

Summary

This report provides quantitative reference intakes for vitamin A, vitamin K, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, vanadium, and zinc. No recommendations are provided for arsenic and silicon. This is one volume in a series of reports that presents dietary reference values for the intake of nutrients by Americans and Canadians. The development of Dietary Reference Intakes (DRIs) expands and replaces the series of Recommended Dietary Allowances (RDAs) in the United States and Recommended Nutrient Intakes (RNIs) in Canada. A major impetus for the expansion of this review is the growing recognition of the many uses to which RDAs and RNIs have been applied and the growing awareness that many of these uses require the application of statistically valid methods that depend on reference values other than RDAs and RNIs. This report includes a review of the roles that micronutrients are known to play in traditional deficiency diseases and evaluates possible roles in chronic diseases.

The overall project is a comprehensive effort undertaken by the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes (the DRI Committee) of the Food and Nutrition Board, Institute of Medicine, The National Academies, with active involvement of Health Canada. (See Appendix A for a description of the overall process and its origins.) This study was requested by the U.S. Federal Advisory Steering Committee for Dietary Reference Intakes in collaboration with Health Canada.

Major new approaches and findings in this report include the following:

- The establishment of new estimates for the conversion of provitamin A carotenoids to vitamin A: 1 μg retinol activity equivalent (μg RAE) is equal to 1 μg all-*trans*-retinol, 12 μg β -carotene, and 24 μg α -carotene or β -cryptoxanthin. This recognizes that 50 percent less bioconversion of carotenoids to vitamin A occurs than was previously thought, a change that means twice as much provitamin A-rich carotenoids contained in green leafy vegetables and certain fruits are required to provide a given amount of vitamin A activity. Given possible future changes in equivalency, weight of carotenoids should be given in food tables.
- The establishment of RDAs for copper and molybdenum.
- The establishment of Tolerable Upper Intake Levels (ULs) for vitamin A, boron, copper, iodine, iron, manganese, molybdenum, nickel, vanadium, and zinc.
- Research recommendations for information needed to advance understanding of human micronutrient requirements and the adverse effects associated with intake of higher amounts.

WHAT ARE DIETARY REFERENCE INTAKES?

Dietary Reference Intakes (DRIs) are reference values that are quantitative estimates of nutrient intakes to be used for planning and assessing diets for apparently healthy people. They include not only Recommended Dietary Allowances (RDAs) but also three other types of reference values (see Box S-1). Although the reference values are based on data, the data were often scanty or drawn from studies that had limitations in addressing the question. Thus, scientific judgment was required for evaluating the evidence and in setting the reference values, and that process is delineated for each nutrient in Chapters 4 through 13.

Recommended Dietary Allowances

The process for setting the RDA depends on being able to set an *Estimated Average Requirement (EAR)*. Before the EAR is set, a specific criterion of adequacy is selected on the basis of a careful review of the literature. In the selection of the criterion, reduction of disease risk is considered along with many other health parameters.

Box S-1 Dietary Reference Intakes

Recommended Dietary Allowance (RDA): *the average daily dietary nutrient intake level sufficient to meet the nutrient requirement of nearly all (97 to 98 percent) healthy individuals in a particular life stage and gender group.*

Adequate Intake (AI): *the recommended average daily intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate—used when an RDA cannot be determined.*

Tolerable Upper Intake Level (UL): *the highest average daily nutrient intake level that is likely to pose no risk of adverse health effects to almost all individuals in the general population. As intake increases above the UL, the potential risk of adverse effects may increase.*

Estimated Average Requirement (EAR): *the average daily nutrient intake level estimated to meet the requirement of half the healthy individuals in a particular life stage and gender group.*

If the standard deviation (SD) of the EAR is available and the requirement for the nutrient is symmetrically distributed, the RDA is set at two SDs above the EAR:

$$\text{RDA} = \text{EAR} + 2 \text{SD}_{\text{EAR}}$$

If data about variability in requirements are insufficient to calculate an SD, a coefficient of variation (CV) for the EAR of 10 percent is assumed, unless available data indicate a greater variation in requirements.

If 10 percent is assumed to be the CV, then twice that amount when added to the EAR is defined as equal to the RDA. The resulting equation for the RDA is then

$$\text{RDA} = 1.2 \times \text{EAR}$$

This level of intake statistically represents 97.5 percent of the requirements of the population. If the distribution of the nutrient requirement is known to be skewed for a population, as with iron,

other approaches are used to find the ninety-seventh to ninety-eighth percentile to set the RDA.

The RDA for a nutrient is a value to be used as a goal for dietary intake for the healthy individual. As discussed in Chapter 14, the RDA is not intended to be used to assess the diets of either individuals or groups or to plan diets for groups. Only if intakes have been observed for a large number of days (i.e., usual intake) and are at or above the RDA, or if observed intakes for fewer days are well above the RDA, should one have a high level of confidence that the intake is adequate (see Box S-2). The EAR is also used as the basis to address diets of groups.

Adequate Intakes

The *Adequate Intake* (AI) is set instead of an RDA if sufficient scientific evidence is not available to calculate an EAR. The main intended use of the AI is as a goal for the nutrient intake of individuals. For example, the AI for young infants, for whom human milk is the recommended sole source of food for most nutrients up through the first 4 to 6 months of age, is based on the daily mean nutrient intake supplied by human milk for apparently healthy, full-term infants receiving human milk. The goal may be different for infants consuming infant formula for which the bioavailability of a nutrient may be different from that in human milk, such as iron, which is high in infant formula due to its lower bioavailability than that found in human milk.

Comparison of Recommended Dietary Allowances and Adequate Intakes

Although both the RDA and AI are to be used as a goal for intake by individuals, the RDA differs from the AI. Intake of the RDA for a nutrient is expected to meet the needs of 97 to 98 percent of the apparently healthy individuals in a life stage and gender group (see Figure S-1). However, because no distribution of requirements is known for nutrients with an AI, it is not possible to know what percentage of individuals are covered by the AI. The AI for a nutrient is expected to exceed the RDA for that nutrient, and thus it should cover the needs of more than 97 to 98 percent of the individuals. The degree to which an AI exceeds the RDA is likely to differ among nutrients and population groups.

For people who have diseases that increase specific nutrient requirements or who have other special health needs, the RDA and

Box S-2 Uses of Dietary Reference Intakes for Healthy Individuals and Groups

<i>Type of Use</i>	<i>For the Individual^a</i>	<i>For a Group^b</i>
Assessment	<p>EAR: use to examine the probability that usual intake is inadequate.</p> <p>RDA: usual intake at or above this level has a low probability of inadequacy.</p> <p>AI^c: usual intake at or above this level has a low probability of inadequacy.</p> <p>UL: usual intake above this level may place an individual at risk of adverse effects from excessive nutrient intake.</p>	<p>EAR: use to estimate the prevalence of inadequate intakes within a group.</p> <p>RDA: do not use to assess intakes of groups.</p> <p>AI^c: mean usual intake at or above this level implies a low prevalence of inadequate intakes.</p> <p>UL: use to estimate the percentage of the population at potential risk of adverse effects from excess nutrient intake.</p>
Planning	<p>RDA: aim for this intake.</p> <p>AI^c: aim for this intake.</p> <p>UL: use as a guide to limit intake; chronic intake of higher amounts may increase the potential risk of adverse effects.</p>	<p>EAR: use to plan an intake distribution with a low prevalence of inadequate intakes.</p> <p>AI^c: use to plan mean intakes.</p> <p>UL: use to plan intake distributions with a low prevalence of intakes potentially at risk of adverse effects.</p>

RDA = Recommended Dietary Allowance
 EAR = Estimated Average Requirement
 AI = Adequate Intake
 UL = Tolerable Upper Level

^aEvaluation of true status requires clinical, biochemical, and anthropometric data.

^bRequires statistically valid approximation of distribution of usual intakes.

^cFor the nutrients in this report, AIs are set for infants for all nutrients, and for other age groups for vitamin K, chromium, and manganese. The AI may be used as a guide for infants as it reflects the average intake from human milk.

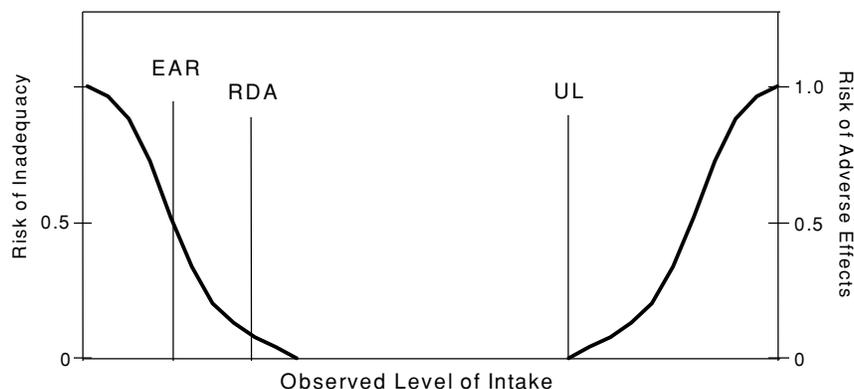


FIGURE S-1 Dietary reference intakes. This figure shows that the Estimated Average Requirement (EAR) is the intake at which the risk of inadequacy is 0.5 (50 percent) to an individual. The Recommended Dietary Allowance (RDA) is the intake at which the risk of inadequacy is very small—only 0.02 to 0.03 (2 to 3 percent). The Adequate Intake (AI) does not bear a consistent relationship to the EAR or the RDA because it is set without being able to estimate the average requirement. It is assumed that the AI is at or above the RDA if one could be calculated. At intakes between the RDA and the Tolerable Upper Intake Level (UL), the risks of inadequacy and of excess are both close to 0. At intakes above the UL, the potential risk of adverse effects may increase.

AI each may serve as the basis for adjusting individual recommendations. Qualified health professionals should adapt the recommended intake to cover higher or lower needs.

Tables S-1 through S-9 provide the recommended intake levels, whether RDAs or AIs, for vitamin A, vitamin K, chromium, copper, iodine, iron, manganese, molybdenum, and zinc by life stage and gender group. For most of these micronutrients, AIs rather than RDAs are proposed for infants to age 1 year. EARs and RDAs, however, are proposed for iron and zinc for infants 7 to 12 months of age because the level of iron and zinc in human milk does not meet the needs of the older infants and because factorial data are available to estimate the average requirement. Neither AIs nor RDAs were proposed for arsenic, boron, nickel, silicon, or vanadium.

Tolerable Upper Intake Levels

The *Tolerable Upper Intake Level* (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects for almost all individuals in the general population (see Table S-10). As intake increases above the UL, the potential risk of adverse effects may increase. The term “tolerable intake” was chosen to avoid implying a possible beneficial effect. Instead, the term is intended to connote a level of intake that can, with high probability, be tolerated biologically. The UL is not intended to be a recommended level of intake. There is no established benefit for apparently healthy individuals if they consume nutrient intakes above the RDA or AI.

ULs are useful because of the increased interest in and availability of fortified foods and the increased use of dietary supplements. ULs are based on total intake of a nutrient from food, water, and supplements if adverse effects have been associated with total intake. However, if adverse effects have been associated with intake from supplements or food fortificants only, the UL is based on nutrient intake from one or both of those sources only, rather than on total intake. The UL applies to chronic daily use.

For vitamin K, arsenic, chromium, and silicon, there are insufficient data for developing a UL. This does not mean that there is no potential for adverse effects resulting from high intake; for example, arsenic is a human poison at high intakes. However, at levels below what is known to be toxic, little data are available. Where data about adverse effects are extremely limited, extra caution may be warranted.

APPROACH FOR SETTING DIETARY REFERENCE INTAKES

The scientific data used to develop Dietary Reference Intakes (DRIs) have come from observational and experimental studies. Studies published in peer-reviewed journals were the principal source of data. Life stage and gender were considered to the extent possible, but the data did not provide a basis for proposing different requirements for men and for nonpregnant and nonlactating women in different age groups for many of the micronutrients. Two of the categories of reference values—the Estimated Average Requirement (EAR) and Recommended Dietary Allowance (RDA)—are defined by specific criteria of nutrient adequacy; the third, the Tolerable Upper Intake Level (UL), is defined by a specific endpoint of adverse effect, when one is available. In all cases, data were examined closely to determine whether a functional endpoint could

TABLE S-1 Criteria and Dietary Reference Intake Values for Vitamin A by Life Stage Group

Life Stage Group	Criterion	EAR (µg)
		Male
0 through 6 mo	Average vitamin A intake from human milk	
7 through 12 mo	Extrapolation from 0 through 6 mo AI	
1 through 3 y	Extrapolation from adult EAR	210
4 through 8 y	Extrapolation from adult EAR	275
9 through 13 y	Extrapolation from adult EAR	445
14 through 18 y	Extrapolation from adult EAR	630
> 18 y	Adequate liver vitamin A stores	625
Pregnancy		
14 through 18 y	Adolescent female EAR plus estimated daily accumulation by fetus	
19 through 50 y	Adult female EAR plus estimated daily accumulation by fetus	
Lactation		
14 through 18 y	Adolescent female EAR plus average amount of vitamin A secreted in human milk	
19 through 50 y	Adult female EAR plus average amount of vitamin A secreted in human milk	

^a EAR = Estimated Average Requirement. The intake that meets the estimated nutrient needs of half of the individuals in a group.

^b RDA = Recommended Dietary Allowance. The intake that meets the nutrient need of almost all (97–98 percent) of individuals in a group.

^c AI = Adequate Intake. The observed average or experimentally determined intake by a

be used as a criterion of adequacy. The quality of studies was examined by considering study design; methods used for measuring intake and indicators of adequacy; and biases, interactions, and confounding factors.

Although the reference values are based on data, the data were often scanty or drawn from studies that had limitations in addressing the various questions that confronted the panel. Therefore, many of the questions raised about the requirements for and recommended intakes of these micronutrients cannot be answered fully because of inadequacies in the present database. Apart from studies of overt deficiency diseases, there is a dearth of studies that address specific effects of inadequate intakes on specific indicators of health status, and a research agenda is proposed (see Chapter 15). The

s for

	EAR ($\mu\text{g RAE/d}$) ^a		RDA ($\mu\text{g RAE/d}$) ^b		AI ($\mu\text{g/d}$) ^c
	Male	Female	Male	Female	
					400
					500
	210	210	300	300	
	275	275	400	400	
	445	420	600	600	
	630	485	900	700	
	625	500	900	700	
		530		750	
		550		770	
vitamin A		885		1,200	
in A		900		1,300	

defined population or subgroup that appears to sustain a defined nutritional status, such as growth rate, normal circulating nutrient values, or other functional indicators of health. The AI is used if sufficient scientific evidence is not available to derive an EAR. For healthy infants receiving human milk, the AI is the mean intake. **The AI is not equivalent to an RDA.**

reasoning used to establish the values is described for each nutrient in Chapters 4 through 13. While the various recommendations are provided as single rounded numbers for practical considerations, it is acknowledged these values imply a precision not fully justified by the underlying data in the case of currently available human studies.

The scientific evidence related to the prevention of chronic degenerative disease was judged to be too nonspecific to be used as the basis for setting any of the recommended levels of intake for all these nutrients. For all of the micronutrients, the EAR is higher than the amount needed to prevent overt deficiency diseases in essentially all individuals in the life stage group and is based on limited data indicating laboratory evidence of sufficiency. The indicators used in deriving the EARs, and thus the RDAs, are described below.

TABLE S-2 Criteria and Dietary Reference Intake Values for Vitamin K by Life Stage Group

Life Stage Group	Criterion	AI (µg/d)
		Male
0 through 6 mo	Average vitamin K intake from human milk	2.0
7 through 12 mo	Extrapolation from 0 through 6 mo AI	2.5
1 through 3 y	Median intake of vitamin K from the Third National Health and Nutrition Examination Survey (NHANES III)	30
4 through 8 y	Median intake of vitamin K from NHANES III	55
9 through 13 y	Median intake of vitamin K from NHANES III	60
14 through 18 y	Median intake of vitamin K from NHANES III	75
> 18 y	Median intake of vitamin K from NHANES III	120
Pregnancy		
14 through 18 y	Adolescent female median intake	
19 through 50 y	Adult female median intake	
Lactation		
14 through 18 y	Adolescent female median intake	
19 through 50 y	Adult female median intake	

^a AI = Adequate Intake. The observed average or experimentally determined intake by a defined population or subgroup that appears to sustain a defined nutritional status, such as growth rate, normal circulating nutrient values, or other functional indicators of health. The AI is used if sufficient scientific evidence is not available to derive an

NUTRIENT FUNCTIONS AND THE INDICATORS USED TO ESTIMATE REQUIREMENTS

Vitamin A functions to maintain normal reproduction, vision, and immune function. A deficiency of vitamin A, although uncommon in North America, can result initially in abnormal dark adaptation (night blindness) followed by xerophthalmia. The method used to set an Estimated Average Requirement (EAR) for vitamin A is based on a computational analysis to assure adequate body stores of vitamin A. The Recommended Dietary Allowance (RDA) for adults for vitamin A is set at 900 µg RAE/day for men and 700 µg RAE/day for women. One µg retinol activity equivalent (µg RAE) is equal to 1 µg all-trans-retinol, 12 µg β-carotene, and 24 µg α-carotene or β-cryptoxanthin.

Vitamin K functions as a coenzyme in the synthesis of the biologically active form of a number of proteins involved in blood coagulation and bone metabolism. Because of the lack of data to set an

s for

	AI (µg/d) ^a	
	Male	Female
	2.0	2.0
	2.5	2.5
Infants (NHANES III)	30	30
	55	55
	60	60
	75	75
	120	90
		75
		90
		75
		90

Estimated Average Requirement (EAR). For healthy infants receiving human milk, the AI is the mean intake. **The AI is not equivalent to a Recommended Dietary Allowance (RDA).**

EAR, an Adequate Intake (AI) is set based on representative dietary intake data from healthy individuals from the Third Nutrition and Health Examination Survey (NHANES III). The AI for adults is 120 and 90 µg/day, for men and women, respectively.

Chromium potentiates the action of insulin in vivo and in vitro. There was not sufficient evidence to set an EAR for chromium. Therefore, an AI was set based on estimated intakes of chromium derived from the average amount of chromium/1,000 kcal of balanced diets and average energy intake from NHANES III. The AI is 35 µg/day for young men and 25 µg/day for young women.

Copper functions to catalyze the activity of many copper metalloenzymes that act as oxidases to achieve the reduction of molecular oxygen. Frank copper deficiency in humans is rare; the deficiency symptoms include normocytic and hypochromic anemia, leukopenia, and neutropenia. The method used to set an EAR for copper is based on the changes in a combination of biochemical indicators

TABLE S-3 Criteria and Dietary Reference Intake Values for Chromium by Life Stage Group

Life Stage Group	Criterion	AI (µg/d)
		Male
0 through 6 mo	Average chromium intake from human milk	0.2
7 through 12 mo	Average chromium intake from human milk and complementary foods	5.5
1 through 3 y	Extrapolation from adult AI	11
4 through 8 y	Extrapolation from adult AI	15
9 through 13 y	Extrapolation from adult AI	25
14 through 18 y	Extrapolation from adult AI	35
19 through 50 y	Average chromium intake based on the chromium content of foods/1,000 kcal and average energy intake ^b	35
≥ 51 y	Average chromium intake based on the chromium content of foods/1,000 kcal and average energy intake ^b	30
Pregnancy		
14 through 18 y	Extrapolation from adolescent AI based on body weight	
19 through 50 y	Extrapolation from adult woman AI based on body weight	
Lactation		
14 through 18 y	Adolescent female intake plus average amount of chromium secreted in human milk	
19 through 50 y	Adult female intake plus average amount of chromium secreted in human milk	

^a AI = Adequate Intake. The observed average or experimentally determined intake by a defined population or subgroup that appears to sustain a defined nutritional status, such as growth rate, normal circulating nutrient values, or other functional indicators of health. AI is used if sufficient scientific evidence is not available to derive an Estimated Average Requirement (EAR). For healthy infants receiving human milk, AI is the

resulting from varied levels of copper intake. The RDA for copper is 900 µg/day for men and women. There were insufficient data to set a different EAR and RDA for each gender.

Iodine is an important component of the thyroid hormones that are involved with the regulation of metabolism. Severe iodine deficiency can result in impaired cognitive development in children and goiter in adults. The method used to set an EAR for iodine is iodine accumulation and turnover. The adult RDA for iodine is 150 µg/day. There were insufficient data to set a different EAR and RDA for each gender.

Iron functions as a component of hemoglobin, myoglobin, cytochromes, and enzymes. Iron deficiency anemia is the most common

s for

	AI (µg/d) ^a	
	Male	Female
	0.2	0.2
	5.5	5.5
	11	11
	15	15
	25	21
	35	24
a content	35	25
a content	30	20
weight		29
y weight		30
		44
mium		45

mean intake. **The AI is not equivalent to a Recommended Dietary Allowance (RDA).**

^bThe average chromium content in well balanced diets was determined to be 13.4 µg/1,000 kcal and the average energy intake for adults was obtained from the Third National Health and Nutrition Examination Survey.

nutritional deficiency in the world, resulting in fatigue and impaired cognitive development and productivity. The required amount of absorbed iron is estimated based on factorial modeling. The EAR is determined by dividing the required amount of absorbed iron by the fractional absorption of dietary iron, estimated to be 18 percent for adults for the typical North American diet. The RDA for men and premenopausal women is 8 and 18 mg/day, respectively. The RDA for pregnant women is 27 mg/day.

Manganese is involved in the formation of bone and in amino acid, lipid, and carbohydrate metabolism. There were insufficient data to set an EAR for manganese. An AI was set based on median intakes reported from the U.S. Food and Drug Administration Total Diet

TABLE S-4 Criteria and Dietary Reference Intake Values for Copper by Life Stage Group

Life Stage Group	Criterion	EAR (µg/
		Male
0 through 6 mo	Average copper intake from human milk	
7 through 12 mo	Average copper intake from human milk and complementary foods	
1 through 3 y	Extrapolation from adult EAR	260
4 through 8 y	Extrapolation from adult EAR	340
9 through 13 y	Extrapolation from adult EAR	540
14 through 18 y	Extrapolation from adult EAR	685
19 through 50 y	Plasma copper, serum ceruloplasmin, and platelet copper concentrations and erythrocyte superoxide dismutase activity	700
≥ 51 y	Extrapolation from 19 through 50 y	700
Pregnancy		
14 through 18 y	Adolescent female EAR plus fetal accumulation of copper	
19 through 50 y	Adult female EAR plus fetal accumulation of copper	
Lactation		
14 through 18 y	Adolescent female EAR plus average amount of copper secreted in human milk	
19 through 50 y	Adult female EAR plus average amount of copper secreted in human milk	

^a EAR = Estimated Average Requirement. The intake that meets the estimated nutrient needs of half of the individuals in a group.

^b RDA = Recommended Dietary Allowance. The intake that meets the nutrient need of almost all (97–98 percent) of individuals in a group.

^c AI = Adequate Intake. The observed average or experimentally determined intake by a

Study. The AI for adult men and women is 2.3 and 1.8 mg/day, respectively.

Molybdenum functions as a cofactor for several enzymes in a form called molybdopterin. An inborn error of metabolism that leads to a deficiency of sulfite oxidase is due to the lack of molybdopterin, which results in neurological dysfunction and mental retardation. Molybdenum balance data were used to set an EAR. The RDA for adults for molybdenum is 45 µg/day for men and women. There were insufficient data to set a different EAR and RDA for each gender.

s for

	EAR ($\mu\text{g}/\text{d}$) ^a		RDA ($\mu\text{g}/\text{d}$) ^b		AI ($\mu\text{g}/\text{d}$) ^c
	Male	Female	Male	Female	
					200
					220
	260	260	340	340	
	340	340	440	440	
	540	540	700	700	
	685	685	890	890	
et xide	700	700	900	900	
	700	700	900	900	
of copper opper		785		1,000	
		800		1,000	
copper er		985		1,300	
		1,000		1,300	

defined population or subgroup that appears to sustain a defined nutritional status, such as growth rate, normal circulating nutrient values, or other functional indicators of health. The AI is used if sufficient scientific evidence is not available to derive an EAR. For healthy infants receiving human milk, the AI is the mean intake. **The AI is not equivalent to an RDA.**

Zinc functions through the catalysis of various enzymes, the maintenance of the structural integrity of proteins, and the regulation of gene expression. Overt human zinc deficiency is rare, and the symptoms of a mild deficiency are diverse due to zinc's ubiquitous involvement in metabolic processes. Factorial analysis of zinc losses and requirements for growth, as well as fractional absorption, were used to set an EAR. The RDA for zinc is set at 11 mg/day for men and 8 mg/day for women.

TABLE S-5 Criteria and Dietary Reference Intake Values for Iodine by Life Stage Group

Life Stage Group	Criterion	EAR ($\mu\text{g}/$
		Male
0 through 6 mo	Average iodine intake from human milk	
7 through 12 mo	Extrapolation from 0 through 6 mo AI	
1 through 3 y	Balance data on children	65
4 through 8 y	Balance data on children	65
9 through 13 y	Extrapolation from adult EAR	73
14 through 18 y	Extrapolation from adult EAR	95
19 through 50 y	Iodine turnover	95
≥ 51 y	Extrapolation of iodine turnover studies from 19 through 50 y	95
Pregnancy		
14 through 18 y	Balance data during pregnancy	
19 through 50 y	Balance data during pregnancy	
Lactation		
14 through 18 y	Adolescent female average requirement plus average amount of iodine secreted in human milk	
19 through 50 y	Adult female average requirement plus average amount of iodine secreted in human milk	

^a EAR = Estimated Average Requirement. The intake that meets the estimated nutrient needs of half of the individuals in a group.

^b RDA = Recommended Dietary Allowance. The intake that meets the nutrient need of almost all (97–98 percent) of individuals in a group.

^c AI = Adequate Intake. The observed average or experimentally determined intake by a

CRITERIA AND PROPOSED VALUES FOR TOLERABLE UPPER INTAKE LEVELS

A risk assessment model is used to derive Tolerable Upper Intake Levels (ULs). The model consists of a systematic series of scientific considerations and judgments. The hallmark of the risk assessment model is the requirement to be explicit in all of the evaluations and judgments made.

The adult ULs for vitamin A (3,000 $\mu\text{g}/\text{day}$), boron (20 mg/day), copper (10,000 $\mu\text{g}/\text{day}$), iodine (1,100 $\mu\text{g}/\text{day}$), iron (45 mg/day), manganese (11 mg/day), molybdenum (2,000 $\mu\text{g}/\text{day}$), nickel (1.0

s for

	EAR ($\mu\text{g}/\text{d}$) ^a		RDA ($\mu\text{g}/\text{d}$) ^b		AI ($\mu\text{g}/\text{d}$) ^c
	Male	Female	Male	Female	
					110
					130
	65	65	90	90	
	65	65	90	90	
	73	73	120	120	
	95	95	150	150	
	95	95	150	150	
	95	95	150	150	
		160		220	
		160		220	
verage		209		290	
amount		209		290	

defined population or subgroup that appears to sustain a defined nutritional status, such as growth rate, normal circulating nutrient values, or other functional indicators of health. The AI is used if sufficient scientific evidence is not available to derive an EAR. For healthy infants receiving human milk, the AI is the mean intake. **The AI is not equivalent to an RDA.**

mg/day), vanadium (1.8 mg/day), and zinc (40 mg/day), as shown in Table S-10, were set to protect the most sensitive individuals in the general population (such as those who might be below the reference adult weight).

Members of the general, apparently healthy population should be advised not to routinely exceed the UL. However, intake above the UL may be appropriate for investigation within well-controlled clinical trials to ascertain if such intakes are of benefit to health for specific reasons. Clinical trials of doses above the UL should not be discouraged, as it is expected that participation in these trials will require informed consent that will include discussion of the possi-

TABLE S-6 Criteria and Dietary Reference Intake Values for Iron by Life Stage Group

Life Stage Group	Criterion	EAR (mg)
		Male
0 through 6 mo	Average iron intake from human milk	
7 through 12 mo	Factorial modeling	6.9
1 through 3 y	Factorial modeling	3.0
4 through 8 y	Factorial modeling	4.1
9 through 13 y	Factorial modeling	5.9
14 through 18 y	Factorial modeling	7.7
19 through 30 y	Factorial modeling	6
31 through 50 y	Factorial modeling	6
51 through 70 y	Factorial modeling	6
> 70 y	Extrapolation of factorial analysis from 51 through 70 y	6
Pregnancy		
14 through 18 y	Factorial modeling	
19 through 50 y	Factorial modeling	
Lactation		
14 through 18 y	Adolescent female EAR minus menstrual losses plus average amount of iron secreted in human milk	
19 through 50 y	Adult female EAR minus menstrual losses plus average amount of iron secreted in human milk	

^a EAR = Estimated Average Requirement. The intake that meets the estimated nutrient needs of half of the individuals in a group.

^b RDA = Recommended Dietary Allowance. The intake that meets the nutrient need of almost all (97–98 percent) of individuals in a group.

^c AI = Adequate Intake. The observed average or experimentally determined intake by a

bility of adverse effects and will employ appropriate safety monitoring of trial subjects.

The ULs for vitamin A, boron, copper, iodine, iron, manganese, molybdenum, nickel, and zinc are based on adverse effects of intake from diet, fortified foods, and/or supplements. ULs could not be established for vitamin K, arsenic, chromium, and silicon because of lack of suitable data, a lack that indicates the need for additional research. The absence of data does not necessarily signify that people can tolerate chronic intakes of these substances at high levels, particularly elements such as arsenic which are known to cause serious adverse effects at very high levels of intake. Like all chemical agents, nutrients and other food components can produce adverse effects

s for

	EAR (mg/d) ^a		RDA (mg/d) ^b		AI (mg/d) ^c
	Male	Female	Male	Female	
					0.27
	6.9	6.9	11	11	
	3.0	3.0	7	7	
	4.1	4.1	10	10	
	5.9	5.7	8	8	
	7.7	7.9	11	15	
	6	8.1	8	18	
	6	8.1	8	18	
	6	5	8	8	
gh 70 y	6	5	8	8	
		23		27	
		22		27	
		7		10	
plus lk verage		6.5		9	

defined population or subgroup that appears to sustain a defined nutritional status, such as growth rate, normal circulating nutrient values, or other functional indicators of health. The AI is used if sufficient scientific evidence is not available to derive an EAR. For healthy infants receiving human milk, the AI is the mean intake. **The AI is not equivalent to an RDA.**

if intakes are excessive. Therefore, when data are extremely limited, extra caution may be warranted.

USING DIETARY REFERENCE INTAKES TO ASSESS NUTRIENT INTAKES OF GROUPS

Suggested uses of Dietary Reference Intakes (DRIs) appear in Box S-2. The transition from using previously published Recommended Dietary Allowances (RDAs) and Reference Nutrient Intakes (RNIs) to using each of the DRIs appropriately will require time and effort by health professionals and others.

For statistical reasons that are addressed in the report *Dietary*

TABLE S-7 Criteria and Dietary Reference Intake Values for Manganese by Life Stage Group

Life Stage Group	Criterion	AI (mg/c
		Male
0 through 6 mo	Average manganese intake from human milk	0.003
7 through 12 mo	Extrapolation from adult AI	0.6
1 through 3 y	Median manganese intake from the Food and Drug Administration's (FDA) Total Diet Study	1.2
4 through 8 y	Median manganese intake from FDA Total Diet Study	1.5
9 through 13 y	Median manganese intake from FDA Total Diet Study	1.9
14 through 18 y	Median manganese intake from FDA Total Diet Study	2.2
≥ 19 y	Median manganese intake from FDA Total Diet Study	2.3
Pregnancy		
14 through 18 y	Extrapolation of adolescent female AI based on body weight	
19 through 50 y	Extrapolation of adult female AI based on body weight	
Lactation		
14 through 18 y	Median manganese intake from FDA Total Diet Study	
19 through 50 y	Median manganese intake from FDA Total Diet Study	

^a AI = Adequate Intake. The observed average or experimentally determined intake by a defined population or subgroup that appears to sustain a defined nutritional status, such as growth rate, normal circulating nutrient values, or other functional indicators of health. The AI is used if sufficient scientific evidence is not available to derive an

Reference Intakes: Applications in Dietary Assessment (IOM, 2000) and briefly in Chapter 14, the Estimated Average Requirement (EAR) is the appropriate reference intake to use in assessing the nutrient intake of groups, whereas the RDA is not appropriate. When assessing nutrient intakes of groups, it is important to consider the variation in intake in the same individuals from day to day, as well as underreporting. With these considerations, the prevalence of inadequacy for a given nutrient may be estimated by using national survey data and determining the percent of the population below the EAR. Assuming a normal distribution of requirements, the percent of surveyed individuals whose intake is less than the EAR equals the percent of individuals whose diets are considered inadequate based on the criteria of inadequacy chosen to determine the requirement. For example, intake data from the Continuing Survey of Food Intakes by Individuals and the Third National Health and Nutrition Examination Survey, which collected 24-hour diet recalls for 1 or 2 days, indicate that:

s for

	AI (mg/d) ^a	
	Male	Female
	0.003	0.003
	0.6	0.6
g	1.2	1.2
study	1.5	1.5
study	1.9	1.6
study	2.2	1.6
study	2.3	1.8
body weight		2.0
weight		2.0
study		2.6
study		2.6

Estimated Average Requirement (EAR). For healthy infants receiving human milk, the AI is the mean intake. **The AI is not equivalent to a Recommended Dietary Allowance (RDA).**

- Between 10 and 25 percent of children 1 to 3 years of age consume dietary vitamin A or its precursors at a level less than the EAR. The percent of adults consuming intakes of vitamin A below the EAR is higher than for children. The EAR is based on a criterion of adequate vitamin A stores in the liver (> 20 µg vitamin A/g liver); thus, these data suggest that a considerable number of people have liver vitamin A stores that are less than desirable. It should be recognized that this does not represent a clinical deficiency state, such as dark adaptation, which is not commonly seen in North Americans.

- Between 5 and 10 percent of adolescent girls consume dietary iron at a level less than the EAR. The criterion chosen for the EAR for this age group was based on iron loss and accretion, using an upper limit of absorption that provides minimal iron stores.

- The prevalence of iron intakes less than the EAR ranges from 15 to 20 percent for premenopausal women which corresponds with a 13 to 16 percent prevalence of low iron status (based on serum ferritin concentration).

TABLE S-8 Criteria and Dietary Reference Intake Values for Molybdenum by Life Stage Group

Life Stage Group	Criterion	EAR (μg)
		Male
0 through 6 mo	Average molybdenum intake from human milk	
7 through 12 mo	Extrapolation from 0 through 6 mo	
1 through 3 y	Extrapolation from adult EAR	13
4 through 8 y	Extrapolation from adult EAR	17
9 through 13 y	Extrapolation from adult EAR	26
14 through 18 y	Extrapolation from adult EAR	33
19 through 30 y	Balance data	34
≥ 31 y	Extrapolation of balance data from 19 through 30 y	34
Pregnancy		
14 through 18 y	Extrapolation of adolescent female EAR based on body weight	
19 through 50 y	Extrapolation of adult female EAR based on body weight	
Lactation		
14 through 18 y	Adolescent female EAR plus average amount of molybdenum secreted in human milk	
19 through 50 y	Adult female EAR plus average amount of molybdenum secreted in human milk	

^a EAR = Estimated Average Requirement. The intake that meets the estimated nutrient needs of half of the individuals in a group.

^b RDA = Recommended Dietary Allowance. The intake that meets the nutrient need of almost all (97–98 percent) of individuals in a group.

^c AI = Adequate Intake. The observed average or experimentally determined intake by a

- A high percentage of pregnant women consume dietary iron at a level less than the EAR; this corresponds with a high prevalence of low hemoglobin concentration (anemia).

CONSIDERATION OF THE RISK OF CHRONIC DEGENERATIVE DISEASE

Close attention was given to the evidence relating intake of all the micronutrients to reduction of the risk of chronic disease. Data linking intake of vitamin K and chromium with the risk of chronic disease in North America were available but insufficient to set Estimated Average Requirements (EARs).

s for

	EAR ($\mu\text{g}/\text{d}$) ^a		RDA ($\mu\text{g}/\text{d}$) ^b		AI ($\mu\text{g}/\text{d}$) ^c
	Male	Female	Male	Female	
					2
					3
	13	13	17	17	
	17	17	22	22	
	26	26	34	34	
	33	33	43	43	
30 y	34	34	45	45	
	34	34	45	45	
n body					
ly weight		40		50	
		40		50	
		35		50	
odenum		36		50	

defined population or subgroup that appears to sustain a defined nutritional status, such as growth rate, normal circulating nutrient values, or other functional indicators of health. The AI is used if sufficient scientific evidence is not available to derive an EAR. For healthy infants receiving human milk, the AI is the mean intake. **The AI is not equivalent to an RDA.**

Bone Health and Osteoporosis

The notion that vitamin K may have a role in osteoporosis was first suggested with reports of lower circulating phylloquinone concentrations in osteoporotic patients having suffered a spinal crush fracture or fracture of the femur. A potential role of vitamin K in bone metabolism has been investigated by studying the vitamin K-dependent bone protein, osteocalcin, and its under- γ -carboxylated form. Increases in undercarboxylated osteocalcin have been associated with an increased risk of hip fracture. These associations should be interpreted with caution because most studies did not control for confounding factors such as other nutrients known to influence

TABLE S-9 Criteria and Dietary Reference Intake Values for Zinc by Life Stage Group

Life Stage Group	Criterion	EAR (mg)
		Male
0 through 6 mo	Average zinc intake from human milk	
7 through 12 mo	Factorial analysis	2.5
1 through 3 y	Factorial analysis	2.5
4 through 8 y	Factorial analysis	4.0
9 through 13 y	Factorial analysis	7.0
14 through 18 y	Factorial analysis	8.5
19 through 50 y	Factorial analysis	9.4
≥ 51 y	Extrapolation of factorial data from 19 through 50 y	9.4
Pregnancy		
14 through 18 y	Adolescent female EAR plus fetal accumulation of zinc	
19 through 50 y	Adult female average requirement plus fetal accumulation of zinc	
Lactation		
14 through 18 y	Adolescent female EAR plus average amount of zinc secreted in human milk	
19 through 50 y	Adult female EAR plus average amount of zinc secreted in human milk	

^a EAR = Estimated Average Requirement. The intake that meets the estimated nutrient needs of half of the individuals in a group.

^b RDA = Recommended Dietary Allowance. The intake that meets the nutrient need of almost all (97–98 percent) of individuals in a group.

^c AI = Adequate Intake. The observed average or experimentally determined intake by a

bone metabolism. Intervention studies using different K vitamers in both physiological and pharmacological dosages have observed a decrease in urinary hydroxyproline and calcium excretion (indicating a reduction in bone loss), as well as an increase in metacarpal bone density. Additional dose response data linking vitamin K and bone health will be needed before bone health can be used as an indicator to estimate the EAR.

Diabetes Mellitus

A number of studies have demonstrated a beneficial effect of chromium on circulating glucose and insulin concentrations; however,

s for

	EAR (mg/d) ^a		RDA (mg/d) ^b		AI (mg/d) ^c
	Male	Female	Male	Female	
					2
	2.5	2.5	3	3	
	2.5	2.5	3	3	
	4.0	4.0	5	5	
	7.0	7.0	8	8	
	8.5	7.3	11	9	
50 y	9.4	6.8	11	8	
	9.4	6.8	11	8	
of zinc		10.0		12	
		9.5		11	
zinc		10.9		13	
secreted		10.4		12	

defined population or subgroup that appears to sustain a defined nutritional status, such as growth rate, normal circulating nutrient values, or other functional indicators of health. The AI is used if sufficient scientific evidence is not available to derive an EAR. For healthy infants receiving human milk, the AI is the mean intake. **The AI is not equivalent to an RDA.**

not all reports of supplementation are positive. Progress in this field has been limited by lack of a simple, widely acceptable method for identification of subjects who are chromium depleted and therefore would be expected to respond to chromium supplementation. Recent studies suggest that a low molecular weight chromium binding substance may amplify insulin receptor tyrosine kinase activity in response to insulin. Additional dose response data linking chromium and prevention of diabetes will be needed before this can be used as an indicator to estimate the EAR.

TABLE S-10 Tolerable Upper Intake Levels (UL)^a, by Life Stage Group

Life Stage Group	Preformed Vitamin A (µg/d)	Boron (mg/d)	Copper (µg/d)	Iodine (µg/d)	Iron (mg/d)
0 through 6 mo	600	ND ^b	ND	ND	40
7 through 12 mo	600	ND	ND	ND	40
1 through 3 y	600	3	1,000	200	40
4 through 8 y	900	6	3,000	300	40
9 through 13 y	1,700	11	5,000	600	40
14 through 18 y	2,800	17	8,000	900	45
≥ 19 y	3,000	20	10,000	1,100	45
Pregnancy					
14 through 18 y	2,800	17	8,000	900	45
19 through 50 y	3,000	20	10,000	1,100	45
Lactation					
14 through 18 y	2,800	17	8,000	900	45
19 through 50 y	3,000	20	10,000	1,100	45

NOTE: Because of the lack of suitable data, ULs could not be established for vitamin K or chromium. In the absence of ULs, extra caution may be warranted in consuming levels of these nutrients above recommended intakes. Although a UL was not determined for arsenic, there is no justification for adding arsenic to food or supplements. In addition, although silicon has not been shown to cause adverse effects in humans, there is no justification for adding silicon to supplements.

^a The highest level of daily nutrient intake that is likely to pose no risk of adverse health effects to almost all individuals in the general population. As intake increases above the

RESEARCH RECOMMENDATIONS

Five major types of information gaps were noted: a lack of data demonstrating a specific role of some of these micronutrients in human health; a dearth of studies designed specifically to estimate average requirements in presumably healthy humans; a lack of data on the micronutrient needs of infants, children, adolescents, the elderly, and pregnant women; a lack of studies to determine the role of these micronutrients in reducing the risk of certain chronic diseases; and a lack of studies designed to detect adverse effects of chronic high intakes of these many of these micronutrients.

Highest priority is thus given to studies that address the following research topics:

SUMMARY

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Iodine (µg/d)	Iron (mg/d)	Manganese (mg/d)	Molybdenum (µg/d)	Nickel (µg/d)	Vanadium (mg/d) ^c	Zinc (mg/d)
ND	40	ND	ND	ND	ND	4
ND	40	ND	ND	ND	ND	5
200	40	2	300	200	ND	7
300	40	3	600	300	ND	12
600	40	6	1,100	600	ND	23
900	45	9	1,700	1,000	ND	34
1,100	45	11	2,000	1,000	1.8	40
900	45	9	1,700	1,000	ND	34
1,100	45	11	2,000	1,000	ND	40
900	45	9	1,700	1,000	ND	34
1,100	45	11	2,000	1,000	ND	40

UL, the risk of adverse effects increases. Unless specified otherwise, the UL represents total nutrient intake from food, water, and supplements.

^bND = not determinable due to lack of data of adverse effects in this age group and concern about lack of ability to handle excess amounts. Source of intake should be from food only to prevent high levels of intake.

^cAlthough vanadium in food has not been shown to cause adverse effects in humans, there is no justification for adding vanadium to food, and vanadium supplements should be used with caution. The UL is based on adverse effects in laboratory animals and this data could be used to set a UL for adults, but not for children or adolescents.

- studies to identify and further understand the functional (e.g., cognitive function, regulation of insulin, bone health, and immune function) and biochemical endpoints that reflect sufficient and insufficient body stores of vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc;

- studies to further identify and quantify the effects of interactions between micronutrients and interactions between micronutrients and other food components, the food matrix, food processing, and life stage on micronutrient (vitamin A, vitamin K, chromium, copper, iron, and zinc) bioavailability and therefore dietary requirement;

- studies to further investigate the role of arsenic, boron, nickel, silicon, and vanadium in human health; and
- studies to investigate the influence of non-nutritional factors (e.g., body mass index, glucose intolerance, infection) on the biochemical indicators for micronutrients currently measured by U.S. and Canadian nutritional surveys, such as for iron and vitamin A.