

Review Article

Systematic classification of evidence for dietary reference intakes for Japanese 2010 (DRIs-J 2010) in adults and future prospects of DRIs in Asian countries

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In Asia, the concept of dietary reference values is shifting from recommended dietary allowances (RDAs) to dietary reference intakes (DRIs). To assist Asian countries that are planning to develop or revise their own DRIs, this study summarizes the scientific literature used in the development of the latest DRIs for the Japanese (DRIs-J 2010): it aims to clarify critical issues on- and discuss future prospects for DRIs in Asia. The criteria and studies used to determine reference values in DRIs-J 2010 in adults were extracted from the DRIs-J 2010 report, systematically classified, and summarized for each nutrient in tables according to the type of DRIs. The classification categories were as follows: criteria, subject ethnicity, year of publication, type of study and study design, number of subjects, and study content. In all, 184 studies were extracted and some issues in DRIs-J 2010 were clarified: 1) some nutrients were lacking in studies based on native populations; 2) only a few and relatively old studies determined tolerable upper intake levels for some nutrients; 3) with the same DRIs, there were inconsistencies among the nutrients in the study criteria. These were considered common issues when determining DRIs in other Asian countries. When establishing DRIs, these issues should be considered, in addition to population health status and country-specific needs.

Key Words: nutrition policy, reference values, diet, Asia, Japan

INTRODUCTION

Dietary reference values are essential for preventing nutritional deficiencies and maintaining health. The concept of recommended dietary allowances (RDAs) was first proposed in the United States in 1941.¹ After many revisions and expansion of the number of nutrients covered, a new concept, dietary reference intakes (DRIs), was established in 1994 to expand the range of application of RDAs.¹ Many Asian countries, such as the Philippines,² Vietnam,³ Taiwan,⁴ Korea,⁵ Singapore,⁶ and Malaysia,⁷ have developed their own RDAs or similar dietary reference values. Among them, Taiwan⁴ and Korea⁵ replaced RDAs with DRIs in 2003 and 2005, respectively.

Japan is an Asian country that has established its own dietary reference values. These values have a long history in Japan: preliminary dietary reference values for Japanese were first established in 1926, and since then several national organizations have developed dietary reference values.⁸ In 1969, the Ministry of Health and Welfare became responsible for establishing RDAs.⁸ Since then, RDAs have been revised every 5 years. The concept of DRIs was introduced in the sixth revision of the RDAs in 2000,⁹ and DRIs eventually superseded RDAs in the “Dietary Reference Intakes for Japanese (DRIs-J) 2005.”¹⁰ The current version is DRIs-J 2010.¹¹ DRIs-J consists of six DRIs, including “Tentative Dietary Goal for Prevent-

ing Lifestyle-Related Diseases”, which is a unique and original dietary reference value for Japanese.

As noted above, the concept of dietary reference values has been shifting from RDAs to DRIs in Asia. More Asian countries are expected to establish DRIs in the future. Sharing information among countries, such as evidence used for establishing DRIs or clarification of issues to be resolved, would help in developing new or improved DRIs in Asia.

In this Review, we aimed to summarize the scientific studies used for DRIs-J 2010, including comparatively new evidence, and to clarify issues that demand attention. We extracted the criteria and studies used to determine dietary reference values from the DRIs-J 2010 report.¹¹ The studies were systematically categorized; we summarized data in tables to determine those nutrients for which

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there was relatively insufficient scientific evidence and the validity of the criteria for each reference value. Based on the results, we assess the future prospects for DRIs in Asia.

MATERIALS AND METHODS

Extracting criteria for reference values and categorizing studies used for DRIs-J 2010

First, we excerpted criteria for reference values for energy and each nutrient from the DRIs-J 2010 report,¹¹ and compared it with that of other nutrients in the same DRIs: estimated energy requirement (EER), estimated average requirement (EAR), adequate intake (AI), tolerable upper intake level (UL), and tentative dietary goal for preventing lifestyle-related diseases (DG). Definitions of each DRI are given in the Appendix. RDA was beyond the scope of the present study because RDA values were calculated based on EAR.

Next, studies used to determine reference values were extracted from the report, and the following classifications were used to categorize each study: subject ethnicity (Japanese or other); year of publication (1940s, 1950s, 1960s, 1970s, 1980s, 1990s, 2000s, or 2010s); type of study (cross-sectional, cohort, case-control, intervention, review, meta-analysis, or case report for scientific articles; and guideline, commentary, report, or other for scientific literature apart from articles); number of study subjects (<10, 10–99, 100–499, 500–999, ≥1000, and unclear). In categorizing each study, the following definitions were applied. 1) The study was defined as Japanese if there was a description of Japanese subjects in the study, or the study was conducted in Japan with no description of non-Japanese subjects. 2) The number of subjects was based on the number indicated in the DRIs-J 2010 report (eg, if both sick and healthy subjects were described in the article, but only the results for healthy subjects appeared in DRIs-J 2010, we used the number of healthy subjects). 3) The number of subjects was not referred to if the study was a review, guideline, or commentary. 4) For balance studies, those in which the main outcome was equilibration, such as nitrogen or water-soluble vitamin balance, were classified as intervention studies; studies such as those measuring energy expenditure by doubly labeled water were classified as cross-sectional studies. Studies were limited to those that were directly concerned with determining reference values (ie, values shown in the study to be directly used as reference values or used for calculating reference values) in adults. We excluded studies used for background information or validation of reference values and studies examining other life stages (infants and children, pregnant and lactating women, and the elderly). After categorizing each study, we counted the number of relevant studies in each category and compared this among the nutrients for each type of reference value.

RESULTS

The criteria for determining DRIs for energy and each nutrient and the results of classifying the studies are shown in Table 1 (EER), Table 2 (EAR), Table 3 (AI), Table 4 (UL), and Table 5 (DG).

Number of studies used for DRIs

In the DRIs-J 2010 report, the number of studies that were directly used to determine DRIs was 14 for EER, 85 for EAR, 19 for AI, 47 for UL, and 19 for DG.

Fourteen studies on basal metabolic rate or physical activity level were used for EER (Table 1). The subjects in those studies were Japanese, and 10 of the studies (71.4%) were published in the 2000s.

By contrast, only 13 of 85 studies with Japanese subjects (15.3%) were used for EAR. No studies dealt with water-soluble vitamins, except vitamin B-6; none deal with sodium or micro-minerals, except iron (Table 2). The nutrient with the largest number of studies used for EAR was protein (n=16), followed by calcium (n=15), zinc (n=9), vitamin A (n=8), and folate (n=7). Fewer than five studies examined other nutrients. Of 16 studies, 15 (93.8%) were published in the 1970s and 1980s, and most were concerned with nitrogen balance.

Subjects in 17 of 19 scientific studies used for AI (89.4%) were Japanese. The report of the National Health and Nutrition Survey in Japan was adopted for most of the nutrients, except vitamin K, biotin, and manganese (Table 3).

With regard to UL, 5 of 47 (10.6%) studies examined Japanese subjects (vitamin E, phosphorus, iodine, and selenium; Table 4). Of 47 studies, 19 (40.4%) were published in the 1970s and 1980s. Values for vitamin A, vitamin D, vitamin B-6, iron, and copper were determined in only one study, which was published in the 1980s.

For DG, 10 of 19 (52.6%) studies examined Japanese subjects (fat, saturated fatty acids [lower limit], n-3 fatty acids, sodium and potassium; Table 5). Japanese studies mainly used the report of the National Health and Nutrition Survey in Japan. Unlike for EAR, AI, and UL, cohort studies with large numbers of subjects or meta-analyses were mainly used for DG.

Criteria for determining each DRI

The criterion for EER was the energy intake for which there was the highest probability of the energy balance being zero. The reference value for EER was determined by a formula using basal metabolic rate and physical activity level (Table 1).

Criteria for EAR varied among nutrients: balance studies (protein, vitamin B-1, vitamin B-2, niacin, sodium, magnesium, chromium, and molybdenum); biomarkers (vitamin A, vitamin B-6, vitamin B-12, folate, vitamin C, copper, iodine, and selenium) and factorial method (calcium, iron, and zinc; Table 2). For most of the nutrients in which biomarkers were used as outcomes, the criterion was based on preventing deficiencies; however, in the case of vitamin C, the criteria were prevention of cardiovascular disease and promotion of antioxidant activity.

AI, which is an alternative value for EAR, was determined mainly based on estimated nutrient intake obtained by dietary surveys (n-6 fatty acids, vitamin E, pantothenic acid, biotin, potassium, phosphorus, and manganese; Table 3). Criteria for vitamin D were based on serum 25-hydroxy vitamin D concentration, though its actual AI value was determined based on median intake of vitamin D according to the National Health and Nutrition Survey in Japan (the survey did not assess serum 25-

Table 1. Criterion for estimated energy intake (EER) and studies used in EER in adults

Criterion	Studies with Japanese subjects					Other studies				
	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
Energy Energy intake for which there was the highest probability of the energy balance being zero (basal metabolic rate× physical activity level)	3-15, 19 [14]	1980s [2] 1990s [2] 2000s [10]	<Articles> X-SECT [12] INTERV [1] Review [1]	10-99 [9] 100-499 [5]	Basal metabolic rate, energy expenditure, and physical activity level	—	—	—	—	—

†Numbers in brackets are the number of studies and the numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of the studies appear in reference 25.

§Abbreviations: X-SECT, cross-sectional study; INTERV, intervention study.

Table 2. Criteria for estimated average requirement (EAR) and studies used in EAR in adults

Nutrients	Criteria	Studies with Japanese subjects					Other studies				
		Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
Protein	Intake to maintain nitrogen balance adjusted by digestion coefficient of protein [Balance]	16–19, 28 [5]	1970s [1] 1980s [4]	<Articles> INTERV [4] <Others> Others [1]	<10 [2] 10-99 [3]	Nitrogen balance and digestion coefficient of protein	13-15, 20-27 [11]	1970s [3] 1980s [7] 1990s [1]	<Articles> INTERV [11]	<10 [6] 10-99 [5]	Nitrogen balance
Fat-soluble vitamins											
Vitamin A	Intake to maintain minimum cumulative liver dosage to prevent deficiency (20 µg/g) [Biomarker]	14 [1]	2000s [1]	<Others> Others [1]	—	Liver weight/kg body weight in adults	8-13,15 [7]	1970s [2] 1980s [1] 2000s [4]	<Articles> X-SECT [1] INTERV [2] Review [4]	10-99 [2] 100-499 [1]	Minimum cumulative liver dosage, coefficient of excretion, amount of excretion of vitamin A, liver weight/kg body weight and ratio of vitamin A storage (liver/body weight) etc.

†Numbers in brackets are the numbers of studies, and the numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of the studies appear in references 26–32.

§Abbreviations: X-SECT, cross-sectional study; INTERV, intervention study.

Table 2. Criteria for estimated average requirement (EAR) and studies used in EAR in adults (cont.)

Nutrients	Criteria	Studies with Japanese subjects					Other studies				
		Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
Water-soluble vitamins											
Vitamin B-1	Intake to maintain vitamin B-1 balance [Balance]	—	—	—	—	—	7 [1]	1960s [1]	<Articles> Meta-analysis [1]	Unclear [1]	Meta-analysis of studies that examined the relation between vitamin B-1 intake and urinary vitamin B-1 excretion
Vitamin B-2	Intake to maintain vitamin B-2 balance [Balance]	—	—	—	—	—	15,16 [2]	1940s [1] 1950s [1]	<Articles> INTERV [2]	10–99 [2]	Studies that examined the relation between vitamin B-2 intake and urinary vitamin B-2 excretion
Niacin	Intake to maintain amount of urinary <i>N</i> ¹ -methyl-nicotinamide (1.0 mg/day) to prevent pellagra [Balance]	—	—	—	—	—	22, 24–26 [4]	1950s [3] 1980s [1]	<Articles> INTERV [3] Review [1]	<10 [1] 10–99 [2]	Studies that examined the relation between niacin intake and urinary niacin excretion
Vitamin B-6	Intake to maintain serum plasma pyridoxal 5'-phosphate (30 nmol/L) to prevent deficiency [Biomarker]	5[1]	2000s [1]	<Articles> INTERV [1]	<10 [1]	Coefficient of pyridoxal 5'-phosphate utilization in the body	41 [1]	1990s [1]	<Others> Guideline [1]	—	Vitamin B-6 intake to maintain serum plasma pyridoxal 5'-phosphate of greater than 30 nmol/L
Vitamin B-12	Intake to maintain hematological states and normal serum vitamin B-12 to prevent pernicious anemia [Biomarker]	—	—	—	—	—	48,49, 53,54 [4]	1950s [1] 1960s [1] 1990s [1] 2000s [1]	<Articles> INTERV [2] Review [1] <Others> Guideline [1]	<10 [2]	Rate of vitamin B-12 absorption and production of red blood cells
Folate	Intake to maintain folate in red blood cells (≥ 300 nmol/L) and serum homocysteine (<14 μ mol/L) [Biomarker]	—	—	—	—	—	70-76 [7]	1980s [2] 1990s [3] 2000s [2]	<Articles> INTERV [7]	10-99 [6] 100-499 [1]	Folate intake to maintain folate in red blood cells and serum homocysteine
Vitamin C	Intake to maintain plasma vitamin C (50 μ mol/L) to prevent cardiovascular disease and promote antioxidant action [Biomarker]	—	—	—	—	—	128 [1]	2000s [1]	<Articles> Meta-analysis [1]	≥ 1000 [1]	Meta-analysis of studies that examined the relation between vitamin C intake and plasma vitamin C concentration

†Numbers in brackets are the numbers of studies, and the numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of the studies appear in references 26–32.

§Abbreviations: X-SECT, cross-sectional study; INTERV, intervention study.

Table 2. Criteria for estimated average requirement (EAR) and studies used in EAR in adults (cont.)

Nutrients	Criteria	Studies with Japanese subjects					Other studies				
		Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
Macro minerals											
Sodium	Intake to make up for unavoidable loss [Balance]	—	—	—	—	—	5–7 [3]	1970s [1] 1980s [1] 1990s [1]	<Articles> Review [1] <Others> Guideline [2]	—	Amount of unavoidable sodium loss in adults
Calcium	(Amount of calcium accumulated in the body + urinary calcium extraction + loss via dermal tissue) / apparent absorption rate [Factorial method]	72,73,83 [3]	2000s [3]	<Articles> INTERV [3]	10–99 [3]	Amount of urinary calcium extraction and apparent absorption rate of calcium	60,61,71,74,77,82,84–87,89,93 [12]	1980s [2] 1990s [4] 2000s [6]	<Articles> X-SECT [8] Cohort study [2] Review [2]	<10 [1] 10–99 [6] 100–499 [2] 500–999 [1]	Amount of calcium accumulated in the body, amount of urinary calcium extraction, and apparent absorption rate
Magnesium	Intake to maintain magnesium balance [Balance]	113 [1]	2000s [1]	<Articles> INTERV [1]	100–499 [1]	Amount of magnesium intake to maintain equilibration	—	—	—	—	—
Micro minerals											
Iron	Healthy adults: (basal iron loss / iron absorption); menstruating women: (basal iron loss + menstrual losses)/iron absorption. [Factorial method]	13,15 [2]	1960s [1] 2000s [1]	<Articles> X-SECT [1] Review [1]	10–99 [1]	Amount of menstrual bleeding, and menstrual cycle	7,16,17 [3]	1960s [1] 1980s [1] 1990s [1]	<Articles> INTERV [1] Review [1] <Others> Report [1]	10–99 [1]	Amount of basal iron loss, concentration of hemoglobin, and iron absorption rate
Zinc	Amount by model formula using the following factors: (zinc excretion, endogenous zinc excretion via the intestine and extent of absorption of dietary zinc) [Factorial method]	—	—	—	—	—	58–64,68,69 [9]	1980s [4] 1990s [3] 2000s [2]	<Articles> INTERV [7] <Others> Guideline [2]	<10 [5] 10–99 [2]	Amount of endogenous zinc excretion via the intestine, amount of zinc excretion, and reference weight in men aged 19–30

†Numbers in brackets are the numbers of studies, and the numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of the studies appear in references 26–32.

§Abbreviations: X-SECT, cross-sectional study; INTERV, intervention study.

Table 2. Criteria for estimated average requirement (EAR) and studies used in EAR in adults (cont.)

Nutrients	Criteria	Studies with Japanese subjects					Other studies				
		Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
Micro minerals											
Copper	Minimum intake to maintain normal plasma copper, urinary copper, salivary copper levels, and plasma superoxide dismutase activity [Biomarker]	—	—	—	—	—	110,111 [2]	1990s [2]	<Articles> INTERV [2]	10-99 [2]	Minimum amount to maintain normal plasma copper, urinary copper and salivary copper levels, and plasma superoxide dismutase activity
Iodine	Based on amount of iodine storage in the thyroid gland [Biomarker]	—	—	—	—	—	150,151 [2]	1960s [2]	<Articles> INTERV [1] <Others> Others [1]	10-99 [1] 100-499 [1]	Amount of iodine storage in the thyroid gland
Selenium	Intake to maintain 2/3 of saturated plasma glutathione peroxidase activity (GPX) level [Biomarker]	—	—	—	—	—	181 [1]	1990s [1]	<Others> Report [1]	—	Amount of selenium intake for maximum saturated plasma GPX activity, and regression formula between the value of GPX activity and selenium intake
Chromium	Intake to maintain chromium balance [Balance]	—	—	—	—	—	218 [1]	1980s [1]	<Articles> INTERV [1]	10-99 [1]	Amount of chromium intake to maintain equilibration
Molybdenum	Intake to maintain molybdenum balance [Balance]	—	—	—	—	—	249 [1]	1990s [1]	<Articles> INTERV [1]	<10 [1]	Amount of molybdenum intake to maintain equilibration

†Numbers in brackets are the numbers of studies, and the numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of the studies appear in references 26–32.

§Abbreviations: X-SECT, cross-sectional study; INTERV, intervention study.

Table 3. Criteria for adequate intake (AI) and studies used in AI in adults

Nutrients	Criteria	Studies with Japanese subjects					Other studies				
		Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
n-6 fatty acid	Median intake of n-6 fatty acid per day [Dietary survey]	2,3 [2]	2000s [2]	<Others> Report [2]	≥1000 [2]	Median intake of n-6 fatty acid according to National Health and Nutrition Survey in 2005 and 2006	—	—	—	—	—
Fat-soluble vitamins											
Vitamin D	Intake to maintain serum 25-hydroxy vitamin D (50 nmol/L) for normal blood parathormone [Biomarker]	55,56 [2]	2000s [2]	<Others> Report [2]	≥1000 [2]	Median intake of vitamin D according to National Health and Nutrition Survey in 2005 and 2006	—	—	—	—	—
Vitamin E	Median intake of vitamin E per day [Dietary survey]	55,56 [2]	2000s [2]	<Others> Report [2]	≥1000 [2]	Median intake of vitamin E according to National Health and Nutrition Survey in 2005 and 2006	—	—	—	—	—
Vitamin K	Intake to maintain normal blood clotting function [Biomarker]	—	—	—	—	—	96 [1]	1980s [1]	<Articles> INTERV [1]	10–99 [1]	Vitamin K intake to prevent latent deficiency
Water-soluble vitamins											
Pantothenic acid	Median intake of pantothenic acid per day [Dietary survey]	110,111 [2]	2000s [2]	<Others> Report [2]	≥1000 [2]	Median intake of pantothenic acid according to National Health and Nutrition Survey in 2005 and 2006	—	—	—	—	—
Biotin	Mean intake of biotin per day [Dietary survey]	115–118 [4]	2000s [4]	<Articles> X-SECT [4]	—	Mean intake of biotin according to total diet study	114 [1]	2000s [1]	<Articles> X-SECT [1]	—	Intake of biotin from total diet study
Macro-minerals											
Potassium	Intake to make up for unavoidable loss and median intake of potassium [Balance and dietary survey]	3,4 [2]	2000s [2]	<Others> Report [2]	≥1000 [2]	Median intake of potassium according to National Health and Nutrition Survey in 2005 and 2006	—	—	—	—	—
Phosphorus	Median intake of phosphorus per day [Dietary survey]	3,4 [2]	2000s [2]	<Others> Report [2]	≥1000 [2]	Median intake of phosphorus according to National Health and Nutrition Survey in 2005 and 2006	—	—	—	—	—

†Numbers in brackets are the numbers of studies, and the numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of the studies appear in references 26–32.

§Abbreviations: X-SECT, cross-sectional study; INTERV, intervention study.

Table 3. Criteria for adequate intake (AI) and studies used in AI in adults (cont.)

Nutrients	Criteria	Studies with Japanese subjects					Other studies				
		Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
Micro-minerals											
Manganese	Mean intake of manganese [Dietary survey]	131 [1]	1990s [1]	<Articles> Review [1]	—	Mean intake of manganese	—	—	—	—	—

†Numbers in brackets are the numbers of studies, and the numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of the studies appear in references 26–32.

§Abbreviations: X-SECT, cross-sectional study; INTERV, intervention study.

Table 4. Criteria of tolerable upper intake level (UL) and studies used in UL in adults

Nutrients	Criteria	Studies with Japanese subjects					Other studies				
		Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
Fat-soluble vitamins											
Vitamin A	Maximum intake without hepatic toxicity	—	—	—	—	—	27 [1]	1980s [1]	<Articles> Case report [1]	<10 [1]	Report of hepatic toxicity by individuals with excessive vitamin A intake (adverse effect reported)
Vitamin D	Maximum intake without hypercalcemia	—	—	—	—	—	70 [1]	1980s [1]	<Articles> INTERV [1]	100-499 [1]	Intervention study with vitamin D given to patients (adverse effect reported)
Vitamin E	Maximum intake without hemorrhagic effect	87 [1]	2000s [1]	<Articles> INTERV [1]	10-99 [1]	Intervention study with α -tocopherol given to subjects (adverse effect not reported)	—	—	—	—	—

†Numbers in brackets are the numbers of studies, and the numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of the studies appear in references 26–32.

§Abbreviations: X-SECT, cross-sectional study; INTERV, intervention study

Table 4. Criteria of tolerable upper intake level (UL) and studies used in UL in adults (cont.)

Nutrients	Criteria	Studies with Japanese subjects					Other studies				
		Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
Water-soluble vitamins											
Niacin	Maximum intake without digestive or hepatic toxicity	—	—	—	—	—	32-35 [4]	1970s [1] 1990s [3]	<Articles> INTERV [2] Review [1] Case report [1]	<10 [1] 10-99 [2]	Intervention studies with nicotinamide or nicotine acid given to patients (adverse effect reported), etc.
Vitamin B ₆	Maximum intake without sensory neuropathy	—	—	—	—	—	46 [1]	1980s [1]	<Articles> INTERV [1]	10-99 [1]	Intervention study with pyridoxine given to patients (adverse effect not reported)
Folate	Maximum intake without adverse effect by pteroylmonoglutamic acid	—	—	—	—	—	84-92 [9]	1980s [4] 1990s [4] 2000s [1]	<Articles> Cohort study [1] Case-control study [1] INTERV [5] Review [1] <Others> Guideline [1]	100-499 [2] ≥1000 [5]	Intervention study with folate given to women (adverse effect not reported), etc.
Macro-minerals											
Calcium	Maximum intake without milk-alkali syndrome	—	—	—	—	—	98-106 [9]	1980s [6] 1990s [3]	<Articles> X-SECT [1] Case report [8]	<10 [8] 10-99 [1]	Report of calcium intake by milk-alkali syndrome patients
Magnesium	Maximum intake without diarrhea	—	—	—	—	—	111,122-125 [5]	1980s [1] 1990s [4]	<Articles> X-SECT [4] <Others> Guideline [1]	10-99 [4]	UL value in American/Canadian DRIs and intervention study with magnesium given to subjects (adverse effect reported)
Phosphorus	Maximum intake that maintains normal serum phosphorus level	113,140 [2]	1980s [1] 2000s [1]	<Articles> INTERV [1] <Others> Commentary [1]	100-499 [1]	Upper limit of serum phosphorus level, rate of phosphorus absorption	139 [1]	1980s [1]	<Articles> Review [1]	—	Normal serum phosphorus level and amount of absorbed phosphorus

†Numbers in brackets are the number of studies, and the numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of studies appear in references 26–32.

§Abbreviations: X-SECT, cross-sectional study; INTERV, intervention study; HDL, high density lipoprotein; LOAEL, lowest observed adverse effect level; NOAEL, no observed adverse effect level; FAO/WHO, Food and Agriculture Organization/World Health Organization.

Table 4. Criteria of tolerable upper intake level (UL) and studies used in UL in adults (cont.)

Nutrients	Criteria	Studies with Japanese subjects					Other studies				
		Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
Micro-minerals											
Iron	Provisional maximal tolerable intake reported by FAO/WHO	—	—	—	—	—	38 [1]	1980s [1]	<Others> Guideline [1]	—	Provisional maximal tolerable intake reported by FAO/WHO
Zinc	Maximum intake without adverse effect (decreasing serum HDL, ferritin, hematocrit, etc.)	—	—	—	—	—	68,69 [2]	2000s [2]	<Others> Guideline [2]	—	LOAEL and uncertainty factor reported by American/Canadian DRIs and reference weight
Copper	Maximum intake without Wilson's disease	—	—	—	—	—	119 [1]	1980s [1]	<Articles> INTERV [1]	<10[1]	Intervention study with copper given to patients (adverse effect not reported)
Manganese	Maximum intake that maintains normal serum manganese level	—	—	—	—	—	130 [1]	2000s [1]	<Others> Guideline [1]	—	NOAEL reported by American/Canadian DRIs
Iodine	Maximum intake without thyroid gland disorder in case of habitual intake	162 [1]	1990s [1]	<Articles> X-SECT [1]	≥1000 [1]	Relation between urine iodine concentration and prevalence of hypothyroidism (adverse effect reported) and mean intake of iodine	—	—	—	—	—
Selenium	Maximum intake without adverse effect (losing hair or nails)	168 [1]	1990s [1]	<Articles> Review [1]	—	Mean selenium intake in Japanese	201–205 [5]	1990s [3] 2000s [2]	<Articles> X-SECT [1] Cohort study [1] INTERV [3]	<10 [1] 10–99 [1] ≥1000 [3]	Intervention study with selenium supplement given to patients (adverse effect reported) and LOAEL of selenium intake, etc.
Molybdenum	Based on UL of molybdenum reported by European Scientific Committee on Food	—	—	—	—	—	258 [1]	2000s [1]	<Others> Others [1]	—	UL of molybdenum reported by European Scientific Committee on Food

†Numbers in brackets are the number of studies, and the numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of studies appear in references 26–32.

§Abbreviations: X-SECT, cross-sectional study; INTERV, intervention study; HDL, high density lipoprotein; LOAEL, lowest observed adverse effect level; NOAEL, no observed adverse effect level; FAO/WHO, Food and Agriculture Organization/World Health Organization

hydroxy vitamin D concentration).

For UL, the criteria focused on adverse effects, such as hepatic toxicity, hypercalcemia, and diarrhea, which can be caused by excess intake of vitamin A, vitamin D, and magnesium, respectively (Table 4). The studies used as their sources were intervention studies for the treatment of disease (vitamin D, niacin, vitamin B-6, copper, and selenium), case reports (vitamin A and calcium), and guidelines in other countries (magnesium, iron, zinc, manganese, and molybdenum). Among these nutrients, adverse effects were reported for excessive intake of vitamin A, vitamin D, niacin, calcium, magnesium, iodine, and selenium. There were no reports of adverse effects for vitamin E, vitamin B-6, folate, or copper.

DG was determined for nineteen nutrients (Table 5). Among them, reference values for n-6 fatty acid and carbohydrates were determined without sufficient evidence. Reference values for n-6 fatty acid were assessed by considering the possible health risk (chronic inflammation) through high intake of n-6 fatty acid. Reference values for carbohydrates were based on estimated energy intake, RDA of protein intake, and DG of fat intake; however, these were not established using definite evidence. Criteria for DG value also varied by nutrient: decreasing the risk of stroke or cardiovascular disease (fat [upper limit], saturated fatty acid, cholesterol, and dietary fiber); median intake with the National Health and Nutrition Survey in Japan (n-3 fatty acid); and an intermediate value between the intake in guidelines for preventing hypertension and the median intake from the National Health and Nutrition Survey in Japan (sodium and potassium).

DISCUSSION

In the present study, we systematically classified the scientific studies used for DRIs-J 2010 to determine the nutrients for which there was insufficient evidence and to examine the validity of the criteria for each DRI. As far as we know, this type of study has not been previously reported. This study will provide useful information not only for Japan but also for other Asian countries with newly established or revised DRIs.

Some issues with DRIs-J 2010 emerged from the present study. The following areas were considered especially important for determining DRIs in other Asian countries: 1) studies conducted on native populations failed to examine some nutrients; 2) UL values for some nutrients were determined only by a few, relatively old studies; and 3) there were inconsistencies in the criteria for nutrients in the same DRIs.

Some countries, such as the United States and Canada, conduct selected updates after sufficient evidence has accumulated. For example, the American/Canadian Dietary Reference Intake for vitamin D was revised in 2011 for the first time in over a decade.¹² By contrast, DRIs-J is revised every 5 years. Though this consistency in the revision period has the advantage of reference values being based on the latest scientific studies, 5 years may be too short a time to accumulate sufficient evidence for some nutrients.

In the future, it is expected that more studies on Japanese subjects will be published. In the present study, we were unable to compare the results for Japanese and non-

Japanese subjects because the latter were used when Japanese data were lacking. However, it has been reported that Asians have a lower BMI than Caucasians, and the risk of type 2 diabetes is significantly higher among Asians than among Caucasians, even after adjusting for the differences in BMI.¹³ In addition, liver fat content, which has been shown to be associated with visceral adipose tissue, dyslipidemia, and insulin resistance, has been found to be higher in Japanese than in Caucasians and liver fat increases with increasing BMI at a higher rate in Japanese.¹⁴ Regarding dietary intake, people in Western countries (United States and United Kingdom) had a higher intake of energy, fat, potassium, and calcium and a lower intake of sodium than people in East Asian countries (Japan and China).¹⁵ Although these findings constitute a small portion of evidence, they suggest the possibility of metabolic and dietary differences between Asian and Caucasian populations. Conversely, it was reported that there were no significant differences in gene polymorphism related to type 2 diabetes among Japanese, Korean, and Chinese subjects.¹⁶ One study also showed similar dietary intakes between Japanese and Chinese.¹⁵ These results indicate that similarities exist among Asians. Considering that there are many ethnic groups in Asia and each group has its own regional and cultural differences, it is expected that DRIs may be established for each ethnic group and shared among Asian countries.

Inconsistency in the criteria among the nutrients with the same DRIs was also considered to be an issue. The concept of DRIs, including EAR, RDA, AI, and UL, was introduced in 1997 in the United States.¹ In Japan, DG, as an original dietary reference value for the primary prevention of lifestyle-related diseases, was added to DRIs. DG has a short history and is still in the process of being developed. Regarding vitamin C, because one study suggests that the minimal intake of 10 mg per day prevents scurvy,¹⁷ using this value as EAR and the current EAR value as DG could be one solution. The difficulty is in overlapping cases; for example, insufficient vitamin D intake is associated with rickets or osteomalacia (it is used for determining EAR), but longitudinally a deficiency of vitamin D is associated with osteoporosis (which is related to DG). As in this example, examining the compatibility with other reference values may be needed when new reference values are established.

In this Review, we clarified the issues in DRIs-J 2010 and examined the future prospects for DRIs in Asia. However, this study has two limitations. The first is that the number of studies used for reference values depended on the kind of criteria. For example, factorial methods tended to require more studies than balance methods; this is because studies corresponding to each factor are needed in factorial methods. The second limitation is that we did not consider the quality of the studies (eg, a meta-analysis, which integrated a number of original articles, was counted as one study). Grading the quality of the evidence was taken into account in the development of guidelines.¹⁸ However, grading the quality of the evidence can be adopted only in cases where the outcomes were similar among different studies. Because the required outcome and study design differed according to the reference value and nutrient, it was difficult to grade the

Table 5. Concept of tentative dietary goal for preventing lifestyle-related diseases (DG) and studies used in DG in adults

Nutrients	Criteria	Studies with Japanese subjects					Other studies				
		Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
Fat (lower limit)	100%- (AI for n-6 fatty acid + AI for n-3 fatty acid + DG for saturated fatty acid + % of energy intake as monounsaturated fatty acid + amount of glycerol)	Unpublished	—	—	—	Median intake of monounsaturated fatty acid according to National Health and Nutrition Survey in 2005 and 2006	—	—	—	—	—
Fat (upper limit)	% of energy intake as fat for decreasing serum total cholesterol, LDL cholesterol, triglyceride, total cholesterol/HDL cholesterol and body weight	2,3 [2]	2000s [2]	<Others> Report [2]	≥1000 [2]	Median value of % of energy intake as fat according to National Health and Nutrition Survey in 2005 and 2006	18 [1]	1990s [1]	<Articles> Meta-analysis [1]	≥1000 [1]	Relation between 30% of energy intake as fat and serum total cholesterol, LDL cholesterol, triglyceride, total cholesterol/HDL cholesterol, and body weight
Saturated fatty acid (lower limit)	% of energy intake as saturated fatty acid for decreasing risk of cerebral hemorrhage	28 [1]	2000s [1]	<Articles> Cohort study [1]	≥1000 [1]	Relation between saturated fatty acid intake and prevalence of cerebral hemorrhage	30 [1]	1980s [1]	<Articles> Cohort study [1]	≥1000 [1]	Relation between saturated fatty acid intake and mortality from stroke
Saturated fatty acid (upper limit)	% of energy intake as saturated fatty acid for decreasing risk of cardiovascular disease	—	—	—	—	—	18,48 [2]	1990s [2]	<Articles> Cohort study [1] Meta-analysis [1]	≥1000 [2]	Meta-analysis of the effect of National Cholesterol Education Program and relation between saturated fatty acid intake and morbidity or mortality from cardiovascular disease
n-6 fatty acid (upper limit)	10% of energy intake as n-6 fatty acid (but there is insufficient evidence)	—	—	—	—	—	—	—	—	—	—

†Numbers in brackets are the number of studies, and numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of the studies appear in references 26–32.

§Abbreviations: AI, adequate intake; WHO/ISH, World Health Organization/International Society of Hypertension

Table 5. Concept of tentative dietary goal for preventing lifestyle-related diseases (DG) and studies used in DG in adults (cont.)

Nutrients	Criteria	Studies with Japanese subjects					Other studies				
		Studies	Year of publication	Type of study (study design)	Number of subjects	Study content	Studies	Year of publication	Type of study (study design)	Number of subjects	Study content
n-3 fatty acid (lower limit)	Median intake of n-3 fatty acid	2,3 [2]	2000s [2]	<Others> Report [2]	≥1000 [2]	Median intake of n-3 fatty acid according to National Health and Nutrition Survey in 2005 and 2006	—	—	—	—	—
Cholesterol (upper limit)	Intake for decreasing the risk of cardiovascular disease	—	—	—	—	—	30 [1]	1980s [1]	<Articles> Cohort study [1]	≥1000 [1]	Relation between cholesterol intake and mortality from cardiovascular disease
Carbohydrate	100% - (% of energy intake as fat + % of energy intake as protein) (but there is insufficient evidence)	—	—	—	—	—	—	—	—	—	—
Dietary fiber	Intake for decreasing risk of myocardial infarction	—	—	—	—	—	19 [1]	2000s [1]	<Articles> Meta-analysis [1]	≥1000 [1]	Relation between dietary fiber intake and mortality from myocardial infarction
Macro-minerals											
Sodium	Intermediate value of sodium intake (6 g/d) for preventing hypertension and median intake of sodium	3,4,21 [3]	2000s [3]	<Others> Guideline [1] Report [2]	≥1000 [2]	Median intake of sodium according to National Health and Nutrition Survey in 2005 and 2006, and guideline by Japanese Society for Hypertension	19,20 [2]	2000s [2]	<Others> Guideline [2]	—	7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and guideline by WHO/ISH
Potassium	Intermediate value of potassium intake for preventing hypertension and median intake of potassium	3,4 [2]	2000s [2]	<Others> Report [2]	≥1000 [2]	Intake of potassium according to National Health and Nutrition Survey in 2005 and 2006	33 [1]	1990s [1]	<Others> Guideline [1]	—	6th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

†Numbers in brackets are the number of studies, and numbers in the study category are the reference numbers in DRIs-J 2010.

‡URLs of the studies appear in references 26–32.

§Abbreviations: AI, adequate intake; WHO/ISH, World Health Organization/International Society of Hypertension

quality of the evidence in such cases. Therefore, we attempted to make an assessment according to the number of studies cited. It is worth noting that some issues in DRIs-J 2010 were clarified in the present study, but a comprehensive assessment method, including the quality of evidence, will need to be developed.

Every time DRIs-J is revised, the evidence base becomes stronger. In the DRIs-J 2010 report, more than 1000 references were cited. Among them, 184 were studies that we summarized in the present investigation; the others were used for background information, validation of reference values, and for reference values for other life stages (infants and children, pregnant and lactating women, and the elderly). Reference values for calcium were AI and DG in DRIs-J 2005,¹⁰ but they were updated to EAR and RDA in DRIs-J 2010.¹¹ In this way, although there are still many nutrients with AI values, it is expected that there will be an increasing number of nutrients with EAR and RDA as evidence accumulates. In addition, introducing other criteria or methods may be appropriate for some nutrients in the future. For example, although the current AI value for vitamin K was determined based on blood-clotting function,¹¹ that vitamin has also been reported as being associated with bone health.^{19,20} Therefore, whether or not the criteria associated with bone health should be introduced is an issue that needs to be discussed. Methods of measuring the protein requirement have also been a contentious area. Conventionally, the nitrogen balance method has been regarded as the gold standard. However, because the method has many limitations,²¹ the amino acid oxidation technique has been used as an alternative in recent years.²²⁻²⁴ There are many topics that are worthy of debate with respect to the subject matter of the present paper; however, the most pertinent issue is a consideration of the health status and the particular needs of the population in one's own country.

In conclusion, this study has clarified issues related to DRIs-J and discussed the future prospects of DRIs in Asia. When determining DRIs, it is necessary to address the issues presented in this study and also to consider the health status and particular needs of the population in one's own country. It is our expectation that the data in the present study will be of use in determining and revising DRIs in various Asian countries.

AUTHOR DISCLOSURES

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Appendix. DRI definitions and nutrients included in DRIs-J 2010

DRIs	Definitions	Nutrients included (in adults)
Estimated energy requirement (EER)	Average dietary energy intake that is assumed to maintain energy balance and good health in a healthy adult of a defined age, sex, weight, height, and physical activity level	Energy
Estimated average requirement (EAR)	Average requirement (50%) for the nutrient for each age and sex group	Protein, vitamin A, vitamin B-1, vitamin B-2, niacin, vitamin B-6, vitamin B-12, folate, vitamin C, sodium, calcium, magnesium, iron, zinc, copper, iodine, selenium, chromium, and molybdenum
Adequate intake (AI)	Less well-defined value; generally, the median of the population without evidence of deficiency	n-6 fatty acid, vitamin D, vitamin E, vitamin K, pantothenic acid, biotin, potassium, phosphorus, and manganese
Recommended dietary allowance (RDA)	Intake that covers the needs of 97.5% of the population for each age and sex group (calculated by $EAR+2SD_{EAR}$; because the variance is usually unknown, the coefficient of variation is adopted instead)	Protein, vitamin A, vitamin B-1, vitamin B-2, niacin, vitamin B-6, vitamin B-12, folate, vitamin C, calcium, magnesium, iron, zinc, copper, iodine, selenium, chromium, and molybdenum
Tolerable upper intake level (UL)	Highest level of intake that can be tolerated without causing adverse effects	Vitamin A, vitamin B-6, vitamin D, vitamin E, niacin, folate, calcium, magnesium, phosphorus, iron, zinc, copper, manganese, iodine, selenium, and molybdenum
Tentative dietary goal for preventing life-style-related diseases (DG)	Value for primary prevention of lifestyle-related diseases	Fat, saturated fatty acid, n-6 fatty acid, n-3 fatty acid, cholesterol, carbohydrate, dietary fiber, sodium, and potassium

Review Article

Systematic classification of evidence for dietary reference intakes for Japanese 2010 (DRIs-J 2010) in adults and future prospects of DRIs in Asian countries

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2010 日本成人膳食營養素參考攝取量(DRIs-J 2010)實證研究之系統性分類及對亞洲國家膳食營養素參考攝取量之未來展望

在亞洲，對膳食參考值的概念正從建議攝取量(RDAs)轉變成膳食營養素參考攝取量(DRIs)。為了協助正計畫發展或修改己國 DRIs 之亞洲國家，本篇研究綜整所有用來發展日本最新 DRIs(DRIs-J 2010)之科學性文獻，目的是釐清當前重要議題並剖析亞洲 DRIs 之未來展望。DRIs-J 2010 中訂定成人參考值的標準與研究主要摘錄自 DRIs-J 2010 報告，並根據 DRIs 中的類型，將每一營養素予以系統性分類並匯整於表中。分類項目如下：量測標準、對象種族、出版年份、研究型態與設計、樣本數及研究內容。在所有文獻中，共挑出 184 篇，並將 DRIs-J 2010 中的部分議題分成以下幾點說明：1) 部份營養素缺乏以當地族群為主之研究；2) 部分營養素僅賴少數或早期幾篇研究來決定其上限容許攝取量；3) 制定相同 DRIs，營養素之量測標準卻不一致。以上這些常見議題亦是其他亞洲國家訂定 DRIs 時會遭遇到。建立 DRIs 時，除了族群之健康狀態和國家特定之需求外，這些議題也需納入考慮。

關鍵字：營養政策、參考值、飲食、亞洲、日本