodium NRV guidelines can be found in Section 7.

Given the purpose of the review was to pilot the application of the Framework, and given time and resource constraints, the Sodium EWG narrowed the scope of the review to focus on the revision of the Suggested Dietary Target and Upper Level of Intake for sodium for adults.

In a general sense, where a NRV has not been reviewed, the value from the 2006 NRVs for Australia and New Zealand stand. Specifically for sodium, the 2006 NRVs for children, the AI for adults, the AI for pregnancy and the AI during lactation still apply. A new NRV, the SDT, has been developed for generally well adults. The new position that no UL value could be set is intended to replace the 2006 UL for adults. The SDT is the most appropriate NRV for

preventive health strategies in the population and in relevant cases the SDT may now be referred to in place of the UL.

The review process complies with the *2011 NHMRC Procedures and requirements for meeting the 2011 NHMRC standard for clinical practice guidelines*.

It is noted by the EWG that as this is a partial review, the remaining NRVs for sodium should be reviewed as soon as possible.

In line with the Framework, the following criteria are triggers for nutrient reviews:

- Changes to and/or developments in NRVs in comparable countries – changes have been made to recommendations for specific nutrients in comparable Organisation for Economic Cooperation and Development countries.
- Emergence of new evidence – the emergence of significant new evidence suggests the current NRV may be inappropriate for the population.
- Public health priority – fortification or widespread supplement use (due to the perceived need for a particular nutrient by the public) may require a review of nutrient recommendations.
- Methodological rigour – there are concerns regarding the strength and/or consistency of the methodology and evidence underpinning the current nutrient recommendations.

Future reviews will be undertaken in accordance with the Framework.

### *3.4 Public consultation*

A draft report of the NRV for sodium was submitted to the Advisory Committee in mid-2015 and was approved for public consultation.

The draft NRV review report for sodium was released for public consultation from 30 October 2015 to 11 December 2015. Public consultation is a requirement for this review under the National Health and Medical Research Council Act (1992).

For more information on the public consultation process and on submissions received please refer to the Review of NRVs for Sodium Public Consultation Report.

### *3.5 Background information - Sodium*

Sodium is a nutrient that is ubiquitous in the food supply and plays an essential role in human physiology. Excess sodium intakes have been associated with increased chronic disease risk, and in particular high blood pressure [2]. A comprehensive overview of the physiological role of sodium in the human body is provided in the Institute of Medicine's Dietary Reference Values document [3]. Briefly, sodium is the primary cation in human extracellular fluid. It has an essential role in the maintenance of key physiological activities such as extracellular fluid volume and cellular membrane potential [4]. Sodium balance is maintained through a range of physiological systems and hormones such as the renin-angiotensin-aldosterone hormone system, the sympathetic nervous system, atrial

natriuretic peptide, the kallikrein-kinin system and other factors that regulate renal and medullary blood flow [5]. In the absence of a situation where excessive sweating may be occurring, urinary sodium excretion in humans is approximately equivalent to intake [3]. Thus urinary sodium excretion is often used as a biomarker of intake.

Sodium is largely consumed as sodium chloride, or 'salt'. The 2006 NRVs accepted the position indicated in the literature that approximately 90% of the total sodium excreted in the urine came from dietary salt [5]. Sodium may also be found in food additives such as sodium phosphate, sodium bicarbonate and sodium benzoate, however these contribute much less to total sodium intakes than dietary salt.

Accurate estimations of dietary sodium intake are of particular importance given the potential negative health effects of excess dietary sodium. The relationship between high sodium intakes and elevated blood pressure has been established both in clinical trial research and large observational studies [6-8]. Elevated blood pressure is an established risk factor for the development of adverse health outcomes such as stroke [9], myocardial infarction [10], and chronic kidney disease [11]. Thus sodium intake is recognised as being of key public health importance. There may also be some value in considering effects of sodium intake on other heart disease risk factors, such as cholesterol levels.

Values for the Upper Level of Intake (UL) have previously been set in 2006 for Australia and New Zealand (Table 3.1). The Suggested Dietary Target (SDT) for adults was set at 1600 mg (70 mmol)/day.

**Table 3.1 Previous values for the UL for Australian/New Zealand populations [5]**

<b>Age groups by categories</b>	<b>Milligrams (mg)</b>	<b>Millimoles (mmol)</b>
<b>Infant</b>		
0–12 months	Not possible to establish. Source of intake should be through breast milk, formula and food only.	
<b>Children</b>		
1-3 yr	1000 mg/day	(43 mmol)
4-8 yr	1400 mg/day	(60 mmol)
9-13 yr	2000 mg/day	(86 mmol)
14-18 yr	2300 mg/day	(100 mmol)
<b>Adults 19+ yr</b>		
Men	2300 mg/day	(100 mmol)
Women	2300 mg/day	(100 mmol)
<b>Lactation</b>		
All ages	2300 mg/day	(100 mmol)

### *3.6 Target Users*

The NRV values are designed to assist dietitians and other health professionals assess the dietary requirements of the population. Public health nutritionists, food legislators and the food industry will also use this recommendation for preventive health strategies, dietary modelling and/or food labelling and food formulation.

Users need to be aware that the NRVs examined here (UL and SDT):

- apply to the generally well adult population;
- are applicable for population targets;
- do not serve as clinical practice guidelines used by health professionals treating individuals; and
- are not intended for assessing the diets of individuals.

However, as the new SDT is a target for the population median intake, most people in the population should be reducing their sodium intake.

## 4. Scope and Purpose

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The purpose of this review is to pilot the Framework and in doing so ensure the currency of NRVs for sodium with scientific methods and knowledge, particularly with relevance to population health. The area is constantly debated in the scientific literature. For example, it was noted that in the 2006 NRVs for Australia and New Zealand, the UL for sodium of 2300 mg/day (100 mmol/day) was based on experimental studies of sodium intake and blood pressure (such as the DASH trial [7]). The NRV document also refers to population studies showing low levels of hypertension and no other observed adverse effects where intakes were below this level. In 2014 there is not only a separate debate on the nature of the relationship between high blood pressure and morbidity and mortality in the population, but also new emerging evidence of associations between high sodium intakes and other endpoints such as stroke and cardiovascular disease [12].

The Expert Working Group (EWG) took the position that the association between high sodium intakes and elevated blood pressure indicated a significant public health problem for populations exposed to high sodium intakes. Given the potential for negative health effects from high sodium intakes, the most relevant NRVs for updating in this context remained the Suggested Dietary Target and the Upper Level of Intake. Further, as most of the available studies providing the evidence base were on adults, the focus of the review was on the SDT and UL for adult men and women. This approach was also adopted in the review of the Australian Dietary Guidelines. Due to time constraints, data relating to the essentiality of sodium were not examined, nor were considerations of whether an EAR or AI could be set to determine essentiality requirements. The effects of a single nutrient (sodium) on chronic disease risk was also considered in view of the fact this is only one component of a whole dietary pattern, whereas food synergies are likely to have the impact on health outcomes [13]. Nevertheless, unlike other single nutrients, the evidence linking sodium intakes to high blood pressure in populations has been recognised by authoritative bodies for some time.

This report focused on the revision of the Suggested Dietary Target (SDT) and Upper Level of Intake (UL) for sodium for adults using the methodological framework for the review of Nutrient Reference Values [14]. The EWG decided not to consider values for children due to time constraints for the pilot review.

The over-arching research question was *'Is it possible to define a level of sodium intake above which there is an increased risk of adverse health outcomes in the general adult population?'*

In conducting the systematic literature review (SLR), the population, intervention, comparator and outcome (PICO) question framework was applied and stated:

*'What is the effect of lower versus higher intakes of sodium on blood pressure, total cholesterol, HDL cholesterol and LDL cholesterol, myocardial infarction, total mortality and stroke within the adult population?'*

A risk analysis approach was applied to the development of the NRVs. The EWG noted the approach to risk assessment for nutrient toxicity utilised by authoritative bodies [15, 16], and that the terms used by the IOM were different from that of the WHO Food Risk Analysis Model [16]. The values derived for the NRVs were compared against existing intakes and recommendations, and interpretations were developed with reference to existing NRVs. The steps in the process reported here included:

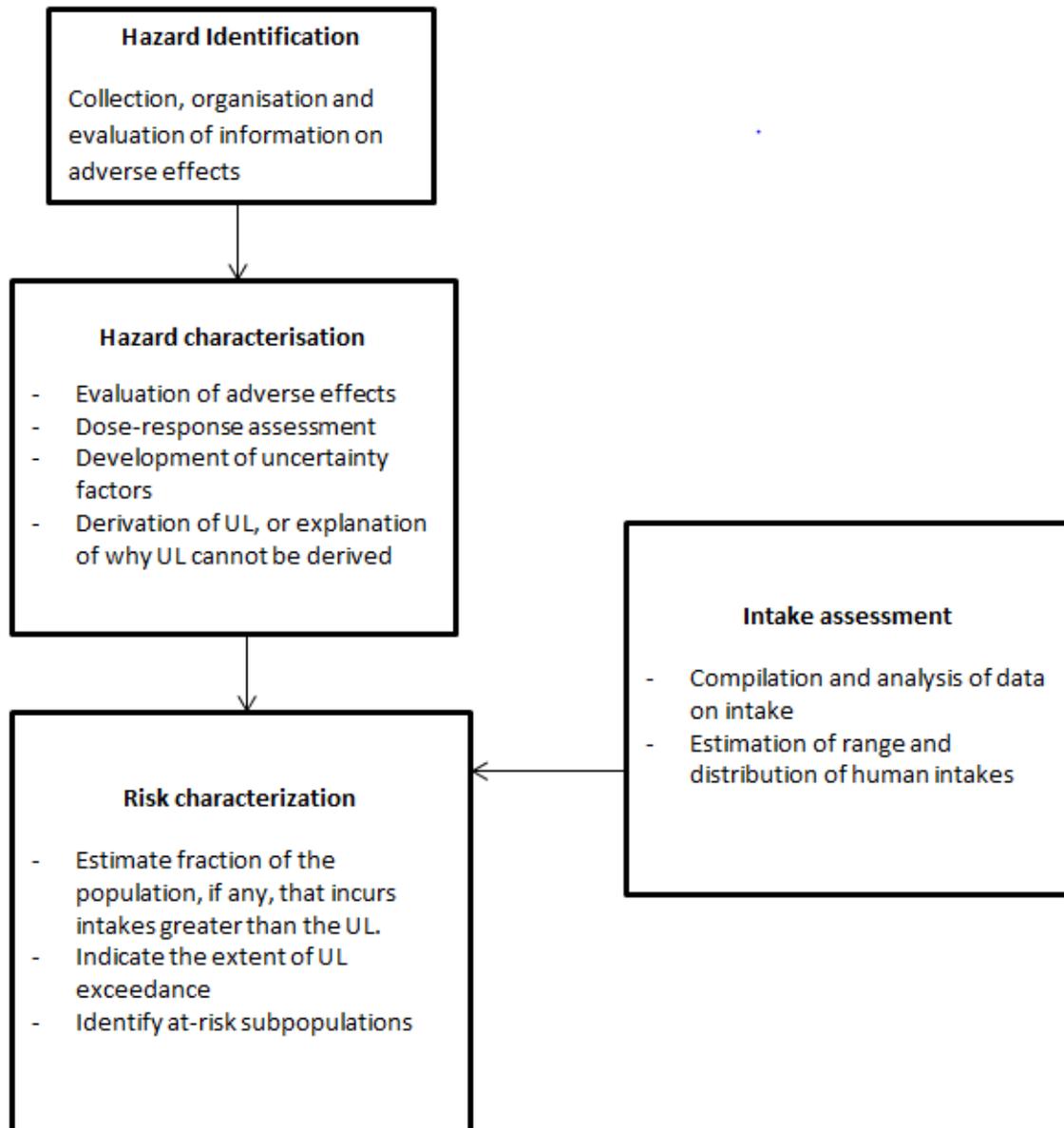
*Hazard identification:* conducted through the identification of biomarkers of intake and effects, and by systematic identification of relevant scientific literature addressing evidence of risks.

*Hazard characterisation:* undertaken by quality appraisal of the literature and statistical analysis of data derived from the studies considered. This was done to evaluate adverse effects and assess dose response relationships. The UL was considered from this analysis.

*Intake assessment:* undertaken via a consideration of the usual intake (referenced as the current AI) for the referent population, and intakes levels commensurate with Dietary Modelling for the Foundation Diets which served as a Support Document for the Australian Dietary Guidelines.

*Risk characterisation:* undertaken with consideration of the generally well adult population that included adults with hypertension.

Figure 4.1 Risk assessment model for nutrient toxicity (adapted from IOM [15] and FAO/WHO [16])



In conducting the review of the **SDT**, the EWG noted the following definition:

The SDT is a daily average intake from food and beverages for certain nutrients that will help in the prevention of chronic disease.

In this case 'average' refers to the median intake of the population. Using the NRV definitions the research question relating to the SDT was:

*'What is the daily average sodium intake from food and beverages that will help in the prevention of chronic disease?'*

The SDT is a recommendation to provide advice for a directional change in the current population dietary intake. Consequently, several things are taken into consideration. Unlike the UL, the selection of a value as the SDT is not solely based on the data from the literature cited in the Systematic Literature Review, and additional considerations such as current population intakes had to be identified and weighed to make the decision.

In conducting the review of the UL, the EWG noted the following definition:

The UL is the *highest average daily nutrient intake level likely to pose no adverse health effects to almost all individuals in the general population. As intake increases above the UL, the potential risk of adverse effects increases.*

Using the NRV definitions the research question relating to the UL was

*'Is it possible to define the highest average daily sodium intake likely to pose no adverse effects to almost all individuals in the general adult population?'*

Once a position on the UL for sodium was established by data analysis, comparisons were made with existing NRVs for sodium, and approaches to the derivation of the UL taken elsewhere.

## 5. Evidence Review (Technical report)

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The evidence review outlines the rationale for the approach taken to assessing the sodium-health relationship for the purposes of the NRVs. It covers the selection of biomarkers for dietary intake of sodium, disease end points, biomarkers of disease end points, and the approach taken to evidence review.

### 5.1 Selection of biomarkers

#### 5.1.1 Description of the biomarkers of dietary intake and study end points selected for the review

*Dietary sodium:* Urinary sodium excretion was considered to be the most robust dietary biomarker of sodium intake.

*Blood pressure:* Systolic, diastolic and mean arterial blood pressure.

*Study end points:* Total, low density lipoprotein (LDL) and high density lipoprotein (HDL) cholesterol were used as biomarkers of disease risk, as adverse effects of sodium restriction on these lipids have been alleged.

*Cardiovascular disease risk:* a range of cardiovascular disease end points including total mortality, stroke and myocardial infarction.

#### 5.1.2 Rationale for the selection of biomarker(s)

*Dietary sodium:* In order to examine the nature of the association between sodium intakes and health risk, accurate estimates of sodium intake are required. Given the known problems of dietary assessment methods, biomarkers of sodium intake were considered with reference to sodium physiology. Under normal circumstances the vast majority of sodium excretion occurs via the urine (around 90%), and some sodium is also lost through the skin in sweat, and in faeces [17].

Limitations to the accuracy of dietary assessment data include lack of quantification of discretionary salt use, accuracy of information about brands of food items reported as consumed, accuracy of food composition databases, and day-to-day variability of sodium intake. Dietary assessment of sodium intakes may therefore underestimate total intake by around 10-20% [18, 19], although a recent validation study suggests that the USDA's Automated Multiple-Pass Method of collecting dietary data using 24 hour recalls reports accurate sodium intake estimates [20]. Food frequency questionnaires (FFQ) are also used, and can overcome issues relating to day-to-day variability by assessing intake over longer periods, however it is difficult to accurately quantify intake using a FFQ, and this method will also depend greatly on the list of food items in the FFQ, and infrequently include information about brands [21].

The most accurate method of estimating total dietary sodium intake is to measure excretion via collection of a 24-hour urine sample, and it is widely regarded as the 'gold standard' for estimating dietary sodium intake in individuals in the previous 24 hours [22]. There are a number of disadvantages in this method however: there is a high level of respondent burden and urine samples may be returned incomplete, thereby reducing their accuracy [23, 24]. Day-to-day variation of salt intake is considerable, and an accurate measure of an individual's usual or long term sodium intake requires several 24-hour assessments [22, 25].

*Blood pressure:* Although blood pressure is a risk factor rather than a disease endpoint, it has been widely used internationally in the determination of NRVs for sodium as there is good evidence from well conducted trials of its relationship with dietary sodium intake, and some evidence for certain cardiovascular disease endpoints. Therefore changes in blood pressure were selected as the primary endpoint for this review.

A consistent association between dietary sodium intake and blood pressure has been demonstrated in observational studies, clinical trials, and meta-analyses [26, 27] although it is well-recognised that not all high blood pressure responds to sodium reduction [28]. Elevated blood pressure has recently been described as the leading risk factor for global burden of disease, due to its association with a wide range of cardiovascular disease endpoints, including ischaemic heart disease and stroke [29]. Traditionally the interpretation of blood pressure levels has resulted in a dichotomisation into clinical terms referred to as hypertension (elevated blood pressure) and normotension (normal blood pressure). Increasingly, however, it is recognised that this distinction is somewhat arbitrary in terms of CVD risk management. Observational studies show that the relationship between blood pressure and ischaemic heart disease and stroke is log-linear, and independent of other risk factors, between at least 115/75 mmHg and 185/115 mmHg [30, 31]. Cut points for the definition of 'hypertension' have varied over time, between countries, and are population specific. Rather than individual risk factor management, overall cardiovascular disease risk management based on multiple risk factors is now favoured in New Zealand and Australia [32, 33]. For this reason the term 'elevated blood pressure' has been used in this report in favour of 'hypertension', unless referring to individual studies which have classified patients in this way.

Having said that, the focus of the revision of the SDT and UL was on chronic disease prevention so the SLR examined the effects of sodium intake in otherwise healthy adult populations. Studies with participants identified as 'hypertensive' were included, as elevated blood pressure is common in the Australian and New Zealand adult populations. For example in the 2008/09 New Zealand Adult Nutrition Survey 15% of adults 15 years and older reported taking medication to lower blood pressure, and 31% could be defined as having hypertension [34]. The 2011-12 Australian Health Survey reported that 21.5% of individuals aged 18 years and older had measured blood pressure greater than 140/90

mmHg. However, this was based only on measurement at the interview and excluded those with normotension who were managing their condition via medication [35].

*Study end points:* Several outcomes were considered owing to suggestions that lowering the sodium content of the diet might have possible adverse effects [36]. The potential for very low sodium diets to be associated with activation of the renin-angiotensin-aldosterone system has been implicated [37]. Thus, studies on serum total cholesterol, LDL and HDL cholesterol were included in the review in order to identify possible adverse effects on overall CVD risk. This was consistent with the approach taken by the Institute of Medicine and World Health Organization [4, 38].

*Cardiovascular disease related endpoints:* Cardiovascular disease (particularly ischaemic heart disease and stroke) remains a leading cause of morbidity and mortality in Australia and New Zealand. Despite a number of studies showing a reduction in CVD associated with lower sodium intakes [39, 40] some recent observational studies have raised the possibility of an association between low sodium diets and increased risk of CVD (for example [81]). Therefore IHD, stroke and total mortality were included in the review to check for potential adverse effects on these outcomes of lowering sodium.

## 5.2 Selection of evidence

Evidence from the scientific literature was sought in two phases. First, systematic literature reviews (SLRs) recently produced by authoritative bodies and informing revisions of sodium NRVs were considered and individual studies referenced in these reviews were noted. Second an independent search was conducted to identify newly published studies or reviews that were not included in the previous reviews. The full body of evidence (all identified studies) then underwent critical appraisal using the GRADE system [42], and data from the studies were analysed for the current purposes.

### 5.2.1 Data used during the review

The evidence for this review was first examined through recently published SLRs reporting effects of reduced sodium intake on blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, myocardial infarction, total mortality or stroke. Six recently published SLRs [4, 43-47] were identified. Two of the SLRs [43, 44] also included data on the relationship between sodium intake and effects on factors that were outside the scope of the review, such as renin, aldosterone, renal function and triglycerides. In addition to the SLRs, references from the previous Institute of Medicine (IoM) Dietary Reference Values for sodium were examined [3].

The second phase of data collection was conducted through a systematic search of the literature as outlined below.

## 5.2.2 Methodology

The methodological framework provided to the Expert Working Group [14] served as a guiding document. The SLR methodology addressed the requirements of the PRISMA statement for Transparent Reporting of Systematic Reviews and Meta-analyses [48].

An expanded PICO framework (PICO TS – Population, Intervention, Comparison, Outcomes, Timing, Study design) was utilised to inform the search strategy relating to the following research question:

*What is the effect of a high versus a low intake of sodium on blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, stroke, myocardial infarction and total mortality in the general adult population?.*

### **Population:**

Adults (defined as individuals aged 18 years and older).

Inclusion criteria: both normotensive individuals and individuals with hypertension (with or without medication), individuals with diabetes (either type 1 or type 2) that has not progressed to nephropathy or chronic kidney disease.

Exclusion criteria: individuals with severe disease such as congestive cardiac failure, end stage renal failure or cancer, pregnant females, children (defined as individuals aged under 18 years).

### **Intervention:**

An intake of sodium achieved either by allocating all subjects to low sodium intakes and randomising all to two or more intakes of sodium via supplements/foods or randomising subjects to two or more different sodium intakes by providing dietary advice and/or foods.

### **Inclusion criteria:**

Three types of studies were eligible for inclusion in the review:

1. studies involving randomised controlled trials with NaCl supplements or sodium enriched food/drink or placebo or other known sodium dose.
2. co-interventions that use simultaneous interventions whereby the role of sodium can be isolated.
3. unblinded dietary advice to reduce sodium compared to usual intake or a different diet.

Studies including urinary sodium excretion data (minimum 8 hours).

**Exclusion criteria:**

Co-intervention studies where the role of sodium may not be isolated, studies without a minimum of 8 hours of urinary sodium excretion data, studies involving exercise as an intervention due to unknown effects on sodium excretion.

**Comparator:**

A second arm was required in which subjects were given a different, well-described intake of sodium.

**Outcome:**

Studies must report one or more of total mortality, stroke, myocardial infarction, total, LDL or HDL cholesterol or blood pressure (must note method of measurement).

**Time:**

Study duration of trials measuring blood pressure, total, HDL or LDL cholesterol must be of at least 4 weeks duration. Studies evaluating myocardial infarction, stroke or total mortality must be of at least 6 months duration.

**Study design:**

Limited to randomised controlled trials.

As outlined above six SLRs examining reduced sodium intake and effects on blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, myocardial infarction, total mortality or stroke were identified. The studies included within these reviews were added to a database of potential literature to be evaluated against the inclusion and exclusion criteria of the current review.

To obtain articles published after the aforementioned systematic reviews (between 2011 and 2014), an additional systematic search was conducted. Of the six SLRs used, Gaudal et al. [44] was identified as having a wider inclusion criteria than that defined by the Expert Working Group whereas the other reviews had narrower criteria. Therefore, the search terms and combinations were selected to align with the Gaudal et al search strategy taking into account the outcomes of interest defined in the present review. This allowed the Gaudal review to be updated. Restrictions to the current analysis were then applied.

The databases Medline, Web of Science, PubMed and the Cochrane Library were searched with the search terms and limits described in Supporting Document 1.

Initially, the search was conducted to cover the time period of 22 July 2011 – 3 December 2013. The search was then updated to identify any new studies published up to November 2014.

All articles identified following both phases of the literature search were scrutinised against the previously defined inclusion and exclusion criteria by experienced researchers to determine their relevance to the current review.

### **5.2.3 Assumptions and limitations**

The document review strategy followed the option of updating a review, as outlined in the Methodological Framework for the Revision of the NRVs [14]. A potential limitation of this approach was the reliance on published high quality SLRs from the peer-reviewed literature or expert groups to have done a thorough search and retrieved all relevant literature. However, the reviews came from several different groups who were working independently and so the risk of oversight was minimal. In addition, this review was limited to NRVs for adults and an evidence base focusing on the relationships between dietary sodium intake and blood pressure. A number of dietary and other factors have been shown to be associated with blood pressure including potassium intake, alcohol intake and weight status [49]. Furthermore, particular population groups such as African Americans, obese adults, and those with pre-existing elevated blood pressure may be more 'salt sensitive', which is reflected in, for example, the 2010 USDA Dietary Guidelines for Americans which recommend a lower SDT for sodium of 1500 mg/day "among persons who are 51 and older and those of any age who are African American or have hypertension, diabetes, or chronic kidney disease" [50]. However the subsequent IOM report has rejected this view, indicating a lack of evidence. The influences of other dietary factors, or specific population groups were not considered in the current analysis, introducing a potential source of error.

### **5.2.4 Rationale for decisions**

Decisions on inclusions and exclusions of studies and on the PICO (TS) framework were made via consensus by the Expert Working Group. This was done in consideration of the methodological framework for the revision of the NRVs [14]. It was pertinent to consider time constraints for the project when evaluating the evidence base, so the population was restricted to adults and the study designs to RCTs. Studies involving individuals with disease states such as congestive cardiac failure or end stage renal failure were excluded as the disease pathology may influence sodium or fluid status.

Studies which only included dietary assessment of sodium intake without measurement of urinary sodium excretion were not considered due to their potential for inaccuracies. Spot urine, overnight urine and 12-hour urine sampling have been used as a convenient alternative to 24-hour urinary collection. While spot urine collection shows promise as a method to estimate population level intake estimates, it is likely to be inaccurate on an individual level and therefore an unreliable measure of intake in clinical trials and observational studies linking sodium intake with health outcomes in individuals [51-53] because the unreliability in measurement can obscure links to potential small changes in health effects. Therefore, when defining the inclusion criteria for the current SLR, studies had to include a collection of urine lasting at least 8 hours.

Study duration was restricted to a minimum of 4 weeks when evaluating changes in biomarkers of disease risk such as blood pressure and cholesterol. This time frame reflects

the minimum time required to observe changes in blood pressure following dietary modification [54]. For studies assessing myocardial infarction, stroke and mortality, a time frame of 6 months was selected based on the chronic nature of these outcomes.

### 5.3 Review of evidence

#### 5.3.1 Methods used

A risk of bias assessment table was developed for each study identified in the review. The table was based on the categories outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* [55]. Additional information was added to the table to ensure that all information required for the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method of appraising the quality of evidence in systematic reviews [42] were captured.

The GRADE approach to appraising the quality of evidence for each outcome was adopted for the current review. GRADEProfiler software (Version 3.6) was utilised to facilitate this process, with decisions on the quality of evidence guided by the strategy outlined by Barbu et al. [39] and Guyatt et al. [56]. Due to time constraints, meta-analyses were not conducted for diastolic blood pressure and mortality outcomes (see Supporting Document 2), therefore GRADE assessments of the quality of evidence could not be conducted for these outcomes. In addition, article summary tables included an assessment of the National Health and Medical Research Council (NHMRC) level of evidence [57].

#### **Primary outcome**

Full details of the statistical analyses on systolic blood pressure are contained in Supporting Document 2. Briefly, data from all included articles were summarised. Where available, data were extracted separately for sex, ethnicity and hypertension status subgroups. Studies were to be further characterised based on their participants' hypertension status, which was classified according to current Australian hypertension cut-offs to ensure currency of data [32] but this information was not always available.

Studies were analysed by comparing the effect on blood pressure in the group with the higher sodium excretion to the group with the lower sodium excretion, irrespective of whether the study author had called the group 'intervention' or 'control'. Because studies tested a wide range of sodium intakes, the high intake in one study might have been the low intake in another. Where studies reported more than two groups [7, 58, 59], the low and intermediate groups (corresponding to sodium intakes of approximately 50 mmol/day and 100 mmol/day respectively) were selected for analysis based on consensus with the Expert Working Group.

Urinary sodium and potassium data was generally reported in mmol in the papers and was converted to mg/24hr. The difference in urinary sodium and potassium excretion between high and low sodium groups was calculated using the following equation:

$$\text{Difference in 24 hour urinary excretion} = \text{24 hour urinary excretion at the end of the low sodium period} - \text{24 hour urinary excretion at the end of the higher sodium period}$$

Where urinary excretion values were measured over an eight hour period, values were converted to 24 hour values by multiplying by 3.8 and 4.9 for sodium and potassium respectively [60].

Outcome data were extracted from Graudal et al [44] with some checking. Some results had to be calculated using the formulas outlined in Supporting Document 2 or from the WHO review if the same formulas had been used. A key aim of the dose-response assessment is the identification of a No Observed Adverse Effect Level (NOAEL) which is defined as ‘the highest intake of a substance at which no adverse effects have been observed’. If there are insufficient data to allow the setting of a NOAEL, the Lowest Observed Adverse Effect level (LOAEL) is then identified. The LOAEL is defined as: ‘the lowest intake of a substance at which an adverse effect has been observed’.

### ***Secondary outcomes***

Analysis of data on diastolic blood pressure was not a focus of this report due to time constraints. The EWG prioritised the analysis of systolic blood pressure data as this has been demonstrated to be of greater clinical importance [61].

### ***Possible adverse effects***

Random-effects meta-analyses were conducted for total cholesterol, HDL cholesterol and LDL cholesterol data (Supporting Document 2). Results of studies reporting the relative risk of stroke, myocardial infarction and mortality were described.

## **5.3.2 Results**

Details of the search findings and applications of exclusion criteria are contained in Supporting Document 1. Briefly, 61 articles describing 57 studies were included in the SLR. One study [62] was identified as meeting the inclusion criteria during the initial 2011 - 2013 search. An additional study [35] was identified in the second search (3 December 2013 – 10 November 2014), however as its results were consistent with the larger body of evidence, inclusion of this study in the quantitative analysis would not influence the results of the review or result in downgrading of the evidence. Therefore it was not included in the meta-analysis. A PRISMA flow diagram detailing the inclusion and exclusion of studies is shown in Supporting Document 1.

The risk of bias assessments for all included studies are shown in Supporting Document 1 as Appendix 6. The summary of findings table including GRADE assessments relevant to each outcome of interest are also shown in Supporting Document 1 (Appendix 7).

The number of included studies conducted in Australia was 14 [35, 63-75], with 2 studies included that were conducted in New Zealand [76, 77]. Of the remaining studies, 28 were conducted in European countries [58, 78-103] and 14 in the USA [7, 59, 60, 62, 104-113]. No included studies were conducted in countries in the continents of Asia or Africa.

Data were available for a total of 2315 intervention participants and 2310 control participants in the parallel studies, with data available for 1574 participants (1549 for the meta-analyses) in the cross-over studies. There were 26 parallel studies relating to sodium and a relevant health effect [60, 64-68, 70-72, 74, 75, 77, 78, 82-84, 90, 94, 95, 98, 101, 104, 105, 108-111] and 31 crossover studies (30 included in the meta-analyses) [7, 35, 58, 62, 63, 69, 73, 76, 80-82, 85-89, 91-93, 96, 97, 99-103, 106, 107, 109, 112, 113].

### ***Resting systolic blood pressure***

Fifty five studies [7, 58, 60, 62-66, 68-113] contributing 66 strata were considered (see Supporting Document 2). Within these studies, 40 studies (46 strata) [58, 63-66, 70-73, 75-91, 93, 95, 97-99, 103-106, 108, 109, 112, 113] were conducted in participants with a degree of hypertension, 11 studies (14 strata) [60, 68, 69, 74, 81, 96, 100, 102, 107, 110, 111] were conducted in normotensive participants and 5 studies (6 strata) [7, 62, 92, 94, 101] were conducted in both normotensive and hypertensive populations (where the participants could not be separated into either hypertensive or normotensive). As one study [81] presented data separately for normotensive and hypertensive participants, this study was included in the total count for both sub-groups. As previously described, an additional study conducted in normotensive participants [35], which found a non-significant reduction in systolic blood pressure, was not included in the meta-analysis but would be unlikely to influence results.

When sub-groups were considered, reductions in systolic blood pressure following a low sodium diet appeared to be different in participants with hypertension, with reported changes ranging from -17 mmHg to 6.3 mmHg, compared to studies of normotensive individuals (range: -10 mmHg to 1.7 mmHg), or those involving both normotensive and hypertensive individuals (range: -12 mmHg to 0.1 mmHg). As data on results in individuals of different ethnicities were only available for two studies [87, 104], it was not considered appropriate to draw conclusions on the impact of ethnicity on blood pressure response.

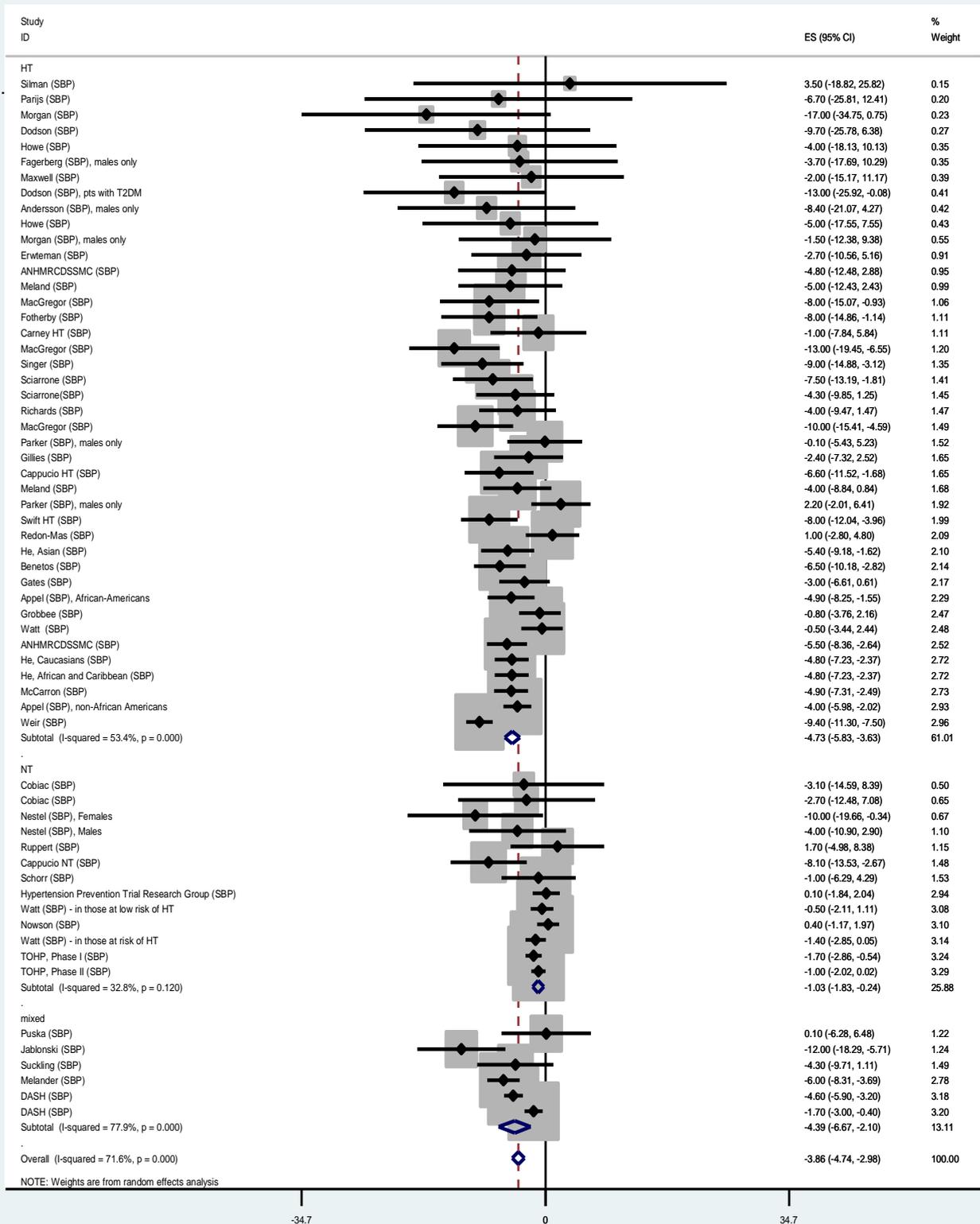
For the meta-analysis, 55 studies yielded 66 strata from which 5 were excluded from analysis owing to incomplete data or extreme values. Overall, there was a weighted average reduction in systolic blood pressure in the low sodium group compared to the high sodium group (-3.9 mm Hg; 95%CI; -4.7 to -3.0 mm Hg). Heterogeneity among the studies was classified as medium overall ( $I^2=72\%$ ). The impact on systolic blood pressure was different in

normotensive people (-1.0 mm Hg) and hypertensive people (-4.7mm Hg). The studies included in the meta-analysis contained a much higher proportion of hypertensive groups than the prevalence in Australia or New Zealand and so the overall meta-analysis results cannot be extrapolated to the two countries. Using a prevalence of 30% (from a survey in Australia that defined hypertension based on either blood pressure measurement at interview or use of medication) to weight the category specific results for hypertensive people and normotensive people yields an estimated reduction of 2.1 mm Hg in systolic blood pressure in the adult population if mean sodium excretion decreases from about 3500 mg/day to about 2100 mg/day.

This meta-analysis confirms the accuracy of data extraction by yielding comparable overall estimates to other reviews. However, it does not allow the location of the UL to be determined because a cut-off point could not be identified, but also because the analysis assumes that the effect of a sodium reduction is unrelated to the actual intake. For a UL to be set, then the analysis would have to take into account the fact that the effect of a particular sodium reduction depends on the actual intake (or excretion).

The association between different measures of sodium excretion and systolic blood pressure were examined in several ways owing to the correlation between the three measures of sodium excretion (in the low group, the high group and the difference between the groups). A point at which increasing sodium excretion increased the impact on systolic blood pressure could not be identified either in all sub-groups or in hypertensive people. The available data covered the range 1200-3300 mg/day sodium in the low sodium group and we conclude that the data are linear in this range. Similarly, no conclusion could be drawn when the study groups were categorised according to the excretion in the high sodium excretion group. Therefore, if there is a point at which the impact of increases in sodium intake increases the size of the effect on systolic blood pressure compared to lower intakes (i.e. a point that could approximate a UL), it does not lie in the range of the data examined. It cannot be extrapolated from the data because the systolic blood pressure response outside the range of the data may not be linear. This was noted, bearing in mind that the dose-response of a physiological parameter also may be non-linear but merely adaptive, and reversible, and therefore not adverse and not appropriate for setting a UL. Conversely, a response could be linear but end up crossing a tolerance threshold at a high enough intake of a substance, resulting in an adverse effect. Either way, the data available did not expose a possible NOAEL or LOAEL from either of these perspectives that could be used to derive a UL.

Therefore the available data do not allow the setting of a LOAEL or a NOAEL, because an intake level at which the dose-response relationship is greater relative to the response at lower intakes has not been established. The same analysis does not allow identification of an SDT.



**Figure 5.2 Meta-analysis of the difference in systolic blood pressure in the group with lower 24 hour urinary Na excretion compared to the group with higher Na excretion, by hypertension status (hypertensive – HT – vs normotensive – NT) of participants at baseline, ordered by decreasing width of 95% confidence interval**

### ***Resting diastolic blood pressure***

Fifty seven studies [7, 35, 58, 60, 62-78, 80-113] contributing 69 strata contributed to the exploration of resting diastolic blood pressure. Within these studies, 41 studies (48 strata) [58, 63-67, 70-73, 75-91, 93, 95, 97-99, 103-106, 108, 109, 112, 113] were conducted in participants with a degree of hypertension, 12 studies (15 strata) [35, 60, 68, 69, 74, 81, 96, 100, 102, 107, 110, 111] were conducted in normotensive participants and 5 studies (6 strata) [7, 62, 92, 94, 101] were conducted in a both normotensive and hypertensive populations (where the participants could not be separated into either hypertensive or normotensive).

As with systolic blood pressure, when sub-groups were considered, reductions in diastolic blood pressure following a low sodium diet appeared to be different in participants with hypertension, with changes ranging from -9 mmHg to 3.8 mmHg, compared to studies of normotensive individuals (range: -5 mmHg to 1.4 mmHg), or those involving both normotensive and hypertensive individuals (range: -3 mmHg to -0.7 mmHg).

### ***Mean arterial pressure***

A total of 7 studies (8 sub-analyses) evaluated the effect of sodium on mean arterial pressure [35, 79, 80, 96, 99, 100, 113] with changes following a low sodium diet ranging from -10 mmHg to 1 mmHg.

### ***Serum cholesterol levels***

The effect of sodium on total cholesterol levels was reported in 14 studies (16 strata) [59, 62, 75, 81, 86, 90, 91, 96, 102, 106, 109, 113-115]. Outcomes for HDL-cholesterol were reported in 11 studies (12 strata) [62, 75, 90, 91, 96, 102, 106, 109, 114, 115] and LDL-cholesterol in 8 studies (10 strata) [62, 75, 96, 102, 106, 109, 114, 115].

Following consumption of a low sodium diet, all studies reported non-significant changes in total, HDL and LDL cholesterol. These changes ranged from -0.200 mmol/L to 0.212 mmol/L for total cholesterol, -0.199 mmol/L to 0.078 mmol/L for HDL cholesterol, and -0.233 mmol/L to 0.209 mmol/L for LDL cholesterol.

There was no significant effect of sodium reduction on total, HDL or LDL cholesterol identified from the meta-analysis (Table 5.1).

**Table 5.1 Pooled results for the effect of sodium reduction on total, HDL and LDL cholesterol (mmol/L)<sup>1</sup>**

<b>Outcome</b>	<b>Intervention group participants (n)</b>	<b>Control group participants (n)</b>	<b>Strata (n)</b>	<b>Weighted mean difference</b>	<b>95% Confidence Intervals</b>
Total cholesterol	804	803	16	0.032	-0.019 to 0.084
HDL cholesterol	661	660	12	-0.006	-0.021 to 0.009
LDL cholesterol	622	621	10	0.013	-0.062 to 0.088

<sup>1</sup> Studies listed in Supporting Document 1

***Stroke, myocardial infarction and total mortality outcomes***

Only one study reported analysed data relating to the effect of dietary sodium intake on the incidence of myocardial infarction and stroke [104], while three studies reported data on the incidence of mortality [60, 66, 111]. There was no significant difference in the number of events in individuals consuming a low or higher sodium diet (Table 5.2).

**Table 5.2 Effect of sodium consumption on the incidence of long term outcomes**

<b>Outcomes</b>	<b>Relative risk</b>	<b>95% confidence</b>
Stroke [104]	0.50	0.05, 5.47
Myocardial Infarction [104]	0.50	0.09, 2.70
Mortality		
Morgan et al. [66]	2.91	0.12, 68.81
Hypertension Prevention Trial [60]	1.04	0.07, 16.54
Whelton [111]	1.50	0.25, 8.96

### 5.3.3 Summary of methods used and decisions made in formulating recommendations

1. The Sodium EWG began with the position that the association between high sodium intakes and elevated blood pressure may indicate a significant public health problem for populations exposed to high sodium intakes. In this context, the relevant NRVs were the SDT and the UL.
2. Evidence of adverse effects from the consumption of sodium was sought through systematic review of the scientific literature. The adverse effects were taken as an increase in blood pressure from increased dietary sodium.
3. Decisions on inclusions and exclusions of studies and on the PICO (TS) framework were made via consensus by the Sodium EWG.
4. Population inclusions were justified as follows:
  - a. Normotensive and hypertensive adults:
    - i. The adverse effect of interest was the relationship between sodium intake and blood pressure, so high blood pressure was relevant and hypertension is prevalent in the community.
    - ii. The classification of 'hypertension' is based on a defined cut off for blood pressure, so the Sodium EWG determined to include data on adults with hypertension /high blood pressure in the analysis. (Sub group analyses for the different groups were conducted in the meta-analyses for SBP and effects were greater in people with hypertension, but effects were still seen in both).
  - b. Adults with diabetes: Diabetes is a chronic condition prevalent in the community and sufferers not progressing to nephropathy or CKD were not likely to have further pathophysiological conditions that may confound effects on BP.
5. Population exclusions were justified as:
  - a. Children: Time constraints in undertaking the review for children.
  - b. Pregnant women: physiological impact on blood pressure from pregnancy
  - c. Individuals with severe diseases (CCF, ESRF, Cancer): as the disease pathology may influence sodium or fluid status.
6. Studies undertaken in the 2011 Cochrane review were accessed and screened, and a further search was undertaken to include any additional studies to December 2013. This was updated again in November 2014. A small number of additional more recent papers were considered by the Sodium EWG following the public consultation in October – November 2015 to address specific issues raised. These papers were not considered to be relevant to the establishment of the SDT or UL and were therefore not included in the report.
7. Articles were summarised and assessed for risk of bias using the Cochrane framework.
8. A meta-analysis was conducted using studies with SBP as the outcome.
9. The GRADE assessment was conducted on the body of evidence for SBP effects.

10. The Sodium EWG accepted the high GRADE assessment for evidence relating to effects on SBP for hypertensive and normotensive people.
11. Based on the GRADE assessment and the meta-analysis the Sodium EWG accepted that the evidence supported an effect of a dose response relationship between sodium intakes and blood pressure.
12. SDT: The Sodium EWG noted that the current intakes of sodium in Australia and New Zealand were within the higher end of the range of sodium intakes in the studies examined (around 2000mg/day). Thus from a *population perspective*, lowering the median intake of sodium should lower blood pressure in the population.
13. The Sodium EWG considered the SDT as the median intake for the population that may help prevent chronic disease, and set the level at 2000mg/day.
14. The Sodium EWG further considered this value as consistent with international recommendations, in particular WHO recommendations.
15. The Sodium EWG also considered this value to be consistent with the sodium levels estimated to emerge from Total Diet models supporting the Australian Dietary Guidelines. Thus, the SDT was consistent with the consumption of a healthy diet in the context of the target population.
16. UL: The Sodium EWG noted that 'ULs should only be developed when there is strong, high quality evidence supporting the potential for significant harm from realistically achievable dietary intakes (from diet and supplements combined), and that ' In cases where the data supporting adverse effects of high intakes of a nutrient is of poor quality, speculative, reliant on biomarkers of uncertain relationship to primary health outcomes, or derived from populations with unusual or deficient diets, alternative options to setting a UL may include setting a provisional UL, not determining a UL, or stating that a UL is not required'.
17. The statistical analysis undertaken to examine the relationship between sodium intake and blood pressure using data from the SLR studies demonstrated that it was not possible to identify an intake where the risk of change in systolic blood pressure shifts from non-existent to present (or from weaker to stronger).
18. The Sodium EWG found that the cutpoint analysis did not reveal a sodium intake at which the magnitude of the relationship between sodium intake and blood pressure changed. Thus it was not possible to determine a value for a UL. This does not mean consumption is safe at any level, but rather, using the new methodology, a point estimate for the UL cannot be determined. On this basis the Sodium EWG made the decision not to set a UL.
19. The final outcomes of the Sodium EWG deliberations were that a new NRV, the SDT, was developed for generally well adults. A revised statement on the UL was agreed upon to replace the 2006 UL for adults. The Sodium EWG was of the position that the SDT was the most appropriate NRV for preventive health strategies in the population. In relevant cases this meant the SDT could be referred to in place of the UL.

## 6. Guideline recommendations

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In a general sense, where a NRV has not been reviewed, the value from the 2006 NRVs for Australia and New Zealand stand. Specifically for sodium, the 2006 NRVs for children, the AI for adults, the AI for pregnancy and the AI during lactation still apply. A new NRV, the SDT, has been developed for generally well adults. A new NRV, the SDT, has been developed for generally well adults. The new position that no UL value could be set is intended to replace the 2006 UL for adults. The SDT is the most appropriate NRV for preventive health strategies in the population and in relevant cases the SDT may now be referred to in place of the UL.

- **The Suggested Dietary Target (SDT) for sodium has been determined as 2000 mg for the generally well adult population.**

The SDT is defined in consideration of the contribution of a nutrient intake to chronic disease risk. There is a convincing relationship between increasing sodium intake and increasing blood pressure in the population within the range across which the analysis was done.

The value is a change from the 2006 SDT. The 2006 value was not developed using the new methodological framework which refers to the desirable median intake of the population. The guidance on the determination of the SDT has been applied and the current value reflects the desirable median intake of the population. This is lower than the likely current median intake (see Section 6.2), so most individuals should be aiming to reduce their sodium intake. This new value is supported by strong evidence that reducing sodium intake from likely current dietary levels to the SDT would reduce systolic blood pressure by 2 mm Hg in the total population. It is the target recently arrived at by WHO using different criteria and aligns well with the dietary modelling for the ADG.

The value for the SDT recognises that sodium intake is one dietary factor that contributes to the prevention of chronic disease, and that the effect of high sodium intakes is also seen in the context of a whole diet.

- **No Upper Level of intake for sodium has been set for the generally well adult population.**

The Upper Level is the highest average daily nutrient intake level likely to pose no adverse health effect to almost all individuals. The evidence on sodium intake and increasing blood pressure in the population appears consistent but it was not possible to define the highest average daily sodium intake where no adverse effects on blood pressure could be observed within the range across which the analysis was done. In other words, while incremental increases in blood pressure were apparent with increasing sodium intake, there was no enhancement of this effect at any point in the range of sodium intakes tested in the studies examined. Thus, applying the definition a UL in the new methodological framework, a UL could not be determined and a PUL is not appropriate.

The recommendation is a change from the 2006 UL, reflecting the new guidance from the methodological framework on the determinants of the UL. Within this framework, there is insufficient evidence to support the determination of a single UL value with confidence. This does not mean consumption is safe at any level, but rather, using the new methodology, a point estimate for the UL cannot be determined. No Upper Level of intake for sodium has been set.

The evidence on sodium intake and blood pressure in the population appears consistent but it was not possible to define the highest average daily sodium intake where no adverse effects on blood pressure could be observed.

## *6.1 Rationale for any changes to previous values*

The revised NRVs represent changes from the previous values. This reflects the revised definitions provided by the Framework document [14], consideration of the outcomes of the evidence review, and changes made by international authorities. A summary of these considerations are presented below.

### **6.1.1 New methodological framework**

The new framework indicated that evidence should be assessed separately for deficiency status and the prevention of chronic disease. The sodium report focused on the latter because deficiency is not an issue for this nutrient. Contextual features were considered, including the feasibility of the NRVs given current food choices. In turn, this also recognised that sodium is delivered in foods that deliver other nutrients, and that there is a need for a diet to provide requirements for all nutrients as well as sodium. Finally global public health efforts for addressing the prevalence of non-communicable diseases related to sodium intake were considered.

Unlike the UL, the consideration of the SDT did not involve a dose-response analysis of potential adverse effects. Concepts such as NOAEL or LOAEL did not apply. In keeping with the new Framework, the SDT was set as a desired target for the population median intake.

In the case of the UL, the Framework [14], states that: 'ULs should only be developed when there is strong, high quality evidence supporting the potential for significant harm from realistically achievable dietary intakes (from diet and supplements combined)'. In cases where the data supporting adverse effects of high intakes of a nutrient is of poor quality, speculative, reliant on biomarkers of uncertain relationship to primary health outcomes, or derived from populations with unusual or deficient diets, alternative options to setting a UL may include setting a provisional UL, not determining a UL, or stating that a UL is not required [14].

**Table 6.1 Criteria for using different categories of Upper Level of Intake [14]**

<b>Option</b>	<b>Criteria</b>	<b>Frequency</b>
<b>Upper Level of Intake</b>	Good evidence of an adverse effect in humans at realistically achievable intakes; AND Sufficient data to support establishment of a dose response relationship.	Expressed per day, week or month as appropriate for individual nutrients.
<b>Provisional UL</b>	Sufficient evidence of adverse effects in humans at realistic levels of intake; AND Nature or extent of the evidence is insufficient to determine a point estimate of the safe upper level with reasonable confidence.	Expressed per day, week or month as appropriate for individual nutrients
<b>Not determined</b>	An absence of evidence of hazard; OR Some evidence of potential adverse effects at high intake levels well above that normally achievable in the diet; OR The evidence is insufficient to support the determination of a UL with any confidence.	N/A
<b>Not required</b>	Good quality evidence demonstrating no adverse outcomes from nutrient intakes well above amounts normally achievable from the diet.	N/A

In order to determine a position with respect to these criteria, a risk analysis approach was taken for nutrient toxicity [15, 16]. Hazard identification involved the collection and evaluation of all available information relating to the adverse effects associated with consumption of a specific nutrient. In this context, the adverse effect, defined as: ‘any significant alteration in the structure or function of the human organism or any impairment of a physiologically important function’ [15] was addressed primarily in terms of an increase in blood pressure from increased dietary sodium intake. The EWG found the model could not be used in its entirety for a number of reasons.

Biomarkers of intake and study end points were consistent with current positions on diet and blood pressure (Section 5.1.2). Relevant literature providing the evidence base for nutrient-health associations was identified (Supporting Document 1). The SLR applied the GRADE quality appraisal process to examine individual studies (Supporting Document 1). The analysis of data derived from these studies confirmed there was an overall effect of sodium intake on blood pressure. The cutpoint analysis did not, however, reveal a sodium

intake at which the magnitude of the relationship between sodium and blood pressure changed. Thus it was not possible to determine a value for a UL.

### **6.1.2 Outcomes of review**

*Evidence of effects:* While the SLR conducted for this report, and the associated statistical analysis, showed a lack of evidence of effects of sodium intake on disease outcomes, mortality, and cholesterol levels, it did show consistent evidence of the effect of reducing sodium intake on reductions in systolic blood pressure in the range examined. Given that mortality and disease end points are likely to be influenced by multiple factors, (of which blood pressure is one), the EWG determined that the blood pressure effects were a significant enough basis for the analysis to try to determine a UL. The effects were viewed progressively for cutpoints between 1100 mg/day and 3700 mg/day Na, by increments of 100 mg Na. Graphical analyses of data from these studies showed that below about 2000 mg/day, the difference in blood pressure was larger in the group of studies above the cutpoint than below the cutpoint (i.e. there was a stronger effect in the studies with higher sodium intakes that were categorised as belonging to a “low sodium group”) but the reverse was true above 2000 mg/day (not corrected for confounding by differences in the sodium range tested). The above-cutpoint groups tested a smaller range of sodium differences than the below-cutpoint set at all cutpoint values. The above- and below-cutpoint groups showed the same mean difference in systolic blood pressure when expressed per 500 mg difference in sodium (about -1.5 mmHg per 500 mg reduction in Na excretion). Therefore differences observed in the analysis of systolic blood pressure above and below 2000 mg/day of sodium intake were due to confounding by variation among the studies in the sodium intakes prescribed between the high and low sodium groups. This analysis did not test for many small differences (for example from 1200 to 1500 mg) but as the relationship appeared present with increasing intakes the assumption was made that the difference was possibly similar. This analysis is shown in full, including graphical presentation, in Supporting Document 2.

*Determination of SDT:* With respect to the SDT, a target for the prevention of raised blood pressure was considered relevant given that in the range of 1200-3300 mg of 24-hour Na excretion, a dose-response relationship can be observed between a decrease in sodium intake and decrease in systolic blood pressure (about 1.5 mmHg/500 mg). The meta-analysis showed a reduction in systolic blood pressure when mean population excretion was lowered from about 3500 mg/day to 2100 mg/day. This would lead to an SDT of an intake that is equivalent to an excretion of 2100 mg/day. The recommended SDT in this report is rounded to 2000 mg/day to reflect:

- Lack of a precision in change in the dose relationship at exactly 2100 mg.
- Consideration of the dietary modelling (below).
- Consistency with international recommendations (such as WHO).

- Acknowledgement that given current population mean intakes in Australia and New Zealand, a SDT of 2000 mg is aspirational. The 2012 WHO guideline for sodium was established at 2000 mg (5 g/day salt) based on a comprehensive review and meta-analysis which concluded that reducing sodium to less than 2000 mg/day was more beneficial to blood pressure than reducing sodium intake but still consuming more than 2000 mg/day.

As population dietary intake levels decrease and more data emerge about the relationship between sodium intake and blood pressure at lower levels (i.e. below 2000 mg/day), further revision of the SDT downwards may be appropriate.

*Relevance to foods and the total diet:* The dietary modelling for the Foundation Diets associated with the Australian Dietary Guidelines produced a value for dietary intake of about 1200 mg sodium/day in the process of working with a judicious combination of foods aimed at delivering all nutrient requirements (Supporting Document 3). These models contained insufficient energy to cover the needs of most of the population, and the 7-day diets for the Total Diet models (which included foods beyond the minimum to meet nutrient requirements and meet energy needs) produced dietary sodium intakes closer to average daily sodium intakes in the order of 1900-2200 mg in young men and 1700-2000 mg in young women of average activity. So setting the SDT at 2000 mg/day means that it is more likely to be achievable in parallel with obtaining a sufficient intake of energy. As parallel initiatives to encourage the food industry to lower the salt content of foods are undertaken, changes to the food supply may occur and it may be possible to achieve an adequate energy intake on lower sodium intakes, so the SDT may be revised downwards.

*Determination of the UL:* Across a range of sodium excretion levels (indicating diet), a relationship between reduction in sodium intake and reduction in systolic blood pressure was found. The relationship between dietary sodium and systolic blood pressure was related to the size of the reduction in sodium excretion in each study and this relationship did not vary across the range of 1200-3300 mg/day in the data examined. The EWG noted that an effect was observed in the DASH study [7] which informed the setting of the UL in 2006. The analysis conducted for this 2014 review indicates a need to revise this position. The 2006 NRV report set the UL for sodium based on two studies [7, 58], but further studies and developments in methodology have expanded the range of inputs. The 2014 review worked from a definition of the UL which implicated a point above which an adverse effect was identifiable, but it was noted that both the studies considered for the 2006 review showed that there was a lessening of effect in the higher intake group. Further, the dose-response relationship between sodium and blood pressure examined in the 2014 review did not have any breakpoints. This means it is not possible to identify the NOAEL across the range of 1200-3300 mg/day in the low sodium group.

In this situation where it is accepted that there is an effect, but a NOAEL cannot be determined, a UL cannot be set. The definitions of “Not determined” and “Not required”

both refer to “well above that normally achievable in the diet”. Our SLR (Supporting Document 1) confirmed previous reviews that there was strong evidence that decreasing intakes of sodium decreased systolic blood pressure (the GRADE quality of evidence assessment was high when hypertensive and normotensive participants were analysed separately). The inclusion of new studies since the earlier versions of the review by He et al [116] (which was the basis of the salt guideline in the 2013 ADG) did not alter the association. Thus the analysis shows that it is not possible to identify an intake where the risk of change in systolic blood pressure shifts from non-existent to present (or from weaker to stronger). In answering the research question, it was not considered possible to define the highest average daily sodium intake likely to pose no adverse effects to almost all individuals in the general adult population. Thus it was not possible to define a UL based on the dose-response relationship between sodium and systolic blood pressure observed.

### **6.1.3 Comparisons with international guidelines**

The issues raised by the different regional groups reflect many of the challenges faced in deriving the NRVs, including SDTs for Australia/ New Zealand as discussed in this report.

The previous UL values for Australia and New Zealand (2006) and USA/Canada were the same, but EFSA and Japan have not set a UL for sodium (Table 6.2). The 2005 IOM report noted that it is difficult to precisely determine a UL due to the ‘progressive and continuous’ nature of the relationship between sodium intake and blood pressure. In 2006 EFSA went further and stated that it was not possible to determine a threshold level of sodium intake below which there is unlikely to be adverse effects on blood pressure. Japan also did not set a UL although specific reasons for this were not detailed. Three of the countries have specified a value for adequacy to compensate for endogenous sodium losses but only Japan has called this an EAR rather than AI.

**Table 6.2 Selected Sodium NRVs: Australia/New Zealand, USA/Canada, EFSA, Japan.**

Country	UL	SDT	AI	Approach
Australia & New Zealand (2006) [5]	2300 mg /day (100 mmol/day)	1600 mg (70 mmol/day)	460-920 mg/day	<p><u>UL</u>: Based on population studies that identified low levels of hypertension and no other observed adverse effects with intakes below this level &amp; experimental data</p> <p><u>SDT</u>: Selected in line with past WHO recommendations</p> <p><u>AI</u>: Set to ensure basic sodium requirements are met and allow for adequate intake of other nutrients</p>
USA & Canada (Institute of Medicine) (2005) [3]	2300 mg /day (100 mmol/day)	Not available	<p>1.5 g/day (65 mmol/day) for adults aged 19-50</p> <p>1.3 g/day (55 mmol/day) for adults aged 51-70</p>	<p><u>UL</u>: Based on clinical trial evidence exploring dose response between blood pressure and sodium (commonly the next level above the adequate intake that was tested)</p> <p><u>AI</u>: based on meeting sodium needs and that of other nutrients in apparently healthy individuals using foods found in a Western-type diet</p>
European Food Safety Authority (EFSA) (2006) [117]	Not available	Not available		<p><u>UL</u>: Report indicated available data not sufficient to establish a UL</p> <p><u>SDT</u>: not set as yet</p>
Japan (2010) [118]	Not available	<9 g salt for males, <7.5 g salt for females	<p>Did not set AI</p> <p>Set an EAR of 600 mg/day</p>	<p><u>SDT</u>: Review of epidemiological evidence of relationship between sodium intake, blood pressure and cancer – taking into consideration Japanese sodium intake and NRVs from Western countries</p>

## 6.2 *Validity and applicability of recommendations*

In the context of this report, the validity of recommendations was considered in line with current dietary sodium intakes. Most studies suggest that adults in Australia and New Zealand have a dietary intake of approximately 3600 mg of sodium/day which is more than double the existing SDT [119].

The estimated level of intake is commensurate with a 2008 review of studies that used the 24 hour urine to measure sodium intake showed intakes of between 2440 mg/day (females only) and 4800 mg/day [120]. Since then several more studies on small population groups using 24 hour urine have been published showing that sodium intake per person per day in Australia varies, for example, 2898 mg/day (Adelaide) [121], 3600 mg/day (Lithgow, NSW) [122] and 3800 mg/day for men and 2800 mg/day for women in Victoria.

The most recent estimate of dietary sodium intake for New Zealand adults is from a population survey of a representative sample of 301 adults aged 18-64 years living in two urban areas (Dunedin and Wellington) in 2012. Participants were recruited from the electoral roll and, due to a relatively low response rate of 23%, the sample was supplemented by 50 volunteers. Assessment of sodium intake was undertaken by 24 hour urine collection. The mean 24 hour sodium excretion was 3373 mg/day (95%CI 3208, 3539). The vast majority (93 %) of participants had a 24 hour sodium excretion that exceeded the SDT of 1600 mg/day while approximately three quarters (76%) had a 24 hour sodium excretion that exceeded the UL for sodium of 2300 mg/day [123]. These estimates are consistent with previous population surveys in New Zealand [124-126], suggesting that dietary sodium intake for adults has remained relatively stable over the past three decades.

The 2011-12 Australian Health Survey analysed the proportion of sodium that comes from the diet, excluding discretionary salt [127]. For the population aged 2 years and older, cereals and cereal products and cereal based product and dishes contribute 43% of dietary sodium (including 14.8% from breads, flat breads and sweet breads and English muffins and 14.6% from mixed dishes where cereal is the major ingredient), 8% of dietary sodium is contributed by milk products and dishes and 6% from processed meat. Although 1.9% of dietary sodium came from snack foods, including potato crisps, this varied by age from 4.8% among those aged 4-8 years to less than 1% in those aged over 50 years [127]. Similar figures have also been reported among an assessment of Australian Indigenous children and non-Indigenous children living in rural NSW (n=215), with 19-21% of sodium in the diet from bread, 14-16% from processed meat, 7-9% from take-away foods, 5.5-7.5% from potato crisps [128].

In New Zealand breads, cereals, and processed meats are likely to contribute most to sodium intake from processed food. Several analyses of results from the 1997 Adult Nutrition Survey matched to food composition data from the New Zealand Food Composition Database, and the New Zealand Total Diet Survey have been undertaken.

These suggest that for all age groups bread made the greatest contribution to sodium intake from processed foods (at approximately 35-43%) [129]. Processed meats, sauces, breakfast cereals and baked products are also likely to be important sources of dietary sodium [130]. Other foods that are likely to contribute significantly to dietary sodium intake in New Zealand include takeaways, dairy products, cereals and pasta, biscuits and cake and meat and meat products [131]. Since these analyses were undertaken the sodium content of bread has been reduced [132], however the effect of this on contribution to sodium intake has not been formally evaluated. Current sodium intake estimates suggest that it is going to be difficult for individuals or groups to reduce intake to levels consistent with the proposed NRVs.

There are clearly challenges in setting NRVs for sodium, that are likely to be similar for a number of nutrients where the setting of NRVs is to reduce chronic disease, rather than reduce dietary deficiency. A precise threshold where intake is associated with increased evidence of harm is unable to be defined given the current evidence available. However, there is a large amount of consistent evidence associating higher sodium intakes and elevated blood pressure. Further clinical trials examining the effect of sodium lowering to levels below 1200 mg/day may in future reveal a threshold level. Lack of NRV guidance on this issue may be interpreted as lack of evidence, rather than lack of precision, and would be inconsistent with the goal of reducing chronic disease, and may undermine public health efforts to reduce sodium intake.

### **Applicability**

The SDT reflects the desirable median intake of the population. Thus it is applicable for population targets and is not intended for individual use. It applies to the generally well adult population and is not meant to replace clinical practice guidelines used by health professionals treating individual people.

Current sodium intake estimates for Australia and New Zealand suggest that sodium intake is higher than the recommended SDT. This means that for the population target to be reached, most people should be aiming to reduce their sodium intake.

The NRVs are health based guidance values serving as reference standards to be considered in developing clinical practice guidelines, and as the basis for public health policy initiatives. They can provide a benchmark for activities that involve monitoring and assessing population sodium intake and sodium levels in the food supply. The recommendations may assist health professionals develop preventive health strategies and public health messages that sodium intake should be reduced to improve health.

## 7. Membership of groups and committees involved in the development process

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### ***Membership of the Nutrient Reference Values Steering Group***

The Steering Group for the project is composed of representatives from the Australian Government Department of Health, and the New Zealand Ministry of Health and makes decisions relating to the strategic, technical and funding elements of the project.

Membership is held by the following positions:

#### **Australian Government Department of Health:**

- Assistant Secretary - Preventive Health Policy Branch, Population Health and Sport Division.
- Director – Food and Nutrition Policy Section, Population Health and Sport Division.

#### **New Zealand Ministry of Health:**

- Director/Deputy Director of Public Health, Protection Regulation and Assurance Business Unit.
- Team Leader & Senior Advisor (Nutrition), Clinical Leadership, Protection and Regulation Business Unit.

### ***Membership of the Nutrient Reference Values Advisory Committee***

The NRV Advisory Committee includes members with technical expertise in the areas of micronutrients, toxicology, nutrition risk assessment, public health, end user needs, research, chronic disease, and nutrition. The role of the Advisory Committee is to provide advice to the Steering Group on the nutrient priorities for review, appointments and to support the nutrient specific Expert Working Groups. Membership of the Advisory Committee is outlined below.

#### **Professor Samir Samman (Chair)**

*Head of the Department of Human Nutrition, University of Otago, New Zealand*

*Expertise:* micronutrients, biomarkers and the role they play in informing nutritional status and disease risk in humans. Professor Samman's interest in micronutrients has involved him in a range of national and international committees including the US National Institutes of Health and UN International Atomic Energy Agency committees that considered nutrient biomarkers.

*Role:* Chair the Advisory Committee meetings and provide expert reference and advice to the Steering Group and guidance to the Expert Working Groups on the development of the reports including on micronutrient research components, and responses to methodological and independent expert reviews.

**Ms Janis Baines**

*Manager, Food Data Analysis Section, Food Standards Australia New Zealand*

*Expertise:* nutrition; chemistry; food regulation; nutrient risk assessment including dietary exposure assessment methods and nutrient fortification assessments; NRV end-use; and food composition. Ms Baines has been an expert member (and chair) of a number of Joint FAO/WHO expert committees in relation to dietary exposure assessment methods for food chemicals, including nutrients.

*Role:* Contribute expert advice to the Steering Group and guidance to the Expert Working Groups on the development of the reports, including on end user needs and dietary exposure assessment aspects. Chair of the Fluoride Expert Working Group.

**Associate Professor Marijka Batterham**

*Director of Statistical Consulting Service in Informatics, University of Wollongong*

*Expertise:* statistics and nutrition research. Dr Batterham is an accredited statistician and advanced accredited practising dietitian. Dr Batterham is the Director of the Statistical Consulting Service in Informatics and works across the University of Wollongong to assist students and staff members with the statistical design and analysis of their research.

*Role:* Contribute expert advice to the Steering Group and guidance to the Expert Working Groups on the development of the reports, including on nutrition research and statistical elements.

**Professor Michael Fenech (until March 2016)**

*Professor, CSIRO Food & Nutritional Sciences*

*Expertise:* micronutrients, genetic toxicology, genome health, nutrition research. Dr Fenech has written reviews relating to biomarkers of genome damage relevant to cancer risk and the role of folate and B12 in prevention of DNA damage.

*Role:* Contribute expert advice to the Steering Group and guidance to the Expert Working Groups on the development of the reports, including on nutrition research elements.

**Professor Mark Lawrence**

*Professor, School of Exercise and Nutrition Sciences, Deakin University*

*Expertise:* public health, food and nutrition policy, and food systems. Professor Lawrence is a technical adviser to the World Health Organisation, a member of the FSANZ Public Health Dialogue and a member of the 2013 Australian Dietary Guidelines Working Committee.

*Role:* Contribute expert advice to the Steering Group and guidance to the Expert Working Groups on the development of the reports, including on public health and end user needs.

**Professor Jim Mann**

*Professor in Human Nutrition and Medicine, University of Otago and Consultant Physician (Endocrinology), Dunedin Hospital*

*Expertise:* nutrition epidemiology; research and public health; chronic disease; endocrinology; and medicine. Professor Mann is the Director of Edgar Diabetes and Obesity Research and the WHO Collaborating Centre for Human Nutrition; the Principal Investigator for the Riddet Institute at Massey University; and has chaired several WHO/FAO Expert Advisory Groups and Scientific Update Groups.

*Role:* Contribute expert advice to the Steering Group and guidance to the Expert Working Groups on the development of the reports, including on nutritional epidemiology, public health and chronic disease elements.

**Professor Murray Skeaff**

*Professor in Human Nutrition, University of Otago*

*Expertise:* nutritional epidemiology and nutrition research. Professor Skeaff is a member of the FSANZ Health Claims Scientific Advisory Group, the New Zealand Heart Foundation's Scientific Advisory Committee and has been a member of the technical advisory groups for the Eating and Health Activity Guidelines and a number of FAO/WHO nutrition expert groups.

*Role:* Contribute expert advice to the Steering Group and guidance to the Expert Working Groups on the development of the reports, including on nutritional epidemiology and research elements.

**Professor Linda Tapsell AM**

*Senior Professor, School of Medicine, University of Wollongong*

*Expertise:* nutrition and dietetics, nutrition research translation, evidence based review and guideline development. Professor Tapsell is a member of the FSANZ Health Claims Scientific Advisory Group, the 2013 Australian Dietary Guidelines Working Committee and several international science advisory committees. Professor Tapsell worked in health services before becoming an academic.

*Role:* Contribute expert advice to the Steering Group and guidance to the Expert Working Groups on the development of the reports, including on nutrition research, evidence based

guideline development aspects, and end-user needs. Chair of the Sodium Expert Working Group.

**Associate Professor Sheila Skeaff (proxy member from March 2015)**

*Professor, Department of Human Nutrition, University of Otago*

*Expertise:* nutrition research. Associate Professor Skeaff's expertise is in trace element research with a particular emphasis on iodine. Associate Professor Skeaff is particularly interested in assessing the iodine status of vulnerable groups of the population including children and pregnant women. Associate Professor Skeaff is the current President of the Nutrition Society of New Zealand.

*Role:* Contribute expert advice to the Steering Group and guidance to the Expert Working Groups on the development of the reports, including on nutrition research. Deputy Chair of the Iodine Expert Working Group.

**Emeritus Professor Christine Thomson (until February 2015)**

*Professor, Department of Human Nutrition, University of Otago*

*Expertise:* nutrition research and public health. Professor Thomson's research involved studies of the nutritional importance of selenium and iodine for New Zealand residents, which has gained international recognition. This research identified a re-emergence of mild iodine deficiency in New Zealand.

*Role:* Contribute expert advice to the Steering Group and guidance to the Expert Working Groups on the development of the reports, including on nutrition research and public health elements. Chair of the Iodine Expert Working Group until February 2015.

**Professor Lynne Daniels (2013)**

*Head of School, Exercise & Nutrition Sciences, Queensland University of Technology*

*Expertise:* nutrition research. Professor Daniels was appointed to a newly established capacity building research chair within the Institute Health and Biomedical Innovation. Professor Daniels research interests include nutrition and feeding in infancy and early childhood, childhood obesity, selenium status of infants and nutrition assessment and support of older adults.

*Role:* Contribute expert advice to the Steering Group and guidance to the Expert Working Groups on the development of the reports, including on nutrition research elements.

### ***Membership of the Nutrient Reference Values Sodium Expert Working Group***

The Sodium Expert Working Group is responsible for examining scientific evidence and establishing nutrient values for sodium. Membership of the Sodium Expert Working Group is outlined below.

#### **Professor Linda Tapsell AM (Chair)**

*Senior Professor, School of Medicine, University of Wollongong*

*Expertise:* nutrition and dietetics, nutrition research translation, evidence based review and guideline development. Professor Tapsell is a member of the FSANZ Health Claims Scientific Advisory Group, the 2013 Australian Dietary Guidelines Working Committee and several international science advisory committees. Professor Tapsell worked in health services before becoming an academic.

*Role:* Chair EWG meetings, report on progress in Advisory Group meetings, contribute to the development of the report, including on nutrition research, evidence based guideline development aspects, and end-user needs. In conjunction with the EWG and Advisory Committee, develop responses to the public consultation and methodological and independent expert reviews.

#### **Dr Barry Fields**

*Senior Toxicologist, Food Standards Australia New Zealand*

*Expertise:* toxicology and risk assessment of food additives, contaminants and processing aids. Dr Fields obtained his PhD in chemistry from the University of Sydney. He has worked as a research fellow at the University of Sydney and a senior toxicologist at the Therapeutic Goods Administration.

*Role:* contribute to development of the report, including advise on toxicological frameworks and tools for use in undertaking risk analysis and on end-user needs.

#### **Professor Vicki Flood**

*Professor of Allied Health, Faculty of Health Sciences, Charles Perkins Centre, University of Sydney*

*Expertise:* nutrition epidemiology and public health nutrition interventions, micronutrient research including folate, vitamin B12 and sodium. Research areas include chronic disease, food security of vulnerable population groups and micronutrient research. Professor Flood has represented Australia at international meetings, such as the World Health Organisation.

*Role:* contribute to development of the report, including advise on public health context relevant to guidelines and nutrition research elements.

**Professor Dorothy Mackerras**

*Chief Public Health Nutrition Advisor, Food Standards Australia New Zealand*

*Expertise:* nutritional epidemiology and dietary methods, public health nutrition, critical appraisal of scientific evidence, statistics, and food standards and guidelines development. Professor Mackerras obtained her PhD in epidemiology in the United States and is well known in Australia for her expertise in nutritional epidemiology and dietary methods.

*Role:* contribute to development of the report, including preparing supporting documents containing statistical analyses and dietary modelling underpinning the development of the NRVs and on end-user needs.

**Dr Rachael McLean**

*Public Health Physician & Senior Lecturer in Public Health Nutrition, University of Otago*

*Expertise:* medical endocrinology and public health, evidence based review and guidelines development. Research interests include monitoring population dietary sodium intake, public health approaches to dietary sodium reduction, and the relationship between dietary sodium and cardiovascular disease.

*Role:* contribute to development of the report, including advise on public health and clinical aspects relevant to the use of the NRVs.

**Dr Jacqui Webster**

*Director, WHO Collaborating Centre on Population Salt Reduction, George Institute  
Senior lecturer in public health, University of Sydney*

*Expertise:* nutritional epidemiology and public health nutrition interventions. Her primary research interest relates to the development and evaluation of population strategies to reduce salt intake. Dr Webster previously established and implemented the UK Government's salt reduction strategy. Dr Webster regularly contributes to national and international policy development.

*Role:* contribute to development of the report, including advise on public health context relevant to guidelines and nutrition research elements.

**Observer****Ms Xenia Cleanthous**

*Manager of Nutrition Data and Analysis, National Heart Foundation of Australia*

*Expertise:* nutrition and dietetics, food and nutrition data analysis, and NGO functions including policy development, program planning and advocacy.

*Role:* to serve as an observer of process as a community member and for a learning opportunity for future reviews.

### **Research Assistants**

#### **Dr Elizabeth Neale**

*Director, Landmark Nutrition Australia*

*Expertise:* nutrition and dietetics and systematic literature review (SLR) methods for evidence based guidelines development.

*Role:* to undertake the SLR process and develop draft reports for consideration by the Sodium EWG.

#### **Dr Deborah Nolan-Clark**

*Director, Landmark Nutrition Australia*

*Expertise:* nutrition and dietetics and systematic review methods for evidence based guidelines development.

*Role:* to undertake the SLR process and develop draft reports for consideration by the Sodium EWG.

#### **Dr Judy Cunningham**

*Consultant*

*Expertise:* food regulation, risk assessment including dietary exposure assessment methods and nutrient fortification assessments, NRV end-use and food composition.

*Role:* scientific editor.

### *Declarations of interest process*

Declarations of interest were made by all members of the Advisory Committee and EWGs during the review process in accordance with the requirements of the *National Health and Medical Research Council Act 1992*. A record of interests was made publicly available on Health's website to ensure transparency. Visit [NRV Advisory Committee membership](#) and [NRV Sodium Expert Working Group membership](#).

Members were required to update their information as soon as they became aware of any changes and there was a standing agenda item at each meeting where declarations of interest were called for and recorded in the meeting minutes. Should a member have identified as having a significant real or perceived conflict of interest, a requirement was that the member would be requested to leave the room or not participate in discussions on matters where a conflict was identified.

## 8. Glossary

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ADG	Australian Dietary Guidelines
AI	Adequate Intake - The average daily nutrient intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate (used when an EAR cannot be determined)
BP	Blood Pressure
CI	Confidence Interval
CVD	Cardiovascular Disease
EAR	Estimated Average Requirement – A daily nutrient level estimated to meet the requirements of half the healthy individuals in a sex <sup>1</sup> and particular life stage group
FFQ	Food Frequency Questionnaire
HDL	High density Lipoprotein
HT	Hypertensive – Usually defined as systolic blood pressure above $\geq 140$ and/or diastolic blood pressure $\geq 90$ mmHg
IHD	Ischaemic Heart Disease
IOM	Institute of Medicine
K	Potassium
LDL	Low Density Lipoprotein
LOAEL	Lowest Observed Adverse Effect level- Lowest dose at which there is a measurable adverse effect from a test substance in a test subject or population.
Na	Sodium

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<sup>1</sup> Given NRVs are based on biological characteristics, the term 'sex' rather than 'gender' has been used to be consistent with recent government guidelines on the use of the term 'sex' and 'gender': the *Standard for Sex and Gender Variables 2016* and the *Australian Government Guidelines on the Recognition of Sex and Gender 2015*. The NRV definitions in the *Methodological Framework for the Review of NRVs 2015* currently uses the term 'gender'.

NOAEL	No Observed Adverse Effect Level - Highest dose at which there is no measurable adverse effect from a test substance in a test subject or population
NHMRC	National Health and Medical Research Council - Australia's peak body for supporting health and medical research; for developing health advice for the Australian community, health professionals and governments; and for providing advice on ethical behaviour in health care and in the conduct of health and medical research
NRV	Nutrient Reference Values - A set of nutritional recommendations, based on current scientific knowledge, used to assess the health status of populations and individuals.
NT	Normotensive – Usually defined as blood pressure below 140/90mmHg
PICO (TS)	Population, intervention, comparator, outcome, time, study design
PUL	Provisional Upper Level of Intake – as with UL (see below) but with some ability to assess and with minimal certainty
SBP	Systolic Blood Pressure
SDT	Suggested Dietary Target - A daily average intake from food and beverages for certain nutrients that may help in the prevention of chronic disease.
SLR	Systematic Literature Review
UF	Uncertainty Factor
UL	Upper Level of Intake - The highest average daily nutrient intake level likely to pose no adverse health effects to almost all individuals in the general population. As intake increases above the UL, the potential risk of adverse effects increases
USDA	United States Drug Administration
WHO	World Health Organization

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## **10. Attachments**

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Supporting Document 1: Systematic literature review

Supporting Document 2: Statistical analyses

Supporting Document 3: Review of dietary modelling