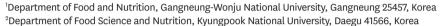


## Review



## Dietary Reference Intakes of sodium for Koreans: focusing on a new DRI component for chronic disease risk reduction

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## **ABSTRACT**

Sodium is a physiologically essential nutrient, but excessive intake is linked to the increased risk of various chronic diseases, particularly cardiovascular. It is, therefore, necessary to accomplish an evidence-based approach and establish the Korean Dietary Reference Intakes (KDRIs) index, to identify both the nutritional adequacy and health effects of sodium. This review presents the rationale for and the process of revising the KDRIs for sodium and, more importantly, establishing the sodium Chronic Disease Risk Reduction Intake (CDRR) level, which is a new specific set of values for chronic disease risk reduction. To establish the 2020 KDRIs for dietary sodium, the committee conducted a systematic literature review of the intake-response relationships between the selected indicators for sodium levels and human chronic diseases. In this review, 43 studies published from January 2014 to December 2018, using databases of PubMed and Web of Science, were finally included for evaluating the risk of bias and strength of evidence (SoE). We determined that SoE of the relationship between dietary sodium and cardiovascular diseases, cerebrovascular disease, and hypertension, was moderate to strong. However, due to insufficient scientific evidence, we were unable to establish the estimated average requirement and the recommended nutrient intake for dietary sodium. Therefore, the adequate intake of sodium for adults was established to be 1,500 mg/day, whereas the CDRR for dietary sodium was established at 2,300 mg/day for adults. Intake goal for dietary sodium established in the 2015 KDRIs instead of the tolerable upper intake level was not presented in the 2020 KDRIs. For the next revision of the KDRIs, there is a requirement to pursue further studies on nutritional adequacy and toxicity of dietary sodium, and their associations with chronic disease endpoint in the Korean population.

Keywords: Sodium; Dietary Reference Intake; South Korea

## INTRODUCTION

Sodium is an essential element that maintains homeostasis and physiological functions. Being a major cation in the extracellular fluid, sodium is involved in osmotic pressure regulation and water balance, and also plays a role in nerve impulse transmission, muscle

https://e-nrp.org

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#### **Conflict of Interest**

The authors declare no potential conflicts of interests.

#### **Author Contributions**

Conceptualization: Kim HJ, Shin MJ; Investigation: Kim HJ, Lee YK, Koo HS, Shin MJ; Supervision: Shin MJ; Writing - original draft: HJ Kim, Shin MJ; Writing - review & editing: HJ Kim, Shin MJ. contraction, and acid-base balance [1]. Therefore, insufficient sodium intake is usually associated with adverse health outcomes. Contrarily, excessive sodium intake is a risk factor for several chronic diseases [2,3], particularly cardiovascular, mainly through the effect of sodium intake on blood pressure (BP) [2,4-6]. It is well known that a reduction in the dietary sodium decreases BP and the incidence of hypertension, which is also associated with reduced morbidity and mortality resulting from cardiovascular diseases (CVDs) [2,3,7].

Dietary Reference Intakes (DRIs) are defined as a set of quantitative reference values for the apparently healthy population. They are traditionally used in planning and assessing diets based on nutrient deficiencies and/or toxicities [8]. Previously, an attempt was made for the Korean population to set the Estimated Average Requirement (EAR) and the recommended nutrient intake (RNI) for sodium adequacy, and the tolerable upper intake level (UL) for preventing health problems arising from sodium toxicity [9], leading to the establishment of the sodium adequate intake (AI) instead of the EAR and RNI, and the sodium intake goal instead of the UL, in the 2015 DRIs for Koreans (KDRIs). This was based taking into account the lack of appropriate indicators of sodium exposure, and insufficient scientific evidence on sodium adequacy or toxicity [9]. However, considering the impact of nutrition on the prevention, treatment and health promotion of chronic diseases, the use of chronic disease endpoints to establish the DRIs has been addressed. Population aging and the increased prevalence of chronic diseases worldwide, along with accumulating scientific evidence on the health effect of sodium intake, further potentiated the establishment of dietary recommendations aimed at reducing chronic diseases [8]. As such, there has been a consensus to include a new DRI category for the prevention of chronic diseases, in addition to the traditional framework of DRIs [10].

Very recently, chronic disease risk reduction intake (CDRR) for dietary sodium (a new category of reference values specific for chronic disease risk reduction) has been proposed in the Consensus Study Reports published by the committee of the National Academies of Sciences, Engineering, and Medicine [8]. In this report, the CDRR is defined as the lowest level of intake where there is sufficient strength of evidence (SoE) to characterize a chronic disease risk reduction, which was established in the DRIs for US and Canada [8]. This implies that reducing the sodium intake above the CDRR established would decrease the risk of chronic disease [8]. For the 2020 KDRIs, the committee comprehensively reviewed the available evidence, and considered the update of current KDRIs for sodium by focusing on the CDRR. A thorough systematic literature review of the relationship between dietary sodium and the risk of chronic diseases resulted in the committee establishing the sodium CDRR to prevent chronic diseases as a new category in the 2020 KDRIs.

This review presents the rationale and processes of establishing the KDRIs for adequacy and toxicity of dietary sodium, as well as specific values of the 2020 KDRIs for dietary sodium, using the 4-step evidence-based approach suggested by the US sodium committee [8], comprising the following steps: Step 1. Review and selection of indicators; Step 2. Assessment of the intake—response relationships of the selected indicators and establishment of DRI values; Step 3. Comparison of current population intake levels and DRI values to characterize the risk; Step 4. Discussion of public health implications and special considerations. This report provides the sodium intake level as an AI and, more importantly, we herein report a new CDRR value for dietary sodium for Koreans.



## INDICATORS TO ESTABLISH THE KDRIs FOR DIETARY SODIUM

## Indicators of sodium adequacy

A critical initial step of the DRIs framework is selection of the indicators for adequate and excessive dietary intakes of sodium. As reported earlier, no sensitive biomarkers are available to help characterize the sodium requirements in a healthy population [8]. For the purpose of the literature review, sodium balance, urinary sodium excretion, and sodium level in blood were selected as indicators of sodium exposure in the 2020 KDRIs. In addition, intermediate biomarkers selected for chronic disease indicators include insulin resistance, plasma renin activity, and BP.

## **Indicators of sodium toxicity**

The UL is defined as the highest intake level at which there is no risk of any adverse health effect in apparently healthy individuals. To set the UL for dietary sodium in the US and Canada, the lowest toxic sodium level was calculated on the basis of an increase in BP due to sodium intake, as the toxicity endpoint in the 2005 DRIs [8]. However, the approach to establish the sodium UL in the report of 2019 jointly developed by the US and Canada differs in that health effects of excessive sodium intakes on BP, stroke and coronary heart need to be considered when establishing the sodium CDRR. Under the synthesis of evidence for the 2020 KDRIs, sodium toxicity should be considered based on toxicity, and not on chronic disease endpoint related indicators.

#### Chronic disease indicators to establish sodium CDRR

While the sodium UL is established based on the toxic effect derived from excessive intake of sodium, the CDRR indicates the decrease in the risks of chronic diseases with reductions in dietary sodium intake [8]. For the 2020 KDRIs, the committee reviewed the causal relationship between sodium intake and indicators that could potentially inform the sodium CDRRs, including chronic disease endpoints and surrogate markers. The scientific evidence and conclusions previously accumulated in the 2015 KDRIs was also considered for this deliberation. To review the causal relationship between sodium intake and chronic disease, we finally selected CVD (cerebrovascular disease and coronary heart disease), hypertension, cancer (gastric cancer and renal cancer), osteoporosis, obesity, diabetes, and chronic kidney disease as potential health outcomes, and renin-angiotensin-aldosterone system (RAAS), high BP, bone mineral density, bone mineral content, body mass index (BMI), and glomerular injury as surrogate markers (Fig. 1). Evidence from these indicators can be accumulated to inform the development of a sodium CDRR. More specifically, if there is moderate to high SoE for a causal relationship and an intake–response relationship between sodium intake and chronic disease indicators, a sodium CDRR would be established [11].

## INTAKE-RESPONSE RELATIONSHIP AND SPECIFICATION OF KDRI VALUES

#### The EAR, RNI, and AI for sodium adequacy

In general, the EAR and RNI are established based on available sufficient scientific evidence for nutrient requirements, in the absence of which the AI is established [12]. Due to insufficient scientific evidence of the intake—response relationship for selected adequacy indicators to establish the EAR and RNI in the 2020 KDRIs (which was similar to the 2015 KDRIs), the



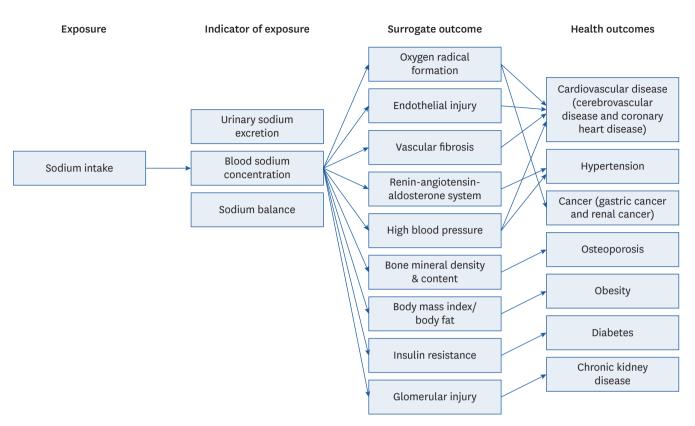


Fig. 1. Indicators of exposure and health outcomes in a systematic review on the causal relationship between sodium intake and chronic disease for establishing the sodium Chronic Disease Risk Reduction Intake level.

committee established the AI of dietary sodium for the 2020 KDRIs. It is generally accepted that AI can be established using the average sodium intake of a healthy population [8] when it is not possible to establish the EAR and RNI. However, the average daily intake of dietary sodium for Koreans was determined to be 3,287 mg according to the 2019 Korea National Health and Nutrition Examination Survey (KNHANES) [13], which is too high to be considered as the sodium AI value. Therefore, the AI for sodium in the 2020 KDRIs was established based on the results of balance studies involving healthy subjects and evidence of the adverse physiological effects of low sodium consumption, such as toxic effects or the occurrence of various diseases [8]. It was established that a diet containing approximately 1,500 mg/day of sodium met the recommended intakes for other nutrients [14]. Increase in plasma levels of total cholesterol was found in the range 460-690 mg/day of sodium intake [15]. When considering the association of sodium intake with insulin resistance, sodium intake lower than 700 mg/day increased insulin resistance [16], while a sodium intake of ≥ 1,200 mg/day was not associated with insulin resistance in non-obese and normotensive men [17]. In addition, evidence from a well-designed balance study conducted among adults [18] reported that sodium intake of 1,525 mg/day among adult men was equivalent to the excreted sodium. Taken together, the appropriateness of the sodium AI value of 1,500 mg/day for adults aged 19-64 years in the 2015 KDRIs was reviewed, and it was decided to recommend this value in the 2020 KDRIs. Since there was no available evidence enough to establish the sodium AI for other age groups, the sodium AI for infants, children, adolescents, and the elderly was calculated by extrapolating from the adult sodium AI value, based on the energy intake involved, as follows [19]:

AI<sub>life stage</sub> = AI<sub>adult</sub> × (Median Energy Intake of Life Stage/Median Energy Intake of Adult)



For males aged 6–8 years, 9–11 years, 12–64 years, 65–74 years, and  $\geq$  75 years, the sodium AI values were established at 1,100 mg/day, 1,300 mg/day, 1,500 mg/day, 1,300 mg/day, and 1,100 mg/day, respectively. For females aged 6–8 years, 9–64 years, 65–74 years, and  $\geq$  75 years, the sodium AI values were established at 1,400 mg/day, 1,500 mg/day, 1,400 mg/day, and 1,100 mg/day, respectively. For children aged 1–2 years and 3–5 years, the AI for sodium was 800 mg/day and 1,000 mg/day, respectively, for both genders. The sodium AI for infants was estimated based on the sodium intakes from breastfeeding, and were determined to be 110 mg/day for infants aged 0–5 months, and 370 mg/day for infants aged 6–11 months (Supplementary Table 1).

## The UL for sodium toxicity

In the 2020 KDRIs, no potential indicators for adverse toxicological effects of sodium were identified subsequent to reviewing the available evidence after excluding the association of sodium intake with chronic disease related indicators. Lethal levels of dietary sodium, primarily due to the ingestion of acute doses, have been previously reported [20-22]. However, they were unsuitable for establishing a sodium UL since the levels did not necessarily reflect the toxicological effects of high sodium intake in our habitual diets. Furthermore, several sodium studies reported that sodium intakes affect the occurrence of headaches [23-25]. However, since the evidence for sodium toxicity was insufficient to determine sodium toxicity risk, the UL for sodium was not established in the 2020 KDRIs. In fact, sodium UL for Koreans has been replaced by intake goal, set at 2,000 mg/day for adults since 2015 KDRIs. The sodium CDRR for reducing the risk of chronic disease is now included as a new category in the 2020 KDRIs; hence, the intake goal of dietary sodium could not be identified in the 2020 KDRIs.

#### The CDRR for sodium based on chronic disease risk reduction

A systematic literature review was thoroughly conducted to identify scientific evidence of the potential detrimental health effects of excessive intake of dietary sodium. The methods and results of the review are as follows.

## Selection of studies for the systematic review

Randomized controlled trials, cohort studies, nested case-control studies, case-control studies, and cross-sectional studies on the relationship between sodium and the risk of several chronic diseases, published between January 2014 and December 2018, were identified using the PubMed (https://pubmed.ncbi.nlm.nih.gov) and Web of Science (https://www.webofknowledge.com) databases. The search keywords used were "salt," "sodium intake," "dietary sodium," and "urinary sodium" for the independent variables, and "CVD," "cerebrovascular disease," "coronary heart disease," "hypertension," "BP," "RAAS," "obesity," "BMI," "osteoporosis," "bone mineral density," "bone mineral content," "osteoporotic fracture," "diabetes," "chronic kidney disease," "proteinuria," "gastric cancer," and "renal cancer" for dependent variables. Studies written in both Korean and English were included for this review.

## Inclusion/exclusion criteria

Articles were extracted based on their titles and abstracts. The inclusion and exclusion criteria were as follows: 1) inclusion of only human studies, 2) in cases of multiple publications involving the same study population, only the most recent study was included, 3) reviews or meta-analyses were excluded. Using these criteria, the studies were reviewed independently by 2 reviewers, and initial disagreements between the reviewers were resolved by eventual consensus between them.



#### Data collection

The following information was collected from each study: author name, publication year, country, diseases examined, study design, study subjects (health status, life stage, age, and sex), confounding or effect-modifying variables, measures of sodium (dietary sodium intake or urinary sodium excretion), category of sodium intake, outcomes (level of incidence, and mortality and controls), adjusted relative risk/odds ratio with 95% confidence intervals, and trends (P).

## Quality evaluation of the study

The quality of each study was evaluated using the Cochrane RoB 2.0 template and the STROBE checklist for intervention and cross-sectional studies, and the Newcastle-Ottawa scale for cohort, nested case-control, and case-control studies. Using these tools, the risk of bias (RoB) level was classified as "low," "some concerns," or "high" for each study. Moreover, the overall SoE was classified into grades I (strong), II (moderate), III (limited), and IV (grade not assignable), based on the criteria employed by the US Department of Agriculture's Nutrition Evidence Library. These grading criteria include quality in relation to RoB, quantity (number of studies and participants), consistency of findings across studies, public health impact (directness and magnitude), and generalizability (references). To establish the sodium CDRR, the SoE for both the causal relationship between sodium intake and chronic disease indicators and their intake—response relationship should be at least moderate, using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system [11].

#### Results of the systematic literature review

A total of 1,033 articles were identified via the initial computerized literature search. Based on the titles and abstracts of the articles, 248 articles were selected independently by the 2 reviewers. Randomized controlled trials, cohort studies, nested case-control studies, case-control studies, and cross-sectional studies were selected, whereas reviews or metaanalyses were excluded. Moreover, multiple publications that included the same population, insufficient study population, or unhealthy subjects, were excluded. Finally, through a full text review of the remaining articles, 43 studies (7 randomized controlled trials, 18 cohort studies, 3 nested case-control studies, and 15 cross-sectional study) were included for evaluating the RoB and SoE of the harmful effects of sodium intake levels on several chronic diseases (Fig. 2 and Table 1). Details of the eligible studies for the systematic review are presented in Tables 2 and 3, Supplementary Tables 2 and 3. We found that SoE of the relationship between dietary sodium and CVD, cerebrovascular disease, hypertension, and their surrogate marker systolic/diastolic BP, was at least moderate. Specifically, there was strong evidence for BP lowering the effect of sodium. Furthermore, there was a moderate SoE for the intake-response relationship between sodium intake and the risk of CVD or cerebrovascular disease. However, evidence associating sodium intake with the risk of coronary heart disease, cancer, bone mineral density, RAAS, and obesity were insufficient (limited or grade not assignable) (Table 4).

In a meta-analysis of 39 randomized clinical trials on the intake–response, there was a strong SoE that sodium reduction decreased the risk of CVD, hypertension, and systolic/diastolic BP in subjects with a sodium intake of 2,300–4,100 mg/day. In addition, there was a moderate SoE that sodium reduction in subjects with a sodium intake of 4,100–5,000 mg/day decreased the effect of systolic/diastolic BP. However, the SoE was weak for intake levels  $\leq$  2,300 mg/day [8]. Taken together, we concluded that there is a moderate-to-high SoE for reduced sodium intake decreasing the risk of CVD, hypertension, and BP in persons with



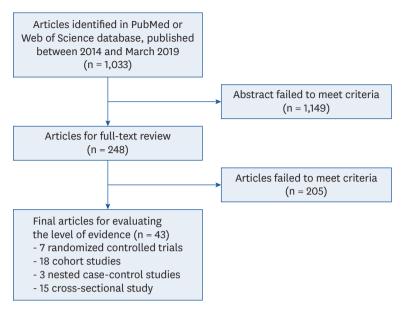


Fig. 2. Study selection process for the systematic review.

sodium intake levels of 2,300–5,000 mg/day. Accordingly, the DRIs jointly developed by US and Canada set 2,300 mg/day as the CDRR of sodium for adults [8]. Based on a systematic review and the CDRR established in the DRIs for US and Canada, the 2020 KDRIs established the CDRR for sodium at 2,300 mg/day for Koreans aged 19–64 years. Moreover, the CDRR for sodium according to age, sex, and life-stage were extrapolated from the adult values by considering the energy intake involved, as follows [19]:

CDRR<sub>life stage</sub> = CDRR<sub>adult</sub> × (Median Energy Intake of Life Stage/Median Energy Intake of Adult)

The sodium CDRR for children aged 1–2 years and 3–5 years was established as 1,200 mg/day and 1,600 mg/day, respectively, for both genders. The CDRR for children aged 6–8 years and 9–11 years was set at 1,800 mg/day and 2,000 mg/day for males, and 2,100 mg/day and 2,300 mg/day for females, respectively, and for adolescents aged 12–18 years the CDRR was set at 2,300 mg for both genders. For the elderly aged 65–74 years and  $\geq$  75 years, the sodium CDRR values were established as 1,900 mg/day and 1,800 mg/day for males, and 2,200 mg/day and 1,700 mg/day for females, respectively (Supplementary **Table 1**).

Table 1. List of studies included in the systemic literature review

Study design	Author	Year	Title
RCT-parallel	Jenkins et al. [38]	2015	The effect of a dietary portfolio compared to a DASH-type diet on blood pressure
	Diaz et αl. [39]	2014	The effects of weight loss and salt reduction on visit-to-visit blood pressure variability: results from a multicenter randomized controlled trial
	Reidlinger et al. [40]	2015	How effective are current dietary guidelines for cardiovascular disease prevention in healthy middle-aged and older men and women? A randomized controlled trial
	Zhou et al. [41]	2016	Intake of low sodium salt substitute for 3years attenuates the increase in blood pressure in a rural population of North China - A randomized controlled trial
	Juraschek et al. [42]	2017	Effects of sodium reduction and the DASH diet in relation to baseline blood pressure
RCT-crossover	Muth et al. [43]	2017	Central systolic blood pressure and aortic stiffness response to dietary sodium in young and middle-aged adults
	Nielsen et al. [44]	2016	Changes in the renin-angiotensin-aldosterone system in response to dietary salt intake in normal and hypertensive pregnancy. A randomized trial

(continued to the next page)



Table 1. (Continued) List of studies included in the systemic literature review

Study design	Author	Year	Title
Cohort	Merino et al. [45]	2015	Is complying with the recommendations of sodium intake beneficial for health in individuals at high cardiovascular risk? Findings from the PREDIMED study
	Kalogeropoulos et al. [46]	2015	Dietary sodium content, mortality, and risk for cardiovascular events in older adults: the Health, Aging, and Body Composition (Health ABC) Study
	Okayama et al. [47]	2016	Dietary sodium-to-potassium ratio as a risk factor for stroke, cardiovascular disease and all-cause mortality in Japan: the NIPPON DATA80 cohort study
	Mente et al. [48]	2018	Urinary sodium excretion, blood pressure, cardiovascular disease, and mortality: a community-level prospective epidemiological cohort study
	Cook et al. [49]	2014	Lower levels of sodium intake and reduced cardiovascular risk
	Willey et al. [36]		Dietary sodium to potassium ratio and risk of stroke in a multiethnic urban population: the Northern Manhattan Study
	Prentice et al. [50]	2017	Associations of biomarker-calibrated sodium and potassium intakes with cardiovascular disease risk among postmenopausal women
	Li et al. [51]		Longitudinal change of perceived salt intake and stroke risk in a Chinese population
	Joosten et al. [52]		Sodium excretion and risk of developing coronary heart disease
	Voortman et al. [53]		Adherence to the 2015 Dutch dietary guidelines and risk of non-communicable diseases and mortality in the Rotterdam Study
	Takase et al. [54]		Dietary sodium consumption predicts future blood pressure and incident hypertension in the Japanese normotensive general population
	Buendia et al. [55] Timpka et al. [56]		Longitudinal effects of dietary sodium and potassium on blood pressure in adolescent girls Lifestyle in progression from hypertensive disorders of pregnancy to chronic hypertension in Nurses' Healt
	Bertoia et al. [57]	2014	Study II: observational cohort study  Mediterranean and Dietary Approaches to Stop Hypertension dietary patterns and risk of sudden cardiac
	Horikawa et al. [58]	2014	death in postmenopausal women  Dietary sodium intake and incidence of diabetes complications in Japanese patients with type 2 diabetes:  analysis of the Japan Diebetes Complications (Fudy (JDCS))
	Umesawa et al. [59]	2016	analysis of the Japan Diabetes Complications Study (JDCS) Salty food preference and intake and risk of gastric cancer: The JACC Study
	Wang <i>et al.</i> [60]		Composite protective lifestyle factors and risk of developing gastric adenocarcinoma: the Singapore Chinese Health Study
	Carbone et al. [61]	2016	Sodium intake and osteoporosis. Findings from the Women's Health Initiative
Nested case	Lee et al. [62]		Hyponatraemia and its prognosis in acute heart failure is related to right ventricular dysfunction
control	Deckers et al. [63]	2014	Long-term dietary sodium, potassium and fluid intake; exploring potential novel risk factors for renal cell cancer in the Netherlands Cohort Study on diet and cancer
	Deckers et al. [64]	2017	Promoter CpG island methylation in ion transport mechanisms and associated dietary intakes jointly influence the risk of clear-cell renal cell cancer
Cross sectional	Kim et al. [65]	2014	The relationship of dietary sodium, potassium, fruits, and vegetables intake with blood pressure among Korean adults aged 40 and older
	Tabara et al. [66]	2015	Descriptive epidemiology of spot urine sodium-to-potassium ratio clarified close relationship with blood pressure level
	Noh et al. [67]	2015	Association between high blood pressure and intakes of sodium and potassium among Korean adults: Korean National Health and Nutrition Examination Survey, 2007–2012
	Xu et al. [68]		Estimation of salt intake by 24-hour urinary sodium excretion: a cross-sectional study in Yantai, China
	Hu et αl. [69]		Prevalence, awareness, treatment, and control of hypertension among Kazakhs with high salt intake in Xinjiang, China: a community-based cross-sectional study
	Park et al. [70]		The effect of the sodium to potassium ratio on hypertension prevalence: a propensity score matching approach
	Navia et al. [71]		Sodium intake may promote weight gain; results of the FANPE study in a representative sample of the adul Spanish population
	Ge et αl. [72]		Are 24 h urinary sodium excretion and sodium:potassium independently associated with obesity in Chines adults?
	Huh et al. [73]		Gender-specific association between urinary sodium excretion and body composition: analysis of the 2008-2010 Korean National Health and Nutrition Examination Surveys
	Murakami et al. [74]		Ability of self-reported estimates of dietary sodium, potassium and protein to detect an association with general and abdominal obesity: comparison with the estimates derived from 24 h urinary excretion
	Ma et αl. [75]		High salt intake: independent risk factor for obesity?
	Grimes et al. [76]		24-h urinary sodium excretion is associated with obesity in a cross-sectional sample of Australian schoolchildren
	Oh et αl. [77]		Associations of sodium intake with obesity, metabolic disorder, and albuminuria according to age
	Nam et al. [78]		Association between 24-h urinary sodium excretion and obesity in Korean adults: a multicenter study
	Zhang <i>et al</i> . [79]	2018	A positive association between dietary sodium intake and obesity and central obesity: results from the National Health and Nutrition Examination Survey 1999–2006

RCT, randomized controlled trial.



 Table 2.
 Association between sodium levels and the risk of chronic diseases (event outcomes)

Author (Year) Nation	7		Study cubiects			Sodium levels	No of cases/	RB/OR (95% CI)	P for Confounding	ROB
المعالم (المعار) المعالما	design	Source of subjects,	Outcome	Follow-up	Measurement	Categories	No. of category	(100,000) 110,611	_	
		Mean age (yrs)/Sex (%)	Mean age (yrs)/Sex (%) (incidence or death rate)		nnit	)			considered	
Cardiovascular disease										
Merino et al. (2015)	Cohor	Cohort Adults, NA (50-88	Incidence (195/2989.0.031)	1 yr	Intake	Decrease in sodium intake	33/1,199	0.66 (0.38, 1.15)	0.040 Demographic,	Low
, , , , , , , , , , , , , , , , , , ,		) - J	(+00.0,000)			Increase in sodium intake		1.72 (1.01, 2.91)	medical factors,	
									lifestyles, and foods	"
Kalogeropoulos et al		Cohort Adults 73 6 (70–79	Incidence	10 vrs	Intake	< 1 500 mg/day	63/917	1 09 (0 79 1 41)	O 470 Demographic	WO
(2015) [46], US		yrs)/Males 48.8%	(572/1,981; 0.289)	5	amounts	1,500-2,300 mg/day	161/576	1.00	anthropic, and	
						> 2,300mg/day	348/1,188	1.02 (0.84, 1.24)	medical factors,	
Okayama <i>et al.</i>	Cohor	Cohort Adults, NA (30-79	Death rate	24 yrs	Intake dietary	1st quintile	110/1,581	1.00	0.005 Demographic,	Low
(2016) [47], Japan		yrs)/Males 44.5%	(579/8,283;0.070)	,	Na-K ratio	2nd quintile	114/1,652	AN	anthropic, and	
						3rd quintile	100/1,686	NA	medical factors,	
						4th quintile	113/1,684	Ϋ́	lifestyles, and foods	"
			:		,	5th quintile	142/1,681	1.39 (1.20, 1.61)	Intake	
Mente et $al.$ (2018)	Cohor	Cohort Adults, 50.4 (35–70	Incidence	8.1 yrs	Intake	1st tertile	Y S	1.00 (-2.00, -0.01)	1.00 (-2.00, -0.01) < 0.001 Demographic,	Low
[40], 10 could les		y13// Mates 42.1.70	((2))		allioulles	and tertile	Y Y	0.24 (-2.12, 2.61)	medical factors,	
									lifestyles	
Cook <i>et al.</i> (2014)	Cohor	Cohort Prehypertensive adults,	Incidence	10-15 yrs	24-h urine	< 2,300 mg/24 h	17/236	0.68 (0.34, 1.37)	0.130 Demographic,	Low
[49], 03		69.5%	(199/2,312, 0.003)			2,300-< 3,600 mg/24 II	01/893	1.00, 1.11)	medical factors.	
						3,000=> 4,800 mg/24hr	41/415	1.05 (0.68, 1.62)	lifestyles, and foods	"
						5			intake	
Prentice <i>et al.</i> (2017) [50], US	Cohor	Cohort Postmenopausal women, NA (50–79 yrs)/Female 100%	Incidence (5,897/86,444; 0.068)	12 yrs	Intake	20% increase in intake	5,897/86,444	1.06 (0.92, 1.23)	NA Demographic, and medical factors, lifestyles	Low
Bertoia <i>et αl.</i> (2014)	Cohor	Cohort Postmenopausal	Death rate	10.5 yrs	Intake	1st quintile	52/18,465	1.00	0.460 Demographic,	Low
[57], US		women, NA (50-79	(237/93,122;0.003)		DASH diet	2nd quintile	56/18,216	1.09 (0.75, 1.60)	anthropic, and	
		yrs)/Female 100%			pattern score	3rd quintile	57/20,220	1.11 (0.75, 1.63)	medical factors,	
						4th quintile	41/17,808	0.95 (0.62, 1.45)	lifestyles, and foods intake	"
7. 4	-	414 - 17 - 17 - 17 - 17 - 17 - 17 - 17 -			1	פרוו לחווורוופ	01/10,413	0.00 (0.34, 1.30)		-
Horikawa et αι. (9014) [58] Janan	Conoc	Conort 12DM adults, NA (40-70 vrs)/Males	Incidence (1 39/1 414:0 09)	8 yrs	Intake	1St quartile	23/354	1.00 0 0 0 0 0 1.00 0 0 0 0 0 0 0 0 0 0	0.030 Demographic,	Low
(2011) Jupan		47.5%	(+04/ +, +++, 000)		3	3rd quartile	39/351	1.47 (0.89, 2.93)	medical factors,	
						4th quartile	41/359	2.07 (1.16, 3.71)	lifestyles, and foods	"
Lee <i>et al.</i> (2018)	Neste	Nested Adults, 67.8 ± 14.9	Prevalence	2 yrs	Serum level	With hyponatraemia	94/116	1.00	< 0.001 Baseline	Low
[62], Korea	case-	yrs/Males 55.7%	(NA)	,		Without hyponatraemia	78/232	8.00 (4.50, 14.22)	characteristics	
Cerebrovascular disease										
Okayama et al.	Cohor	Cohort Adults, NA (30-79	Death rate	24 yrs	Intake dietary	1st quintile	45/1,581	1.00	0.002 Demographic,	Low
(2016)[47], Japan		yrs)/Males 44.5%	(273/8,283; 0.033)		Na-K ratio	2nd quintile	46/1,652	ď :	anthropic, and	
						srd quintile	55/1,686	Ψ.	lifectyles and foods	,
						4th quintile 5th quintile	53/1,684	NA 1.43 (1.17, 1.76)	intake	2
Mente et al. (9018)	Cohor	Cohort Adults 50.4 (35-70	Incidence	8.1 vrs	Intake	1st tertile	ĄZ		< 0.001 Demographic	WO
[48], 18 countries		yrs)/Males 42.1%	(NA)	1	amounts	2nd tertile	Z Z		anthropic, and	
						3rd tertile	N N	0.54 (0.12, 0.96)	ineuicat iactors, lifestyles	

(continued to the next page)



Table 2. (Continued) Association between sodium levels and the risk of chronic diseases (event outcomes)

					`					
Author (Year), Nation	Study	Study subjects		S	Sodium levels	No. of cases/	RR/OR (95% CI)	P for Confor	Confounding	RoB
			Follow-up	Measurement	Categories	No. of category		trend variables	səlqı	
	Mean age (yrs)/Sex (%)	Mean age (yrs)/Sex (%) (incidence or death rate)	duration	unit				considered	dered	
Willey <i>et al.</i> (2017) [36], US	Cohort Adults, 69 ± 10 yrs/ Males 36%	Incidence (274/2,496; 0.110)	12 yrs	Intake dietary Na-K ratio	Increase in Na-K ratio	274/2,496	1.58 (1.20, 2.06)	NA Demographic, and anthropic, and medical factors, lifestyles, and foods intake	spoo	Low
Prentice <i>et al.</i> (2017) [50], US	Cohort Postmenopausal women, NA (50-79 yrs)/Female 100%	Incidence (2,843/86,444; 0.033)	12 yrs	Intake	20% increase in intake	2,843/86,444	0.98 (0.85, 1.13)	NA Demographic, and medical factors, lifestyles		Low
Li et αl. (2018) [51], China	Cohort Adults, 53.6 ± 12 yrs/ Males 77.8%	Incidence (1,564/79,490; 0.020)	5 yrs	Intake changing pattern	Moderate-stable Moderate-decreasing Moderate-increasing Low-increasing	1,225/59,241 141/9,268 72/2,975 54/2,879	1.00 0.77 (0.64, 0.91) 1.04 (0.82, 1.32) 0.92 (0.70, 1.22)	NA Demographic, anthropic, and medical factors, lifestyles	ις.	Low
Voortman et al. (2017) [53], Netherlands	Cohort Adults, 64.1 (49-83 yrs)/Males 41.9%	Incidence (979/29,442; 0.104)	10.2 yrs	Intake Dutch dietary guidelines	Ingirucucaanig 1st quintile 2nd quintile 3rd quintile 4th quintile 5th quintile	7	1.01 1.00 0.93 (0.78, 1.12) 0.88 (0.73, 1.06) 0.97 (0.80, 1.17) 0.92 (0.75, 1.13)	0.520 Demographic, and anthropic factors, lifestyles, and foods intake	S	Low
Hypertension Takase et al. (2015) [54], Japan	Cohort Adults, 54.1 ± 10.9 yrs/Males 64.2%	Incidence (1,027/4,523; 0.227)	3.1 yrs	Intake amounts	Lower intake Higher intake	Ą Ą	1.25 (1.04, 1.50)	< 0.001 Demographic, anthropic, and medical factors, and lifestyles	s, and	Low
Timpka e <i>t al.</i> (2017) [56], US	Cohort	Incidence (572/90,887 PY) Incidence	<b>∀</b>	Intake dietary Na-K ratio Intake dietary	1st quartile 2nd quartile 3rd quartile 4th quartile 1st quartile	4 4 4 4 2 2 2 2 2	1.00 1.07 (0.82, 1.40) 0.98 (0.75, 1.27) 1.07 (0.83, 1.38) 1.00	O.650 Demographic, and anthropic factors, lifestyles, and foods intake     O.030	ω	Low
	yrs)/Females 100% Adults, NA (50-59 yrs)/Females 100%	(5,716/334,976 PY) Incidence (5,366/20,207 PY)	₹ Z	Na-K ratio Intake dietary Na-K ratio	2nd quartile 3rd quartile 4th quartile 1st quartile 2nd quartile 3rd quartile 4th quartile		1.04 (0.96, 1.13) 1.10 (1.02, 1.19) 1.09 (1.00, 1.18) 1.00 1.07 (0.99, 1.15) 1.14 (1.05, 1.23)	0.006		
Noh et <i>al.</i> (2015) [67], Korea	Cross- Adults, NA (> 19 yrs)/ sectional Males 50.3%	Prevalence (2,812/24,096; 0.120)	1	Intake combinations of Na and K intakes	Low Na/High K High Na/High K Low Na/Low K High Na/Low K	9.50%/4,516 10.30%/7,532 11.80%/7,532 12.40%/4,516	1.00 0.99 (0.84, 1.18) 1.19 (1.01, 1.40) 1.21 (1.02, 1.44)	<ul> <li>&lt; 0.001 Demographic, and anthropic factors, lifestyles, and foods intake</li> </ul>	S	Low
Hu et al. (2017) [69], China	Cross- Adults, 46.5 (> 30 yrs)/ sectional Males 46.7%	/ Prevalence (NA/1,668; 0.455)	1	Intake amounts	1st quartile 2nd quartile 3rd quartile 4th quartile	~		< 0.001 Demographic factors Low	hicfactors	Low
Park <i>et al.</i> (2016) [70], Korea	Cross- Adults, 46.1 (20-79 sectional yrs)/Males 31.8%	Prevalence (NA/30,206; 0.196)		Intake dietary Na-K ratio	1st quartile 2nd quartile 3rd quartile 4th quartile	19.27%/2,356 18.00%/2,356 19.44%/2,356 21.52%/2,356	0.00 1.02% point 2.74% point 3.44% point	NA Propensity score matching		Low

A moderate to strong strength of evidence was determined for the relationship between sodium and cardiovascular disease, cerebrovascular disease, and hypertension. RR, relative risk; OR, odds ratio; CI, confidence interval; ROB, risk of bias; NA, not available; PY, person years; T2DM, type 2 diabetes mellitus.



 Table 3. Association between sodium levels and the risk of chronic diseases (continuous outcomes): hypertension

ALTON VARIATION	Study	517	Study subjects			Sodium levels	No of cases/	Mean (95% CI)	P-values	P-values Confounding variables	Rog
المطاوا (احطا)، المطاواا	doping		na sanjana	:			No of octoring	(in 6/ 66) limai.		comodinating variables	
	design	Source of subjects, Mean age (yrs)/Sex (%)	Outcome	Follow-up duration	Measurement unit	Categories	No. or category			considered	
Jenkins <i>et al.</i> (2015) [38], Canada	RCT	Hyperlipidemia adults, NA (20-85 yrs)/Males	Mean arterial pressure	24 wks	Intake	Dietary portfolio DASH-type diet	159 82	-2.1 (-3.0, -1.3) -0.3 (-1.5, 1.0)	0.026	ı	Low
		39.0%	Systolic blood			Dietary portfolio	159	-2.5 (-3.7, -1.2)	0.045		
			pressure Diastolic blood			DASH-type diet Dietary nortfolio	82	-0.4 (-2.1, 1.4) -9.0 (-9.8 -1.9)	0.096		
			pressure			DASH-type diet	82	-0.2.(-1.4, 0.9)			
Diaz et αl. (2014)	RCT		Visit-to-visit blood	36 mon	Intake	Sodium light lifestyle	452	$7.1 \pm 3.0$	0.290		Low
[39], US		43.9 ± 6.1 yrs/Males 66.0%	pressure			Usual care control	463	$6.9 \pm 2.9$			
Reidlinger et al.	RCT	Adults, 53 (40–70	Systolic blood	12 wks	Intake	Restriction on salt and	80	-4.1 (NA)	0.003	1	Low
(2015) [40], UK		yrs)/males 39.0%	pressure			sugar Control diet	c	(AN) R O			
			Diaetolic blood			Restriction on salt and	80	(AN) 0.0 (AN) 0 6-	6000		
			pressure			sugar		( ) ( ) ( )	0		
						Control diet	82	-0.2 (NA)			
Zhou <i>et αl.</i> (2016)	RCT	Families, $46.4 \pm 13.6$	Systolic blood	3 yrs	Intake	Low salt	224	-8.9 (NA)	NA		Low
[41], China		yrs/Males 49.0%	pressure			Normal salt	238	-5.8 (NA)			
			Diastolic blood			Low salt	224	-4.7 (NA)	NA		
			pressure			Normal salt	238	-2.4 (NA)			
Juraschek et al.	RCT	Pre- or stage 1	Systolic blood	4 wks	Intake	DASH diet	204	-10.4 (-15.5, -5.3)	0.020		Low
(2017) [42], US		hypertension adults,	pressure			Control diet	200	-7.0(-12.9, -1.2)			
		49.1 ± 10.4 yrs/Males 43.0%									
Muth et αl. (2017)	RCT	Young adults, 27.0 ±	Systolic blood	14 days	Intake	Low sodium diet	85 Ye	Young adults: -4.0 (NA)	0.012		Some
[43], US		1.0 yrs Middle-aged adıılts	pressure				2	Middle-aged: -0 0 (NA) / O 001	00.0		concerns
		52.0 ± 1.0 yrs/Males				High sodium diet	85	Young adults: NA	AN A		
		51.0%						Middle-aged: NA	ΝΑ		
Buendia et al. (2015) Cohort	Cohort	_	Systolic blood	10 yrs	Intake dietary	Intake dietary < 2,000 mg/day	425	108.8 (108.0, 109.7)	0.550	Demographic, and	Low
[55], US		(9–10 yrs)/Females	pressure		Na-K ratio	2,500-3,000 mg/day	644	109.3 (108.3, 109.6)		anthropic factors,	
		100%				3,000-4,000 mg/day	905	108.9 (108.6, 109.7)		lifestyles, and foods	
						> 4,000 mg/day		108.1 (108.0, 110.4)		intake	
			Diastolic blood			< 2,000 mg/day	425	65.6 (64.8, 66.4)	0.560		
			pressure			2,500-3,000 mg/day	644	65.6 (64.9, 66.2)			
						3,000-4,000 mg/day	902	65.5 (65.0, 66.0)			
						> 4,000 mg/day	211	64.9 (63.8, 66.1)			

(continued to the next page)



Table 3. (Continued) Association between sodium levels and the risk of chronic diseases (continuous outcomes): hypertension

500000000000000000000000000000000000000	), second				mana cama	the state of the s					
Author (Year), Nation		Study	Study subjects		0)	Sodium levels	No. of cases/	Mean (95% CI)	<i>P</i> -values	P-values Confounding variables	RoB
	design	Source of subjects, Mean age (vrs)/Sex (%)	Outcome	Follow-up	Measurement	Categories	No. of category			considered	
3 1000		(c) \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	-	5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	-	-				-	
Kim et al. (2014)	Cross-		Systolic blood		Intake	Male				Demographic, and	Low
[65], Korea	sectional		pressure		amonnts	1st quintile	488	124.6 (123.0, 126.1)	0.600	anthropic factors,	
		Males 38.9%				2nd quintile	489	124.4 (123.0, 125.9)		lifestyles, and foods	
						3rd quintile	489	124.3 (122.8, 125.7)		intake	
						4th quintile	480	195 5 (194 1 197 0)			
						לבון למווינונס	0 0	1011(12411,1210)			
						stn quintile	884	125./(124.1,127.3)			
						Female					
						1st quintile	768	121.5 (120.2, 122.8)	0.610		
						2nd quintile	768	122.5 (121.3, 123.7)			
						3rd quintile	768	191.9 (120.7, 193.1)			
						4th quintile	768	1917(190 5 193 0)			
						למו למווינונ	0 0	1010(1200), 1200)			
						stn quintile	897	121.2 (119.7, 122.4)			
			Diastolic blood			Male					
			pressure			1st auintile	488	78.8 (77.8.79.7)	0.020		
			-			مانیت کردر	700	(200 000)			
						anii daii da	0 0	(0.00,00.0)			
						3rd quintile	984	80.5 (79.6, 81.4)			
						4th quintile	489	80.7 (79.9, 81.6)			
						5th quintile	488	80.6 (79.7, 81.6)			
						Female					
						1st quintile	768	76 8 (75 9 77 3)	0005		
						Tac dament	0 0	10.0 (7.0.0, 7.7.0)			
						Znd quintile	89/	78.3 (77.5, 79.0)			
						3rd quintile	768	77.4 (76.7, 78.1)			
						4th quintile	768	78.1 (77.4, 78.9)			
						5th quintile	768	78.4 (77.7, 79.1)			
Tabara et al. (2015)	Cross-	Adults. 54 (30-74	Blood pressure		Spot urine	Linear increase in urinary	9.144	0.112 (NA)	< 0.001	Demographic.	Low
[661. Japan	sectional	sectional vrs)/Males 52.2%	_		<u>-</u>	Na-K ratio				anthropic, and medical	
-										factors, lifestyles	
Noh et al. (2015)	Cross-	Adults. NA (> 19 vrs)/	Systolic blood	,	Intake	Low Na/High K	4.516	$113.0 \pm 0.30$	< 0.001	Demographic, and	Low
[67]. Korea	sectional		pressure		combinations	High Na/High K	7.539			anthropic factors.	
50 D. ( )					of Na and K	16.1.4.4.1.16.1.17	,, ,	N 00 0 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		lifestyles and foods	
					ייין ביין ביין	LOW Na/LOW K	7,532	$114.2 \pm 0.24$		illestytes, alld 100ds	
					Intakes	High Na/Low K	4,516	$114.8 \pm 0.31$		Intake	
			Diastolic blood		Intake	Low Na/High K	4,516	$73.9 \pm 0.21$	< 0.001		
			pressure		combinations	High Na/High K	7,532	$75.0 \pm 0.17$			
					of Na and K	Low Na/Low K	7,532	74.6 ± 0.17			
					intakes	High Na/Low K	4,516	75.8 ± 0.22			
Xu et al. (2014) [68], Cross-	Cross-	Adults, 42.3 (18-69	Systolic blood		24-h urine	Linear increase in urinary	191	0.16 (NA)	0.010	Demographic, and	Low
China	sectional	sectional vrs)/Males NA	pressure		) ; ;	sodium excretion	! !			anthropic factors	
			Diastolic blood			Linear increase in urinary	191	0.12 (NA)	0.060	_	
			pressure			sodium excretion					
Park et al. (2016)	Cross-		Average treatment		Intake dietary	1st quartile	2,356	0.00	NA	,	Low
[70], Korea	sectional	sectional yrs)/Males 31.8%	effects on systolic		Na-K ratio	2nd quartile	2,356	$1.10 \pm 0.51$			
			blood pressure			3rd quartile	2,356	$0.90 \pm 0.52$			
						4th quartile	2,356	$1.40 \pm 0.54$			
			Average treatment			1st quartile	2,356	0.00			
			effects on diastolic			2nd quartile	2,356	$0.80 \pm 0.32$			
			blood pressure			3rd quartile	2,356	$0.20 \pm 0.33$			
						4th quartile	2,356	$0.90 \pm 0.34$			
Moderate to strong	strenoth	Moderate to strong strength of evidence was determined for the relationship between sodium and hypertension	ned for the relation	nshin hetw	e milipos uga	nd hvnertension					

Moderate to strong strength of evidence was determined for the relationship between sodium and hypertension. CI, confidence interval; RoB, risk of bias; NA, not available; RCT, randomized controlled trial.



Table 4. Level of risk of bias and strength of evidence for the relationship between sodium intakes and chronic diseases

	· · · · · · · · · · · · · · · · · · ·		
Health outcomes	Authors (Year)	RoB	Overall SoE
Cardiovascular disease	Bertoia et al. (2014) [57], Cook et al. (2014) [49], Horikawa et al. (2014) [58], Kalogeropoulos et al. (2015) [46], Okayama et al. (2016) [47], Merino et al. (2015) [45], Prentice et al. (2017) [50], Lee et al. (2018) [62], Mente et al. (2018) [48]	Low: 8	Moderate
Cerebrovascular disease	Okayama et al. (2016) [47], Prentice et al. (2017) [50], Voortman et al. (2017) [53], Willey et al. (2017) [36], Li et al. (2018) [51], Mente et al. (2018) [48]	Low: 6	Moderate
Coronary heart disease	Joosten <i>et al.</i> (2014) [52], Kalogeropoulos <i>et al.</i> (2015) [46], Prentice <i>et al.</i> (2017) [50], Voortman <i>et al.</i> (2017) [53]	Low: 4	Limited
Hypertension	Diaz et al. (2014) [39], Kim et al. (2014) [65], Xu et al. (2014) [68], Buendia et al. (2015) [55], Jenkins et al. (2015) [38], Noh et al. (2015) [67], Reidlinger et al. (2015) [40], Tabara et al. (2015) [66], Takase et al. (2015) [54], Timpka et al. (2015) [56], Park et al. (2016) [70], Zhou et al. (2016) [41], Hu et al. (2017) [69], Muth et al. (2017) [43], Juraschek et al. (2017) [42]	Low: 14 Some concerns: 1	Strong
Gastric cancer	Umesawa et αl. (2016) [59], Wang et αl. (2017) [60]	Low: 2	Limited
Renal cancer	Deckers et al. (2014) [63], Deckers et al. (2017) [64]	Low: 2	Limited
Bone mineral density	Carbone et al. (2016) [61]	High: 1	Grade not assignable
RAAS	Nielsen et al. (2016) [44]	Some concerns: 1	Grade not assignable
Obesity	Navia et al. (2014) [71], Ge et al. (2016) [72], Huh et al. (2015) [73], Ma et al. (2015) [75], Murakami et al. (2015) [74], Grimes et al. (2016) [76], Nam et al. (2017) [78], Oh et al. (2017) [77], Zhang et al. (2018) [79]	Low: 8 Some concerns: 1	Limited

RoB, risk of bias; SoE, strength of evidence; RAAS, renin-angiotensin-aldosterone system.

## INTAKE ASSESSMENT TO CHARACTERIZE RISK

Currently, majority of the populations are reported to consume dietary sodium above the recommended WHO levels [7], while countries consuming less than 2,000 mg of sodium per day are the poor with malnutrition problems [26]. Especially in Asian countries, the mean sodium intakes are higher than 4,600 mg/day [27]. According to the 2019 KNHANES, the average daily sodium intake was 3,287 mg/day (males, 3,851 mg/day; females, 2,699 mg/ day) in South Korea, and the percentage of excessive sodium intake of ≥ 2,000 mg/day was 74.0% (84.5% for males and 63.5% for females) among Koreans aged ≥ 9 years [28]. In both developed and developing countries, including South Korea, where various processed foods produced by the modern food supply system are consumed, the feasibility of achieving a sodium intake goal of 2,000 mg/day is constantly questioned. Therefore, it is necessary to set a flexible goal for sodium intake for Koreans, based on the eating habits and food system in this population. Considering the food sources of dietary sodium, the predominant sources of dietary sodium for the Korean population are reported to be salt and kimchi, followed by soy sauce, ramen and soybean paste [13,29]. Moreover, the highest sodium source per serving was ramen (1,563 mg per serving), followed by salted seafood (jeotgal) (956 mg per serving), buckwheat noodles (891 mg per serving), and sandwich/hamburger/pizza (830 mg per serving) [13,29].

# PUBLIC HEALTH IMPLICATIONS AND SPECIAL CONSIDERATIONS

Contrary to the conventional idea that a lower sodium intake is healthy, recent studies have reported a U-shaped or J-shaped curve for the association between sodium intake and CVD risks, rather than a continuously increasing positive association [5,30]. Although there is a continuous positive linear relationship between sodium intake and BP, a sodium intake of < 3 g or > 7 g/d increases the risk of CVD in a U-shaped curve, when compared to an intake of 4-5 g/d [30]. Future studies on the effect of very low sodium intakes, and balance studies on adequate sodium intake, are required to establish the AI for sodium in the Korean



population. It should be acknowledged that the absence of reference values of UL or intake goal for dietary sodium does not indicate that there are no adverse toxicological effects of excessive sodium intake. Rather, it means that there is a lack of evidence for the toxicological effects of sodium in healthy populations. Therefore, further studies using the toxicological risk assessment approach are needed in order to set the UL in the future.

It has also been reported that the ratio between dietary sodium and potassium (Na:K ratio) is associated with health outcomes [31-33]. Specifically, a high Na:K ratio is reported to be associated with increased BP, and risk of hypertension and stroke [34-36]. Despite national efforts of reducing sodium intake at the population level, the Na:K ratio remains high among Koreans (ratio of 2.20 in 2019) [37]. Therefore, a health policy that targets lowering of the Na:K ratio is needed to improve public health in the Korean population.

The main limitation is insufficient evidence necessary to assess the relationship between sodium intake and chronic diseases in the Korean population. However, there is considerable evidence worldwide, for understanding the association between sodium intake and chronic disease. Furthermore, a meta-analysis on intake—response conducted by the US committee studying the DRIs of sodium, included Japanese and Chinese studies. Therefore, the CDRR established by the US committee can be used as the provisional CDRR for Koreans. Considering the increasing prevalence of hypertension and CVDs in South Korea, establishing and promoting this CDRR would be beneficial. Further studies on the relationship between sodium intake and chronic diseases are required to establish the CDRR for sodium in the Korean population. Moreover, since the majority of Koreans consume sodium at levels above the CDRR, there is a need to find new solutions, including technological innovations, that can reduce sodium in the food supply and in consumption.

## **CONCLUSIONS**

The 2020 KDRIs established the AI value for dietary sodium intake at 1,500 mg/day for adults aged 19–64 years, which is the same as in the 2015 KDRIs. Moreover, on the basis of a systematic review, the CDRR for sodium was set at 2,300 mg/day for adults aged 19–64 years as a new reference value, specific to chronic disease risk reduction. Intake goal for dietary sodium established in the 2015 KDRIs (instead of the UL) was not presented in the 2020 KDRIs. For the next revision of the KDRIs, further studies are required on sodium adequacy and toxicity, and their associations with chronic diseases, in the Korean population.

## SUPPLEMENTARY MATERIALS

## **Supplementary Table 1**

2020 Dietary Reference Intakes for Koreans for sodium and potassium by age, sex, and life stage

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## **Supplementary Table 2**

Association between sodium levels and the risk of chronic diseases (event outcomes)

Click here to view



## Supplementary Table 3

Association between sodium levels and the risk of chronic diseases (continuous outcomes)

Click here to view

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