Australian Government
Department of Health and Ageing
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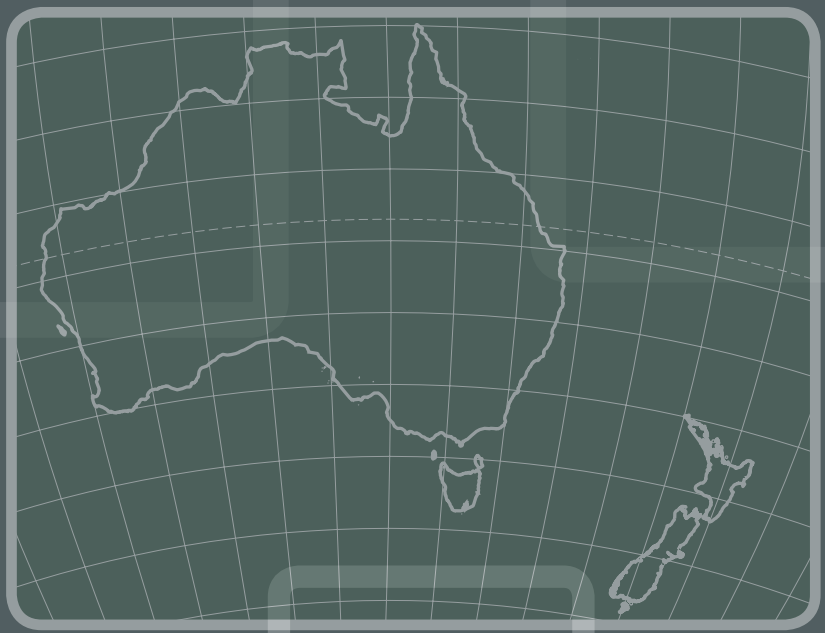
MINISTRY OF HEALTH
MANATŪ HAUORA

Nutrient Reference Values for Australia and New Zealand

Including Recommended Dietary Intakes



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NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND

INCLUDING RECOMMENDED DIETARY INTAKES

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Disclaimer

This document is a general guide. The recommendations are for healthy people and may not meet the specific nutritional requirements of all individuals. They are designed to assist nutrition and health professionals assess the dietary requirements of individuals and groups and are based on the best information available at the date of compilation.

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Food and Nutrition Board: Institute of Medicine. *Dietary Reference Intakes for calcium, phosphorus, magnesium, vitamin D and fluoride*. Washington DC: National Academy Press, 1997.

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PREFACE

The Australian and New Zealand Governments have been providing nutrition advice to the public for more than 75 years. This advice has included information on 'Recommended Dietary Intakes' (RDIs) or 'Allowances', which are the amounts of specific nutrients required on average on a daily basis for sustenance or avoidance of deficiency states. Advice has also been provided in the form of 'Dietary Guidelines', and culturally-relevant food and dietary patterns that will not only achieve sustenance, but also reduce the risk of chronic disease. The last revision of *Recommended Dietary Intakes for use in Australia* began in 1980 and was published in 1991 (NHMRC 1991). The reviews used as the source of information were published collectively in a book (Truswell et al 1990). The Australian recommendations were also later formally adopted by the New Zealand Ministry of Health for use in New Zealand.

In July 1997, a workshop of invited experts, including representatives from New Zealand, was held in Sydney to discuss the need for a revision of the 1991 NHMRC *Recommended Dietary Intakes for use in Australia.* Under the auspices of the Strategic Inter-governmental Nutrition Alliance (SIGNAL), a second workshop was held in July 1999 to scope the July 1997 recommendations and define the project parameters for the review. Amongst other considerations, it was agreed that:

- a joint Australia New Zealand RDI review should proceed as soon as possible;
- a set of reference values for each nutrient was required and the term 'Nutrient Reference Values' (NRVs) would be used to describe the set;
- the review should build primarily upon concurrent work being undertaken in the United States and Canada, while also taking into consideration recommendations from the United Kingdom, Germany and the European Union, recent dietary survey data collected in Australia and New Zealand, scientific data and unique Australasian conditions.

At the time of the 1999 workshop, the joint US and Canadian revision had begun to release its recommendations as a series of Dietary Reference Intakes. The revision of most of the major minerals and vitamins was completed by 2001 and this round of revisions was completed by 2004.

Bearing in mind the progress with the joint US:Canada revisions and the high cost and time lines associated with de novo revisions of this kind, in 2001, the Commonwealth Department of Health and Ageing asked the National Health and Medical Research Council (NHMRC) to undertake a scoping study in relation to a potential revision of the Australian/New Zealand RDIs. The New Zealand Ministry of Health funded some initial work for the review process that provided expert input into the revision of the two key nutrients, iodine and selenium. The NHMRC was then commissioned in 2002 to manage the joint Australian/New Zealand revision process. An expert Working Party was appointed to oversee the process with representation from both Australia and New Zealand, including end users from the clinical and public health nutrition research sector, the food industry, the dietetics profession, the food legislative sector and the Australian and New Zealand governments. The current publication, its recommendations and its associated Appendix, are the result of that review process. The understanding of many aspects of good nutrition is by no means complete. Where expert judgement had to be applied, public health and safety were the priorities.

Consumption of food not only provides for the physiological needs of human life, but also contributes to our social and emotional needs. Consequently, it is possible to prescribe a diet that would meet the physiological needs of a group yet fail to meet the social or emotional needs of a significant percentage of that group. Whilst physiological needs are the primary determinant of NRVs, they are developed with consideration given to the other aspects of food intake.

Research has shown that a healthy diet containing adequate amounts of the various nutrients need not be a costly diet. This is discussed in more detail in the NHMRC's *Dietary Guidelines for Australian Adults* which, together with the *Dietary Guidelines for Children and Adolescents in Australia*, the *Dietary Guidelines for Older Australians* and the *New Zealand Food and Nutrition Guidelines for the ages and stages of the lifecycle*, are companion documents to this publication on NRVs. Together with

the Australian Guides to Healthy Eating, the Dietary Guidelines translate the nutrient recommendations addressed in the current document into food and lifestyle patterns for the community. Revision of all of these documents is an ongoing process as the various sets of recommendations are closely interrelated.

These recommendations are for healthy people and may not meet the specific nutritional requirements of individuals with various diseases or conditions, pre-term infants, or people with specific genetic profiles. They are designed to assist nutrition and health professionals assess the dietary requirements of individuals and groups. They may also be used by public health nutritionists, food legislators and the food industry for dietary modelling and/or food labelling and food formulation.

This document is one of a series of three which also includes the evidence base for the NRVs and a summary or reference document containing the tabulated and annotated NRVs for everyday use by practitioners developed as a result of submissions and comments received at the workshops. The NRVs will also be available in electronic format on the NHMRC website.

Katrine Baghurst, June 2005
Chair of the Working Party
Editor

INTRODUCTION

WHAT ARE NUTRIENT REFERENCE VALUES?

In the 1991 *Recommended Dietary Intakes (RDI) for use in Australia* (NHMRC 1991) an RDI value, sometimes presented as a range, was developed for each nutrient. The RDI was defined as: "*the levels of intake of essential nutrients considered, in the judgement of the NHMRC, on the basis of available scientific knowledge, to be adequate to meet the known nutritional needs of practically all healthy people…they incorporate generous factors to accommodate variations in absorption and metabolism. They therefore apply to group needs. RDIs exceed the actual nutrient requirements of practically all healthy persons and are not synonymous with requirements.*"

Despite the emphasis on the population basis of the RDI, the RDIs were often misused in assessing dietary adequacy of individuals, or even foods, not only in Australia and New Zealand but also in many other countries. To overcome this misuse, many countries have moved to a system of reference values that retains the concept of the RDI while attempting to identify the average requirements needed by individuals. In 1991, the UK (Dept Health 1991) became the first country to develop a set of values for each nutrient. More recently, the Food and Nutrition Board: Institute of Medicine (FNB:IOM 1997, 1998a, 2000a, 2001, 2002, 2004) adopted a similar approach on behalf of the US and Canadian Governments.

After due consideration, the Working Party decided to adopt the approach of the US:Canadian Dietary Reference Intakes (DRIs) but vary some of the terminology, notably to retain the term 'Recommended Dietary Intake'.

Definitions adapted from the FNB:IOM DRI process

EAR **Estimated Average Requirement**

A daily nutrient level estimated to meet the requirements of half the healthy individuals in a particular life stage and gender group.

RDI **Recommended Dietary Intake**

The average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97–98 per cent) healthy individuals in a particular life stage and gender group.

AI **Adequate Intake (used when an RDI cannot be determined)**

The average daily nutrient intake level based on observed or experimentally-determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate.

EER **Estimated Energy Requirement**

The average dietary energy intake that is predicted to maintain energy balance in a healthy adult of defined age, gender, weight, height and level of physical activity, consistent with good health. In children and pregnant and lactating women, the EER is taken to include the needs associated with the deposition of tissues or the secretion of milk at rates consistent with good health.

UL **Upper Level of Intake**

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

For each nutrient, an Estimated Average Requirement (EAR) was set from which an RDI could be derived. (Note that the US: Canadian terminology is 'Recommended Dietary Allowance', or 'RDA'). Whilst the various NRVs are expressed on a per day basis, they should apply to intakes assessed over a period of about 3 to 4 days. If the standard deviation (SD) of the EAR is available and the requirement for the nutrient is symmetrically distributed, the RDI is set at 2SD above the EAR. Such that

$RDI = EAR + 2SD_{EAR}$.

If data about variability in requirements are insufficient to calculate an SD (which is usually the case), a coefficient of variation (CV) is used. A CV of 10% for the EAR is assumed for nutrients unless available data indicate that greater variation is probable. The 10% is based on extensive data on variation in basal metabolic rate and protein requirements (FAO:WHO:UNA 1985, Garby & Lammert 1984, Elia 1992).

If 10% is assumed to be the CV, then twice that amount added to the EAR is defined as equal to the RDI. Thus for a CV of 10%, the RDI would be 1.2 x EAR; for a CV of 15% it would be 1.3 x EAR and for a CV of 20% it would be 1.4 x EAR.

Where evidence was insufficient or too conflicting to establish an EAR (and thus an RDI) an Adequate Intake (AI) was set, either on experimental evidence or by adopting the most recently available population median intake and assuming that the Australian/New Zealand populations were not deficient for that particular nutrient. Both the RDI and AI can be used as a goal for individual intake, but there is less certainty about the AI value as it depends to a greater degree on judgement. An AI might deviate significantly from and be numerically higher than an RDI if the RDI could be determined. Thus AIs should be interpreted with greater caution.

Where AIs were based on median population intakes, these were derived from a re-analysis of the complete databases of the National Nutrition Surveys of Australia, 1995 (Australian Bureau of Statistics 1998) and New Zealand 1991, 1997, 2002 (LINZ Activity and Health Research Unit 1992, Ministry of Health 1999, 2003) using the appropriate age bands. The two-day adjusted data were used for the estimates.

For infants of 0 to 6 months, all recommendations are in the form of Adequate Intakes based on the composition of breast milk from healthy mothers, using a standard milk volume. The bioavailability of nutrients in formulas may vary from that in breast milk, so formula-fed babies may need higher nutrient intakes. As formulas can vary in the chemical form and source of the nutrients, it is not possible to develop a single reference value for all formula-fed infants.

For energy, an Estimated Energy Requirement (EER) was set for a range of activity levels for individuals of a specified age, gender and body size.

For each nutrient, an Upper Level of Intake (UL) was set, which, unless otherwise stated, includes intake from all sources including foods, nutrients added to foods, pills, capsules or medicines. The UL is the highest average daily nutrient intake level likely to pose no adverse health effects to almost all individuals in the general population. In setting the UL, any adverse health effect were considered, including those on chronic disease status. The UL is not a recommended level of intake. It is based on a risk assessment of nutrients that involves establishment of a No Observed Adverse Effect Level (NOAEL) and/or a Lowest Observed Adverse Effect Level (LOAEL) and application of an Uncertainty Factor (UF) related to the evidence base and severity of potential adverse effects. Members of the general population should be advised not to routinely exceed the UL. Intakes above the UL may be appropriate for some nutrients for investigation in well-controlled clinical trials as long as signed informed consent is given and as long as the trials employ appropriate safety monitoring of trial subjects. Readers are referred to the relevant FNB:IOM documents and the report of the UK Expert Group on Vitamins and Minerals (2003) for more details about the potential toxicological effects of high intakes of nutrients. In Australia, vitamin and mineral supplements are regulated under the Therapeutic Goods Act (1989) that also sets some standards for these products. In New Zealand, dietary supplements are generally regulated under the New Zealand Dietary Supplements Regulations (New Zealand Government 1985), but supplements with nutrients at higher/pharmacological doses than the specified maximum daily doses need to meet the requirements of the Medicines Regulations (1984).

Further details of the approach used in setting ULs are given in the FNB:IOM publication *Dietary Reference Intakes. A risk assessment model for establishing upper intake levels for nutrients* (1998b) and in the relevant nutrient chapters of the DRI publications.

The uses of the various NRVs are summarised in the table below that was adapted from the FNB:IOM (2000b) publication, *Dietary Reference Intakes. Applications in Dietary Assessment.* This document also provides further details of potential applications.

Nutrient Reference Value	For individuals:	For groups:
Estimated Average Requirement (EAR)	Use to examine the probability that usual intake is inadequate	Use to estimate the prevalence of inadequate intakes within a group
Recommended Dietary Intake (RDI)	Usual intake at or above this level has a low probability of inadequacy	Do not use to assess intakes of groups
Adequate Intake (AI)	Usual intake at or above this level has a low probability of inadequacy. When the AI is based on median intakes of healthy populations, this assessment is made with less confidence	Mean usual intake at or above this level implies a low prevalence of inadequate intakes. When the AI is based on median intakes of healthy populations, this assessment is made with less confidence
Upper Level of Intake (UL)	Usual intake above this level may place an individual at risk of adverse effects from excessive nutrient intake	Use to estimate the percentage of the population at potential risk of adverse effects from excessive nutrient intake

In contrast to the US:Canadian approach, the Working Party agreed to retain the traditional concept of adequate physiological or metabolic function and/or avoidance of deficiency states as the prime reference point for establishing the EAR and RDIs and to deal separately with the issue of chronic disease prevention. It was felt that assessing nutrient needs for chronic disease prevention in a quantitative manner was still problematical. Research findings related to chronic disease prevention often relate to nutrient mixes or food intake patterns, rather than the intake of individual nutrients.

To address the issue of chronic disease prevention, two additional sets of reference values were developed for selected nutrients for which sufficient evidence existed. The set dealing with the macronutrients was adapted from the work of the FNB:IOM DRI review of macronutrients (2002) and is called the Acceptable Macronutrient Distribution Range (AMDR). The second set of reference values was termed Suggested Dietary Targets (SDTs). These related to nutrients for which there was a reasonable body of evidence of a potential chronic disease preventive effect at levels substantially higher than the EAR and RDI or AI. As the evidence base for chronic disease prevention is mainly derived from studies and health outcomes in adults, these AMDRs and SDTs apply only to adults and adolescents of 14 years and over.

AMDR: Acceptable Macronutrient Distribution Range: The AMDR is an estimate of the range of intake for each macronutrient for individuals (expressed as per cent contribution to energy), which would allow for an adequate intake of all the other nutrients whilst maximising general health outcome.

SDT: Suggested Dietary Target: A daily average intake from food and beverages for certain nutrients that that may help in prevention of chronic disease.

THE NUTRIENTS REVIEWED

Having considered emerging evidence on the connections between diet and health and the recent recommendations from other countries, the preliminary workshops identified more than 40 nutrients for the Working Party to consider. The document *Recommended Dietary Intakes for use in Australia* (NHMRC 1991), which had also been adopted for use in New Zealand, contained recommendations for 19 nutrients and dietary energy. During this review, dietary energy requirements and requirements for the nutrients were considered. Those for which values were set are listed below:

Macronutrients	Vitamins	Minerals & trace elements
Energy	Vitamin A	Calcium
Protein	Thiamin	Chromium
Fat (for infants only)	Riboflavin	Copper
n-6 fatty acids (linoleic)	Niacin	Fluoride
n-3 fatty acids (α-linolenic)	Vitamin B_6	Iodine
LC n-3 fatty acids (omega-3	Vitamin B_{12}	Iron
fats, DHA, DPA, EPA)	Folate	Magnesium
Carbohydrate (for infants only)	Pantothenic acid	Manganese
Dietary fibre	Biotin	Molybdenum
Water	Choline	Phosphorus
	Vitamin C	Potassium
	Vitamin D	Selenium
	Vitamin E	Sodium
	Vitamin K	Zinc

In addition to the nutrients listed above, the Working Party also reviewed the literature on total fat (for ages and life stages other than infancy), carbohydrate (for ages and life stages other than infancy), cholesterol, arsenic, boron, nickel, silicon and vanadium. For these nutrients or age bands and life stages, it was agreed that there was little or no evidence for their essentiality in humans. This was generally in line with the findings of the US:Canadian DRI review recommendations. However, the DRI reviews set upper limits for some of these nutrients (FNB:IOM 1998, 2001) and the reader is referred to these for information.

The reviews were based on assessment of the applicability of the recently developed US:Canadian Dietary Reference Intakes (FNB:IOM 1997, 1998a,b, 2000a,b, 2001, 2002, 2004) to Australia and New Zealand, with reference to recommendations from other countries such as the UK (1991, 2003), Germany:Austria:Switzerland (DACH recommendations 2002) and from key organisations such as the FAO:WHO (2001).

REFERENCE BODY WEIGHTS

In developing the recommendations it was necessary to standardise body weights for the various age/gender groups. Assessment of the data on measured body weights and heights for relevant age/gender categories from the most recent National Nutrition Survey of Australia, 1995 (ABS 1998) and New Zealand, 1997 and 2002 (MOH 1999, 2003) showed that the body weights were similar to those used in the earlier US:Canadian DRI publications. From the 2002 publication onwards, the US:Canadian DRI review panels changed their standard body weights in response to availability of new data showing markedly lighter body weights than previously used. As the most recent Australian/New Zealand data more closely resembled those in the earlier US:Canadian reports, these were adopted for use throughout these recommendations.

The standard body weights for all adults were based on that for 19–30 year olds, although body weight in most western populations tends to increase throughout adulthood because of increasing body fat.

Gender	Age	Reference body weight (kg)
Both	2–6 months	7
Both	7–11 months	9
Both	1–3 years	13
Both	4–8 years	22
Males	9–13 years	40
	14–18 years	64
	19+ years	76
Females	9–13 years	40
	14–18 years	57
	19+ years	61

EXTRAPOLATION PROCESSES

Experimental data are often only available for a limited age/gender group. The setting of recommendations for other groups may require extrapolation of the data. This is sometimes based on energy requirements, but more commonly on a metabolic body weight. In extrapolating data from one group to another, the processes and formulae used were those developed by the US:Canadian DRI panels unless otherwise indicated in the text.

Extrapolations from adult Estimated Average Requirements (EAR) to children's requirements were mostly done using the formula:

$$EAR_{child} = EAR_{adult} \times F$$

$$\text{where } F = (Weight_{child}/Weight_{adult})^{0.75} \times (1 + \text{growth factor}).$$

The growth factors used were 0.3 from 7 months to 3 years of age and 0.15 for 4–13 years of age for both genders. For boys aged 14–18 years, the growth factor used was 0.15 but for girls of this age, the growth factor was set at zero.

When extrapolating from the Adequate Intake (AI) for younger infants aged 0-6 months, to older infants aged 7-12 months, the formula used was:

$$AI_{7–12\ months} = AI_{0–6\ months} \times F$$

$$\text{where } F = (Weight_{7–12\ months}/Weight_{0–6\ months})^{0.75}$$

When estimating the Upper Level of Intake for children, the UL was extrapolated down from the adults UL using the formula:

$$UL_{child} = UL_{adult} \times (Weight_{child}/Weight_{adult})^{0.75}$$

This allows both body mass and metabolic differences between adults and children to be incorporated as necessary. More details can be found in the methodology sections of the US:Canadian FNB:IOM reports.

IMPLICATIONS

The implications for adoption of these revised NRVs include:

- The need to address ongoing education of both health and food industry professionals in the end use of the various reference values and related tools for their use.
- The need to update a number of documents and educational tools based on the previous RDIs, including:
  - The NHMRC Core Food Groups analysis (NHMRC 1994)
  - *The Australian Guide to Healthy Eating* and the *Dietary Guidelines for Australian Adults*, the *Australian Guidelines for Children and Adolescents in Australia* and the *Dietary Guidelines for Older Australians*
  - *The New Zealand Food and Nutrition Guidelines for the ages and stages of the lifecycle.*

In Australia, the Core Food Groups analysis addressed the translation of the nutrient recommendations into amounts of core foods (eg cereals, fruits and vegetables, meats, fish, poultry, dairy, fats and oils) required to meet these nutrient recommendations in Australia. These in turn were used as the basis for the development of the *Australian Guide to Healthy Eating* and the *Australian Dietary Guidelines for Adults*, the *Dietary Guidelines for Children and Adolescents in Australia* and the *Dietary Guidelines for Older Australians*.

New Zealand has Food and Nutrition Guidelines covering the ages and stages of the lifecycle. There are currently seven in the series including infants and toddlers (0–2 years), children (2–12 years), adolescents, pregnant women, breastfeeding women, adults and older people. These publications include a background paper for health professionals and an accompanying health education pamphlet for the public.

The interrelationships between these various recommendations and the underpinning evidence are shown in Figure 1.

- The need for regular monitoring of dietary intake and nutrient status in the population, including the use of fortified foods and supplements, to underpin the ongoing revisions of the NRVs, notably the Adequate Intake values which, by definition, are often based on population median dietary intakes.
- The need for research funds to enable more accurate assessment of requirements for both sustenance and prevention of chronic disease, including studies on issues such as biomarkers for nutritional status and nutrient bioavailability, and adverse effects of high intakes.
- The need to update and expand existing food databases for the analysis of national nutrition survey data, including information on the levels of fortification in foods.
- The need to change computerised dietary analysis programs that use the existing RDI values as reference values.
- The need for the redevelopment of relevant standards for the use of NRVs for food legislative purposes, including issues such as food labelling and food fortification.
- The need to consider the implications of changes in the NRVs for the food and dietary supplementation industry.

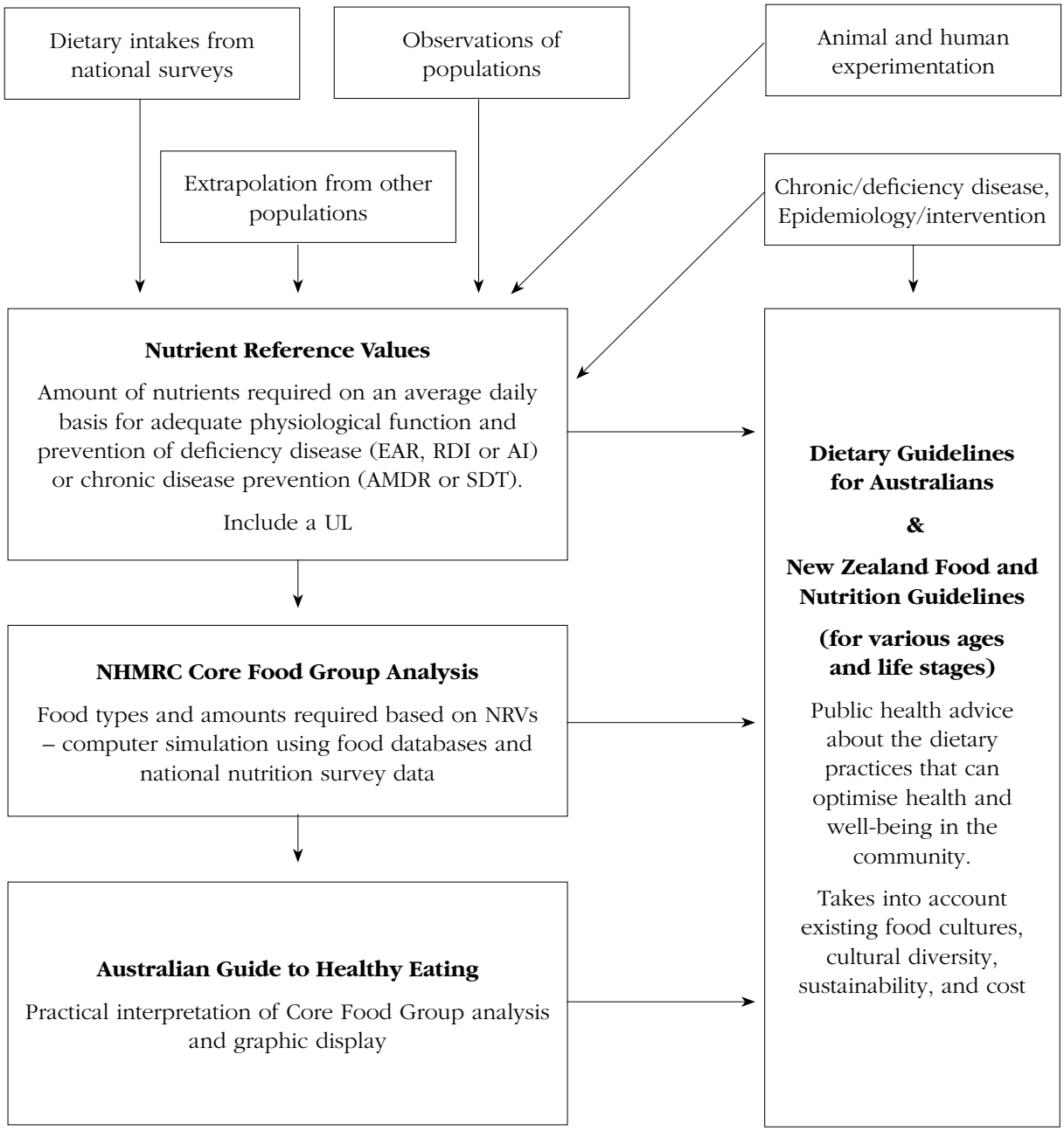

FIGURE 1. INTERRELATIONSHIPS BETWEEN THE EVIDENCE BASE, NRVS, CORE FOOD GROUP ANALYSIS, DIETARY AND FOOD GUIDELINES AND HEALTHY EATING GUIDES

WHAT ARE THE IMPLICATIONS OF CHANGES IN RECOMMENDATIONS FOR CERTAIN NUTRIENTS?

Consumption of a diet conforming to the NRVs need not, in itself, be more expensive for the individual (Baghurst 2003), however addressing the needs for implementation outlined above will involve ongoing costs that are difficult to quantify. The financial expense associated with inadequate nutrition in the community is likely to far outweigh that of implementing the necessary changes. Crowley et al (1992) have estimated the economic cost of diet-related disease in Australia in terms of both direct health care (hospitals, medical expenses, allied health professional services, pharmaceutical expenses and nursing homes) attributable to diet and indirect costs (due to sick leave and the net present value of forgone earnings due to premature death). The estimate of direct costs, excluding consideration of alcohol, was $1,432 million and that for indirect, $605 million, giving a total of $2,037 million for 1989–1990.

The RDI for some nutrients has substantially increased from that in the previous edition due to the availability of new data or changes in the way needs are assessed. In the past, needs at the individual level were often assessed in the practical situation by reference to 70% RDI in the absence of a specific EAR value. The NHMRC Core Food Group assessment, which is the basis for the *Australian Guide to Healthy Eating*, was also modelled on 70% RDI. In the background papers to the previous RDIs (Truswell et al 1990), figures called Lower Diagnostic Levels were given for some nutrients, but these were not officially adopted. They were used to derive the previous RDIs with 'generous factors' to accommodate variation in absorption and metabolism. They were therefore not used in practice. The existence of a specific EAR in the current NRVs overcomes the need to extrapolate from the RDI when attempting to assess adequacy of individual diets.

The new RDI for iron in young women of 18 mg/day appears to have increased from the previous RDI (12–16 mg/day), however the EAR for this group (of 8 mg/day) is actually less than 70% of the old RDI of 8.4–11.2 mg/day. This reflects the very high variability in iron requirements in this group because of variability in menstrual loss. Thus if 70% RDI had been used in the past as a benchmark for assessing the needs of individuals, the apparent requirement would likely have decreased somewhat. For pregnant women, 70% of the old RDI was 15.4–29.0 mg/day whilst the new EAR is 22.0 mg/day. For lactation, 70% of the old RDI was 8.4–11.2 mg/day but the new EAR is 6.5 mg/day.

In the case of zinc, another nutrient known to be borderline for adequacy in the community, the estimate of average needs for men has risen from 8.4 mg/day (70% old RDI) to 12 mg/day (EAR) but that for women has fallen from 8.4 mg/day (70% old RDI) to 6.5 mg/day, partly due to recognition that absorptive capacity for zinc varies across the genders and that men have significant losses in semen.

The EAR is well above 70% of the previous RDI for other nutrients, including the B vitamins thiamin, niacin, riboflavin, vitamin B_6 and B_{12}, calcium and magnesium, which are all about 50% higher, and folate, which is about 100% higher, than 70% of the respective old RDIs. The increase in the B vitamin reference values reflects the ways they were set in the earlier version. In the 1981–1989 RDIs, the values for B vitamins were generally set in relation to energy needs for thiamin, riboflavin and niacin or protein needs for vitamin B_6. Energy and protein needs were, in turn, set on figures recommended at that time by the FAO:WHO. The EARs for B vitamins in the current reference values were set using the results of metabolic studies with specific biochemical endpoints in blood, tissues or urine related to potential deficiency states, or depletion-repletion studies.

For folate, the higher RDI marks a return to the RDI that was in place in Australia before the 1981–1989 revision, when it was lowered from 400 µg to 200 µg/day on the basis that the amount of absorbed folate required to treat or fully prevent deficiency disease was 100 µg/day, that the average absorption from food was 50% and that average total folate consumption in Britain and North America at that time was about 200 µg/day. Other countries such as the US and Germany had an RDI of 400 µg at that time (although they later reduced it) as they felt that the availability of folate was between 25% and 50% and that 100–200 µg absorbed folate/day were needed.

The new Australian/NZ RDI for folate is based on the current recommendations from the US and Canada and new data on dietary intake in relation to maintenance of plasma folate, erythrocyte folate and homocysteine levels that suggest a need for about 300 µg/day. The folate RDI is expressed in terms of dietary folate equivalents in recognition of the difference in bioavailability between food folate and folic acid. The latter, which is the form used for supplements and fortification of foods, is twice as well absorbed as food folate.

In relation to calcium, the difference between the old and new RDIs relates almost entirely to the recognition that losses through sweat of some 60 mg/day were not accounted for in previous estimates. The additional intake required to account for the decrease in absorption of calcium with increased intake is 320 mg.

In the case of magnesium, the new EARs and RDIs were based on maintenance of whole body magnesium over time from balance studies mostly published since the last Australian/New Zealand RDIs were set. Recent studies of people on total parenteral nutrition that indicated lower needs than earlier balance studies were also considered. In the background paper for the earlier magnesium RDI for Australia, Dreosti stated "more, conventional magnesium balance studies are necessary at this stage in order to resolve the question of requirements" (Truswell et al 1990).

Thus, the increased requirements for some nutrients since the previous revision are based on data not available at the time or on a different approach to assessing needs. This outcome may appear to imply that people need to consume more food at a time when obesity is a major public health problem in the community. However, achievement of the new RDIs requires the consumption of different types of foods, not the consumption of more food. If energy-dense, nutrient-poor foods and drinks are replaced with plenty of vegetables, fruits and wholegrain cereals, moderate amounts of lean meats, fish, poultry and reduced fat dairy foods and small amounts of polyunsaturated or monounsaturated fats and oils as well as plain water, then all the nutrients required can be obtained within energy requirements. It should be remembered also that increased levels of activity make dietary choices more flexible and have the benefits of assisting in the maintenance of acceptable body weight and reducing a range of chronic diseases.

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Note: All the FNB:IOM Dietary Reference Intake publications can be accessed on line through the website of the National Academy Press at http://www.nap.edu

DIETARY ENERGY

DIETARY ENERGY

BACKGROUND

Energy is not a nutrient but is required in the body for metabolic processes, physiological functions, muscular activity, heat production, growth and synthesis of new tissues. It is released from food components by oxidation. The main sources of energy are carbohydrates, proteins, fats and, to a lesser degree, alcohol.

> The unit of energy is the kilojoule (kJ) or megajoule (1 MJ = 1,000 kJ)
> 4.18 kilojoules are equal to 1 kilocalorie

Allowing for intestinal absorption and for the nitrogenous parts of protein that cannot be completely oxidised, the average amount of energy released ranges from approximately 16.7 kJ/g for carbohydrates or protein to 29.3 kJ/g for alcohol and 37.7 kJ/g for fats (FAO:WHO:UNU 2004).

Humans need energy for basal metabolism which comprises a set of functions necessary for life such as cell metabolism, synthesis and metabolism of enzymes and hormones, transport of substances around the body, maintenance of body temperature and ongoing functioning of muscles including the heart, and brain function. The amount of energy needed for this purpose in a defined period of time is called the basal metabolic rate (BMR). BMR represents about 45–70% of daily energy expenditure, depending on age, gender, body size and composition. Physical activity is the most variable determinant of energy need and is the second largest user of energy after BMR. Humans perform a number of physical activities including the obligatory demands of an individual's economic, social and cultural environment (eg occupational, schoolwork, housework) or discretionary activity (eg energy expended for optional exercise or sport, or in additional social or cultural interactions).

Energy is also required to process food into nutrients resulting in increases in heat production and oxygen consumption often described by the terms 'dietary-induced thermogenesis', 'specific dynamic action of food' or 'thermic effect of feeding'. The metabolic response to food increases the BMR by about 10% over the day in people eating a mixed diet. Growth also requires energy for synthesis of tissues. In the first three months of life, growth uses about 35% of total energy needs. This falls to 5% at 12 months, less than 2% in the second year of life, 1–2% until mid-adolescence and zero by 20 years of age (FAO:WHO:UNU 2004). Additional energy is also needed in pregnancy and lactation to cover the needs of the growing fetus, the placenta and expanding maternal tissues and additional maternal effort at rest and in physical activity, as well as the production of breast milk.

The best method of assessing energy needs is the doubly-labelled water technique. When this method is applied over a 24-hour period, it includes estimates of dietary-induced thermogenesis and the energy cost of tissue synthesis. For adults, this equates to daily energy requirements. The additional needs in infancy and childhood, in adolescence, pregnancy and lactation need to be estimated from growth velocity or weight gain equations, composition of weight gain and average volume and composition of breast milk. When direct data are not available, factorial estimates based on time allocated to habitually performed activities and knowledge of the energy cost of these activities may be used.

As energy requirements vary with age, gender, body size and activity, recommendations are needed for each age and gender group.

Recommendations for energy intake differ from those for nutrient intake in that:

- they are not increased to cover the needs of most members of the group or population, as this level of intake would lead to overweight or obesity in most people.
- there are differences between the actual energy requirements needed to maintain current body size and level of physical activity and the desirable energy requirements needed to maintain body size and levels of physical activity consistent with good health. Desirable energy requirements may be lower than actual requirements for people who are overweight or obese. Desirable requirements may be higher than actual for inactive people. For people who are both overweight/obese and physically inactive, the difference between actual and desirable will depend on the balance between degree of overweight and level of inactivity.
- they can be applied cautiously to individuals, using estimates of energy expenditure. However, predictive estimates are much less accurate for individuals than for groups, and variations in energy expenditure can be large, even between apparently similar individuals.
- there is wide inter-individual variation in the behavioural, physiologic and metabolic components of energy needs. The average energy intake recommended for a defined group cannot be applied to other groups or individuals who differ from the defined group average in gender, age, body size, activity level and possibly other factors.

Two separate terms can therefore be used to express and determine Estimated Energy Requirements (EER):

- The *Estimated Energy Requirement for Maintenance* (EERM, or actual energy requirement) is the dietary energy intake that is predicted to maintain energy balance (plus extra needs for pregnancy, lactation and growth) in healthy individuals or groups of individuals at current levels of body size and level of physical activity.
- The *Desirable Estimated Energy Requirement* (DEER, or energy reference value) is the dietary energy intake that is predicted to maintain energy balance (plus extra needs for pregnancy, lactation and growth) in healthy individuals or groups of individuals of a defined gender, age, weight, height and level of physical activity consistent with good health and/or development.

Use of, and distinction between, these two terms is necessary because of the various ways in which estimates of energy requirements are used and because of the risk of over-prescription of desirable energy intakes in people who do not follow recommendations for increased physical activity. In some clinical situations, it may be necessary to estimate actual energy requirements (eg when prescribing a diet intended to produce an energy deficit leading to a 0.25–1.0 kg/week weight loss).

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants and children

TABLE 1 ESTIMATED ENERGY REQUIREMENTS (EER) OF INFANTS AND YOUNG CHILDREN

Age (months)	*Reference weight (kg)*		*EER (kJ/day)*	
	Boys	*Girls*	*Boys*	*Girls*
1	4.4	4.2	2,000	1,800
2	5.3	4.9	2,400	2,100
3	6.0	5.5	2,400	2,200
4	6.7	6.1	2,400	2,200
5	7.3	6.7	2,500	2,300
6	7.9	7.2	2,700	2,500
7	8.4	7.7	2,800	2,500
8	8.9	8.1	3,000	2,700
9	9.3	8.5	3,100	2,800
10	9.7	8.9	3,300	3,000
11	10.0	9.2	3,400	3,100
12	10.3	9.5	3,500	3,200
15	11.1	10.3	3,800	3,500
18	11.7	11.0	4,000	3,800
21	12.2	11.6	4,200	4,000
24	12.7	12.1	4,400	4,200

Adapted from FNB:IOM (2002); Reference weights from Kuczmarski et al (2000).

***Rationale*:** For infants and 1–2 year-olds, the equations used for estimating energy expenditure were those produced by the Food and Nutrition Board in developing the US:Canadian DRI values (FNB:IOM 2002). There are some 14 doubly-labelled water (DLW) studies in infants (Butte 2001), mostly done in the UK and the US. This method involves consideration of gender, age, body weight and height/length and use of these to derive total energy expenditure (TEE). Physical activity level (PAL) categories are not used in calculating the requirements of infants. Requirements for growth (FNB:IOM 2002) are added to the TEE estimate (89 x weight of infant in kg –100), assuming an additional need of 730 kJ/day for 0–3 months, 230 kJ/day for 4–6 months, 90 kJ/day for 7–12 months and 85 kJ/day for 1–2 years using the estimates of energy content of tissue deposition from Butte et al (2000) in conjunction with the 50th centile for weight gain at various ages (Guo et al 1991).

Four studies with breast-fed and formula-fed infants have shown higher TEE in formula-fed infants (Butte et al 1990, 2000, Jiang et al 1998, Davies et al 1990), averaging +12% at 3 months, +7% at 6 months, +6% at 9 months and +3% at 12 months. No differences were seen at 18 and 24 months (Butte 2001).

Children and adolescents

TABLE 2 ESTIMATED ENERGY REQUIREMENTS FOR CHILDREN AND ADOLESCENTS (MJ/DAY)

Age guide[a,b] *(years)*	*Reference weight*[c] *(kg)*	*Reference height (m)*	*BMR*[d] *(MJ/day)*	*PAL 1.2*[e]	*PAL 1.4*[e]	*PAL 1.6*[e]	*PAL 1.8*[e]	*PAL 2.0*[e]	*PAL 2.2*[e]
Boys									
3	14.3	0.95	3.4	4.2	4.9	5.6	6.3	6.9	7.6
4	16.2	1.02	3.6	4.4	5.2	5.9	6.6	7.3	8.1
5	18.4	1.09	3.8	4.7	5.5	6.2	7.0	7.8	8.5
6	20.7	1.15	4.1	5.0	5.8	6.6	7.4	8.2	9.0
7	23.1	1.22	4.3	5.2	6.1	7.0	7.8	8.7	9.5
8	25.6	1.28	4.5	5.5	6.4	7.3	8.2	9.2	10.1
9	28.6	1.34	4.8	5.9	6.8	7.8	8.8	9.7	10.7
10	31.9	1.39	5.1	6.3	7.3	8.3	9.3	10.4	11.4
11	35.9	1.44	5.4	6.6	7.7	8.8	9.9	11.0	12.0
12	40.5	1.49	5.8	7.0	8.2	9.3	10.5	11.6	12.8
13	45.6	1.56	6.2	7.5	8.7	10.0	11.2	12.4	13.6
14	51.0	1.64	6.6	8.0	9.3	10.6	11.9	13.2	14.6
15	56.3	1.70	7.0	8.5	9.9	11.2	12.6	14.0	15.4
16	60.9	1.74	7.3	8.9	10.3	11.8	13.2	14.7	16.2
17	64.6	1.75	7.6	9.2	10.7	12.2	13.7	15.2	16.7
18	67.2	1.76	7.7	9.4	10.9	12.5	14.0	15.6	17.1
Girls									
3	13.9	0.94	3.2	3.9	4.5	5.3	5.8	6.4	7.1
4	15.8	1.01	3.4	4.1	4.8	5.5	6.1	6.8	7.5
5	17.9	1.08	3.6	4.4	5.1	5.7	6.5	7.2	7.9
6	20.2	1.15	3.8	4.6	5.4	6.1	6.9	7.6	8.4
7	22.8	1.21	4.0	4.9	5.7	6.5	7.3	8.1	8.9
8	25.6	1.28	4.2	5.2	6.0	6.9	7.7	8.6	9.4
9	29.0	1.33	4.5	5.5	6.4	7.3	8.2	9.1	10.0
10	32.9	1.38	4.7	5.7	6.7	7.6	8.5	9.5	10.4
11	37.2	1.44	4.9	6.0	7.0	8.0	9.0	10.0	11.0
12	41.6	1.51	5.2	6.4	7.4	8.5	9.5	10.6	11.6
13	45.8	1.57	5.5	6.7	7.8	8.9	10.0	11.1	12.2
14	49.4	1.60	5.7	6.9	8.1	9.2	10.3	11.5	12.6
15	52.0	1.62	5.8	7.1	8.2	9.4	10.6	11.7	12.9
16	53.9	1.63	5.9	7.2	8.4	9.5	10.7	11.9	13.1
17	55.1	1.63	5.9	7.2	8.4	9.6	10.8	12.0	13.2
18	56.2	1.63	6.0	7.3	8.5	9.7	10.9	12.1	13.3

[a] EERs were calculated using BMR predicted from weight, height and age

[b] The height and or weight to age ratio may differ markedly in some ethnic groups. In this case, if BMI is in the acceptable range, it would be more relevant to use body weight as the main guide to current energy needs

[c] Reference weights from Kuczmarski et al (2000) (see also FNB:IOM 2002)

[d] Estimated using Schofield et al (1985) equations for weight, height and age group 3–10, 10–18

[e] PALs (physical activity levels) incorporate relevant growth factor for age. They correspond to the following activities: 1.2 – bed rest; 1.4 – very sedentary; 1.6 – light activity; 1.8 – moderate activity; 2.0 – heavy activity; 2.2 – vigorous activity

***Rationale*:** For children over 2 years and adolescents, a method was used that estimates energy expenditure at any physical activity level (PAL), similar to that used in the previous Australian/New Zealand RDI (NHMRC 1991) and by the D.A.CH Reference Values report (German Nutrition Society 2002). This approach is limited by the choice of equation (Schofield et al 1985) used to calculate basal metabolic rate, and by lack of easily interpretable activity tables for children. Nevertheless it was considered more appropriate than the alternative approach used in the US: Canadian DRI (FNB:IOM 2002), which limits physical activity categories.

The method used involves firstly determining body weight and height for each age/gender category for the group or individual. To determine actual or maintenance energy requirements (EERM), the current body weight is used. To determine desirable energy requirements (DEER), the current body weight is used if it falls within the healthy weight range for children and adolescents of various ages (Cole et al 2000). Where the BMI is above the recommended level, the desirable body weight is determined by assuming a BMI within the acceptable range for children of that age.

For some ethnic groups in the Australian and New Zealand population, average body weights for a given age for children or adults may vary markedly from the reference values given above. Where average body weight does not align with the reference values shown above, body weight rather than age should be used for estimating the EERM. For the DEER, body weight in relation to the acceptable BMI range should be used as the key determinant.

The acceptable BMI range may vary across ethnic groups but there are limited data on which to base ethnic-specific BMI ranges. The figures for assessment of overweight in children (Cole et al 2000) were established using data from many different groups worldwide. For the elderly, a somewhat higher acceptable BMI range of 22–27 may be warranted as somewhat higher than normal BMIs in the elderly have been associated with better health outcomes and as such are used in National Screening Initiatives for the elderly.

Next, the basal metabolic rate (BMR) of the group or individual is determined using indirect calorimetry or predicting from the Schofield equations (Schofield et al 1985). To account for activity, the approximate physical activity level (PAL) of the group or individual is estimated from the amount of time spent in different activities and energy expenditure is determined by multiplying the BMR by the PAL expressed as a multiple of BMR.

For adults, a PAL above 1.75 is considered by some authorities to be compatible with a healthy lifestyle (FAO:WHO:UNU 2004, FNB:IOM 2002). This value of 1.75 may also be relevant for adolescence but it is not certain whether it applies to childhood, particularly early childhood.

To this is added an estimate of extra energy requirements for growth of 85 kJ/day for 4–8 years, and 105 kJ/day for 9–18 years, using the estimates of energy content of tissue deposition from Butte et al (2000), in conjunction with the 50th centile for weight gain at various ages (Guo et al 1991).

The estimate of energy requirement is then corrected for the composition of the Australian/New Zealand diet (FAO 2003, ABS 1998, MOH 1999, 2003). Further details are given in the Evidence Appendix.

Adults

TABLE 3 ESTIMATED ENERGY REQUIREMENTS OF ADULTS USING PREDICTED BMR X PAL

Age *yr*	*BMI = 22.0*[a]		*BMR* *MJ/d*	*Physical activity level (PAL)*[b] *Males MJ/day*						*BMR* *MJ/d*	*Physical activity level (PAL)*[b] *Females MJ/day*					
	Ht (m)	*Wt (kg)*	*Male*	*1.2*	*1.4*	*1.6*	*1.8*	*2.0*	*2.2*	*Female*	*1.2*	*1.4*	*1.6*	*1.8*	*2.0*	*2.2*
19-30	1.5	49.5	-	-	-	-	-	-	-	5.2	6.1	7.1	8.2	9.2	10.2	11.2
	1.6	56.3	6.4	7.7	9.0	10.3	11.6	12.9	14.2	5.6	6.6	7.7	8.8	9.9	11.1	12.2
	1.7	63.6	6.9	8.3	9.7	11.0	12.4	13.8	15.2	6.0	7.2	8.4	9.6	10.8	12.0	13.2
	1.8	71.3	7.4	8.9	10.3	11.8	13.3	14.8	16.3	6.5	7.7	9.0	10.3	11.6	12.9	14.2
	1.9	79.4	7.9	9.5	11.1	12.6	14.2	15.8	17.4	7.0	8.4	9.7	11.1	12.5	13.9	15.3
	2.0	88.0	8.4	10.1	11.8	13.5	15.2	16.9	18.6	-	-	-	-	-	-	-
31-50	1.5	49.5	-	-	-	-	-	-	-	5.2	6.3	7.3	8.4	9.4	10.4	11.5
	1.6	56.3	6.4	7.6	8.9	10.2	11.4	12.7	14.0	5.5	6.5	7.6	8.7	9.8	10.9	12.0
	1.7	63.6	6.7	8.0	9.4	10.7	12.1	13.4	14.8	5.7	6.8	8.0	9.1	10.3	11.4	12.5
	1.8	71.3	7.1	8.5	9.9	11.3	12.7	14.2	15.6	6.0	7.2	8.3	9.5	10.7	11.9	13.1
	1.9	79.4	7.5	9.0	10.4	11.9	13.4	14.9	16.4	6.2	7.5	8.7	10.0	11.2	12.5	13.7
	2.0	88.0	7.9	9.5	11.0	12.6	14.2	15.8	17.3	-	-	-	-	-	-	-
51-70	1.5	49.5	-	-	-	-	-	-	-	4.9	6.0	6.9	7.9	8.9	9.8	10.9
	1.6	56.3	5.8	7.0	8.2	9.3	10.4	11.5	12.7	5.2	6.2	7.3	8.3	9.3	10.4	11.4
	1.7	63.6	6.1	7.3	8.6	9.8	11.1	12.3	13.6	5.4	6.5	7.6	8.7	9.8	10.7	12.0
	1.8	71.3	6.5	7.8	9.1	10.4	11.7	13.1	14.4	5.7	6.9	8.0	9.1	10.3	11.4	12.6
	1.9	79.4	6.9	8.3	9.6	11.1	12.4	13.8	15.2	6.0	7.2	8.4	9.6	10.8	12.0	13.2
	2.0	88.0	7.3	8.8	10.2	11.7	13.2	14.7	16.1	-	-	-	-	-	-	-
>70	1.5	49.5	-	-	-	-	-	-	-	4.6	5.6	6.5	7.4	8.3	9.3	10.2
	1.6	56.3	5.2	6.3	7.3	8.3	9.4	10.4	11.5	4.9	5.9	6.9	7.8	8.8	9.8	10.8
	1.7	63.6	5.6	6.7	7.8	8.9	10.0	11.2	12.3	5.2	6.2	7.2	8.3	9.3	10.3	11.4
	1.8	71.3	6.0	7.1	8.3	9.5	10.7	11.9	13.1	5.5	6.6	7.7	8.7	9.8	10.9	12.0
	1.9	79.4	6.4	7.6	8.9	10.2	11.4	12.7	14.0	5.8	6.9	8.1	9.2	10.4	11.5	12.7
	2.0	88.0	6.8	8.1	9.5	10.8	12.2	13.5	14.9	-	-	-	-	-	-	-

[a] A BMI of 22.0 is approximately the mid point of the WHO (1998) healthy weight range (BMI 18.5–24.9)

[b] PAL ranges from 1.2 (bed rest) to 2.2 (very active or heavy occupational work). PALs of 1.75 and above are consistent with good health. PALs below 1.4 are incompatible with moving around freely or earning a living. PALs above 2.5 are difficult to maintain for long periods

Note: The original Schofield equations (Schofield 1985) from which these tables were derived used 60+ years as the upper age category. For people aged 51–70 years, the estimates were derived by averaging those for the adults (31–50 years) and older (>70 years) adults.

***Rationale*:** The method used to estimate energy needs may be applied to both groups and individuals. However, it must be recognised that estimates of food energy requirements obtained by these methods are only approximate, especially for individuals in whom variations in energy requirements can be very large, even if they have the same age, sex and body size and apparently similar levels of activity. For example, spontaneous activity such as fidgeting can make a substantial contribution to the daily energy expenditure of some people, while others expend very little energy in this way. When used to predict the energy requirements of individuals, these values should be used cautiously. It is desirable that BMR is measured where possible rather than predicted, and that PAL is estimated from actual records of usual activity patterns.

The method used here is similar to that used in the D.A.CH report (German Nutrition Society 2002). It has the advantage of estimating energy expenditure at any physical activity level, but is limited by there being only three age ranges for the equations used to calculate BMR and by the fact that the equations probably over-estimate BMR in older people. The method is also limited by uncertainty regarding the exact level of PAL to use. However, this method is similar in approach to the method used to derive the previous Australian recommendations for energy intake (NHMRC 1991) and to that used in the most recent FAO report (FAO:WHO:UNU 2004).

Firstly, the gender, age, body weight and height of the group or individual are determined. To estimate EERM, the current body weight is used. To determine DEER, the current body weight is used if it falls within the healthy weight range (ie BMI in the range 18.5–24.9). If the BMI is 25.0 or above, the desirable body weight is determined by assuming a BMI of 22.0, or in the range 18.5–24.9, as appropriate.

The BMR of the group or individual may be measured using indirect calorimetry or predicted from gender, age and weight from the Schofield equations (NHMRC 1991, Schofield et al 1985). For pregnant and lactating women, the pre-pregnant body weight is used in the appropriate equations.

The approximate PAL of the group or individual is assessed from the information in Table 4 or from estimates or measures of the amount of time spent in different activities as outlined in the US:Canadian DRI report (FNB:IOM 2002) or other appropriate factorial method. To determine actual PAL (for the EERM), a description of current activity level is used. To determine desirable PAL (for the DEER), a value of 1.75 or higher is assumed (FNB:IOM 2002, FAO:WHO:UNU 2004).

The energy expenditure is estimated by multiplying the BMR by the PAL expressed as a multiple of BMR. This energy expenditure value includes estimates of the amount of dietary-induced thermogenesis from typical Western diets.

Finally, the estimate of the energy requirement is corrected for composition of the diet. For typical Australian/New Zealand diets, defined as containing 10–20% energy from protein, 0–6% energy from alcohol, and 1–3% of energy from fibre (ABS 1998, MOH 1999), no correction is necessary as any error will be less than 2.5% (FAO 2003). For diets that are very high in protein and/or fibre and/or alcohol, the estimate of energy requirement may be increased according to the calculations shown in the Energy Chapter, Evidence Appendix for NRVs.

Using this approach for the reference body weight male (76 kg), energy requirements for those aged 19–30 years would range from 10.8 MJ for sedentary activity to 13.8 MJ for moderate activity; for 31–50 year-olds, requirements for this activity range would be from 11 MJ to 16.1 MJ; for 51–70 year-olds, from 9.5 MJ to 12.1 MJ and for people older than 70 years, from 7.4 MJ to 13.6 MJ. For the reference body weight adult female (61 kg), requirements across these activity levels would range from 8.1 MJ for those who are sedentary to 10.5 MJ in moderately active 19–30 year-olds; from 7.9 to 10.1 MJ at 31–50 year; 7.6 to 9.6 MJ at 51–70 years and 7.1 to 9.1 MJ at ages over 70 years.

TABLE 4 ENERGY EXPENDITURE LEVELS FOR DIFFERENT LIFESTYLES AS ASSESSED FROM DOUBLY-LABELLED WATER MEASURES

Description of lifestyle	Examples of occupations	PAL
1. At rest, exclusively sedentary or lying (chair-bound or bed-bound).	Old, infirm individuals. Unable to move around freely or earn a living	1.2
2. Exclusively sedentary activity/seated work with little or no strenuous leisure activity[a]	Office employees, precision mechanics	1.4–1.5
3. Sedentary activity/seated work with some requirement for occasional walking and standing but little or no strenuous leisure activity[a]	Laboratory assistants, drivers, students, assembly line workers	1.6–1.7
4. Predominantly standing or walking work[a]	Housewives, salespersons, waiters, mechanics, traders	1.8–1.9
5. Heavy occupational work or highly active leisure	Construction workers, farmers, forest workers, miners, high performance athletes	2.0–2.4
6. Significant amounts of sport or strenuous leisure activity in addition to 2, 3 or 4 above		Add extra PAL units[a]

Adapted from Black et al (1996), German Nutrition Society (2002) and FNB:IOM (2002)

Abbreviations: PAL, physical activity level

[a] Note: For sports and strenuous leisure activities (30–60 minutes, 4–5 times per week) add 0.3 PAL units per day, or calculate how much extra PAL to add from data in Chapter 12 of US:Canadian DRI report (FNB:IOM 2002)

Pregnancy Estimated Energy Requirement

All ages

1st trimester **No additional requirement**

2nd trimester **Additional 1.4 MJ/day**

3rd trimester **Additional 1.9 MJ/day**

***Rationale*:** After estimating the PAL as above for adult women**,** extra requirements for pregnancy are added using results from DLW studies (Forsum et al 1992, Goldberg et al 1991, 1993, Koop-Hoolihan et al 1999) together with the estimated energy content of the gain in both fetal and maternal body mass (de Groot et al 1994, Forsum et al 1988, Goldberg et al 1993, Koop-Hoolihan et al 1999, Lederman et al 1997, Lindsay et al 1997, Pipe et al 1979, Sohlstrom & Forsom 1997, van Raaij et al 1988). This latter estimate is based on the additional body fat (using standard anthropometric techniques) and estimated protein deposition. The average extra requirement for pregnancy is nil in the first trimester, 1.4 MJ/day in the second trimester and 1.9 MJ/day in the third trimester of pregnancy (FNB:IOM 2002).

There are large variations in these requirements according to the pre-pregnancy body fat in the mother (Goldberg et al 1993), so care should be taken when applying these additional requirements to individuals. A report by the European Commission (1993) also refers to studies supporting a need for what they define as thin women (BMI <20) to gain more weight overall, especially during the second and third trimesters, than women above this level of body fat. Conversely, the report states that overweight women do not need to gain as much weight as those with BMI in the normal range and thus have less additional energy needs. A UK report (COMA 1991) suggests a possible (unspecified) greater requirement for energy in underweight pregnant women than those in the normal weight range, but does not address the possibility of a lower requirement in overweight/obese women.

Lactation Estimated Energy Requirement

All ages **Additional 2.0–2.1 MJ/day**

***Rationale*:** Due to variations in milk production (individual variation, stage of lactation and extent of weaning), weight loss during lactation and changes in physical activity level, it is difficult to make a single recommendation for energy needs during lactation.

However, the average additional requirement in lactation may be taken as an extra 2.0–2.1 MJ/day, assuming full breast feeding in the first six months and partial breast feeding thereafter (FAO:WHO: UNU, 2004). The value of 2 MJ/day assumes milk production of 0.78 L/day, an energy content of milk of 2.8 kJ/g, 80% efficiency and an assumed weight loss equivalent to 720 kJ/day in the mother in the first few months of lactation, with no change in physical activity level. In the second six months, milk production is assumed to average 0.60 L/day but due to the depletion of maternal fat stores, additional energy requirements are almost the same.

UPPER LEVEL OF INTAKE - DIETARY ENERGY

It is not possible to set a UL.

***Rationale*:** Body weight within the range desired for good health (BMI 18.5–25 kg/m^2) whilst maintaining adequate levels of physical activity is the critical indicator of adequacy of energy intake. Since any energy intake above the estimated requirement is likely to result in weight gain and increased morbidity, a UL cannot be calculated for dietary energy.

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MACRONUTRIENTS AND WATER

PROTEIN

BACKGROUND

Protein occurs in all living cells and has both functional and structural properties. Amino acids, assembled in long chains, are the building blocks of protein. Of the 20 amino acids found in proteins, some can be made by the body while others are essential in the diet. Amino acids are used for the synthesis of body proteins and other metabolites and can also be used as a source of dietary energy. The proteins of the body are continually being broken down and resynthesised in a process called protein turnover.

Protein is the body's main source of nitrogen which accounts for about 16% the weight of protein. Non-protein nitrogenous compounds are usually present in the diet in minimal amounts. Thus, in assessing dietary protein sources, the total amount of protein, its digestibility and its content of essential amino acids need to be considered. Proteins also contain carbon, oxygen, hydrogen and, to a lesser extent, sulphur.

The nine indispensable or essential amino acids, defined as those that the body is unable to synthesise from simpler molecules, are histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan and valine. Cysteine and tyrosine can partly replace methionine and phenylalanine, respectively. Under certain extreme physiological conditions such as in prematurity or during some catabolic illnesses, the non-essential amino acids arginine, cysteine, glutamine, glycine, proline and tyrosine may be required in the diet. Under normal conditions, glutamine, glutamate or aspartate can supply arginine; methionine and serine can be converted to cysteine; glutaminic acid and ammonia can be converted to glutamine; serine or choline can supply glycine; glutamate can provide proline and phenylalanine can be converted to tyrosine. These amino acids are sometimes termed conditionally indispensable. Alanine, aspartic acid, asparagine, glutamic acid and serine are non-essential. The amino acids act as precursors for many coenzymes, hormones, nucleic acids and other molecules.

Proteins in the diet and the body are associated with a number of other vitamins and minerals and are more complex and variable than other energy sources such as fat and carbohydrate. The polypeptide chains that make up proteins are folded into three-dimensional structures that include helical regions and sheet-like structures due to interaction between the amino acids in the chain. The final shape of a mature protein often reflects its function and also interactions with other molecules. The protein's structure may influence its digestibility.

The body of a 76 kg man contains about 12 kg of protein. Nearly half of this protein is present as skeletal muscle, while other structural tissues such as blood and skin contain about 15% (Lentner 1981). Myosin, actin, collagen and haemoglobin account for almost half of the body's total protein content. Only 1% of the body's store is labile (Waterlow 1969, Young et al 1968), so its availability as a reserve energy store, compared to body fat, is limited. Unlike carbohydrate and fats, the body does not maintain an energy storage form of protein.

Proteins are found in both animal and plant foods. The amino acid profile of animal proteins is closer to that of humans but all of the necessary amino acids can be provided in the amounts needed from plant sources. The major sources in the Australian and New Zealand diet are meat, poultry and fish (about 33%), cereals and cereal-based foods (about 25%) and dairy foods (about 16%). Vegetables also provide about 8%. Certain proteins can cause allergic responses in some individuals notably milk, eggs, peanuts and soy in children and fish, shellfish, peanuts and tree nuts in adults.

The efficiency of dietary protein digestion is high. After ingestion, proteins are denatured by acid in the stomach and cleaved to smaller peptides. A number of gut enzymes including trypsin, chymotrypsin, elastase and carboxypeptidases, complete the process. The free amino acids and small peptides that result are absorbed into the mucosa by specific carrier systems. After intracellular hydrolysis of absorbed peptides, free amino acids are secreted to the portal blood where some of the amino acids are taken up and the remainder pass into systemic circulation for delivery to, and use by, peripheral tissues.

There is wide variation in dietary protein intake, to which the body is able to adapt over a few days. However, severe disease states or fasting can cause substantial body protein losses as energy needs take priority. The protein lost is, however, also necessary to the functioning of the body. A serious depletion in the body mass protein can be life threatening with muscle loss, including loss of heart muscle (Hansen et al 2000). Thus, not only must sufficient protein be provided for sustenance, but also sufficient non-protein energy so the carbon skeletons of amino acids are spared from providing energy. Similarly, unless amino acids are present in the right balance, protein utilisation will be compromised (Duffy et al 1981). Protein-energy malnutrition (PEM) is common on a worldwide basis in both children and adults (Stephenson et al 2000) causing the death of 6 million children a year (FAO 2000). In countries like Australia and New Zealand, PEM is seen most commonly associated with other diseases and in the elderly. Protein deficiency affects all organs including the developing brain (Pollitt 2000), as well as the immune system (Bistrian 1990) and gut mucosal function (Reynolds et al 1996).

There are two key methods for assessing protein requirements, factorial methods and nitrogen balance. For infants, the amount provided by the milk of healthy mothers is used to estimate the adequate intake.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Protein**
0–6 months	**10 g (1.43 g/kg body weight)**	
7–12 months	**14 g (1.60 g/kg body weight)**	

***Rationale*:** An AI for protein for 0–6 months was calculated by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of protein in breast milk of 12.7 g/L (Dewey et al 1983, 1984, Butte et al 1984, Nommsen et al 1991, Mitoulas et al 2002) and rounding. An AI for infants aged 7 to 12 months was calculated by multiplying the concentration of protein in breast milk at this stage of lactation of 11 g/L (Dewey et al 1984, Mitoulas et al 2002, Nommsen et al 1991) by the volume of breast milk (0.6 L) and adding an allowance for complementary foods of 7.1 g/day from the US, NHANES III data (FNB:IOM 2002) to give an AI of 14 g/day (or 1.6 g/kg body weight/day, assuming a reference weight of 9 kg). It is important that the digestibility and comparative protein quality of formulas is taken into account as these will be different to human milk.

Children & adolescents	**EAR**	**RDI**	**Protein**
All			
1–3 yr	**12 g/day (0.92 g/kg)**	**14 g/day (1.08 g/kg)**	
4–8 yr	**16 g/day (0.73 g/kg)**	**20 g/day (0.91 g/kg)**	
Boys			
9–13 yr	**31 g/day (0.78 g/kg)**	**40 g/day (0.94 g/kg)**	
14–18 yr	**49 g/day (0.76 g/kg)**	**65 g/day (0.99 g/kg)**	
Girls			
9–13 yr	**24 g/day (0.61 g/kg)**	**35 g/day (0.87 g/kg)**	
14–18 yr	**35 g/day (0.62 g/kg)**	**45 g/day (0.77 g/kg)**	

***Rationale*:** There are limited data on which to estimate EARs for children and adolescents. Requirements were estimated using the factorial method including estimates of the amount needed for growth and maintenance on a fat-free mass basis. An overall CV of 12% for the EAR was used to derive the RDI.

Adults	**EAR**	**RDI**	**Protein**
Men			
19–30 yr	**52 g/day (0.68 g/kg)**	**64 g/day (0.84 g/kg)**	
31–50 yr	**52 g/day (0.68 g/kg)**	**64 g/day (0.84 g/kg)**	
51–70 yr	**52 g/day (0.68 g/kg)**	**64 g/day (0.84 g/kg)**	
>70 yr	**65 g/day (0.86 g/kg)**	**81g/day (1.07 g/kg)**	
Women			
19–30 yr	**37 g/day (0.60 g/kg)**	**46 g/day (0.75 g/kg)**	
31–50 yr	**37 g/day (0.60 g/kg)**	**46 g/day (0.75 g/kg)**	
51–70 yr	**37 g/day (0.60 g/kg)**	**46 g/day (0.75 g/kg)**	
>70 yr	**46 g/day (0.75 g/kg)**	**57 g/day (0.94 g/kg)**	

***Rationale*:** There are limited data except for younger adult males. Requirements were estimated using the factorial method including estimates of the amount needed for growth and maintenance on a fat-free mass basis. An overall CV of 12% was used to derive the RDIs. Adults older than 53 years appeared to have 25% higher requirements for maintenance than younger adults in an analysis by Rand et al (2003). However, there were only 14 subjects and the difference did not reach significance. Other researchers from the same institute have also suggested a need for higher intakes in older adults (Campbell & Evans 1996, Campbell et al 2001). For this reason, the EAR for adults >70 years was increased by 25% over that of younger adults, although it should be recognised that the data supporting this increase are limited. The RDI is estimated assuming a CV of 12% for the EAR based on the analysis of Rand et al (2003).

Pregnancy	**EAR**	**RDI**	**Protein**
(2nd and 3rd trimesters)			
14–18 yr	**47 g/day (0.82 g/kg)**	**58 g/day (1.02 g/kg)**	
19–30 yr	**49 g/day (0.80 g/kg)**	**60 g/day (1.00 g/kg)**	
31–50 yr	**49 g/day (0.80 g/kg)**	**60 g/day (1.00 g/kg)**	

***Rationale*:** No additional requirement was set for the first trimester as there is little additional weight gain during this time. The recommendations are for the second and third trimesters. One third of the pregnancy weight gain occurs in the second trimester and two thirds in the third trimester. The increase in body weight requires an additional 0.2 g/kg/day during this phase of pregnancy based on the mid-trimester weight gain and efficiency of utilisation observed in the meta analysis of Rand et al (2003), making the EAR at this stage of 0.8 g/kg/day. The RDI is estimated using a CV of 12% for the EAR giving an RDI in the second and third trimesters of pregnancy of 1.00–1.02 g/kg/day or 60 g/day with rounding.

Lactation	**EAR**	**RDI**	**Protein**
14–18 yr	**51 g/day (0.90 g/kg)**	**63 g/day (1.1 g/kg)**	
19–30 yr	**54 g/day (0.88 g/kg)**	**67 g/day (1.1 g/kg)**	
31–50 yr	**54 g/day (0.88 g/kg)**	**67 g/day (1.1 g/kg)**	

***Rationale*:** Using a factorial approach, the additional requirement in pregnancy was estimated as 21.2 g/day (FNB:IOM 2002), assuming that all nitrogen in human milk is provided by extra protein. This was the figure used by the US:Canadian Committee. However, about 20–25% of the nitrogen in milk is non-protein and can be provided by the unused portion of the maintenance protein intake. On this basis, the additional need is about 17 g/day or 0.28 mg/kg body weight. The RDI was set assuming a CV of 12% for the EAR.

UPPER LEVEL OF INTAKE - PROTEIN

No UL was set as there are insufficient data. However, a UL of 25% protein as energy is recommended for which the rationale is provided in the 'Chronic disease' section of this document.

***Rationale*:** Humans consume widely varying amounts of proteins. Although some adverse effects have been reported with moderate to high levels of supplementation, the risk of adverse effects from foods consumed as part of everyday diets is very low. This consideration, together with the limited data available, makes it impossible to set an upper limit in terms of grams per day. However caution is needed. Intakes of individual amino acids that may be consumed as supplements should not exceed those normally found in the diet.

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FATS: TOTAL FAT AND FATTY ACIDS

BACKGROUND

Fats are the most concentrated form of energy for the body (37 kJ/g). They also aid in the absorption of the fat-soluble vitamins, A, D, E and K and other fat-soluble biologically-active components. Chemically, most of the fats in foods are triglycerides, made up of a unit of glycerol combined with three fatty acids which may be the same or different. The differences between one triglyceride and another are largely due to the fatty acids content. Other dietary fats include phospholipids, phytosterols and cholesterol.

There are three major types of naturally-occurring fatty acids – saturated, *cis*-monounsaturated and *cis*-polyunsaturated. A fourth form, the *trans* fatty acids, are produced by partial hydrogenation of polyunsaturated oils in food processing and they also occur naturally in ruminant animal foods. Saturated fats are found mainly in animal-based foods and polyunsaturates and monounsaturates predominate in plant-based foods.

Saturated fatty acids contain no double bond; they are fully saturated with hydrogen. They are the main type of fatty acids found in milk, cream, butter and cheese, meats from most of the land animals, palm oil and coconut oil as well as in products such as pies, biscuits, cakes and pastries. Saturated fatty acids have both physiological and structural functions. They can be synthesised by the body so are not required in the diet.

The main monounsaturated fatty acid is oleic acid with one double bond. Olive, canola and peanut oils are rich in oleic acid. The monounsaturates are also synthesised by the body and are thus not required in the diet.

Polyunsaturated fatty acids contain two or more double bonds. The most common is linoleic acid (LA, 18:2). It is described as 'n-6' due to the position of the double bonds and occurs in seed oils, eg sunflower, safflower and corn. Other n-6 fatty acids include γ-linolenic (18:3), dihomo-γ-linolenic (20:3), arachidonic acid (20:4) and adrenic acid (22:4). LA is the precursor of arachidonic acid, a substrate for eicosanoid production which is also involved in the regulation of gene expression (Ou et al 2001). LA is also found as a structural component of cell membranes and is important in cell signalling. High intakes of n-6 polyunsaturated fats have been associated with blood lipid profiles associated with a lower risk of coronary heart disease (eg lower total and LDL cholesterol, increased HDL cholesterol and reduced triacylglycerol) (Arntzenius et al 1985, Becker et al 1983, Sonnenberg et al 1996).

Smaller amounts of polyunsaturated fatty acids with double bonds in the n-3 position also occur in the diet. These are sometimes referred to as omega fatty acids. Humans are unable to insert a double bond at the n-3 position of a fatty acid and thus require a dietary source. The parent fatty acid of the n-3 series is α-linolenic (ALA, 18:3). ALA is found in legumes, canola oils and margarines, linseed oils and products, certain nuts such as walnuts, and in small amounts in leafy vegetables. Canola oils and margarines and linseed oils are rich sources and legumes contribute some. A second group of n-3 fatty acids are the long chain (LC) acids eicosapentaenoic acid (EPA, 20:5), docosahexaenoic acid (DHA, 22:6) and docosapentaenoic acid (DPA, 22:5) that are found predominantly in oily fish such as mackerel, herrings, sardines, salmon and tuna and other seafood. Whilst α-linolenic acid predominates in western diets, the fish oils, DHA, EPA and DPA predominate in other communities consuming their traditional diet, such as the Inuit (Holman et al 1982).

ALA primarily functions as a precursor for the synthesis of EPA which in turn forms DHA but may also have an independent role in protection against coronary heart disease via different mechanisms (Crawford et al 2000). Conversion of ALA to EPA and DHA is limited and varies according to the intakes of other fatty acids (Burdge et al 2003, Emken 2003, Pawlosky et al 2001). Thus, a typical intake of ALA may be less able to satisfy the physiological requirements for LC n-3 fatty acids than the smaller and often more variable intakes of pre-formed LC n-3 fatty acids.

DHA plays an important role as a structural membrane lipids, particularly in nerve tissue and the retina, and can also act as a precursor to certain eicosanoids. EPA is the precursor of the 3 series of prostaglandins and the 5 series of leukotrienes. In recent years, research has shown both cardiovascular and anti-inflammatory benefits of LC n-3 fatty acids (Albert et al 1998, 2002, Burr et al 1989, Dallongeville et al 2003, Djousse et al 2001, Dolecek 1992, GISSI-Prevenzione Investigators 1999, Hu et al 1999, Pischon et al 2003, WHO 2003). Early on, because of the nature of the fish oils used in studies, these benefits were attributed to EPA and its impact on eicosanoid production (Simopoulos 1991) but recent studies suggest that DHA is the primary mediator of cardiovascular benefits, influencing gene expression of key metabolic regulators, particularly in endothelial cells (Mori et al 1999). The potential role of DPA, as a very minor component of fish oil, has been largely ignored, despite the fact that recent research shows DPA contributes almost 30% of total LC n-3 in our diet (Howe et al 2003, 2005).

Until dose-response relationships have been established, the relative efficacy of EPA, DPA and DHA remains uncertain. Moreover, the extent of their interconversion is also uncertain. Hence it is not possible to differentiate between intake requirements for EPA, DPA and DHA at this stage.

A lack of dietary n-6 or n-3 polyunsaturated fatty acids is characterised by rough, scaly skin, dermatitis, increased transepidermal water loss, reduced growth and a high triene: tetraene ratio (Goodgame et al 1978, Holman et al 1982, Jeppersen et al 2000, Mascioli et al 1996, O'Neill et al 1977). They cannot be formed in the body and is therefore essential in the diet. Studies on patients given fat-free parenteral feeding have provided insight into the levels at which essential fatty acid deficiency occurs but are not sufficient to establish an average requirement (Fleming et al 1976, Goodgame et al 1978, Jeppersen et al 1998, Riella et al 1975).

There is some evidence that the ratio of n-6 to n-3 fatty acids may be important. Jensen et al (1997) reported that infants fed formulas containing an LA:ALA ratio of 4.8:1 had lower arachidonic acid concentrations and impaired growth compared to infants fed ratios of 9.7:1 or above. However, more recent large trials of ratios of 5:12 and 10:1 found no evidence of reduced growth or other problems (Simmer 2002). Various authorities have recommended ratios of LA:ALA or n-6:n-3 ratios ranging from 5:1 to 10:1 or 5:1 to 15:1 or 6:1 to 16:1 for infant formula (ESPGAN, Committee on Nutrition 1991, ISSFAL 1994, LSRO 1998).

A number of studies have looked at the n-6:n-3 ratio in relation to heart disease with inconsistent results (Dolecek & Graditis 1991, Ezaki et al 1999, Hu et al 1999, Kromhout et al 1985, Lands et al 1990, 1992, Nelson et al 1991, Shekelle et al 1985). However, on the basis of these results, the FAO:WHO Consultation on Fats and Oils (1994) recommended that the ratio of LA to ALA in the diet should be between 5:1 and 10:1 and suggested that individuals with a ratio greater than 10:1 should be encouraged to consume more n-3-rich foods. In contrast, an expert workshop in the Netherlands (de Deckere 1998) concluded that setting an n-6:n-3 ratio would not be helpful. They also proposed that there should be separate recommendations for plant (18:3) and marine (20:5, 22:5, 22:6) n-3 fatty acids.

Based on the concept of essentiality and given the lack of dose-response data to derive EARs for those components considered essential, AIs have been set for LA (n-6 in infants), ALA and the combined LC n-3 fatty acids, DHA:EPA:DPA. The AIs are based on median population intakes in Australia.

For children, adolescents and adults an EAR, RDI or AI for total fat was not set as it is the type of fats consumed that relate to essentiality and to many of the physiological and health outcomes. A suggested range of per cent energy as fat in relation to chronic disease prevention is addressed in the 'Chronic disease' section. In infancy, as fat is the major single source of energy in breast milk, an AI recommendation for total fat has been made based on breast milk composition. Recommendations for fatty acids in infancy are also based on total n-6 or n-3 derived from the composition of breast milk.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Fats**
0–6 months	**Total fat**	**31 g/day**
	n-6 polyunsaturated fats	**4.4 g/day**
	n-3 polyunsaturated fats	**0.5 g/day**
7–12 months	**Total fat**	**30 g/day**
	n-6 polyunsaturated fats	**4.6 g/day**
	n-3 polyunsaturated fats	**0.5 g/day**

***Rationale*:** The AI for 0–6 months was set by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of fat, n-6 or n-3 in breast milk (40; 5.6 and 0.63 g/L, respectively) from nine studies reviewed by FNB:IOM (2002) and rounding. The AI for 7–12 months was set by multiplying together the average intake of breast milk (0.6 L/day) and the average concentration of fat, n-6 or n-3 in breast milk (40; 5.6 and 0.63 g/L respectively) from nine studies reviewed by FNB:IOM (2002) and adding the median intake from complementary foods (5.7, 1.2 and 0.11 g/day, respectively) from the US CSFII data for 1994–96 (FNB:IOM 2002).

Children, adolescents & adults	**AI**		**Fats**
	Linoleic acid	**α-linolenic acid**	**Total LC n-3 (DHA+EPA+DPA)**
Boys and girls			
1–3 yr	**5 g/day**	**0.5 g/day**	**40 mg/day**
4–8 yr	**8 g/day**	**0.8 g/day**	**55 mg/day**
Boys			
9–13 yr	**10 g/day**	**1.0 g/day**	**70 mg/day**
14–18 yr	**12 g/day**	**1.2 g/day**	**125 mg/day**
Girls			
9–13 yr	**8 g/day**	**0.8 g/day**	**70 mg/day**
14–18 yr	**8 g/day**	**0.8 g/day**	**85 mg/day**
Adults 19+ yr			
Men	**13 g/day**	**1.3 g/day**	**160 mg/day**
Women	**8 g/day**	**0.8 g/day**	**90 mg/day**

***Rationale*:** The AIs for LA and ALA were based on the highest median intakes of any of the gender-related age groups taken from an analysis of the National Nutrition Survey of Australia of 1995 (Howe et al 2003, 2005). For LC n-3, to overcome a marked gender disparity caused by particularly higher relative intakes in younger adult males (19–30 years), the AI was based on the median intake for all adults of the relevant gender. As national data were not available for New Zealand, similar values were assumed. The AIs do not necessarily reflect optimal intakes but are the values found in a population with no apparent essential fatty acid deficiency. (The 'Chronic disease prevention' section includes a suggested dietary target.)

Pregnancy	AI			Fats
	Linoleic acid	α-linolenic acid	Total LC n-3 (DHA+EPA+DPA)	
14–18 yr	10 g/day	1.0 g/day	110 mg/day	
19–50 yr	10 g/day	1.0 g/day	115 mg/day	

***Rationale*:** Demand for n-6 and n-3 fatty acids for placental and fetal tissue must be met from maternal stores or by increased dietary intake, but there is a lack of data for assessing additional needs. The AIs for pregnancy were therefore based on that of the non-pregnant women, with an additional amount based on the increased average body weight in pregnancy (x 1.25).

Lactation	AI			Fats
	Linoleic acid	α-linolenic acid	Total LC n-3 (DHA+EPA+DPA)	
14–18 yr	12 g/day	1.2 g/day	140 mg/day	
19–50 yr	12 g/day	1.2 g/day	145 mg/day	

Rationale: There is a lack of data about the requirements in pregnancy, so the AIs were based on that for non-pregnant, non-lactating women plus that of the infant. As the infant recommendation includes only an AI for total n-3 based on milk concentration, this amount was apportioned between ALA and LC omega-3 in the same ratio as in the maternal AI when assessing the additional requirement.

UPPER LEVEL OF INTAKE - TOTAL FAT AND FATTY ACIDS

Linoleic acid: **No UL was set because there is no known level at which adverse effects may occur.**

α-linolenic acid: **No UL was set because there is no known level at which adverse effects may occur. The longer chain DHA, EPA and DPA fatty acids derived from ALA are more biologically-potent than ALA itself.**

LC n-3 fatty acids (DHA, EPA, DPA):

Infants 0–12 months	**Not possible to establish**
Children, adolescents and adults	**3,000 mg/day**

***Rationale*:** There is some evidence to suggest that high levels of these fatty acids may impair immune response and prolong bleeding time. However the immune function tests were performed in vitro and it is unclear how the results would translate to the in vivo situation. Prolonged bleeding times have been seen in the Inuit, but it is not known if they were caused by high LC n-3 consumption. The US Food and Drug Administration (DHHS 1997) has set a 'Generally Regarded as Safe' level of 3000 mg/day for LC n-3 which has been adopted here as the upper level of intake for children, adolescents and adults. (Note that is unlikely that this level of intake would be reached by consumption of seafood alone. If it were, then consideration would need to be given to the possible effects of concomitant intakes of other potential toxins such as mercury.) It is not possible to estimate an upper level of intake for infants.

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CARBOHYDRATE

BACKGROUND

The primary role of dietary carbohydrate is the provision of energy to cells, particularly the brain that requires glucose for its metabolism. Other nutrients (eg fat , protein and alcohol) can provide energy but there are good reasons to limit the proportion of energy provided by these nutrients as discussed in the 'Chronic disease' section. Carbohydrate is also necessary to avoid ketoacidosis. However, as limited data exist on which to base an estimate of requirements, it was not possible to set an EAR, RDI or AI for carbohydrates (either collectively or individually) for most age/gender groups.

The lack of an RDI or AI for total carbohydrates in no way reflects a lack of value as a key component of the diet. The type of carbohydrate consumed is paramount in terms of health outcome (see 'Chronic disease' section and FNB:IOM 2002).

It was deemed inappropriate to set an upper level of intake for carbohydrates, however, evidence of the role of various carbohydrates in relation to chronic diseases is discussed in the 'Chronic disease' section where an acceptable range of intake is given.

Some exceptions have been made as detailed below.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Carbohydrate**
0–6 months	**60 g/day**	
7–12 months	**95 g/day**	

***Rationale*:** In infancy, the brain is large relative to body size and uses 60% of the infant's total energy intake (Gibbons 1998). Animal experiments indicate that the infant brain can use keto acids as fuel (Edmond et al 1985, Sokoloff 1973). It is also known that the gluconeogenic pathway is highly developed, even in premature infants (Sunehag et al 1999).

However, it is not known whether gluconeogenesis can provide all of the glucose requirements of infants, so an AI has been set based on the average carbohydrate (mostly lactose) content of breast milk (74 g/L) and an average daily milk volume of 0.78 L in the first 6 months, giving 60 g/day (with rounding). For ages 7–12 months, an estimate was made based on an average volume of 0.60 L/day milk at 74 g/L (44 g/day) plus an amount from complementary foods of 51 g/day (from NHANES III as detailed in FNB:IOM 2002).

Pregnancy and lactation

Although no specific EAR, RDI or AI recommendations are made for pregnancy and lactation, these physiological states require additional fuel to support the development, growth and metabolism of maternal and fetal tissues, or for milk production, respectively. Glucose is the optimal fuel, particularly for the maintenance of maternal and fetal brain function, although keto acids can meet some needs (Patel et al 1975).

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DIETARY FIBRE

BACKGROUND

Adequate dietary fibre is essential for proper functioning of the gut and has also been related to risk reduction for a number of chronic diseases including heart disease, certain cancers and diabetes (see 'Chronic disease' section for further discussion).

There is no single definition of dietary fibre, which is a component of all plant materials. What can be said with certainty is that most of the components of dietary fibre are carbohydrate in nature, lignin being an exception. Hipsley first used the term 'dietary fibre' in 1953 to describe plant cell walls in the diet, which were thought to protect against toxaemia of pregnancy. This term, later taken up by Trowell (1972), encompassed only components of the plant cell wall that resisted digestion by secretions of the human alimentary tract, namely cellulose, hemicelluloses, pectin and lignin.

Trowell described dietary fibre as either 'the skeletal remains of cell walls' or as 'remnants of the plant cell wall' (Trowell 1972, 1975). As it is difficult to determine whether indigestible materials from plants came from the cell wall or other parts, the definition was expanded to include all indigestible components of plant origin (Trowell et al 1976). In 1987, the Life Sciences Research Office of the Federation of American Societies for Experimental Biology (1987) adopted a definition of dietary fibre as 'the endogenous components of plant materials in the diet which are resistant to digestion by enzymes produced by humans'. This definition can be considered to include some components of what is now known as resistant starch (RS). As pointed out by Southgate (1991), this definition is virtually identical to that for 'unavailable carbohydrates' as originally defined in McCance & Lawrence (1929).

One difficulty with the word endogenous in this definition is that it excludes, for example, those forms of RS that arise as a consequence of cooking and processing techniques. It also excludes substances which are intimately associated with the major components of dietary fibre and which are capable of having important nutritional and/or physiologic effects such as phytates, lectins, saponins, non-polymeric polyphenols, and inorganic constituents. Recent data have indicated that while non-starch polysaccharides (NSP) are important for human health, RS may be as significant if not more so for many health conditions (Topping & Clifton, 2001).

Food Standards Australia New Zealand (FSANZ) defines Dietary Fibre as follows:

> 'Dietary fibre means that fraction of the edible parts of plants or their extracts, or synthetic analogues, that are resistant to the digestion and absorption in the small intestine, usually with complete or partial fermentation in the large intestine. Dietary fibre includes polysaccharides, oligosaccharides (degree of polymerisation >2) and lignins, and promotes one or more of the following beneficial physiological effects:
>
> (i) laxation
>
> (ii) reduction in blood cholesterol
>
> (iii) modulation of blood glucose'.

This definition was gazetted in Standard 1.2.8 of the ANZ Food Standards Code in August 2001. The code also prescribes a number of acceptable Association of Official Analytical Chemists (AOAC) methods of analysis for total dietary fibre or its components that led to the inclusion of inulin, fructo-oligosaccharides and polydextrose in the category of dietary fibre. At the time of publication of the current document, FSANZ has not assessed a method for assaying RS.

In Australia, the National Nutrition Survey of 1995 indicated that 45% of dietary fibre comes from breads and other cereal foods, 10% from fruit and 30% from vegetables (NNS 1998). The distribution is similar in New Zealand, with 44% from breads and cereals, 13% from fruit and 28% from vegetables (MOH 1999). However, it is worth noting that the food data bases for dietary fibre used for these surveys do not equate precisely to the FSANZ definition as the analytical methods used (AOAC in Australia and

Englyst in New Zealand) measure a different set of components. Nevertheless, the differences have been assumed to be relatively small.

Resistant starch comes within the FSANZ definition but is only partially assessed using currently approved methods that account for only about 40% of RS. Baghurst et al (1996) estimated intakes of RS in Australia and New Zealand based on national nutrition surveys in the mid 1980s for Australia and early 1990s for New Zealand. This analysis showed an average figure of 4.0 g RS/100 g starch for men, 4.7 g RS/100 g starch for women and 4.5 g RS/100 g starch for children.

It has been postulated that diets high in fibre have a lower energy density and may therefore help in moderating obesity. The exact mechanisms by which these apparent health benefits may arise have not been determined. In almost every instance, there exists the possibility that the observed associations are indirect as a consequence of chemoprotective effects of non-nutrients closely associated with the fibre components of fruits, vegetables and cereal foods. Further discussion of the potential role of fibre in relation to chronic disease is given in the 'Chronic disease' section.

Only in the case of laxation is there evidence of both protective (Sanjoaquin et al 2004) and therapeutic actions (Topping & Clifton 2001). This laxative effect accounts for the role of dietary fibre in conditions such as hiatus hernia, diverticular disease and haemorrhoids. These latter conditions may also be affected by adequacy of fluid ingestion. Regional differences in the occurrence of these diseases generated the original hypothesis of Burkitt & Trowell (1975). However, there are few studies that have looked at the role of dietary fibre in the aetiology, rather than treatment, of these diseases. Dietary fibre is the most effective treatment for all forms of constipation due to its influence on faecal bulk and consistency.

Assessment of dietary fibre needs is complex as the endpoints are ill defined. There is no biochemical marker that can be used to determine dietary fibre needs, so appearance or disappearance of clinical endpoints needs to be considered. In keeping with the concept of setting EARs and RDIs or AIs for prevention of deficiency states, the endpoints chosen in the estimation of requirements were adequate gastrointestinal function and adequate laxation rather than reduction of risk for chronic disease.

From a meta analysis of about 100 studies of changes in stool weight with various forms of fibre, the increase in faecal weight due to ingestion of fibre has been estimated (Cummings 1993). An increase of 1 g in faecal bulk can be achieved with an additional 3 g of isolated cellulose, 5.4 g of wheat bran, 1.3 g of isolated pectin and 4.9 g of fruit and vegetables (Hillman 1983). Resistant starch has very limited effect (Behall & Howe 1996, Cummings et al 1996, Heijnen et al 1998, Jenkins et al 1998). However, increased faecal weight does not necessarily equate to enhanced laxation as other factors such as water can affect laxation directly or be a necessary adjunct to increased fibre intakes (Anti et al 1998).

Assessing the stool weight that will promote laxation and prevent constipation is very difficult. For these reasons, it is not possible to establish an EAR. Instead, an AI has been derived based on median intakes in populations like Australia and New Zealand where laxation problems are not common.

The potential benefits of higher than AI intakes on chronic disease aetiology are discussed in the 'Chronic disease' section.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Dietary Fibre**
0–6 months	**No AI has been set**	
7–12 months	**No AI has been set**	

***Rationale*:** There are no functional criteria for dietary fibre in infants. Human milk contains no dietary fibre and as such no AI is set.

Children & adolescents	AI	Dietary Fibre
All		
1–3 yr	**14 g/day**	
4–8 yr	**18 g/day**	
Boys		
9–13 yr	**24 g/day**	
14–18 yr	**28 g/day**	
Girls		
9–13 yr	**20 g/day**	
14–18 yr	**22 g/day**	

***Rationale*:** The AI is set at the median for dietary fibre intake in Australia and New Zealand for children of these ages based on the National Dietary Surveys of Australia undertaken in 1995 and New Zealand undertaken in 2002 (ABS 1998, MOH 2003) plus an allowance ranging from 2–4 g/day for the different age/gender groups for a component of RS not included in the food data base used for these surveys, and rounding.

Adults	AI	Dietary Fibre
Men		
19–30 yr	**30 g/day**	
31–50 yr	**30 g/day**	
51–70 yr	**30 g/day**	
>70 yr	**30 g/day**	
Women		
19–30 yr	**25 g/day**	
31–50 yr	**25 g/day**	
51–70 yr	**25 g/day**	
>70 yr	**25 g/day**	

***Rationale*:** The AI is set at the median for dietary fibre intake in Australia and New Zealand based on the 1995 National Nutrition Survey of Australia (ABS 1998) and the 1997 National Nutrition Survey of New Zealand (MOH 1999). The value within each gender was set for all ages at the highest median of any of the age groups plus an allowance of slightly more than 4 g/day for men and slightly less than 3 g/day for women for the component of RS not included in the food data base for dietary fibre used for these surveys, and rounding.

Pregnancy	AI	Dietary Fibre
14–18 yr	**25 g/day**	
19–30 yr	**28 g/day**	
31–50 yr	**28 g/day**	

***Rationale*:** There is no evidence for increased metabolic needs in pregnancy. To allow for additional body weight, the AI is increased in relation to increased energy needs of about 12%, with rounding.

Lactation	AI	Dietary Fibre
14–18 yr	**27 g/day**	
19–30 yr	**30 g/day**	
31–50 yr	**30 g/day**	

***Rationale*:** There is no evidence for increased metabolic needs in lactation. The AI is increased in relation to additional energy needs of about 20%, with rounding.

UPPER LEVEL OF INTAKE - DIETARY FIBRE

There is no UL set for dietary fibre.

***Rationale*:** A number of potential adverse effects have been identified for high intakes of dietary fibre. Potential adverse effects on mineral and vitamin bioavailability were first identified in McCance & Widdowson (1942). However, Gordon et al (1995) stated in a review of the literature: 'We are of the strong conviction and can find no convincing scientific evidence that any dietary fibre, even when consumed in large amounts (ie 50 g total dietary fibre per day), has or should have any adverse effect on mineral absorption or nutrition in humans.'

There are three other potential adverse effects of diets high in dietary fibre. The first relates to the potential increase in the incidental intake of pesticides and other agricultural chemicals, heavy metals, nitrates and antinutrients such as lectins, haemagglutinins and solanine (National Research Council 1989) associated particularly with consumption of the bran layer or skins of plants. The second is the possibility of the development of food intolerances due to alteration of gut microflora (British Nutrition Foundation, 1990). Thirdly, diets with a high content of leafy vegetables may cause problems with benzoar formation in people with upper gastrointestinal dysfunction (Vinik & Jenkins 1988). However, in practice, these potential adverse effects are not likely to cause problems at the levels of recommended intake if dietary fibre is derived from a variety of sources.

Dietary fibre is variable in composition, so it is difficult to link a specific fibre with a particular adverse outcome, especially if phytate is present. A high intake of dietary fibre will not produce substantial deleterious effects when part of a healthy diet, so no upper level of intake is set.

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WATER

BACKGROUND

Water is defined as an essential nutrient because it is required in amounts that exceed the body's ability to produce it. All biochemical reactions occur in water. It fills the spaces in and between cells and helps form structures of large molecules such as protein and glycogen. Water is also required for digestion, absorption, transportation, dissolving nutrients, elimination of waste products and thermoregulation (Kleiner 1999).

Water accounts for 50–80% of body weight, depending on lean body mass. On average, men have a higher lean body mass than women and higher percentage of body mass as water than in women. The relative mass of water decreases in both men and women with age. Human requirements for water are related to metabolic needs and are highly variable. They depend to some extent on individual metabolism.

Solid foods contribute approximately 20% of total water intake or about 700–800 mL (NNS 1995). The remainder of the dietary intake comes from free water and/or other fluids (NHMRC 2003). An additional 250 mL or so of water is also made available to the body from metabolism (water of oxidation). The body must retain a minimal amount to maintain a tolerable solute load for the kidneys. Excluding perspiration, the normal turnover of water is approximately 4% of total body weight in adults. In a 70 kg adult, this is equivalent to 2,500–3,000 mL/day.

Water losses from lungs and skin (insensible losses) are responsible for 50% of the total water turnover. They are sensitive to environmental conditions and can be increased at high temperatures, high altitude and low humidity. During summer, when heat stress may be high, water depletion can lead to heat exhaustion, loss of consciousness and heat stroke (Cheung et al 1998, Hubbard & Armstrong 1988). Unfit, overweight, older people may be especially at risk, particularly if they are subjected to strenuous exercise. Infants and dependent children may also be at risk if not offered sufficient fluids. The remainder of the losses are from urine and stools.

Dehydration of as little as 2% loss of body weight results in impaired physiological responses and performance. The reported health effects of chronic mild dehydration and poor fluid intake include increased risk of kidney stones (Borghi et al 1996, Hughes & Norman 1992, Iguchi et al 1990, Embon et al 1990), urinary tract cancers (Bitterman et al 1991, Wilkens et al 1996, Michaud et al1999), colon cancer (Shannon et al 1996) and mitral valve prolapse (Lax et al 1992) as well as diminished physical and mental performance (Armstrong et al 1985, Brooks & Fahey 1984, Brouns et al 1992, Cheung et al 1998, Kristel-Boneh et al 1988, Torranin et al 1979, Sawka & Pandolf 1990).

Oral health may also be affected by fluid consumption. Apart from the beneficial effects of fluoride added to tap water in many communities in Australia and New Zealand, fluid intake can affect saliva production. Saliva, which is primarily water, is essential for maintenance of oral health. Decreased body water has been associated with salivary dysfunction, especially in older adults. However, one investigation (Ship & Fischer 1997) found that decreased salivary gland function was associated with dehydration, independent of age.

Several factors increase the possibility of chronic, mild dehydration, including a poor thirst mechanism (Sagawa et al 1992, Sansevero 1997), dissatisfaction with the taste of water (Meyer et al 1994, Weissman 1997), consumption of common diuretics such as caffeine (Meyer et al 1994) and alcohol, participation in exercise (Convertino et al 1996) and environmental conditions (Sagawa et al 1992).

Kidney function can decline as part of the normal ageing process with decrease in kidney mass, declines in renal blood flow and glomerular filtration rate, distal renal tubular diluting capacity, renal concentrating capacity, sodium conservation and renal response to vasopressin. This decline in kidney function together with hormonal changes and factors such as decreased thirst perception, medication, cognitive changes, limited mobility and increased use of diuretics and laxatives make older adults a

group of particular concern (NHMRC 1999). Numerous studies have shown diminished thirst sensations in the elderly. Despite the fact that these changes may be normal adaptations of the ageing process, the outcomes of dehydration in the elderly are serious and range from constipation to cognitive impairment, functional decline, falls or stroke.

Hydration status, assessed by plasma or serum osmolality is the indicator of choice to assess water requirements. However, the body's needs vary widely according to environmental conditions, physical activity and individual metabolism. The body can also compensate in the short term for over or under-hydration, so it is difficult to establish an EAR experimentally. There is no single level of water intake that would ensure adequate hydration and optimal health for half of all the apparently healthy people in the population, in all environmental conditions. Thus an AI has been established based on median population intakes in Australia.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Water**
0–6 months	**0.7 L/day (from breast milk or formula)**	
7–12 months	**0.8 L/day (from breast milk, formula, food, plain water and other beverages, including 0.6 L as fluids)**	

***Rationale*:** Infants exclusively fed breast milk do not require supplemental water. Breast milk is 87% water. The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average amount of water in breast milk (0.87 L/L), and rounding. For infants of 7–12 months, the breast milk intake is assumed to be 600 mL/day. This would supply 0.52 L water/day. An amount of 0.32 L/day is added for water from complementary foods as estimated from the US CSFII data (FNB:IOM 2004) to give a total of 0.84 L/day rounded to 0.8 L/day.

Children & adolescents	**AI**		**Water**
	Total water (Food and fluids)	**Fluids (Including plain water, milk and other drinks)**	
All			
1–3 yr	**1.4 L/day**	**1.0 L/day (about 4 cups)**	
4–8 yr	**1.6 L/day**	**1.2 L/day (about 5 cups)**	
Boys			
9–13 yr	**2.2 L/day**	**1.6 L/day (about 6 cups)**	
14–18 yr	**2.7 L/day**	**1.9 L/day (about 7–8 cups)**	
Girls			
9–13 yr	**1.9 L/day**	**1.4 L/day (about 5–6 cups)**	
14–18 yr	**2.2 L/day**	**1.6 L/day (about 6 cups)**	

***Rationale*:** The National Nutrition Survey of Australia, 1995 (ABS 1998) showed that for children and adolescents, some 70% of water intake came from beverages and milk, leaving 30% from foods. Children living in extremely hot climates may require higher than AI amounts to remain hydrated, especially if they are highly active.

Adults	AI	Water
	Total water (Food and fluids)	**Fluids (Including plain water, milk and other drinks)**
Men		
19–30 yr	**3.4 L/day**	**2.6 L/day (about 10 cups)**
31–50 yr	**3.4 L/day**	**2.6 L/day (about 10 cups)**
51–70 yr	**3.4 L/day**	**2.6 L/day (about 10 cups)**
>70 yr	**3.4 L/day**	**2.6 L/day (about 10 cups)**
Women		
19–30 yr	**2.8 L/day**	**2.1 L/day (about 8 cups)**
31–50 yr	**2.8 L/day**	**2.1 L/day (about 8 cups)**
51–70 yr	**2.8 L/day**	**2.1 L/day (about 8 cups)**
>70 yr	**2.8 L/day**	**2.1 L/day (about 8 cups)**

***Rationale*:** Intakes for adults were based on the median intake from the National Nutrition Survey of Australia, 1995 (ABS 1998). The NNS showed that for adults, some 75% of water intake came from beverages (alcoholic and non-alcoholic) and milk, leaving 25% from foods. The AIs for men and women were set at the level of the highest median intake from any of the four age categories for each gender. Adults living and or working in extremely hot climates may require higher than AI amounts to remain hydrated, especially if they are very active.

Pregnancy	AI	Water
	Total water (Food and fluids)	**Fluids (Including plain water, milk and other drinks)**
14–18 yr	**2.4 L/day**	**1.8 L/day (about 7 cups)**
19–30 yr	**3.1 L/day**	**2.3 L/day (about 9 cups)**
31–50 yr	**3.1 L/day**	**2.3 L/day (about 9 cups)**

***Rationale*:** A pregnant woman has slightly increased water requirements because of expanding extracellular fluid space, the needs of the fetus and the amniotic fluid. While there are differences in plasma osmolality in pregnancy (Davison et al 1981, 1984, Lindheimer & Davison 1995) the differences are short-term and do not seem to relate to poor hydration. Thus, an AI was set based on median intakes in pregnancy. As there are few data for water intake in pregnancy in Australia and New Zealand, data were sourced from US surveys (FNB:IOM 2004) that showed an increase of approximately 10% in total water consumption. Women living and/or working in extremely hot climates may require higher than AI amounts to remain hydrated, especially if they are very active.

Lactation	AI	Water
	Total water (Food and fluids)	**Fluids (Including plain water, milk and other drinks)**
14–18 yr	**2.9 L/day**	**2.3 L/day (about 7 cups)**
19–30 yr	**3.5 L/day**	**2.6 L/day (about 9 cups)**
31–50 yr	**3.5 L/day**	**2.6 L/day (about 9 cups)**

***Rationale*:** There is no evidence that renal function and hydration are different in lactation. However, a lactating woman must replace fluid lost in breast milk. Water accounts for 87% of milk and the average milk production in the first six months of lactation is 0.78 L/day (equivalent to 0.70 L water). The increased total water need is therefore some 0.70 L/day above basic needs. Women living and/or working in extremely hot climates may require higher than AI amounts to remain hydrated, especially if they are very active.

UPPER LEVEL OF INTAKE - WATER

No upper level of intake has been set.

***Rationale*:** Excess water intake can cause hyponatremia, but this is a rare occurrence in the general population. There are no data on habitual consumption resulting in specified hazards in apparently healthy people. In addition, there is a significant self-regulation of excess water consumption in healthy people in temperate climates. Thus no UL for water has been set.

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VITAMINS

VITAMIN A

BACKGROUND

Vitamin A is a fat-soluble vitamin which helps maintain normal reproduction, vision and immune function. It comes in a number of forms (as retinol, retinal, retinoic acid or retinyl ester).

The term vitamin A is used in the context of dietary requirements to include provitamin A carotenoids that are dietary precursors of retinol. Of the many carotenoids in nature, several have provitamin A activity but food composition data are only readily available for α-carotene, β-carotene and β-cryptoxanthin. Preformed vitamin A is found only in animal-derived foods, whereas dietary carotenoids are found primarily in oils, fruits and vegetables.

Vitamin A intakes or requirements are generally expressed in terms of retinol equivalents (RE). One RE is defined as the biological activity associated with 1 µg of all-*trans* retinol. Although there is some ongoing discussion in the literature about the conversion rates for carotenes, 6 µg all-*trans* β-carotene and 12 µg of α-carotene, β-cryptoxanthin and other provitamin A carotenoids have been retained as the conversion figures as being equivalent to 1 RE. These traditional conversion rates align more with the sources of carotenes in the Australian and New Zealand diets. They are also in line with the most recent decision of the FAO, (FAO:WHO 2001) who concluded that the literature to date was insufficient to justify a change in conversion rates.

1 µg Retinol Equivalent	=	1 µg of all-*trans* retinol
	=	6 µg all-*trans* β-carotene
	=	12 µg of α-carotene, β-cryptoxanthin and other provitamin A carotenoids
1 International Unit (IU) retinol	=	0.3 µg Retinol Equivalents

Retinol is required for the integrity of epithelial cells throughout the body (Gudas et al 1994). Retinoic acid regulates the expression of various genes that encode structural proteins, enzymes, extracellular matrix proteins and retinol binding proteins and receptors. Retinoic acid plays an important role in embryonic development, particularly in the development of the spinal cord and vertebrae, limbs, heart, eye and ears (Morris-Kay & Sokolova 1996). It is also required to maintain differentiation of the cornea and conjunctiva, preventing xerophthalmia, as well as for photoreceptor rod and cone cells in the retina (Sommer & West 1996). The retinal form of vitamin A is also required by the eye to change light to neural signals for vision (Saari 1994). Retinol and its metabolites are necessary for maintenance of immune function (Katz et al 1987, Trechsel et al 1985, Zhao & Ross 1995).

An adequate supply of vitamin A also plays a role in preventing morbidity and mortality from infectious disease, particularly in children (Glasziou & Mackerras 1993). Infection and infestation can cause malabsorption of vitamin A (Mahalanabis et al 1979, Sivakumar & Reddy 1972, 1975). The matrix of foods eaten can affect the release of carotenoids from foods, however, processing of food (cutting up, cooking etc) greatly improves availability and thus absorption of carotenoids from foods (Micozzi et al 1992, Tang et al 2000, Torronen et al 1996). Some studies show improved absorption of carotenoids with increased fat intake (Jalal et al 1998, Reddy & Srikantia 1966, Roels et al 1963) but the data are not consistent (Borel et al 1997, Figuera et al 1969).

Positive interactions between iron or zinc status and vitamin A status have been reported in animal studies (Amine et al 1970, Rosales et al 1999) or within human population groups in developing countries (Bloem et al 1989) but the relevance to the Australia and New Zealand population is unclear. Deficiency can result in abnormal dark adaptation, followed by xerophthalmia but is uncommon in Australia and New Zealand. The New Zealand Children's Survey, 2002 (MOH 2003) did, however, state

that a significant proportion of Pacific children and Maori males might be at risk of inadequate intakes. Chronically high levels of alcohol ingestion can negatively affect vitamin A status through an effect on the liver (Wang 1999).

Vitamin A status has been assessed using a variety of indicators including a dark adaptation test (Carney & Russell 1980), a pupillary response test (Stewart & Young 1989), plasma retinol concentration (Underwood 1984), total liver reserves by isotope dilution (Bausch & Rietz 1977, Furr et al 1989), relative dose response methods (Amedee-Manesme et al 1984, 1987, Loerch et al 1979, Mobarhan et al 1981) and/or immune function assessment (Butera & Krakowka 1986, Carman et al 1989, 1992, Cohen & Elin 1974, Friedman & Sklan 1989, Smith et al 1987). However, these methods have limitations in the context of setting EARs for the population. They are too specific (ie only related to visual outcomes), accurate only across a limited intake range or susceptible to confounding (FNB:IOM 2001).

The method used to set the EARs in the current document was thus based on an estimate of the amount of dietary vitamin A required to maintain a given body-pool size in well-nourished subjects (Olson 1987, FNB:IOM 2001). The modifications to this approach that were needed to determine requirements for specific age groups or for pregnancy and lactation are noted below.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Vitamin A**
0–6 months	**250 µg/day of retinol (as retinyl esters)**	
7–12 months	**430 µg/day of retinol equivalents (REs)**	

***Rationale*:** The AI for 0–6 months of 250 µg retinol as retinyl esters is calculated from multiplying the average intake of breast milk (0.78 L/day) by the average concentration of retinol present as retinyl esters in human milk, 310 µg/L, (Canfield et al 2003) to give 242 µg retinol, and rounding up. It assumes no contribution from carotenes in breast milk. For 7–12 months, the equivalent calculation is average intake of breast milk (0.6 L/day) x concentration of retinol (310 µg/L) plus a contribution of 244 µg from complementary foods that includes some contribution from carotenes, giving an AI of 430 RE.

Children & adolescents	**EAR**	**RDI**	**Vitamin A (as retinol equivalents)**
All			
1–3 yr	**210 µg/day**	**300 µg/day**	
4–8 yr	**275 µg/day**	**400 µg/day**	
Boys			
9–13 yr	**445 µg/day**	**600 µg/day**	
14–18 yr	**630 µg/day**	**900 µg/day**	
Girls			
9–13 yr	**420 µg/day**	**600 µg/day**	
14–18 yr	**485 µg/day**	**700 µg/day**	

***Rationale*:** No data are available to estimate average requirement of children and adolescents. The computational method used by the US:Canadian DRI committee (FNB:IOM 2001) was adopted for setting the EAR. The RDI was set by using a CV for the EAR of 20% based on calculated half-life values for liver vitamin A and rounded to the nearest 100 µg.

Adults	EAR	RDI	Vitamin A (as retinol equivalents)
Men			
19–30 yr	**625 µg/day**	**900 µg/day**	
31–50 yr	**625 µg/day**	**900 µg/day**	
51–70 yr	**625 µg/day**	**900 µg/day**	
>70 yr	**625 µg/day**	**900 µg/day**	
Women			
19–30 yr	**500 µg/day**	**700 µg/day**	
31–50 yr	**500 µg/day**	**700 µg/day**	
51–70 yr	**500 µg/day**	**700 µg/day**	
>70 yr	**500 µg/day**	**700 µg/day**	

***Rationale*:** The computational approach of the US:Canadian DRI committee (FNB:IOM 2001) was adopted. This is based on the amount of dietary vitamin A required to maintain a given body-pool size in well-nourished subjects.

The formula used was: Average requirement = A x B x C x D x E x F where:

A = % body vitamin A stores lost per day when ingesting a vitamin A-free diet, B = minimum acceptable liver vitamin A reserve, C = liver weight:body weight ratio, D = reference weight for a specific age group and gender, E = ratio of total body:liver vitamin A reserves and F = efficiency of storage of ingested vitamin A. The RDI was set using a CV of 20% for the EAR, with rounding to the nearest 100 µg.

Pregnancy	EAR	RDI	Vitamin A (as retinol equivalents)
14–18 yr	**530 µg/day**	**700 µg/day**	
19–30 yr	**550 µg/day**	**800 µg/day**	
31–50 yr	**550 µg/day**	**800 µg/day**	

***Rationale*:** Direct studies are lacking. The model used to set the EAR is the US:Canadian DRI approach based on the accumulation of vitamin A in the liver of the fetus during gestation and an assumption that liver contains approximately 50% of the body's vitamin A when liver stores are low, as for newborns. The RDI was set on the basis of a CV of 20% for the EAR with rounding to the nearest 100 µg.

Lactation	EAR	RDI	Vitamin A (as retinol equivalents)
14–18 yr	**780 µg/day**	**1,100 µg/day**	
19–30 yr	**800 µg/day**	**1,100 µg/day**	
31–50 yr	**800 µg/day**	**1,100 µg/day**	

***Rationale*:** An average of 250 µg/day retinol (AI for infants 0–6 months) is added to the EAR for non-pregnant adolescent girls and women. The RDI was set assuming a CV of 20% for the EAR, with rounding to the nearest 100 µg.

UPPER LEVEL OF INTAKE - VITAMIN A AS RETINOL

Infants	
0–12 months	**600 µg/day**
Children and adolescents	
1–3 yr	**600 µg/day**
4–8 yr	**900 µg/day**
9–13 yr	**1,700 µg/day**
14–18 yr	**2,800 µg/day**
Adults 19+ yr	
Men	**3,000 µg/day**
Women	**3,000 µg/day**
Pregnancy	
14–18 yr	**2,800 µg/day**
19–50 yr	**3,000 µg/day**
Lactation	
14–18 yr	**2,800 µg/day**
19–50 yr	**3,000 µg/day**

***Rationale*:** The UL is set based on causality, quality and completeness of available data. The critical adverse event used for women of childbearing age was teratogenicity and for other adults it was liver abnormalities, notably abnormal liver pathology (FNB:IOM 2001). For infants, reports of hypervitaminosis A were used to derive the UL. There was a paucity of evidence for children and adolescents, so the UL was determined by extrapolation from adult data on the basis of relative body weight.

Those with high alcohol intake, pre-existing liver disease, hyperlipidaemia or severe protein malnutrition may be particularly susceptible to excess intake of preformed vitamin A and may not be protected by the UL for the general population.

UPPER LEVEL OF INTAKE - BETA-CAROTENE

The UL for β-carotene cannot be established for supplemental use and does not need to be established for food use.

***Rationale*:** Although β-carotene is a precursor of vitamin A, excess intake has not been associated with vitamin A toxicity in humans as the metabolic conversion of β-carotene is regulated by vitamin A status. Beta-carotene is of low toxicity in both animals and humans. Until recently, β-carotene was thought to be without adverse effect other than a yellowing of the skin that occurred after sustained high intake. However, human studies in the 1990s have indicated that excess intake through supplements (20 mg/day or more) by smokers and subjects previously exposed to asbestos has been associated with an increased risk of lung cancer (ATBC trial 1994, Omenn et al 1996). However, there is insufficient scientific basis to set a precise figure for an UL for β-carotene, as no dose-response relationship for the observed effects is available either from the intervention trials in humans or from appropriate animal models (FNB:IOM 2000, European Commission 2000).

In conclusion, there is insufficient evidence to establish a UL for β-carotene for supplemental use, but high intakes can cause yellowing of the skin and may be harmful to smokers. A UL for β-carotene from food does not need to be established, based on an absence of adverse effects.

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THIAMIN

BACKGROUND

Thiamin is a water-soluble substance that occurs in free or phosphorylated forms in most plant and animal tissue. It plays an essential role in the supply of energy to the tissue, in carbohydrate metabolism and in the metabolic links between carbohydrate, protein and fat metabolism. Following ingestion, absorption of thiamin occurs mainly in the jejunum, actively at low concentrations and passively at high concentrations. It is transported in blood in both plasma and red blood cells. If intake is high, only a small amount of the thiamin is absorbed and elevated serum values result in active urinary excretion (Davis et al 1984). The total body content of the vitamin is about 30 mg.

Although there is a lack of direct evidence, it is thought that a relationship exists between thiamin requirement, energy supply and energy expenditure. This arises from the role of thiamin as thiamin pyrophosphate in the metabolism of carbohydrate. Thus a small adjustment (about 10%) to estimated requirements is often made to reflect differing body size and energy requirements between genders and in physiological states such as pregnancy and lactation.

Thiamin is found predominantly in cereal foods. There is mandatory thiamin enrichment of baking flour in Australia but not in New Zealand. There is little information about the bioavailability of thiamin. It has been shown that absorption does not differ from supplements given with breakfast or on an empty stomach (Levy & Hewitt 1971).

Low levels of thiamin intake may be associated with biochemical and possibly clinical evidence of thiamin depletion. The early stages of deficiency, however, may be overlooked (Lonsdale & Shamberger 1980) as signs are non-specific. The two distinct major diseases from deficiency of thiamin are beri beri and Wernicke-Korsakoff syndrome. They do not usually occur together.

Beri beri is now rare in countries where it was originally described – Japan, Indonesia and Malaysia – in those living on polished rice. In Western countries, occasional cases are seen in alcoholics. In acute beri beri there is a high output cardiac failure, warm extremities, bounding pulse, oedema and cardiac enlargement. These features appear to be the result of intense vasodilation from the accumulation of pyruvate and lactate in blood and tissues. There are few ECG abnormalities. Response to thiamin treatment is prompt, with diuresis and usually a full recovery. Chronic beri beri affects the peripheral nerves rather than the cardiovascular system. There is inability to lift the foot up (foot drop), loss of sensation in the feet and absent ankle reflexes.

Wernicke's encephalopathy is usually seen in people who have been drinking alcohol heavily and eating very little. Alcohol requires thiamin for its metabolism and alcoholic beverages do not contain it. Occasional cases are seen in people on a prolonged fast (such as hunger strikers) or with persistent vomiting (as in severe vomiting of pregnancy). Clinically, there is a state of quiet confusion, a lowered level of consciousness and ataxia. The characteristic feature is paralysis of one or more of the external movements of the eyes (ophthalmoplegia). This, and the lowered consciousness, respond to injection of thiamin within two days, but if treatment is delayed the memory may never recover. This memory disorder, with inability to retain new memories and sometimes confabulation, is called Korsakoff's psychosis after the Russian psychiatrist who first described it. Wernicke-Korsakoff syndrome (WKS) was apparently more common in Australia than other countries that fortified bread with thiamin. Since mandatory fortification of Australian bread with thiamin in 1991, WKS has become very uncommon (Truswell 2000).

It is not clear why one deficient person develops beri beri and another develops WKS or why the two deficiency diseases seldom occur together. Possibly acute beri beri occurs in people who use their muscles for heavy work and so accumulate large amounts of pyruvate, producing vasodilation and increased cardiac work, while encephalopathy is the first manifestation in inactive people.

There are several indicators for estimating requirements of thiamin (Brin 1970, Schrijver 1991, Wood et al 1980) including low urinary excretion; low erythrocyte transketolase activity; low erythrocyte thiamin or elevated thiamin pyrophosphate effect. Urinary thiamin is the most widely used indicator, but erythrocyte transketolase activity is regarded as the best functional test of thiamin status (McCormick & Greene 1994). However, erythrocyte transketolase activity has some limitations when setting an EAR, as it can be affected by factors other than diet. Erythrocyte thiamin is more stable in frozen erythrocytes, easier to standardise and less susceptible to other factors influencing enzyme activity (Baines & Davies 1988).

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Thiamin**
0–6 months	**0.2 mg/day**	
7–12 months	**0.3 mg/day**	

***Rationale*:** The AI for 0–6 months of 0.2 mg thiamin is calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of thiamin in human milk of 0.21 mg/L (Committee on Nutrition 1985), and rounding up. The FNB:IOM found that the AI estimate using intake data for thiamine for 7–12 months was unreasonably high when compared to extrapolation data from either younger infants or adults. Thus the AI for 7–12 months was extrapolated using a reference body weight method for younger infants (0.2 mg) or adults (0.3 mg) together with consideration of variance in the measures for adults. The greater of the two estimates was adopted.

Children & adolescents	**EAR**	**RDI**	**Thiamin**
All			
1–3 yr	**0.4 mg/day**	**0.5 mg/day**	
4–8 yr	**0.5 mg/day**	**0.6 mg/day**	
Boys			
9–13 yr	**0.7 mg/day**	**0.9 mg/day**	
14–18 yr	**1.0 mg/day**	**1.2 mg/day**	
Girls			
9–13 yr	**0.7 mg/day**	**0.9 mg/day**	
14–18 yr	**0.9 mg/day**	**1.1 mg/day**	

***Rationale*:** There is little direct evidence of requirements in children and adolescents so the EARs for these age groups were extrapolated from adult recommendations on a metabolic body weight basis including growth considerations (FNB:IOM 1998). The RDI was set assuming a CV of 10% for the EAR.

Adults	EAR	RDI	Thiamin
Men			
19–30 yr	**1.0 mg/day**	**1.2 mg/day**	
31–50 yr	**1.0 mg/day**	**1.2 mg/day**	
51–70 yr	**1.0 mg/day**	**1.2 mg/day**	
>70 yr	**1.0 mg/day**	**1.2 mg/day**	
Women			
19–30 yr	**0.9 mg/day**	**1.1 mg/day**	
31–50 yr	**0.9 mg/day**	**1.1 mg/day**	
51–70 yr	**0.9 mg/day**	**1.1 mg/day**	
>70 yr	**0.9 mg/day**	**1.1 mg/day**	

***Rationale*:** The EARs for adults were set on the basis of a number of metabolic studies using various endpoints (Anderson et al 1986, Bamji 1970, Brin 1962, Elsom et al 1942, FNB:IOM 1998Folz et al 1944, Henshaw et al 1970, Hoorn et al 1975, Horwitt et al 1948, Kraut et al 1966, Oldham 1962, Reuter et al 1967, Sauberlich et al 1979, Wood et al 1980, Ziporin et al 1965). Consideration of these studies indicated a requirement of at least 0.8 mg/day of thiamin with intakes of 1.0 mg/day being marginally adequate for normal transketolase activity and generally adequate for urinary thiamin excretion (FNB: IOM 1998). The EAR was thus set at 1.0 mg/day for men and 0.9 mg/day for women based on body size and energy needs. The RDI was set assuming a CV for the EAR of 10%. Despite reduced activity at older ages, maintenance of the same EARs and RDIs at this age is recommended as needs are higher. There may be increased needs for healthy people if they are engaged in strenuous occupations or in competitive athletics that demands continuous daily activity with high energy expenditure.

Pregnancy	EAR	RDI	Thiamin
14–18 yr	**1.2 mg/day**	**1.4 mg/day**	
19–30 yr	**1.2 mg/day**	**1.4 mg/day**	
31–50 yr	**1.2 mg/day**	**1.4 mg/day**	

***Rationale*:** In pregnancy, requirement is increased by about 30% based on maternal and fetal growth 20% and a 10% increase in energy use (Chong & Ho 1970, Daum et al 1948, Hathaway & Strom 1946, Heller et al 1974, Lockhart et al 1943, Oldham et al 1946, 1950, Slobody et al 1949, Tripathy 1968). This results in an increased requirement after rounding of 0.3 mg/day. The RDI was set assuming a CV for the EAR of 10%.

Lactation	EAR	RDI	Thiamin
14–18 yr	**1.2 mg/day**	**1.4 mg/day**	
19–30 yr	**1.2 mg/day**	**1.4 mg/day**	
31–50 yr	**1.2 mg/day**	**1.4 mg/day**	

***Rationale*:** Assuming an average milk production of 0.78 L/day, about 0.16 mg thiamin per day is transferred to breast milk (see infant recommendations). An additional 0.1 mg/day is also needed to cover the energy cost of milk production, giving an increased overall requirement of 0.26 mg/day compared to non-pregnant, non-lactating women (FNB:IOM 1998). With rounding this gives an EAR in lactation of 1.2 mg/day. The RDI was set assuming a CV of 10% for the EAR.

UPPER LEVEL OF INTAKE - THIAMIN

The upper level of intake of thiamin cannot be estimated.

There are no reports of adverse effects from consumption of excess thiamin by ingestion of food but there were reports from the 1940s of sensitivity to continuous high doses of oral thiamin in fortified foods or supplements (Laws 1941, Leitner 1943, Stein & Morgenstern 1944, Stiles 1941). There have also been reports of anaphylaxis and death after inappropriate parenteral administration (Reingold & Webb 1946, Schiff 1941, Stephen et al 1992) and of allergic sensitivity and pruritis with intramuscular administration (Royer-Morrot et al 1992, Wrenn et al 1989). However, there are insufficient data to estimate a UL. Existing evidence available from clinical studies as well as the long history of therapeutic use indicate that current levels of intake from thiamin from all sources do not represent a health risk for the general population.

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RIBOFLAVIN

BACKGROUND

Riboflavin is a water-soluble vitamin. The bioactive forms of riboflavin are the oxidised and reduced forms of flavin adenine dinucleotide (FAD and $FADH_2$, respectively) and flavin mononucleotide (FMN and $FMNH_2$, respectively) (FNB:IOM 1998, McCormick 2000, Thurnham 2000). They function as co-enzymes for key reactions in the catabolism of fuel molecules (eg β-oxidation of fatty acids, Krebs cycle), and in certain biosynthetic pathways (eg fatty acid synthesis). Riboflavin and its derivatives are important for the body's handling of some other nutrients including conversion of vitamin B-6 to its bioactive form, pyridoxal phosphate; conversion of tryptophan to niacin and conversion of methylenetet rahydrofolate (MTHF) to methylTHF by the enzyme methyleneTHF reductase (MTHFR).

As methylTHF is essential for the conversion of homocysteine to methionine, riboflavin deficiency can result in raised plasma levels of homocysteine that are associated with increased cardiovascular risk. A cross-sectional study (McNulty et al 2002) suggested that this association is much more likely to occur in individuals with the TT genetic variant of MTHFR (ie homozygous for the C677T polymorphism), which is found in about 12% of humans, than those with the CT or CC variants. Powers (2003) also noted that riboflavin deficiency is often associated with anaemia, which may result from problems in the body's handling of iron.

The metabolism of riboflavin is tightly controlled and depends on the riboflavin status of the individual (Lee & McCormick 1983). Riboflavin is converted to coenzymes mostly in the small intestine, liver, heart and kidney (Brown 1990, Darby 1981). Surplus riboflavin is excreted in urine, either as riboflavin itself (about two-thirds of total excretion) or as a range of metabolites. In deficiency, only small amounts are excreted.

Most of the riboflavin in our foods occurs as the nucleotides FAD/$FADH_2$ and FMN/$FMNH_2$ in a complex of food protein (Merrill et al 1981, Nicholalds 1981). This is released as free riboflavin by digestive enzymes in the small intestine and absorbed into the bloodstream. The major sources are milk and milk products and fortified breads and cereals. The bioavailability of riboflavin is high, probably about 95% (Zempleni et al 1996), but our capacity to absorb riboflavin from the small intestine is only moderate.

The classic disease of riboflavin deficiency is ariboflavinosis, which manifests in growth disturbances, seborrhaeic dermatitis, inflammation of the oral mucosa and tongue, cracks at the corner of the mouth and normocytic anaemia (Wilson 1983).

A range of indicators has been used to assess riboflavin status. These include clinical assessment of the classic physical symptoms of deficiency indicating severe deficiency, urinary excretion of riboflavin, erythrocyte flavin levels and determination of the erythrocyte glutathione reductase activity coefficient (EGRAC) in which erythrocyte glutathione reductase is assayed in the presence and absence of added FAD to establish an in vitro activity coefficient. This value provides an indirect indicator of cellular FAD levels and, by extrapolation, an indicator of whole body riboflavin status. Unfortunately, different studies have used different reference ranges for EGRAC. All of these methods are reasonably satisfactory indicators (Hustad et al 2002), however erythrocyte flavin has not been widely used.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Riboflavin**
0–6 months	**0.3 mg/day**	
7–12 months	**0.4 mg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of riboflavin in breast milk (0.35 mg/L) from the studies of Roughead & McCormick (1990) and WHO (1965), and rounding (FNB:IOM 1998). The FNM: IOM found that the AI estimate using intake data for thiamine for 7–12 months were unreasonably high when compared to extrapolation data from either younger infants or adults. The AI for 7–12 months was derived from estimating requirements on a body weight basis from the value for younger infants of 0.35 mg/day and from adults, using a metabolic weight ratio, including consideration for growth (0.35 mg/day) and rounding.

Children & adolescents	**EAR**	**RDI**	**Riboflavin**
All			
1–3 yr	**0.4 mg/day**	**0.5 mg/day**	
4–8 yr	**0.5 mg/day**	**0.6 mg/day**	
Boys			
9–13 yr	**0.8 mg/day**	**0.9 mg/day**	
14–18 yr	**1.1 mg/day**	**1.3 mg/day**	
Girls			
9–13 yr	**0.8 mg/day**	**0.9 mg/day**	
14–18 yr	**0.9 mg/day**	**1.1 mg/day**	

***Rationale*:** As there are limited data specific to these age groups, EARs were derived from the adult recommendations using a metabolic body weight ratio estimate including an allowance for growth. The RDI was set assuming a CV of 10% for the EAR.

Adults	**EAR**	**RDI**	**Riboflavin**
Men			
19–30 yr	**1.1 mg/day**	**1.3 mg/day**	
31–50 yr	**1.1 mg/day**	**1.3 mg/day**	
51–70 yr	**1.1 mg/day**	**1.3 mg/day**	
>70 yr	**1.3 mg/day**	**1.6 mg/day**	
Women			
19–30 yr	**0.9 mg/day**	**1.1 mg/day**	
31–50 yr	**0.9 mg/day**	**1.1 mg/day**	
51–70 yr	**0.9 mg/day**	**1.1 mg/day**	
>70 yr	**1.1 mg/day**	**1.3 mg/day**	

***Rationale*:** The EARs for adults from 19–70 years were based on a series of studies addressing clinical deficiency signs and biochemical markers, including EGRAC, in relation to measured dietary intake (Belko et al 1983, Bessey et al 1956, Boisvert et al 1993, Brewer et al 1946, Davis et al 1946, Horwitt et al 1949, 1950, Keys et al 1944, Kuizon et al 1992, Roe et al 1982, Sebrell et al 1941, Williams et al 1943). The RDI was derived assuming a CV of 10% for the EAR (FNB:IOM 1998).

As energy expenditure decreases with age, it would be expected that the EAR for older people may also decrease. However two studies question this assumption. Boisvert et al (1993) showed that for elderly Guatemalans, normalisation of EGRAC was achieved with 1.3 mg/day riboflavin and that a sharp increase in urinary riboflavin occurred at intakes above 1.0–1.1 mg/day, suggesting that needs were similar to those of younger adults.

A well-controlled UK study of free-living (ie not in residential care) elderly people over 65 years (Madigan et al 1998) showed that in a population where nearly all subjects had intakes above 1.3 mg/day for men and 1.1 mg/day for women, 12% were deficient (>1.4 EGRAC) and a further 33% had low riboflavin status. Thus the EAR for the elderly was set at 1.3 mg/day for men and 1.1 mg/day for elderly women. The RDI was set assuming a CV of 10% for the EAR.

Pregnancy	**EAR**	**RDI**	**Riboflavin**
14–18 yr	**1.2 mg/day**	**1.4 mg/day**	
19–30 yr	**1.2 mg/day**	**1.4 mg/day**	
31–50 yr	**1.2 mg/day**	**1.4 mg/day**	

***Rationale*:** In pregnancy, an additional requirement of 0.3 mg/day is estimated based on increased growth in maternal and fetal tissues and an increase in energy expenditure (FNB:IOM 1998). This added to the requirement for non-pregnant women to give an EAR of 1.2 mg/day. The RDI was set assuming a CV of 10% for the EAR.

Lactation	**EAR**	**RDI**	**Riboflavin**
14–18 yr	**1.3 mg/day**	**1.6 mg/day**	
19–30 yr	**1.3 mg/day**	**1.6 mg/day**	
31–50 yr	**1.3 mg/day**	**1.6 mg/day**	

***Rationale*:** In lactation it is assumed that 0.3 mg/day of riboflavin is transferred into milk. Use of riboflavin for milk production is estimated as 70% (WHO 1965) meaning that 0.4 mg/day is required. This amount is added to the EAR recommended for non-pregnant, non-lactating women and the RDI is set by assuming a CV of 10% for the EAR.

UPPER LEVEL OF INTAKE - RIBOFLAVIN

The upper level of intake cannot be estimated.

No adverse events have been associated with riboflavin consumption as food or supplements so no upper level of intake can be set. Studies using large doses of riboflavin have been undertaken, but they were not designed to assess adverse effects systematically (Schoenen et al 1998, Stripp 1965, Zempleni et al 1996). The only evidence of adverse effects comes from in vitro studies indicating a potential increase in photosensitivity to ultraviolet radiation (Ali et al 1991, Floersheim 1994, Spector et al 1995).

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NIACIN

BACKGROUND

Niacin is a generic descriptor for the closely related compounds, nicotinic acid and its amide nicotinamide, which act similarly as nutrients. The amino acid tryptophan is converted to nicotinamide with an average conversion efficiency of 60:1 and can thus contribute to requirements (Horwitt et al 1981) although this can vary depending on a number of dietary and metabolic factors (McCormick 1988).

> Niacin intakes and requirements are often expressed as niacin equivalents where 1 mg niacin equivalent is equal to 1 mg niacin or 60 mg tryptophan.

Niacin functions as a component of the reduced and oxidised forms of the coenzyme nicotinamide adenine dinucleotide ($NADH_2$ and NAD, respectively), both of which are involved in energy metabolism, and nicotinamide adenine dinucleotide phosphate ($NADPH_2$ and NADP, respectively). These coenzymes function in dehydrogenase-reductase systems involving the transfer of a hydride ion (McCormick 1988, 1997). NAD is also needed for non-redox adenosine diphosphate-ribose transfer reactions involved in DNA repair and calcium mobilisation. It functions as part of the intracellular respiration system and with enzymes involved in oxidation of fuel substrates. Because of their role in energy metabolism, niacin requirements are, to some extent, related to energy requirements

Niacin is found in a wide range of foods. Important sources of preformed niacin include beef, pork, wholegrain cereals, eggs and cow's milk. Human milk contains a higher concentration of niacin than cows' milk. In unprepared foods, niacin is present mainly as cellular NAD and NADP. Enzymatic hydrolysis of the coenzymes can occur during the course of food preparation. In mature grains, most of the niacin is bound and is thus only 30% available, although alkali treatment of grain increases availability (Carpenter & Lewin 1985, Carter & Carpenter 1982). The niacin in meats is in the form of NAD and NADP and is more bioavailable. Some foods, such as beans and liver, contain niacin in the free form that is highly available.

The requirement for preformed niacin depends to some extent on the availability of tryptophan. Inadequate iron, riboflavin or vitamin B_6 status decreases the conversion of tryptophan to niacin (McCormick 1989).

Deficiency of niacin causes the disease pellagra which is associated with inflammation of the skin on exposure to sunlight, resembling severe sunburn except that the affected skin is sharply demarcated (McCormick 1988, 1997). These skin lesions progress to pigmentation, cracking and peeling. Often the skin of the neck is involved. Pellagra is the disease of 'three Ds', namely dermatitis, diarrhoea and (in severe cases) delirium or dementia. There is also likely to be an inflamed tongue (glossitis). In mild chronic cases, mental symptoms are not prominent. Pellagra was a major problem in the Southern states of the US in poor Blacks and Whites whose diet consisted of maize (American corn) and little else. Unlike other cereals maize is low in bioavailable niacin and tryptophan is the first limiting amino acid. Pellagra only disappeared after niacin was discovered and mandatory fortification of maize meal was introduced in 1941.

Indicators that have been used to assess niacin requirements include urinary excretion, plasma concentrations, erythrocyte pyridine nucleotides, transfer of adenosine diphosphate ribose and appearance of pellagra. Biochemical changes appear well before overt signs of deficiency. The most reliable and sensitive measures are urinary excretion of N1-methyl nicotinamide and its derivative, N1-methyl-2-pyridone-5-carboxyamide.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	AI	Niacin
0–6 months	**2 mg/day of preformed niacin**	
7–12 months	**4 mg/day of niacin equivalents**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of niacin in breast milk, and rounding (FNB:IOM 1998). The figure for breast milk concentration of preformed niacin used was 1.8 mg/L based on the studies of Ford et al (1983). The tryptophan content of breast milk is 210 mg/L (Committee on Nutrition, 1985). The standard conversion rate is likely to overestimate tryptophan conversion from milk because of the high protein turnover and the net positive nitrogen retention in infancy. The AI was therefore set on the preformed niacin figure and rounded up. Because of limited data, the AI for 7–12 months was derived from the recommended intake for adults on a body weight basis accounting for growth needs and as such is expressed on a niacin equivalence base.

Children & adolescents	EAR	RDI	Niacin (as niacin equivalents)
All			
1–3 yr	**5 mg/day**	**6 mg/day**	
4–8 yr	**6 mg/day**	**8 mg/day**	
Boys			
9–13 yr	**9 mg/day**	**12 mg/day**	
14–18 yr	**12 mg/day**	**16 mg/day**	
Girls			
9–13 yr	**9 mg/day**	**12 mg/day**	
14–18 yr	**11 mg/day**	**14 mg/day**	

***Rationale*:** As there are limited data to set an EAR for these ages, the children's and adolescents' EARs were set by extrapolation from the adult data on a body weight basis accounting for growth needs (FNB:IOM 1998). The RDI was set using a CV of 15% for the EAR.

Adults	EAR	RDI	Niacin (as niacin equivalents)
Men			
19–30 yr	**12 mg/day**	**16 mg/day**	
31–50 yr	**12 mg/day**	**16 mg/day**	
51–70 yr	**12 mg/day**	**16 mg/day**	
>70 yr	**12 mg/day**	**16 mg/day**	
Women			
19–30 yr	**11 mg/day**	**14 mg/day**	
31–50 yr	**11 mg/day**	**14 mg/day**	
51–70 yr	**11 mg/day**	**14 mg/day**	
>70 yr	**11 mg/day**	**14 mg/day**	

***Rationale*:** The EAR for adults was set on a number of studies of niacin intake and urine N_1-methylnicotinamide (Goldsmith et al 1952, 1955, Horwitt et al 1956, Jacob et al 1989) with a 10% decrease for energy in women (FNB:IOM 1998). The RDI was set using a CV of 15% for the EAR derived from these studies.

Pregnancy	**EAR**	**RDI**	**Niacin (as niacin equivalents)**
14–18 yr	**14 mg/day**	**18 mg/day**	
19–30 yr	**14 mg/day**	**18 mg/day**	
31–50 yr	**14 mg/day**	**18 mg/day**	

***Rationale*:** There is no direct evidence to suggest a change in requirements in pregnancy, but an additional 3 mg/day would be needed to cover increased energy utilisation and growth (FNB:IOM 1998). This was added to the unrounded EAR for non pregnant women and the RDI was derived assuming a CV of 15% for the EAR.

Lactation	**EAR**	**RDI**	**Niacin (as niacin equivalents)**
14–18 yr	**13 mg/day**	**17 mg/day**	
19–30 yr	**13 mg/day**	**17 mg/day**	
31–50 yr	**13 mg/day**	**17 mg/day**	

***Rationale*:** An extra 1.4 mg of preformed niacin is secreted daily during lactation. This, together with the additional amount of 1 mg to cover additional energy needs, gives an additional 2.4 mg/day of niacin equivalents for women (FNB:IOM 1998). This was added to the unrounded EAR for non lactating women and the RDI was derived assuming a CV of 15% for the EAR.

UPPER LEVEL OF INTAKE - NIACIN AS NICOTINIC ACID

For intake from fortified foods or supplements

Infants	
0–12 months	**Not possible to establish; source of intake should be breast milk, formula or food only**
Children and adolescents	
1–3 yr	**10 mg/day**
4–8 yr	**15 mg/day**
9–13 yr	**20 mg/day**
14–18 yr	**30 mg/day**
Adults 19+ yr	
Men	**35 mg/day**
Women	**35 mg/day**
Pregnancy	
14–18 yr	**30 mg/day**
19–50 yr	**35 mg/day**

Lactation

14–18 yr	**30 mg/day**
19–50 yr	**35 mg/day**

***Rationale*:** There are no data to set a NOAEL. The data used to set an LOAEL for nicotinic acid were based on flushing reactions (FNB:IOM 1998). A LOAEL of 50 mg/day was set based on the study of Sebrell & Butler (1938) supported by data from Spies et al (1938). An uncertainty factor of 1.5 was selected as the flushing is transient. After rounding, a UL of 35 mg/day was therefore set for adults. The only reports of flushing associated with the ingestion of nicotinic acid with food have occurred following the addition of free nicotinic acid to the food prior to consumption. For infants, a UL could not be set as there were few data. No data were found to show that other age groups or physiological states had increased sensitivity, so the limits for pregnancy and lactation were set at those for other adults and the limits for children and adolescents were set on a body weight basis.

UPPER LEVEL OF INTAKE - NIACIN AS NICOTINAMIDE

For total intake from all sources

Infants

0–12 months	**Not possible to establish; source of intake should be breast milk, formula or food only**

Children and adolescents

1–3 yrs	**150 mg/day**
4–8 yrs	**250 mg/day**
9–13 yrs	**500 mg/day**
14–18 yrs	**750 mg/day**

Adults 19+ yrs

Men	**900 mg/day**
Women	**900 mg/day**

Pregnancy

14–18 yrs	**Not possible to establish, source of intake should be from food only**
19–50 yrs	**Not possible to establish, source of intake should be from food only**

Lactation

14–18 yrs	**Not possible to establish, source of intake should be from food only**
19–50 yrs	**Not possible to establish, source of intake should be from food only**

***Rationale*:** Nicotinamide is not a vasodilator (so does not cause the flushing that occurs with nicotinic acid) and has potential therapeutic value (Knopp 2000). For nicotinamide taken in supplemental form, a UL of 900 mg/day for men and non-pregnant, adult women is suggested. This is in line with recommendations from the European Commission (2002).

Large doses of nicotinamide (up to 3,000 mg/day for periods of up to 3 years) appear to be well tolerated, as reported in trials on the possible benefits of nicotinamide in patients with, or at risk of developing, diabetes. The NOAEL from these studies is approximately 1,800 mg/day. This value represents the lowest reported dose in a number of high quality trials of (Lampeter et al 1998, Pozilli

et al 1995). Many of these used sensitive biomarkers of hepatic function and glucose homeostasis, and included a range of age groups, with some subjects treated with up to 3,600 mg/day. A UF of 2 was used to allow for the fact that adults may eliminate nicotinamide more slowly than the study groups, many of which were children, and that data for children would not reflect the full extent of intersubject variability that could occur in an older population.

There is a lack of data on the safety of nicotinamide in pregnancy and lactation, and no relevant animal data. This level does not therefore apply to pregnant and lactating women.

Infants should get all their niacin from food, breast milk or formula only.

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VITAMIN B_6

BACKGROUND

Vitamin B_6 comprises six compounds – pyridoxal, pyridoxine, pyridoxamine and their respective 5' phosphates (see table below). It acts as a coenzyme in the metabolism of amino acids, glycogen and sphingoid bases. The most common form in human tissue is the 5'-phosphate form of pyridoxal (PLP) most of which is found in muscle bound to phosphorylase. The second most common is the 5'-phosphate form of pyridoxamine (PMP). Plant foods contain primarily pyridoxine (PN) and its 5'-phosphate (PNP), sometimes in the form of a glucoside.

Absorption in the gut involves phosphatase-mediated hydrolysis and transport of the non-phosphorylated form to the mucosal cells. Quite large doses of PLP and PMP are well absorbed (Hamm et al 1979). PN glucoside is less well absorbed. Most of the absorbed non-phosphorylated vitamin B_6 goes to the liver where conversion to the phosphorylated form occurs. The major excretory product is 4-pyridoxic acid that accounts for about half the B_6 compounds in urine (Shultz & Leklem 1981).

FORMS AND EQUIVALENCE OF VITAMIN B_6 COMPOUNDS

	Units of measurement		
Pyridoxine (PN)	1g = 5.9 mmol	1mmol = 170 mg	Three naturally inter-convertible forms in the tissues
Pyridoxal (PL)	1g = 6.0 mmol	1mmol = 167 mg	
Pyridoxamine (PM)	1g = 6.0 mmol	1mmol = 168 mg	
Pyridoxal-5-phosphate (PLP)	1g = 4.1 mmol	1mmol = 247 mg	Principal active form
4-Pyridoxic acid (4-PA)	1g = 5.5 mmol	1mmol = 183 mg	Principal excretory form
Pyridoxine hydrochloride (PN.HCl)	1g = 4.9 mmol	1mmol = 206 mg	Usual form of supplements

Vitamin B_6 is found in a wide range of foods including organ meats, muscle meats, breakfast cereals, vegetables and fruits. Bioavailability is generally in the region of 75% in a mixed diet (Tarr et al 1981). It has been proposed that vitamin B_6 requirements may be increased at higher protein intake (Baker et al 1964, Hansen et al 1996a, Linkswiler 1978), although other studies have not shown this (Pannemans et al 1994). Nevertheless, protein intake is generally taken into consideration in setting requirements for vitamin B_6.

Clinical deficiency is rare. The symptoms of deficiency include seborrhaeic dermatitis (Mueller & Vilter 1950), microcytic anaemia (Snyderman et al 1953), convulsions (Bessey et al 1957, Coursin 1954) and depression and confusion (Hawkins & Barsky 1948).

Indicators used to assess requirements have ranged from measures of vitamin concentrations in plasma, blood cell or urine to functional measures such as erythrocyte aminotransferase saturation by pyridoxal 5'-phosphate or tryptophan metabolites. Most of these indicators change with dietary intake, but there is little information about what level would indicate a deficiency state. A review (Lui et al 1985) suggested that plasma PLP is probably the best single indicator as it reflects tissue stores.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Vitamin B_6**
0–6months	**0.1 mg/day**	
7–12 months	**0.3 mg/day**	

***Rationale*:** The AI for 0–6 months is calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of vitamin B_6 present in human milk (0.13 mg/L) based on the studies of West & Kirksey (1976). For 7–12 months, the AI was extrapolated from that of the younger infants using a metabolic weight ratio (FNB:IOM 1998).

Children & adolescents	**EAR**	**RDI**	**Vitamin B_6**
All			
1–3 yr	**0.4 mg/day**	**0.5 mg/day**	
4–8 yr	**0.5 mg/day**	**0.6 mg/day**	
Boys			
9–13 yr	**0.8 mg/day**	**1.0 mg/day**	
14–18 yr	**1.1 mg/day**	**1.3 mg/day**	
Girls			
9–13 yr	**0.8 mg/day**	**1.0 mg/day**	
14–18 yr	**1.0 mg/day**	**1.2 mg/day**	

***Rationale*:** As there are few data on children and adolescents, the EARs were set based on the adult EARs adjusted for metabolic body weight and growth (FNB:IOM 1998). In the absence of information on the standard deviation of requirement, the RDI was set assuming a CV of 10% for the EAR.

Adults	**EAR**	**RDI**	**Vitamin B_6**
Men			
19–30 yr	**1.1 mg/day**	**1.3 mg/day**	
31–50 yr	**1.1 mg/day**	**1.3 mg/day**	
51–70 yr	**1.4 mg/day**	**1.7 mg/day**	
>70 yr	**1.4 mg/day**	**1.7 mg/day**	
Women			
19–30 yr	**1.1 mg/day**	**1.3 mg/day**	
31–50 yr	**1.1 mg/day**	**1.3 mg/day**	
51–70 yr	**1.3 mg/day**	**1.5 mg/day**	
>70 yr	**1.3 mg/day**	**1.5 mg/day**	

***Rationale*:** Clinical deficiency is rarely seen at intakes below 0.5 mg/day, but various depletion-repletion studies suggest an average daily requirement of 1.1 mg/day in younger men for maintenance of tissue stores, although the range of study results was quite wide (Baker et al 1964, FNB:IOM 1998, Linkswiler 1978, Miller & Linkswiler 1967, Miller et al 1985, Selhub et al 1993, Yess et al 1964). For younger women, the average requirement seems to be similar (Brown et al 1975, FNB:IOM 1998, Hansen et al 1996a,b, 1997, Huang et al 1998, Kretsch et al 1995). The EAR appears to be higher for older people (Madigan et al 1998) and men have higher requirements than women. The increase due to age and gender appears to be about 0.2 to 0.3 mg of food vitamin B_6 per day. RDIs for all groups were set assuming a CV of 10% for the EAR.

Pregnancy	EAR	RDI	Vitamin B_6
14–18 yr	**1.6 mg/day**	**1.9 mg/day**	
19–30 yr	**1.6 mg/day**	**1.9 mg/day**	
31–50 yr	**1.6 mg/day**	**1.9 mg/day**	

***Rationale*:** The EAR in pregnancy was based on additional requirements shown by studies of changes in plasma concentrations in pregnancy, fetal sequestration data and supplemental studies (Cleary et al 1975, Hamfelt & Tuvemo 1972, Contractor & Shane 1970, Shane & Contractor 1980, Lumeng et al 1976) that suggested that an additional allowance of 0.5 mg/day was justifiable. Because of the approximation of this figure, the adolescent EAR was set at the same level as that for older women. The RDI was set assuming a CV of 10% for the EAR.

Lactation	EAR	RDI	Vitamin B_6
14–18 yr	**1.7 mg/day**	**2.0 mg/day**	
19–30 yr	**1.7 mg/day**	**2.0 mg/day**	
31–50 yr	**1.7 mg/day**	**2.0 mg/day**	

***Rationale*:** The vitamin B_6 in breast milk varies according to maternal vitamin B_6 levels. The amount of vitamin B_6 required to increase breast milk by a small increment is much higher than that increment. Accordingly, the additional requirement in lactation is higher than that suggested by the amount secreted in milk (Borschel et al 1986, West & Kirksey 1976). To ensure a breast milk vitamin B_6 concentration of 0.13 mg/L, five times that amount must be consumed in addition to the EAR of 1.1 mg for non-lactating women. Because of the approximation of the estimate, the adolescent EAR was set as for older women. The RDI is set assuming a CV of 10% for the EAR.

UPPER LEVEL OF INTAKE - VITAMIN B_6 AS PYRIDOXINE

Infants	
0–12 months	**Not possible to establish; source of intake should be breast milk, formula or food only**
Children and adolescents	
1–3 yr	**15 mg/day**
4–8 yr	**20 mg/day**
9–13 yr	**30 mg/day**
14–18 yr	**40 mg/day**
Adults 19+ yr	
Men	**50 mg/day**
Women	**50 mg/day**
Pregnancy	
14–18 yr	**40 mg/day**
19–50 yr	**50 mg/day**
Lactation	
14–18 yr	**40 mg/day**
19–50 yr	**50 mg/day**

***Rationale*:** The ULs were set using results of studies involving long-term oral administration of pyridoxine at doses of less than 1g/day (Berger & Schaumburg 1984, Bernstein & Lobitz 1988, Dalton 1985, Dalton & Dalton 1987, Del Tredici et al 1985, FNB:IOM 1998, Parry & Bredesen 1985). A NOAEL of 200 mg/day was identified from the studies of Bernstein & Lobitz (1988) and Del Tredici et al (1985). These studies involved subjects who had generally been on the supplements for 5 to 6 months or less. The study of Dalton and Dalton (1987), however, suggested that symptoms might take substantially longer than this to appear. In this latter retrospective survey, subjects who reported symptoms had been on supplements for 2.9 years on average. Those reporting no symptoms had taken supplements for 1.9 years. Symptoms disappeared 6 months after cessation of supplements. Given these findings, a UF of 4 was used to derive the UL based on the limitations of the data involving pyridoxine doses of less than 500 mg/day (Berger & Schaumburg 1984, Parry & Bredesen 1985, Dalton 1985, Dalton & Dalton 1987, FNB:IOM 1998) and the limited duration of the studies. The UL for adults was thus set at 50 mg/day. The same figure was set for pregnancy and lactation as there is no evidence of teratogenicity at this level. The UL was set based on metabolic body size and growth considerations for all other ages and life stages except infancy. It was not possible to set a UL for infants, so intake is recommended in the form of food, milk or formula.

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VITAMIN B_{12}

BACKGROUND

Vitamin B_{12} is the generic descriptor for those corrinoid compounds exhibiting qualitatively the biological activity of cyanocobalamin. The main cobalamins with physiological action are hydroxycobalamin, methylcobalamin and deoxyadenosylcobalamin. Vitamin B_{12} is required for the synthesis of fatty acids in myelin and, in conjunction with folate, for DNA synthesis. Adequate intake of vitamin B_{12} is essential for normal blood function and neurological function. It can be stored in the liver for many years.

Vitamin B_{12} can be converted to either of the two cobalamin coenzymes that are active in humans; methylcobalamin and 5-deoxyadenosylcobalamin. Vitamin B_{12} is a cofactor for the enzymes methionine synthase and L-methylmalonyl-CoA mutase and is involved in the conversion of homocysteine to methionine and of L-methylmalonyl-coenzyme A (CoA) to succinyl-CoA. In vitamin B_{12} deficiency, folate may accumulate in serum as a result of slowing of the vitamin B_{12}-dependent methyltransferase.

Whilst there are some plant-based sources of vitamin B_{12}, such as certain algae and plants exposed to bacterial action or contaminated by soil or insects, humans obtain almost all of their vitamin B_{12} from animal foods. About 25% of vitamin B_{12} comes from red meats (Baghurst et al 2000). For adults and children, about 30% and 50%, respectively, is from milk and dairy products (Cobiac et al 1999).

Absorption of vitamin B_{12} is now known to be more complex than was once thought. In foods, methyl-, deoxyadenosyl-, or hydroxocobalamin are bound to enzymes in meat and other animal foods. The cobalamin is released by the action of acid and pepsin that digest the binding protein in the (normal) stomach. The freed cobalamin forms a stable complex with R binder, a glycoprotein secreted in saliva or by the stomach. Meanwhile, intrinsic factor (IF), a 50 kDa glycoprotein that binds cobalamin, is secreted after a meal by the parietal cells of the stomach. However, the binding of cobalamin to IF does not take place in the stomach as was once thought because its affinity is very low at acid pH.

The R binders are partly degraded in the duodenum by pancreatic proteases. The cobalamin then binds IF with high affinity in the more alkaline environment. Unlike R binders, IF is not digested by pancreatic enzymes. Vitamin B_{12} from the bile duct can also combine with IF, forming an enterohepatic cycle. The vitamin B_{12}-IF complex then passes unchanged down the small intestine and is absorbed in the terminal ileum by endocytosis after attachment to a specific 460 kDa IF membrane receptor. The receptor only binds vitamin B_{12} that is attached to IF and does not bind vitamin B_{12} analogues.

Vitamin B_{12} absorption increases with increasing intake (Adams et al 1971, Chanarin 1979). It is absorbed at varying rates from different foods ranging from 11% from liver, 24–40% from eggs and trout, to more than 60% from mutton and chicken (Doscherholmen et al 1975, 1978, 1981, Heyssel et al 1966). The low absorption rate from liver probably relates to the liver's very high content of B_{12}. No studies have been reported on red meat, pork or dairy foods or fish other than trout, so a conservative adjustment for bioavailability of 50% for healthy adults with normal gastric function was assumed in developing the intake requirements. If people consumed large amounts of foods naturally rich in vitamin B_{12}, the absorption rate would be lower.

Vitamin B_{12} added to foods (eg beverages, meat analogues or soy milks) in crystalline form has a similar absorption rate if added in low amounts (<5 µg per dose), but very low absorption (1% or less) if added at 500 µg per dose or above (Berlin et al 1968, Heyssel et al 1996). Excretion of vitamin B_{12} is generally through the faeces and is proportional to body stores (Adams 1970, Heinrich 1964, Mollin & Ross 1952). Other losses occur through the skin and through metabolic reactions.

Requirements for vitamin B_{12} can be affected by age, although not all studies confirm this (van Asselt et al 1996). The age effect may act through the influence of increasing levels of atrophic gastritis (Krasinski et al1986) or reduced gastric acidity (Scarlett et al 1992). Rates of atrophic gastritis in the elderly ranging from 10-30% have been reported in Australia (Andrews et al 1967), the US (Hurwitz et al 1997, Krasinski et al 1986) and Scandinavia (Johnsen et al 1991).

Under utilisation of vitamin B_{12} may occur in those with genetic defects including deletions or defects in MMA-CoA mutase, transcobalamin II or enzymes in the cobalamin adenosylation pathway.

Vitamin B_{12} deficiency can produce haematological, neurological or gut symptoms. The haematological effects are indistinguishable from folate deficiency. They include a range of effects generally associated with anaemia such as skin pallor, lowered energy and exercise tolerance, fatigue, shortness of breath and palpitations. The underlying problem is interference with DNA synthesis leading to production of abnormally large erythrocytes.

Neurological complications are present in about 75–90% of people with frank deficiency. These complications appear to be inversely related to the occurrence of the haematological symptoms (Healton et al 1991, Savage et al 1994). They include sensory disturbances in the extremities, motor disturbance and cognitive changes from memory loss to dementia, with or without mood change. There may also be visual disturbances, impotency and impaired bowel and bladder control. A study by Louwman et al (2000) indicated that cobalamin deficiency in the absence of haematological signs may also affect cognitive function in adolescence.

The indicators that are available for estimating requirements for vitamin B_{12} include haematological response as well as measures of serum or plasma vitamin B_{12}, MMA, homocysteine, formiminoglutamic acid, propionate and methylcitrate and holo-transcobalamin II.

Haematological responses that have been assessed include increases in haemoglobin, haematocrit and erythrocyte count or decreases in MCV or an optimal rise in reticulocyte numbers. Of these, MCV has limited use because of the 120 days needed to see change, and whilst erythrocyte, haemoglobin and haematocrit are robust they are slow to change. However, reticulocyte count is useful as increases in response to diet are apparent within 48 hours and reach a peak in 5–8 days.

Serum or plasma vitamin B_{12} reflects both intake and stores but acceptable levels can be maintained for some time after deficiency occurs because of compensatory release of vitamin B_{12} from tissues. Low levels would, however, represent long-term deficiency or chronic low intakes. MMA exhibits a four-fold range in the normal population but rises when the supply of vitamin B_{12} is low or when absorption is affected (Joosten et al 1996). Elevated MMA levels can be reduced by vitamin B_{12} administration (Joosten et al 1993, Naurath et al 1995, Norman & Morrison 1993, Pennypacker et al 1992).

As the presence of elevated MMA represents a vitamin B_{12}-specific change, MMA is the preferred indicator of vitamin B_{12} status. However, there are not sufficient data available to use MMA levels to set dietary recommendations. Homocysteine concentration does change in response to vitamin B_{12} status but it is not specific to vitamin B_{12}, responding also to folate or vitamin B_6 status or both, and formiminoglutamic acid also changes with folate status. Proprionate and methylcitrate both respond to changes in vitamin B_{12} status (Allen et al 1993), however they offer no advantages over MMA. Measures of holotranscobalamin II are insufficiently robust to allow the assessment of requirements.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Vitamin B_{12}**
0–6months	**0.4 µg/day**	
7–12 months	**0.5 µg/day**	

***Rationale*:** The AI for 0–6 months is based on the Vitamin B_{12} intake of infants fed breast milk. The AI was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of vitamin B_{12} in breast milk, and rounding (FNB:IOM 1998). Reported values of breast milk concentration vary widely, partly because of differences in analytical methods and partly because of variation in maternal vitamin B_{12} status and current intake. Median values are substantially lower than mean values. In a study of 9 well-fed Brazilian mothers whose infants were exclusively breastfed, the average concentration in breast milk was 0.42 µg/L at 2 months and 0.34 µg/L at 3 months (Trugo &

Sardinha 1994). The 2-month value was chosen to ensure adequate intake and multiplied by the daily milk volume (0.42 µg/L x 0.78 L/day = 0.33 µg/day) and rounded up to give the AI of 0.4 µg. As there are few data for the vitamin B_{12} content of weaning diets, the AI for 7–12 months was estimated by extrapolating up from the 0–6 month AI. This was cross-checked by extrapolating from the adult EAR and adjusting for the expected variance to estimate a recommended intake. The former estimate gave a value of 0.5 µg/day after rounding up and the latter, 0.6 µg/day. The AI was set at 0.5 µg/day.

***Note*:** To ensure adequate vitamin B_{12} status in their infants, and prevent severe outcomes including cognitive impairment or even coma in the infant, vegan mothers should supplement their diets with vitamin B_{12} at the RDI level throughout pregnancy and lactation on the basis of evidence that stores in infants of vegan mothers at birth are low and the milk may supply only very small amounts (Specker et al 1990). Soy formula used during weaning needs to be fortified with vitamin B_{12} to an equivalent level. If the mother is not supplemented in pregnancy and lactation and the child is breast fed, then the infant will need supplements from birth.

Children & adolescents	**EAR**	**RDI**	**Vitamin B_{12}**
All			
1–3 yr	**0.7 µg/day**	**0.9 µg/day**	
4–8 yr	**1.0 µg/day**	**1.2 µg/day**	
Boys			
9–13 yr	**1.5 µg/day**	**1.8 µg/day**	
14–18 yr	**2.0 µg/day**	**2.4 µg/day**	
Girls			
9–13 yr	**1.5 µg/day**	**1.8 µg/day**	
14–18 yr	**2.0 µg/day**	**2.4 µg/day**	

***Rationale*:** There are few data on children or adolescents on which to base the EAR so the EAR was set by extrapolation from adult data adjusting for body weight and with reference to growth needs, and rounding up (FNB:IOM 1998). In the absence of information on the standard deviation of the requirement, the RDI was set assuming a CV of 10% for the EAR. Note that vegan children will need supplementation.

Adults	**EAR**	**RDI**	**Vitamin B_{12}**
Men			
19-30 yr	**2.0 µg/day**	**2.4 µg/day**	
31-50 yr	**2.0 µg/day**	**2.4 µg/day**	
51-70 yr	**2.0 µg/day**	**2.4 µg/day**	
>70 yr	**2.0 µg/day**	**2.4 µg/day**	
Women			
19-30 yr	**2.0 µg/day**	**2.4 µg/day**	
31-50 yr	**2.0 µg/day**	**2.4 µg/day**	
51-70 yr	**2.0 µg/day**	**2.4 µg/day**	
>70 yr	**2.0 µg/day**	**2.4 µg/day**	

***Rationale*:** The EAR for adults was set on the basis of haematological evidence and serum vitamin B_{12} levels (FNB:IOM 1998). Sufficient data were not available to discern differences in requirements for men and women. In the absence of information on the standard deviation of the requirement, the RDI was set assuming a CV of 10% for the EAR. Note that strict vegans will need supplementation with vitamin B_{12}.

Note: The natural vitamin B_{12} in foods may be less bioavailable to the substantial number of older adults who have atrophic gastritis with low stomach acid secretion. People with this condition may require higher intakes of vitamin B_{12}-rich foods, vitamin B_{12}-fortified foods or supplements.

Pregnancy	**EAR**	**RDI**	**Vitamin B_{12}**
14–18 yr	**2.2 µg/day**	**2.6 µg/day**	
19–30 yr	**2.2 µg/day**	**2.6 µg/day**	
31–50 yr	**2.2 µg/day**	**2.6 µg/day**	

Rationale: The EAR was set on the basis of the maternal EAR plus an allowance for fetal and placental needs. Fetal accumulation averages 0.1–0.2 µg/day (Baker et al 1962, Loria et al 1977, Vaz Pinto et al 1975) but placental accumulation is only 14 ng/L (Muir & Landon 1985). An additional 0.2 µg/day was therefore added to the maternal requirement and the RDI was then derived assuming a CV of 10% for the EAR. Vegan mothers will need supplementation throughout pregnancy and during lactation in sufficient amounts to ensure adequate supplies for themselves and their child.

Lactation	**EAR**	**RDI**	**Vitamin B_{12}**
14–18 yr	**2.4 µg/day**	**2.8 µg/day**	
19–30 yr	**2.4 µg/day**	**2.8 µg/day**	
31–50 yr	**2.4 µg/day**	**2.8 µg/day**	

***Rationale*:** The EAR for lactation was set by adding the average amount secreted in milk (0.33 µg/day) to the maternal EAR, and rounding up. The RDI was set assuming a CV of 10% for the EAR. Vegan mothers will need supplementation in lactation in sufficient amounts to ensure adequate supplies for themselves and their child.

UPPER LEVEL OF INTAKE - VITAMIN B_{12}

There are insufficient data to allow setting of a UL.

There is no evidence that the current levels of intake from foods and supplements represent a health risk. No adverse effects have been associated with excess vitamin B_{12} intake from food or supplements in healthy individuals. There is weak evidence from animal studies that vitamin B_{12} may potentiate the effects of carcinogenic chemicals (Day et al 1950, Georgadze 1960, Kalnev et al 1977, Ostryanina 1971) but other studies contradict this (Rogers 1975). The apparent lack of toxicity could relate to the body's ability to decrease absorption in response to high intakes. As there are no dose-response data, no UL can be set.

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FOLATE

BACKGROUND

Folate is the commonly used group name for folic acid (pteroyl glutamic acid, or PGA) and its derivatives with similar activity. In foods and in the body folates are usually in the reduced form (tetrahydrofolate, or THF) and conjugated with up to seven glutamate residues and one of several types of one-carbon groups. PGA is used in supplements and for food fortification as it is more stable than the other derivatives.

Folate functions as a coenzyme in single-carbon transfers in the metabolism of nucleotides and amino acids. It is essential for the formation of thymidylate (TMP) for DNA synthesis, so that without folate, living cells cannot divide. The need for folate is higher when cell turnover is increased, such as in fetal development. It is also involved in purine synthesis, in the generation of formate and in amino acid interconversions. Homocysteine is methylated by methyl-THF to produce methionine, which is in turn used for the synthesis of *S*-adenosyl-methionine an important methylating agent *in vivo* (Wagner 1996).

Food folates are hydrolysed to monoglutamate forms in the gut to allow their absorption across the intestine. The monoglutamates enter the portal circulation and are metabolised to polyglutamate derivatives in the liver. They are either retained, or released to the blood as reconverted monoglutamates or to bile. The liver contains about 50% of the body stores of folate.

Folate is a substrate and vitamin B_{12} is a coenzyme for the formation of MTHF that depends on the regeneration of THF, the parent compound in the homocysteine-to-methionine conversion. If either folate or vitamin B_{12} is deficient, megaloblastic changes occur in bone marrow and other replicating cells from lack of 5,10-MTHF for DNA synthesis.

The bulk of excretion products are folate cleavage products. Intact urinary folate accounts for only a small percentage of dietary folate. Biliary excretion of folate can be as high as 100 µg/day (Herbert & Das 1993, Whitehead 1986), however much of this is reabsorbed.

Folate is difficult to measure in foods because it is present in different forms, so food databases can be inaccurate. However, the main sources of folate in Australia and New Zealand according to the National Nutrition Surveys undertaken in 1995 and 1997, respectively (ABS 1998, MOH 1999), are cereals, cereal products and dishes based on cereals (about 27%) and vegetables and legumes (about 29%). Fruit provides about 8–10%. Orange juice is contributing a greater amount than in the past due to the recent introduction of fortification with folate.

Folate requirements can be affected by bioavailability, nutrient interactions, smoking, certain drugs and genetic variations. Notably, the C667T polymorphism that causes MTHF reductase deficiency is found in 2–16% of white populations (van der Put et al 1995). It is likely that individuals who are homozygous for this polymorphism may have a higher requirement for folate.

Bioavailability of folates in food is about 50–60% whereas that of the folic acid used to fortify foods or as a supplement is about 85% (Sauberlich et al 1987, Gregory 1989, 1995, 1997, Pfeiffer et al 1997, Cuskelly et al 1996). Folic acid as a supplement is almost 100% bioavailable on an empty stomach. Picciano et al (2004) have recently demonstrated that the inclusion of cows' milk in the diet enhances the bioavailability of food folate as assessed by changes in erythrocyte folate and plasma total homocysteine concentrations, but not when assessed by plasma folate concentrations. Some controlled studies to assess requirements have used a defined diet containing food folate and supplemented with folic acid, so the term dietary folate equivalents (DFE) has been used to accommodate the varying bioavailabilities.

1 µg dietary folate equivalent (DFE)	= 1 µg food folate
	= 0.5 µg folic acid on an empty stomach
	= 0.6 µg folic acid with meals or as fortified foods

Inadequate folate intake leads to decreased serum folate, then decreased erythrocyte folate, a rise in homocysteine and megaloblastic changes in bone marrow and other rapidly dividing tissues (Eichner & Hillman 1971). As depletion progresses, macrocytic cells are produced and macrocytic anaemia develops. Eventually, full-blown anaemia results in weakness, fatigue, irritability and palpitations. Folic acid supplementation in pregnancy can reduce both the occurrence and recurrence of neural tube defects in the newborn (Bower & Stanley 1989, CDC 1992, Czeizel & Dudas 1992, Kirke et al 1993, Laurence et al 1981, Wald et al 1991).

Indicators of folate requirement include erythrocyte, serum or urinary folate, plasma homocysteine and haematological status measures as well as clinical endpoints such as neural tube defects or chronic degenerative disease. Of these, erythrocyte folate is generally regarded as the primary indicator as it reflects tissue folate stores. For some age groups, erythrocyte folate is used in conjunction with plasma homocysteine and plasma or serum folate.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Folate (as dietary folate equivalents)**
0–6 months	**65 µg/day (as folate)**	
7–12 months	**80 µg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of folate in breast milk of 85 µg/L (Asfour et al 1977, Ek & Magnus 1982, FNB:IOM 1998, Salmenpera et al 1986, Smith et al 1983, 1985), and rounding.

The AI for 7–12 months was set by the reference body weight ratio, estimating up from young infants or down from adults. Both estimates gave an AI of 80 µg/L which is also consistent with data for older, fully breast-fed or fully formula-fed infants in the studies of Asfour et al (1977), Ek & Magnus (1982), Salmenpera et al (1986) and Smith et al (1983).

Children & adolescents	**EAR**	**RDI**	**Folate (as dietary folate equivalents)**
All			
1–3 yr	**120 µg/day**	**150 µg/day**	
4–8 yr	**160 µg/day**	**200 µg/day**	
Boys			
9–13 yr	**250 µg/day**	**300 µg/day**	
14–18 yr	**330 µg/day**	**400 µg/day**	
Girls			
9–13 yr	**250 µg/day**	**300 µg/day**	
14–18 yr	**330 µg/day**	**400 µg/day**	

***Rationale*:** As there are no experimental data for children, the EARs were set by extrapolation from adult data using metabolic body weight ratios with an allowance for growth as per FNB:IOM (1998). In the absence of information on the standard deviation of the requirement, the RDI was set assuming a CV of 10% for the EAR.

Adults	**EAR**	**RDI**	**Folate (as dietary folate equivalents)**
Men			
19–30 yr	**320 µg/day**	**400 µg/day**	
31–50 yr	**320 µg/day**	**400 µg/day**	
51–70 yr	**320 µg/day**	**400 µg/day**	
>70 yr	**320 µg/day**	**400 µg/day**	
Women			
19–30 yr	**320 µg/day**	**400 µg/day**	
31–50 yr	**320 µg/day**	**400 µg/day**	
51–70 yr	**320 µg/day**	**400 µg/day**	
>70 yr	**320 µg/day**	**400 µg/day**	

***Rationale*:** The EAR for younger adults was set by reference to metabolic balance studies, notably the long term maintenance study in women that found no difference in mean final erythrocyte folate at 400 µg/day compared to 200–300 µg/day but a higher number of subjects with low erythrocyte folate, lower mean plasma folate and increased homocysteine levels (O'Keefe et al 1995). Other studies taken into account as cited in FNB:IOM (1998) were Herbert (1962a,b), Jacob et al (1994), Krumdieck et al (1978), Milne et al (1983), Sauberlich et al (1987), Stites et al (1997), von der Porten (1992) and Zalusky & Herbert (1961). For adults over 51 years, the requirements were based on metabolic, observational and epidemiological studies (Bates et al 1980, Garry et al 1982, Jagerstad 1977, Jagerstad & Westesson 1979, Koehler et al 1996, Ortega et al 1993, Rosenburg 1992, Sayoun 1992, Sayoun et al 1988, Selhub et al 1993, Tucker et al 1996, 1984).

In the absence of information on the SD of the requirement, the RDI was set assuming a CV of 10% for the EAR.

***Special note*:** Evidence about the levels of folic acid needed in women to prevent neural tube defects did not form the basis for the adult EARs and RDIs. Women capable of, or planning, pregnancies should consume additional folic acid as a supplement or in the form of fortified foods at a level of 400 µg/day folic acid for at least one month before and three months after conception, in addition to consuming food folate from a varied diet.

Pregnancy	**EAR**	**RDI**	**Folate (as dietary folate equivalents)**
14–18 yr	**520 µg/day**	**600 µg/day**	
19–30 yr	**520 µg/day**	**600 µg/day**	
31–50 yr	**520 µg/day**	**600 µg/day**	

***Rationale*:** Folate requirements increase substantially in pregnancy. This recommendation does not include consideration of additional needs to prevent neural tube defects as the neural tube is formed before most women know they are pregnant. The data indicate that maximal protection against NTD is obtained when the mother is consuming very high levels (5,000 µg) of folic acid as supplements, in the

month preceding conception and in the first trimester (Wald et al 2001). Recommendations are based on evidence from controlled metabolic studies (Caudill et al 1997) and a series of population studies (Chanarin et al 1968, Colman et al 1975, Dawson 1966, Hansen & Rybo 1967, Lowenstein et al 1966, Qvist et al 1986, Willoughby 1967, Willoughby & Jewel 1966). The RDI was estimated assuming a CV of 10% for the EAR.

Lactation	**EAR**	**RDI**	**Folate (as dietary folate equivalents)**
14–18 yr	**450 µg/day**	**500 µg/day**	
19–30 yr	**450 µg/day**	**500 µg/day**	
31–50 yr	**450 µg/day**	**500 µg/day**	

***Rationale*:** To estimate total folate requirement for lactation, the amount needed to provide sufficient breast milk folate (including a 50% bioavailability correction factor) was added to the EAR for adult women using the formula 0.78 L (volume) x 85 µg/L (concentration) x 2 (for bioavailability) = 133 µg/day (+ 320 µg/day). The RDI was estimated assuming a CV of 10% for the EAR.

UPPER LEVEL OF INTAKE - DIETARY FOLATE EQUIVALENTS

Infants	
0–12 months	**Not possible to establish for supplemental folic acid. Source of intake should be milk, formula and food only**
ULs from fortified foods or supplements	
Children and adolescents	
1–3 yr	**300 µg/day as folic acid**
4–8 yr	**400 µg/day as folic acid**
9–13 yr	**600 µg/day as folic acid**
14–18 yr	**800 µg/day as folic acid**
Adults 19+ yr	
Men	**1,000 µg/day as folic acid**
Women	**1,000 µg/day as folic acid**
Pregnancy	
14–18 yr	**800 µg/day as folic acid**
19–50 yr	**1,000 µg/day as folic acid**
Lactation	
14–18 yr	**800 µg/day as folic acid**
19–50 yr	**1,000 µg/day as folic acid**

***Rationale*:** No adverse effects have been associated with consumption of the amounts of dietary folate equivalents normally found in foods or fortified foods (Butterworth & Tamura 1989). High supplemental intakes of folic acid have been shown to be related to adverse neurological effects in people with B_{12} deficiency as they can precipitate or exacerbate the B_{12} deficiency (Israels & Wilkinson 1949, Schwartz et al 1950, Spies et al 1948, Will et al 1959). General toxicity (Hunter et al 1970), increased carcinogenesis (Selby et al 1989) and adverse reproductive and developmental effects have also been reported (Czeizel & Dudas 1992, Czeizel et al 1994, Holmes-Siedle et al 1992, Kirke et al 1992, Lawrence et al 1981, Mukerjee et al 1984, Smithells et al 1981, Vergel et al 1990, Wald et al 1991).

In line with the FNB:IOM (1998) findings, setting of the LOAEL was based on the neurological effects seen with B_{12} deficiency, as this is a fairly common deficiency in the population and as these data have some dose-response characteristics. A LOAEL of 5 mg/day was set on the basis of the studies described above, as there were 100 cases of neurological damage above this level but only 8 below. A UF of 5 was used as the dose-response data were not well controlled, the adverse effects are severe and a LOAEL only, rather than a NOAEL, was available.

The UL was therefore estimated to be 1 mg folic acid (1,000 µg)/day for adults. There are no data to suggest increased susceptibility in pregnancy or lactation, so the adult UL was applied to these groups as well. There is little direct evidence for other ages, so the UL was set on a relative body weight basis for children and adolescents. It was not possible to set a UL for infants.

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PANTOTHENIC ACID

BACKGROUND

Pantothenic acid is a component of coenzyme A (CoA) and phosphopantetheine, both of which are involved in fatty acid metabolism (Tahikliani & Beinlich 1991). It is essential to almost all forms of life and is widely distributed in foods. Chicken, beef, potatoes, oat-based cereals, tomato products, liver, kidney, egg yolks and whole grains are major sources in western diets (Plesofsky-Vig 1996, Walsh et al 1981). Little information is available about bioavailability, with estimates ranging from 40 to 61% (Tarr et al 1981). Neither is there much information about interactions with other nutrients, although there is some information that implies that thiamin, and to a lesser extent riboflavin, can affect pantothenate metabolism and excretion (Koyanagi et al 1969).

Absorption is by active transport at low concentrations and by passive transport at high concentrations. The active system can be saturated, so absorption is less efficient at higher intakes. Pantothenic acid can be synthesised by microbes but the extent to which this happens in man is unknown.

CoA is synthesised from pantothenate in a reaction catalysed by pantothenate kinase. In the form of acetyl CoA and succinyl CoA, CoA plays an important role in the synthesis of fatty acids and membrane phospholipids and also of amino acids, steroid hormones, vitamins A and D, porphyrin and corrin rings, and neurotransmitters. CoA is also needed for acetylation and acylation of proteins. CoA is hydrolysed to pantothenate and the pantothenic acid is excreted intact in urine. Pantothenic acid deficiency is only seen in individuals fed synthetic diets (Fry et al 1976) or in those fed an antagonist (Hodges et al 1958, 1959), although it was implicated in 'burning feet' syndrome in Asia during World War II (Glusman 1947). The symptoms include irritability, restlessness, fatigue, apathy, malaise, sleep disturbance, nausea, vomiting and cramping, numbness and staggering gait, as well as hypoglycaemia and increased insulin sensitivity.

A number of markers have been used to assess adequacy of intake including urinary excretion (Eissenstat et al 1986, Fry et al 1976, Tarr et al 1981) and blood levels (Annous & Song 1995, Baker et al 1969, Cohenour & Calloway 1972, Eissenstat et al 1986, Wittner et al 1989).

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Pantothenic acid**
0–6 months	**1.7 mg/day**	
7–12 months	**2.2 mg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of pantothenate in breast milk of 2.2 mg/L (Picciano 1995), and rounding (FNB:IOM 1998). For 7–12 months, the AI was derived by extrapolating up from younger infants using metabolic body weight ratios.

Children & adolescents	AI	Pantothenic acid
All		
1–3 yr	**3.5 mg/day**	
4–8 yr	**4.0 mg/day**	
Boys		
9–13 yr	**5.0 mg/day**	
14–18 yr	**6.0 mg/day**	
Girls		
9–13 yr	**4.0 mg/day**	
14–18 yr	**4.0 mg/day**	

***Rationale*:** As there are no data to set EARs and thus RDIs, AIs were set for children and adolescents. AIs were set on the median intake level from National Dietary Surveys in Australia, 1995 and New Zealand, 1991 (Baghurst & Record 2004, LINZ 1992), with cross-referencing to some dietary intake/urinary excretion data for children (Eissenstat et al 1986, Kathman & Kies 1984, Kerrey et al 1968, Pace et al 1961, Wittner et al 1989).

Adults	AI	Pantothenic acid
Men		
19–30 yr	**6 mg/day**	
31–50 yr	**6 mg/day**	
51–70 yr	**6 mg/day**	
>70 yr	**6 mg/day**	
Women		
19–30 yr	**4 mg/day**	
31–50 yr	**4 mg/day**	
51–70 yr	**4 mg/day**	
>70 yr	**4 mg/day**	

***Rationale*:** As there are limited data to set EARs, AIs were set for adults using the median population intake data from Australia and New Zealand men and women (Baghurst & Record 2004, LINZ 1992). As dietary intake data often underestimate intakes somewhat, the highest intake for any age category for the men or women was applied to the other age groups within that gender. The data for women are supported by the only study of the relationship between dietary intake and excretion in adults (Fox & Linkswiler 1961) that showed that a pantothenic acid intake of 4 mg/day was adequate.

Pregnancy	AI	Pantothenic acid
14–18 yr	**5 mg/day**	
19–30 yr	**5 mg/day**	
31–50 yr	**5 mg/day**	

***Rationale*:** There are limited data about the needs for pantothenic acid in pregnancy. The AI was therefore set by reference to the non-pregnant intake data with an allowance for the average additional body weight in pregnancy.

Lactation	AI	Pantothenic acid
14–18 yr	**6 mg/day**	
19–30 yr	**6 mg/day**	
31–50 yr	**6 mg/day**	

***Rationale*:** Needs in lactation increase as a substantial amount of pantothenate is secreted in human milk (1.7 mg/day). An additional 2 mg/day is therefore added to the non-pregnant, non-lactating AI.

UPPER LEVEL OF INTAKE - PANTOTHENIC ACID

A UL cannot be determined at this stage.

There are no reports of adverse effects of oral pantothenic acid in either humans or animals on which to base a quantitative estimate. Thus a UL cannot be determined at this stage, but current intakes are unlikely to be associated with adverse health effects.

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BIOTIN

BACKGROUND

Biotin is a cofactor for four carboxylase enzymes found in mammals – pyruvate carboxylase, methyl-crotonyl-CoA carboxylase, proprionyl-CoA carboxylase and acetyl-CoA carboxylase. The first three of these are mitochondrial and the fourth is both mitochondrial and cytosolic. They are involved in a range of actions including catabolising acetyl CoA, carboxylation of pyruvate, degradation of leucine and carboxylation of proprionyl-CoA. Biotin is found in free and protein-bound forms in food but little is known about its bioavailability. It is found in the protein-bound form in meats and cereals, although it seems to be less bioavailable in the latter (Mock 1996).

There are very few data about the biotin content of foods. Liver is known to be a very concentrated source, providing 100 µg/100 g compared to only 1 µg/100 g in meats and plant foods. Avidin, a protein found in raw egg white, binds biotin in the gut and prevents its absorption (Mock 1996). In the intestines, biotin is transported across the brush border membrane by a biotin carrier, against a sodium ion gradient. It can also be synthesised by intestinal microflora (Bonjour 1991) but it is not clear whether this is an additional potential source in humans. About half the biotin undergoes metabolism to bisnorbiotin and biotin sulfoxide before excretion. Urinary excretion and serum concentrations of biotin and its metabolites increase in similar proportions in response to intravenous or oral administration of large doses (Mock & Heird 1997, Zempleni et al 1997).

Although rare, biotin deficiency has been seen in people who consume raw egg white over long periods (Baugh et al 1968) and in total parenteral nutrition. Symptoms include dermatitis, conjunctivitis, alopecia and CNS abnormalities, including developmental delay in infants (Mock 1996). People with genetic biotinidase deficiency will have increased requirements.

The most useful information about requirements comes from assessment of clinical signs in patients on biotin-free intravenous nutrition, in those eating raw egg white or from the results of biotin bioavailability and pharmacokinetic experiments. The most sensitive end points are decreased biotin excretion and/or increased 3-hydroxyisovalerate excretion (Mock et al 1997a, 2002a).

Evidence about biotin requirements is not sufficient to set an EAR and RDI so AIs were set based on extrapolation from data on infants, and on some population intake data from New Zealand for people over 15 years of age (LINZ 1992).

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Biotin**
0–6 months	**5 µg/day**	
7–12 months	**6 µg/day**	

***Rationale*:** The AI for 0–6 months was set by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of biotin in breast milk (6 µg/L) from the studies of Hirano et al (1992), Paul & Southgate (1978) and Salmentera et al (1985). The AI for 7–12 months was extrapolated from the AI for younger infants using the reference body weight method.

Children & adolescents	AI	Biotin
All		
1–3 yr	**8 µg/day**	
4–8 yr	**12 µg/day**	
Boys		
9–13 yr	**20 µg/day**	
14–18 yr	**30 µg/day**	
Girls		
9–13 yr	**20 µg/day**	
14–18 yr	**25 µg/day**	

***Rationale*:** In the absence of adequate data, the AIs for children and adolescents were extrapolated from those for infants using the relative body weight extrapolation with an allowance for growth, and rounding up. Using a food data base developed by DSIR in New Zealand, population intake data from New Zealand (LINZ 1992) gave a median intake of 37.9 µg/day for males aged 15–18 years and 26.7 µg/day for females aged 15–18 years. There are no population intake data for Australia.

Adults	AI	Biotin
Men		
19–30 yr	**30 µg/day**	
31–50 yr	**30 µg/day**	
51–70 yr	**30 µg/day**	
>70 yr	**30 µg/day**	
Women		
19–30 yr	**25 µg/day**	
31–50 yr	**25 µg/day**	
51–70 yr	**25 µg/day**	
>70 yr	**25 µg/day**	

***Rationale*:** In the absence of adequate data, the AIs for adults were extrapolated from those for infants using relative body weights with an allowance for growth. Use of the DSIR data base, population intake data from New Zealand (LINZ 1992) gave an estimated median intake of 33 µg/day for men 19 years and over and 27 µg/day for women. There are no population intake data for Australian children.

Pregnancy	AI	Biotin
14–18 yr	**30 µg/day**	
19–30 yr	**30 µg/day**	
31–50 yr	**30 µg/day**	

Rationale: Studies by Mock & Stadler (1997) and Mock et al (1997b, 2002b) have raised questions about the adequacy of biotin status in pregnancy. Some studies have detected low plasma concentrations of biotin and its metabolites in pregnancy (Bhagavan 1969, Dostalova 1984) but others have not (Mock & Stadler 1997). Emerging evidence suggests that marginal biotin deficiency is teratogenic (Zempleni & Mock 2000). More evidence is needed to assess whether lower plasma concentrations in pregnancy are a natural consequence of haemodilution or indicate inadequate intake. The AI for pregnancy was increased over that of the non-pregnant mother in line with the additional body size associated with placental and fetal tissues.

Lactation	AI	Biotin
14–18 yr	**35 µg/day**	
19–30 yr	**35 µg/day**	
31–50 yr	**35 µg/day**	

***Rationale*:** The AI in lactation was set to cover the additional amount of biotin secreted in milk (5 µg/day).

UPPER LEVEL OF INTAKE - BIOTIN

There is insufficient evidence of adverse effects in humans or animals to set a UL for any age.

Two rat studies showed effects on inhibition of fetal and placental growth and resorption of fetuses (Paul & Duttagupta 1975, 1976) but both used very high doses of injected biotin without a control group. The data were therefore not useful for setting human ULs. In *ex vivo* experiments, 600 µg biotin produced a significant reduction of 33% or greater in mitogen-induced proliferation and cytokine-response of lymphocytes (Zempleni et al 2001). These biomarkers are indicative of a weakened immune response but are not sufficient to allow the setting of a UL. It is unlikely that current levels of intake would be associated with adverse health effects.

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CHOLINE

BACKGROUND

Choline is a precursor for a number of compounds including the neurotransmitter acetylcholine and the membrane constituents phospholipid and sphingomyelin, platelet activating factor and betaine, which is required by kidney cells and plays a role in donating methyl groups to homocysteine to form methionine. It is also important for lipid and cholesterol transport and metabolism if methyl groups.

There is some evidence that choline may improve cognitive function and memory at all ages and, by extension, choline deficiency has been implicated in poor performance for groups such as the institutionalised elderly (Fioravanti &Yanagi 2004, McDaniel et al 2003). There is also evidence that choline may reduce serum and urinary carnitine (Hongu & Sachan 2003).

Choline can be made in the body, but the ability of the body to produce enough depends on the methyl-exchange relationships between choline and folate, Vitamin B_{12} and methionine (Zeisel & Blusztajn 1994). The dietary essentiality of choline was demonstrated in a study of healthy men with normal folate and vitamin B_{12} status who developed liver damage with lower plasma choline and phosphatidylcholine concentrations when fed a choline-deficient diet (Zeisel et al 1991). However, few countries have included choline in their nutrient intake recommendations.

There is little information about requirements for most age and gender groups. Evidence from animal studies suggests that females may have a lower requirement than males. Female rats are less sensitive to choline deficiency than male rats, perhaps because of an enhanced capacity to form choline *de novo* (Tessitore et al 1995). If this is true for women, it is possible that the enhanced capacity may decrease after menopause (Lindblad & Schersten 1976) as animal experiments again have shown that oestrogens increase hepatic phosphatidyl-ethanolamine-*N*-methyltransferase activity (Drouva et al 1986, Young 1971).

Choline is widely distributed throughout the food supply, mostly in the form of phosphatidylcholine in membranes. Milk, liver, eggs and peanuts are particularly good sources. Vegetarians consuming significant quantities of refined products have a risk of becoming choline deficient. Wheat germ and dried soybeans are good sources of choline for this group (Zeisel et al 2003). Endogenous biosynthesis of choline does not meet physiological requirements and chronic deficiency leads to hepatic dysfunction.

Choline is absorbed in the small intestine both intact and after bacterial metabolism to betaine. Some betaine is also formed by oxidation of choline in liver and kidney (Bianchi & Azzone 1964, Weinhold & Sanders 1973). There appear to be no competitors for the choline transporter mechanism in the gut. The tissues of the body accumulate choline by diffusion and mediated transport (Zeisel 1981) and a specific carrier mechanism allows transport across the blood-brain barrier. This carrier has very high capacity in the neonate.

Although choline is essential, there appear to have been no reports of deficiency in the general population. Deficiencies have been seen in experimental situations and also in total parenteral nutrition (Buchman et al 1992, 1993, 1995, Chalwa et al 1989, Shapira et al 1986, Sheard et al 1986). Individuals with obesity, insulin resistance or diabetes, and middle-aged women have a propensity to develop fatty liver syndrome. This may in part be due to deficiencies of nutrients such as carnitine, essential fatty acids or choline, but there is little evidence. Given the propensity of visceral obesity in western countries including Australia and New Zealand, consideration of choline intake, amongst other nutrients, needs to be further explored.

Markers of liver dysfunction and plasma concentrations have been used to assess choline requirements, but both have limitations. Animal experiments show that hepatic choline and choline metabolites in liver decrease in choline deficiency (Zeisel et al 1989). Phosphocholine concentration in liver correlates highly with dietary choline and is also sensitive to modest changes in dietary intake. However, it is not easy to measure (Cohen et al 1995).

Plasma concentration of choline varies in response to diet (Buchman et al 1993, Burt et al 1980, Chalwa et al 1989, Sheard et al 1986, Zeisel et al 1991). The disadvantage of using it as a functional marker is that concentrations do not decline to less than 50% of normal, possibly due to hydrolysis of membrane phospholipids to maintain plasma levels (Savendahl et al 1997). Plasma phosphatidylcholine concentrations also decrease in choline deficiency, but phosphocholine concentrations are also influenced by factors that change plasma lipoprotein levels, so it is not a specific marker for choline deficiency (Zeisel et al 1991).

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Choline**
0–6 months	**125 mg/day**	
7–12 months	**150 mg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of choline in breast milk, and rounding. Breast milk from well-nourished mothers contains an average of 160 mg/L of choline delivered as choline, phosphocholine, glycerophosphocholine, phosphatidylcholine and sphingomyelin (Holmes-McNary et al 1996, Zeisel et al 1986). Infant formulas derived from soy or bovine milk contained significantly less phosphocholine than human milk (Holmes-McNary et al 1996). The AI was thus set at 125 mg/day (160 mg/L x 0.78 L/day and rounded), or 18 mg/kg for the reference weight of 7 kg at this age.

Although the free choline moiety is adequately provided by infant formulas and bovine milk, re-evaluation of the concentration of other choline esters, in particular glycerophosphocholine and phosphocholine, may be warranted. As there are no data on the availability of choline from foods for this age group, the AI for 7–12 months was set by using the reference body weight ratio methods to extrapolate either from the AI for 0–6 months or that for adults. This gave a figure of 150 mg/day.

Children & adolescents	**AI**	**Choline**
All		
1–3 yr	**200 mg/day**	
4–8 yr	**250 mg/day**	
Boys		
9-13 yr	**375 mg/day**	
14–18 yr	**550 mg/day**	
Girls		
9–13 yr	**375 mg/day**	
14–18 yr	**400 mg/day**	

***Rationale*:** As there are no data to set EARs, AIs for children and adolescents were set by extrapolating from the adult data on a body weight basis and allowing for growth needs.

Adults	AI	Choline
Men		
19–30 yr	**550 mg/day**	
31–50 yr	**550 mg/day**	
51–70 yr	**550 mg/day**	
>70 yr	**550 mg/day**	
Women		
19–30 yr	**425 mg/day**	
31–50 yr	**425 mg/day**	
51–70 yr	**425 mg/day**	
>70 yr	**425 mg/day**	

***Rationale*:** As data are too limited to allow the setting of an EAR, an AI for adults was set using data from experimental studies. In one study, an intake level of 500 mg/day (approximately 7 mg/kg body weight) prevented alanine aminotransferase abnormalities in healthy men (Zeisel et al 1991). This estimate is uncertain, but is within the range of adequacy for patients on total parenteral nutrition for whom 2 mg/kg/day (150 mg/day for the standard body weight of men) did not prevent deficiency and 31 mg/kg/day (about 2400 mg/day) did. The AI is therefore set at 550 mg/day for men (7 mg/kg body weight x 76 kg and rounding up). Animal data have suggested that women may use choline more efficiently. The female AI was set using the data from men and adjusting for body weight (7 mg/day x 61 kg), and rounding.

Pregnancy	AI	Choline
14–18 yr	**415 mg/day**	
19–30 yr	**440 mg/day**	
31–50 yr	**440 mg/day**	

***Rationale*:** There are limited data on the needs for choline in pregnancy. The AI is based on the fetal and placental accumulation of choline plus turnover in the mother. From the data of Pompfret et al (1989), Widdowson (1963) and Welsch (1976), the combined fetal and placental choline content has been estimated at 312 mg/kg (FNB:IOM 1998). Assuming there is no additional synthesis in pregnancy and no contribution from fetal and placental synthesis, the additional requirement is 3,000 mg (assuming a 3 kg fetus and 7 kg organs of pregnancy) which equates to 11 mg/day. The AI was therefore set by adding 11 mg/day and rounding.

Lactation	AI	Choline
14–18 yr	**525 mg/day**	
19–30 yr	**550 mg/day**	
31–50 yr	**550 mg/day**	

***Rationale*:** Needs in lactation increase, as a substantial amount of choline is secreted in breast milk. For an average volume of 0.78 L/day of breast milk with an average choline content of 160 mg/L, the increase is 125 mg/day which was added to the mother's requirement.

UPPER LEVEL OF INTAKE - CHOLINE

Infants	
0–12 months	**Not possible to establish. Source of intake should be breast milk, formula and food only**
Children and adolescents	
1–3 yr	**1,000 mg/day**
4–8 yr	**1,000 mg/day**
9–13 yr	**1,000 mg/day**
14–18 yr	**3,000 mg/day**
Adults 19+ yr	
Men	**3,500 mg/day**
Women	**3,500 mg/day**
Pregnancy	
14–18 yr	**3,000 mg/day**
19–50 yr	**3,500 mg/day**
Lactation	
14–18 yr	**3,000 mg/day**
19–50 yr	**3,500 mg/day**

***Rationale*:** The data used to set the UL included a single case report of hypotension and several studies involving cholinergic effects and body odour effects after large choline doses. There are no data to establish a NOAEL. A LOAEL of 7.5 g/day was derived from the study of Boyd et al (1977) of seven dementia patients receiving choline therapy and reports of hypotension, cholinergic responses and fishy body odour in other patients undergoing treatment (Gelenberg et al 1979, Growdon et al 1977a,b, Lawrence et al 1980). In these studies, intakes of 4 g/day showed no effect in terms of hypotension, nausea, diarrhoea or other cholinergic effects but at 7.5 g/day or over, these effects were reported in some patients. A UF of 2 was selected because of limited data, giving a UL of 3.5 g/day (3,500 mg/day) after rounding down. There are no data to suggest that during pregnancy or lactation, there is increased susceptibility, so the same UL was set.

For infants, there were no data on which to set a UL. The only source should be breast milk, formula and food. For older children and adolescents, the UL was set on a body weight basis from the adult value, and rounded down.

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VITAMIN C

BACKGROUND

Vitamin C (L-ascorbic acid or ascorbate) is the generic descriptor for compounds having antiscorbutic activity. Most animals can synthesise vitamin C from D-glucose but humans and other primates, together with guinea pigs, fruit bats, some passeriform birds, some fish and some insects, are exceptions. Humans and primates lack a key enzyme, L-3 gulonolactone oxidase, necessary for the biosynthesis of vitamin C (Nishikimi et al 1994).

Vitamin C is a reducing agent (antioxidant) and it is likely that all of its biochemical and molecular functions relate to this property. In humans, vitamin C acts as an electron donor for eight enzymes, of which three are involved in collagen hydroxylation (including aspects of norepinephrine, peptide hormone and tyrosine metabolism) and two are involved in carnitine biosynthesis (Dunn et al 1984, Eipper et al 1993, 1992, Kaufmann 1974, Kirirkko & Myllyla 1985, Levine et al 1991, Procop & Kiviikko 1995, Peterkovsky 1991, Rebouche 1991). Vitamin C is found in high concentrations in gastric juices (Schorah et al 1991) where it may prevent the formation of N-nitroso-compounds, which are potential mutagens (Correa 1992).

Vitamin C has been shown to protect lipids in human plasma and low density lipoprotein in *ex vivo* experiments against oxidative damage (Frei 1991). But there is no evidence of *in vivo* protection. Vitamin C also interacts with other nutrients. It aids in the absorption of iron and copper (Hallberg 1985, Harris & Perceval 1991), the maintenance of glutathione in the reduced form (Henning et al 1991, Johnston et al 1993), the regeneration, or sparing, of alpha-tocopherol (Halpner et al 1998) and the stabilisation of folate (Stokes et al 1975).

Ascorbate is found widely in fruits and vegetables. Fruits such as blackcurrants, guava, citrus, and kiwi fruit and vegetables such as broccoli and sprouts are good sources. The Australian bush food *terminalia ferdinandiana* is the richest source (Brand et al 1982). However, because of their longer periods of availability, vegetables often contribute more ascorbate to the diet than fruits. In Australia, some 40% of the vitamin C comes from vegetables and 19% from fruits and a further 27% from fruit and vegetable juices (ABS 1998). Vitamin C is very labile and its content in foods varies. Vitamin C content can be affected by season, transport, shelf life, storage time, cooking practices and chlorination of water. Cutting, bruising, heating and exposure to copper, iron or mildly alkaline conditions can destroy ascorbate. It can also be leached into water during cooking.

Intestinal absorption of vitamin C occurs through a sodium-dependent active transport process that is saturable and dose dependent (Rumsey & Levine 1998, Tsao 1997). Kallner et al (1979) showed that some 70–90% of usual intake is absorbed and that absorption fell to 50% or less with increasing doses above 1 g/day. Dose-dependent absorption and renal regulation of ascorbate allow conservation of vitamin C in the body during periods of low intake and regulation of plasma levels at high intakes.

There is a sigmoidal relationship between intake and plasma concentration of vitamin C (Levine et al 1996, Newton et al 1983). Newton et al (1983) showed that for intakes up to 30 mg/day, plasma concentrations are about 11 µmol/L (or 0.2 mg/dL). Above this intake, plasma concentrations increase steeply to 60 µmol/L and plateau at 80 µmol/L, the renal threshold. Levine et al (1996) found that the steep portion of the plasma concentration curve occurred with a daily dose of vitamin C of between 30 and 100 mg and that complete saturation occurred at 1,000 mg daily. Close to steady states, plateau concentrations are reached above 200 mg/day. Absorption is also to some extent dependent on the dosing regimen of vitamin C. For example, there would be better absorption with 250 mg as supplements taken four times daily than 1,000 mg taken once daily.

High levels of vitamin C are found in the pituitary and adrenal lands, leukocytes, eye tissues and fluids and the brain (Horning et al 1975). The biologic half-life of vitamin C is 8–40 days (Kallner et al 1979) and catabolic turnover varies widely, averaging 2.9% over a wide range of intakes (Baker et al 1971). A body pool of less than 300–400 mg is associated with the symptoms of scurvy (Baker et al 1969).

At saturation, the whole body content in males is about 20 mg/kg or 1,500 mg (Baker et al 1969, Kallner et al 1979).

Plasma vitamin C concentrations are reduced by 40% in male smokers. This may be partly due to smokers tending to eat less fruits and vegetables, but after correcting for intakes of fruit and vegetables, smokers still show lower plasma ascorbate than non-smokers (Lykkesfeldt et al 2000). The metabolic turnover of ascorbate is markedly accelerated in smokers (Kallner et al 1981).

Vitamin C deficiency causes scurvy, symptoms of which include skeletal and vascular lesions with gingival changes, pain in the extremities, haemorrhage, oedema, ulcerations and death. In adults, clinical signs occur at intakes of 7–8 mg/day or less (Goldsmith 1961, Rajajalakshmi et al 1965, van Eekelen 1953). In infantile scurvy, the changes are mainly at the sites of active bone growth and include a pseudoparalysis of the limbs (McLaren 1992).

There are several potential indices of vitamin C requirements in humans, including assessment of clinical outcomes, vitamin C turnover and biochemical indices of status (eg plasma, urine, leukocyte). Some studies have raised the question of whether vitamin C has beneficial effects on normal human subjects at intakes, and tissue levels, considerably greater than those needed to prevent or cure scurvy. However, the evidence has been conflicting. There is potential confounding in food intake studies related to the issue of concomitant intakes of other protective nutrients in fruits and vegetables, such as phytochemicals. In addition, studies generally do not provide the dose-response data on which average requirements can be ascertained (COMA 1991, FNB:IOM 2000, FAO:WHO 2002).

As a result, the estimates of vitamin C requirements in this report are based on prevention of scurvy, vitamin C turnover studies and biochemical indices of vitamin C status in man.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Vitamin C**
0–6 months	**25 mg/day**	
7–12 months	**30 mg/day**	

***Rationale*:** Breast milk concentration varies widely according to maternal intake and does not necessarily reflect infant needs (Irwin & Hutchins 1976, Olson & Hodges 1987, van Zoeren-Grobben et al 1987). Human milk generally can vary from 30 mg/L to 80 mg/L or more, depending on the intake of the mother (Bates & Prentice 1988, WHO 1998). Clinical scurvy has not been observed in fully breast-fed infants, even in communities where the vitamin C intakes of the mothers are low. Scurvy is seen only at intakes of about 7–8 mg/day or less, generally in non-breast-fed babies. The AI for 0–6 months was therefore calculated by multiplying together the average intake of breast milk (0.78 L/day) and a breast milk concentration of 30 mg/L, and rounding up. The AI for 7–12 months was calculated on a body weight basis from that of younger infants.

Children & adolescents	**EAR**	**RDI**	**Vitamin C**
All			
1–3 yr	**25 mg/day**	**35 mg/day**	
4–8 yr	**25 mg/day**	**35 mg/day**	
Boys			
9–13 yr	**28 mg/day**	**40 mg/day**	
14–18 yr	**28 mg/day**	**40 mg/day**	
Girls			
9–13 yr	**28 mg/day**	**40 mg/day**	
14–18 yr	**28 mg/day**	**40 mg/day**	

***Rationale*:** In the absence of adequate data for children and following the approach of the FAO:WHO (2002), the EARs were interpolated from the adult and infant recommendations, although these figures are somewhat arbitrary. The RDI was set assuming a CV of 20% for the EAR, as for adults.

Adults	**EAR**	**RDI**	**Vitamin C**
Men			
19–30 yr	**30 mg/day**	**45 mg/day**	
31–50 yr	**30 mg/day**	**45 mg/day**	
51–70 yr	**30 mg/day**	**45 mg/day**	
>70 yr	**30 mg/day**	**45 mg/day**	
Women			
19–30 yr	**30 mg/day**	**45 mg/day**	
31–50 yr	**30 mg/day**	**45 mg/day**	
51–70 yr	**30 mg/day**	**45 mg/day**	
>70 yr	**30 mg/day**	**45 mg/day**	

***Rationale*:** The EAR for adult men was set on the assumption that the best indicator of adequacy currently available is the intake at which body content is halfway between tissue saturation and the point at which clinical signs of scurvy appear. This equates to 900 mg body content. Assuming an absorption efficiency of 85%, a catabolic rate of 2.9%, and rounding, the EAR for adults was set at 30 mg/day (900 x 2.9/100 x 100/85). This EAR provides enough vitamin C for smokers. There is a known CV for catabolism of 21% (2.9%/day, SD = 0.6%) (Baker et al 1971) which, with rounding, gives an RDI of 45 mg/day. Plasma concentrations of vitamin C fall more rapidly in women than men (Blanchard 1991), so the male recommendation was retained for women although women have lower body sizes.

Pregnancy	**EAR**	**RDI**	**Vitamin C**
14–18 yr	**38 mg/day**	**55 mg/day**	
19–30 yr	**40 mg/day**	**60 mg/day**	
31–50 yr	**40 mg/day**	**60 mg/day**	

***Rationale*:** There is a moderate drain on vitamin C during pregnancy, particularly in the last trimester, probably due to haemodilution as well as transfer to the fetus. Given that 7 mg/day will prevent scurvy in young infants, (Goldsmith 1961, Rajalalakshmi et al 1965, van Eekelen 1953), an extra 10 mg/day in pregnancy should enable reserves to accumulate to meet the extra demands of the growing fetus. The EAR is therefore set at 40 (or 38) mg/day and the RDI set assuming a CV for the EAR of 20%, and rounding up.

Lactation	**EAR**	**RDI**	**Vitamin C**
14–18 yr	**58 mg/day**	**80 mg/day**	
19–30 yr	**60 mg/day**	**85 mg/day**	
31–50 yr	**60 mg/day**	**85 mg/day**	

***Rationale*:** The EARs for lactation are estimated from the EAR for non-lactating women plus needs for the infant. The RDI is set assuming a CV for the EAR of 20%.

UPPER LEVEL OF INTAKE - VITAMIN C

It is not possible to establish a UL for vitamin C, but 1,000 mg/day is a prudent limit.

***Rationale*:** It is not possible to establish with any certainty a UL for supplementary vitamin C, as data are too inconclusive. However, expert bodies have suggested that intakes of no more than 1,000 mg/day for adults would be prudent (UK Expert Group on Vitamins and Minerals 2003, German Nutrition Society 2002).

The UK Expert Group on Vitamins and Minerals (2002) has suggested a guidance level of 1,000 mg based on a LOAEL of 3,000–4,000 mg/day from the study of Cameron & Campbell (1974), applying an UF of 3 to extrapolate to a NOAEL of 1,000 mg/day. The US Food and Nutrition Board used the same data but applied an UF of only 1.5 to give a NOAEL of 2,000 mg which it adopted as the Tolerable Upper Intake for adults ranging down to 400 mg in children aged 1–3 years.

Gastrointestinal effects are the most common adverse effects associated with acute, high doses of vitamin C given over a short period of time. Other reported effects include metabolic acidosis, changes in prothrombin activity and 'conditioned need' scurvy (low ingestion in pregnancy conditioning the need for higher amounts in the infant). It has also been suggested that vitamin C consumption may increase oxalate excretion. However, studies in humans have not revealed a substantial increase in urinary oxalate stones with high intakes of vitamin C. Key studies include those of Auer et al (1998), Cameron & Campbell (1974), Cook et al (1984), Gokce et al (1999), Levine et al (1996, 1999), Mai et al (1990), Morton et al (2001), Urivetsky et al (1992), and Wandilak et al (1994). These studies suggest that vitamin C is not associated with significant adverse effects and there are no obvious specific key toxic endpoints.

Vitamin C can also enhance non-haem iron absorption and thus may increase iron-induced tissue damage in individuals with haemochromatosis (McLaran et al 1982). Haemochromatosis is a condition of glucose-6-phosphate dehydrogenase deficiency that occurs in about 1 in 300 people of northern European descent (George & Powell 1997). However, the possibility of such adverse effects in this group has not been systematically examined.

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VITAMIN D

BACKGROUND

The major function of Vitamin D in humans is to maintain appropriate serum calcium concentrations by enhancing the ability of the small intestine to absorb calcium from the diet. Vitamin D also plays a role in enhancing absorption of phosphorus from the diet, but the blood concentration of phosphorus is not well regulated and varies according to supply and the renal excretory threshold.

Vitamin D maintains the blood calcium at supersaturating levels such that it is deposited in the bone as calcium hydroxyapatite. When dietary calcium is inadequate for the body's needs, 1,25-dihydroxyvitamin D [1,25$(OH)_2$D or calcitriol] – the active form of vitamin D – together with parathyroid hormone, can mobilise stem cells in bone marrow to become mature osteoclasts which in turn increase the mobilisation of calcium stores from bone. However, there is a limited capacity to mobilise sufficient calcium from bone to have a significant effect on blood calcium levels.

Vitamin D occurs in two forms. One is produced by the action of sunlight on skin (D_3 or cholecalciferol) and the other is found in a limited range of foods (D_2 or ergocalciferol). With current food supplies and patterns of eating, it is almost impossible to obtain sufficient vitamin D from the diet alone (Fuller & Casparian 2001). Vitamin D in foods is fat soluble and is biologically less active. Its metabolite, 1.25-dihydroxyvitamin D (1,25(OH_2)D, or calcitriol) is the biologically active hormone responsible for its physiological actions. In the circulation, vitamin D appears as 25-hydroxyvitamin D (25(OH)D) which is five times more potent than cholecalciferol.

Vitamin D status is generally maintained in the population by exposure to sunlight (Glerup et al 2000, Holick 1996, Rasmussen et al 2000). If sunlight exposure is adequate, dietary vitamin D can be considered unnecessary (Holick 2001). In skin, 7-dehydrocholesterol is converted to pre-vitamin D_3 by a narrow band of solar ultraviolet radiation (290–320 nm) which undergoes isomerisation in a temperature-dependent manner to vitamin D_3.

Thus, vitamin D is not a nutrient in the usual sense, since under normal conditions it is supplied mainly by the skin. In addition, its physiological actions are attributable to the active metabolite, 1,25-dihydroxyvitamin D which, because it is synthesised in the kidneys and acts elsewhere, is often called a hormone.

1 µg cholecalciferol is equal to 0.2 µg 25(OH)D.
Vitamin D is also sometimes expressed in International Units where 1 IU equals 0.025 µg cholecalciferol or 0.005 µg 25(OH)D.

Seasonal changes have been shown to have a significant effect on the cutaneous production of cholecalciferol (Pettifor et al 1996, Webb et al 1990). In the winter months in temperate latitudes, solar UV light in the wavelength range of 290–320 nm is absorbed by the atmosphere. People also spend less time outdoors and wear more clothing. For this reason, vitamin D deficiency is more common in the winter months (Holick 1995).

Despite the sunny climate, a seasonal variation in vitamin D levels also occurs in Australia. In the Geelong Osteoporosis Study, the mean vitamin D levels for winter were 58 nmol/L compared with 70 nmol/L in summer (Pasco et al 2001). However, after regular sun exposure, people under the age of 50 can produce and store approximately 6 months' worth of vitamin D, so vitamin D stored in the body is available during the winter when production is minimal (Holick 1996). However, in older people, the efficiency of cutaneous synthesis of vitamin D is significantly less than that in younger people (Holick et al 1989, Need et al 1993).

Other environmental factors such as the angle of the sun, distance from the equator, the amount of cloud cover and the amount of particulate matter in the atmosphere (Holick 1995, Kimlin et al 2003, Madronich et al 1998) can affect the amount of vitamin D produced. Comparative data indicate that Northern and Southern latitudes are not equivalent. It has been estimated that ultraviolet levels in summer are up to 40% higher in New Zealand than in the equivalent Northern latitudes (Madronich et al 1998).

Deficiency of Vitamin D results in inadequate mineralisation or demineralisation of the skeleton. This can lead to rickets in young children, causing bowed legs and knocked knees. A study in China showed that vitamin D given as a supplement over 2 years increased both total body bone mineral content and bone mineral density in older children (Du et al 2004). In adults, deficiency can lead to increased bone turnover and osteoporosis and less commonly to osteomalacia for which the associated secondary hyperparathyroidism enhances mobilisation of calcium from the skeleton, resulting in porotic bone. Vitamin D may also affect fracture rates via mechanisms other than its influence on bone mass. Bischoff-Ferrari et al (2004) showed that on the basis of five RCTs involving 1,237 participants, vitamin D reduced the number of falls by 22% compared with patients receiving calcium or placebo.

Vitamin D is also thought to play a role in maintaining the immune system (Brown et al1999, DeLuca 1998) and helping maintain healthy skin (DeLuca 1998, Jones et al 1998) and muscle strength (Brown et al 1999).

There is increasing recognition that a significant number of Australians and New Zealanders may have less than optimal 25(OH)D status, however limited published information of the prevalence of vitamin D deficiency in Australia is available, other than from relatively small subpopulations (Nowson & Margerison 2002, Pasco et al 2004). Some information is available currently in unpublished form, from the national surveys of 1997 and 2002 in New Zealand (Green et al 2004a,b). Recent analyses of blood samples from these surveys showed that 31% of New Zealand children aged 5–14 years whose bloods were sampled in 2002 had a serum 25(OH)D concentration indicative of vitamin D insufficiency. Between 0% (for 5–6 year olds of European background) and 14% (for girls aged 11–14 years of Pacific Island backgrounds) had vitamin D deficiency. For adolescents at or above 15 years and adults whose bloods were sampled in 1997, the prevalence of deficiency, defined as <17.5 nmol/L, was 2.8%, but the prevalence of insufficiency, defined as <37.5 nmol/L, was 27.6%. Vitamin D concentrations were lower in winter than summer and lower in Pacific peoples and Mäori than those of European and other origins.

The groups thought to be at particular risk in Australia and New Zealand include older persons living in the community, those in residential care with limited mobility for whom frank deficiency may be 22–67% and mild deficiency may be 45–84%, dark-skinned peoples and veiled women who have limited exposure to sunlight (as many as 80% having mild deficiency) and breast-fed infants of these groups of women. Some of these groups (eg the institutionalised elderly) are often not represented in National Surveys.

Adolescents and young children growing rapidly who are on marginal calcium intakes may also have increased requirements for vitamin D that may not be met in winter, when reduced exposure to sunlight depletes the body's stores of vitamin D. There is also some evidence that up to 8% of younger women (20–39 years) may have a frank vitamin D deficiency at the end of winter and 33% may have a marginal deficiency. People who wear protective clothing, always use sunscreen and those who have intestinal, hepatic, renal or cardiopulmonary disease or are taking anticonvulsants may also be at increased risk (Compston 1998, Fitzpatrick et al 2000, Fuller & Casparian 2001, Thomas et al 1998).

Very few foods contain significant amounts of vitamin D (Holick 2001, Vieth 1999). In Australia, fortified margarine appears to be the major dietary source of vitamin D, together with fatty fish such as salmon, herring and mackerel, and eggs (Baghurst & Record 2002).

Accurate estimates of dietary intakes of vitamin D in Australia and New Zealand are not yet available as local food databases are limited. Some estimates have been made using a mix of local and overseas information on food composition with figures between 2-3mg/day for adults (Baghurst & Record 2002,

LINZ 1992). Currently in Australia, vitamin D fortification is mandated for edible oil spreads (table margarine) and voluntary for modified and skim milks, powdered milk, yoghurts and table confections and cheese. In New Zealand, fortification of margarine or milk products with vitamin D is not mandated, however since 1996, voluntary fortification of margarine, fat spreads and their reduced fat counterparts has been permitted. It is also permitted to add vitamin D to dried milk, dried skim milk and non-fat milk solids, skim milk and reduced fat cows' milk, legume beverages and 'food' drinks.

Serum 25(OH)D is the indicator of choice for assessing requirements since it accounts for both dietary and cutaneous sources of the vitamin. However, there is some disagreement in the literature and clinical practice over quantification of the optimal range. A 25(OH)D below 27.5 nmol/L is consistent with vitamin D deficiency in infants, neonates and young children (Specker et al 1992) and is thus used as the key indicator for determining a vitamin D reference value. Little information is available on the levels required to maintain normal calcium metabolism and peak bone mass in children, or young and middle-aged adults but in a recent position statement a Working Group of the Australian and New Zealand Bone and Mineral Society, the Endocrine Society of Australia and Osteoporosis Australia (2005) defined mild deficiency for adults as serum 25-OHD levels between 25 and 50nmol/L; moderate deficiency as between 12.5 and 25nmol/L and severe, below 12.5nmol/L based on various indicators such as increases in parathyroid hormone secretion and various bone indicators. There is mounting evidence for the elderly to support increased dietary requirements for the maintenance of normal metabolism and maximum bone health (Dawson-Hughes et al 1991, Krall et al 1989, Lips et al 1988) and some researchers recommend levels of 75–100 nmol/L, especially for the elderly, on the basis of optimising bone (Dawson-Hughes 2004, Dawson-Hughes et al 1997, Heaney 1999, 2004, Kinyamu et al 1998, Sahota 2000, Vieth et al 1999, Vieth 2004).

When 25(OH)D concentrations are in the deficient range, serum PTH levels are inversely proportional to 25(OH)D levels, and can therefore also be a valuable indication of inadequate vitamin D status, as can skeletal health including bone development and prevention of rickets in infants and children and bone mineral content, bone mineral density and fracture risk in adults.

The recommendations herein assume no, or minimal, exposure to sunlight as sunlight exposure factors and environmental factors can vary widely between individuals across Australia and New Zealand. An assessment of the effect of environmental and personal factors in reducing this requirement is also given, although data are limited.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Vitamin D**
0–6 months	**5.0µg/day**	
7–12 months	**5.0µg/day**	

***Rationale*:** Maternal vitamin D status in pregnancy affects the status of the infant for the first few months of life. If maternal vitamin D status is good during the last stages of pregnancy the newborn child should have adequate vitamin D status for some time after birth in the absence of significant input from the diet. Human milk has very little vitamin D, so infants not exposed to sunlight are unlikely to obtain adequate vitamin D from mother's milk beyond early infancy (Nakao 1988, Specker et al 1985). The AI for infants 0–12 months is based on the lowest dietary intake of vitamin D associated with a mean serum 25 (OH)D concentration of greater than 27.5 nmol/L (lower limit of normal) assuming little or no exposure to sunlight (FNB:IOM 1997). In these circumstances, a minimal intake of 2.5 µg/day will likely prevent rickets in babies 0–6 months (Glaser et al 1949, Specker et al 1992). At this intake, in the absence of sunlight, many will have 25(OH)D levels within the range sometimes seen in rickets (Specker et al 1992). Thus the AI is set at 5 µg/day. Several studies have shown that this level would also be adequate for older babies (Greer et al 1982a, Leung et al 1989, Markestad & Elzouki 1991) and for formula-fed infants (Koo & Tsang 1995, Markestad & Elzouki 1991).

Role of sunlight exposure: Estimates from the Midwest in the US suggest that to get sufficient vitamin D from sunlight alone, infants need to be exposed for 2 hours a week if just their face is exposed or 30 minutes a week with just a nappy on (Specker et al 1985). With habitual small doses of sunshine, breast or formula-fed infants do not require supplemental vitamin D. However, the infants of dark-skinned and/or veiled women may be at higher risk of developing rickets (Grover & Morley 2001). Their mothers often have marginal or frank vitamin D deficiency resulting in low status at birth. The vitamin D status of the infants is further compromised by restricted exposure to sunlight, and reduced ability to synthesise 25(OH)D due to skin pigmentation.

Children & adolescents	**AI**	**Vitamin D**
All		
1–3 yr	**5.0 µg/day**	
4–8 yr	**5.0 µg /day**	
Boys		
9–13 yr	**5.0 µg/day**	
14–18 yr	**5.0 µg/day**	
Girls		
9–13 yr	**5.0 µg/day**	
14–18 yr	**5.0 µg/day**	

***Rationale*:** In the absence of data on how much vitamin D is required to prevent deficiency in 1–8-year olds, recommendations were derived from data on slightly older children with limited sunlight exposure (Aksnes & Aarskog 1982, Gultekin et al 1987). Most children with a dietary intake of 1.9–2.5 µg/day had no evidence of deficiency as defined by blood levels of 25(OH)D below 27.5 nmol/L. Adolescents and young children growing rapidly who are on marginal calcium intakes may have increased requirements for vitamin D which may not be met in winter, when reduced exposure to sunlight depletes the body stores of vitamin D. A requirement of 2.5 µg/day regardless of sunlight was seen as prudent and was doubled to cover the needs of all children of this age to give the AI of 5 µg/day (FNB:IOM 1997).

Role of sunlight exposure: With regular sun exposure, there would not be a dietary need for vitamin D in children and adolescents (Ala-Houhala et al 1984, Gultekin et al 1987, Pettifor et al 1978, Riancho et al 1989, Taylor & Norman 1984). However, children living in far southern latitudes and those with dark skins such as indigenous Australians and New Zealanders, and certain migrant groups, or those who are covered for cultural reasons, may be unable to synthesise enough vitamin D in their skin in store for winter. Jones et al (1999) showed that 10% of children in southern Tasmania assessed in mid-winter had plasma 25(OH)D lower than 25 nmol/L, a level considered insufficient. There has been a reported increase in the presentation of rickets in Victorian children, mainly due to restricted sun exposure in mothers who are often dark skinned and veiled. In New Zealand, from national survey data, 4% of children aged 5–14 years had levels below 17.5 nmol/L and 1–2% of adolescents aged 15–18 years (Green et al 2004a,b).

Adults	AI	Vitamin D
Men		
19–30 yr	**5.0 µg /day**	
31–50 yr	**5.0 µg /day**	
51–70 yr	**10.0 µg /day**	
>70 yr	**15.0 µg /day**	
Women		
19–30 yr	**5.0 µg /day**	
31–50 yr	**5.0 µg /day**	
51–70 yr	**10.0 µg /day**	
>70 yr	**15.0 µg /day**	

***Rationale*:** The AI for younger adults (19–50 years) is based on the amount of vitamin D required to maintain serum 25(OH)D at a level of at least 27.5 nmol/L with minimal exposure to sunlight. One study of US women of this age (Kinyamu et al 1997) showed that an average intake of 3.3–3.4 µg/day resulted in serum 25(OH)D of greater than 30 nmol/L. A study of females in Australia undertaken across both the summer and winter months at latitude 38° (Pasco et al 2001), assessed median intakes to be only 1.3 µg/day (much lower than other estimates for Australia and New Zealand), but had only 7% of subjects with serum 25(OH)D below 28 nmol/L in summer and 11% in winter. A vitamin D intake of 2.5 µg/day was seen as prudent for this age group. There are no data on men on which to set a figure except from one study of submariners not exposed to sunlight, whose status was assessed with or without a 15 µg/day supplement (Holick, 1994). However, the effects of lower doses were not assessed in this study. It is therefore assumed that requirements for men will be the same as those for women.

To cover the needs of all adults in the age range of 19–50 years, regardless of exposure to sunlight and in recognition of the fact that the available data were collected in women, a figure of 5 µg/day was set as the AI for younger adults. The AI was raised to 10 µg/day for adults aged 51–70 years to account for the reduced capacity for the skin to produce vitamin D with ageing (Holick et al 1989, Need et al 1993). Data on bone loss and vitamin D supplementation in women were also taken into consideration (Dawson-Hughes et al 1991, 1995). For adults over 70 years, the AI was raised to 15 µg/day. Studies of elderly people with intakes of 9.6 µg, 7.1 µg or 5.2 µg vitamin D/day showed that 8, 14 and 45%, respectively had low levels of serum 25(OH)D (Gloth et al 1995, Kinyamu et al 1997, O'Dowd et al 1993). A value of 7.5 µg/day was considered prudent for those with limited sun exposure and was doubled to 15 µg/day to cover the needs of all adults of this age, regardless of sun exposure or body stores.

It should be noted that the effect of increasing the dietary intake of vitamin D on 25(OH)D concentration in blood varies according to the existing vitamin D status of the individual. The status of those with low 25(OH)D levels in plasma will be improved to a more significant degree than of those with pre-existing high status (eg plasma levels above about 50 nmol/L) who may benefit little from the additional dietary intake.

Role of sunlight exposure: There is evidence from selected subpopulations that about 4–8% of adults in Australia have serum 25(OH)D levels below 28 nmol/L and about 30% have levels below 50 nmol/L (Pasco et al 2001, MacGrath et al 2001, Vasikaran et al 2000). National surveys in New Zealand have indicated that some 2.8% of adults have levels of less than 17.5 nmol/L and 27.6% have levels below 37.5 nmol/L. Both sunlight and diet play an essential role in vitamin D status in younger adults. Kimlin et al (2003) estimated that for an older woman with fair skin, exposure of 6% of the body surface (face, hands, forearm) to sunlight for 15–30 minutes, 2–3 times per week would provide the equivalent of 15 µg vitamin D/day. Because of reduced cutaneous production, young adults (19–50 years) who live in southern latitudes such as Tasmania and the southern island of New Zealand are particularly at risk of becoming vitamin D deficient during the winter months.

For dark-skinned peoples such as indigenous Australians and New Zealanders and certain migrant groups and veiled women, there is evidence in Australia of high rates of vitamin D deficiency. Grover et al (2001) found that 80% of pregnant dark-skinned, veiled women attending one antenatal clinic in a large teaching hospital had vitamin D levels of less than 22 nmol/L. For people with little access to sunlight a supplement of 10 µg/day would not be excessive.

***Institutionalised elderly*:** Several studies in Australia and New Zealand have shown high rates of deficiency in very elderly people with restricted access to sunlight, many of whom live in institutions. Estimates of deficiency range from 15–52% in Australia (Bruce et al 1999, Flicker et al 2003, Inderjeeth et al 2000, Stein 1996). Ley et al (1999) found that 49% of older New Zealand subjects in winter and 33% in summer had low serum 25(OH)D while McAuley et al (1997) reported 69% of subjects in Dunedin having low levels in winter, but only 26% in summer. Data from the National Nutrition Survey of New Zealand (Green et al 2004b) showed that 1.6% of males over 65 years and 5.8% of females had blood levels below 17.5 nmol/L for serum 25(OH)D and that 20.5% of men and 39.6% of women had levels below 37.5 nmol/L. This survey did not include institutionalised people. The recommendation of 15 µg/day for those over 70 years relates to the general population over 70 years. A number of recent studies demonstrate protection from falls and fractures with supplemental intakes of vitamin D in the elderly.

For institutionalised or bed-bound elderly who have very restricted exposure to sunlight often accompanied by reduced food intake, supplementation with vitamin D in the order of 10–25 µg/day may be necessary (Brazier et al 1995, Byrne et al 1995, Chapuy et al 1992, Egsmose et al 1987, Fardellone et al 1995, Kamel et al 1996, McKenna 1992, Sebert et al 1995, Sorva et al 1991).

Pregnancy	**AI**	**Vitamin D**
14–18 yr	**5.0 µg/day**	
19–30 yr	**5.0 µg/day**	
31–50 yr	**5.0 µg/day**	

***Rationale*:** Although there is placental transfer of vitamin D and its metabolites from mother to fetus, the amounts are too small to affect the mother's vitamin D requirement, particularly as there is a rise in serum calcitriol (probably of placental origin) and a rise in calcium absorption in late pregnancy (Paunier et al 1978, Specker 2004). However, maternal deficiency of vitamin D can affect the fetus and needs to be prevented. Pregnant women who receive regular exposure to sunlight do not require supplementation. However, at intakes of less than 3.8 µg/day, pregnant women in winter months at high latitudes have been shown to have low serum 25(OH)D (Paunier et al 1978). For women who have little access to sunlight, a supplement of 10 µg/day prenatally would not be excessive. In the last trimester of pregnancy there is quite a large transfer of 25(OH)D across the placenta.

Lactation	**AI**	**Vitamin D**
14–18 yr	**5.0 µg/day**	
19–30 yr	**5.0 µg/day**	
31–50 yr	**5.0 µg/day**	

***Rationale*:** There is no evidence that lactation increases the AI of the mother for vitamin D. Thus, if sunlight is inadequate, an AI of 5 µg/day is needed. As noted above, the infants of dark-skinned and/or veiled women may be at higher risk of developing rickets partly because of marginal or frank vitamin D deficiency in the mother. For mothers and their babies with limited exposure to sunlight, a supplemental intake during lactation of 10 µg/day would not be excessive.

UPPER LEVEL OF INTAKE - VITAMIN D

Infants	
0–12 months	**25 µg /day**
Children and adolescents	
1–3 yr	**80 µg/day**
4–8 yr	**80 µg/day**
9–13 yr	**80 µg/day**
14–18 yr	**80 µg/day**
Adults 19+ yr	
Men	**80 µg/day**
Women	**80 µg/day**
Pregnancy	
14–18 yr	**80 µg/day**
19–50 yr	**80 µg/day**
Lactation	
14–18 yr	**80 µg/day**
19–50 yr	**80 µg/day**

***Rationale*:** The UL for infants was set on the basis of a NOAEL of 45 µg/day (Fomon et al 1966, Jeans & Stearns 1938) together with a UF of 1.8 (FNB:IOM 1997) because of the small sample sizes and insensitivity of the endpoint used (linear growth). For children and adolescents, there are little available data, so the recommendation for adults was adopted.

The UL for adults was based on studies assessing the effect of vitamin D on serum calcium in humans (Honkanen et al 1990, Johnson et al 1980, Narang et al 1984, Vieth et al 2001). Johnson et al (1980) and Honkanen et al (1990) conducted studies with supplementation at 50 µg/day or 45 µg/day for several months and saw no adverse effects. Narang et al (1984), using dosages of 60 µg and 95 µg/day over several months in a non-randomised trial that included 30 normal controls, saw increases above 2.75 mmol/L in serum calcium levels a level considered as defining hypercalcaemia, at 95 µg/day but not at 60 µg/day. However, a recent, well-designed, RCT by Vieth et al (2001) saw no adverse effect of dosages of 25 µg/day or 100 µg/day over six months in 30 subjects. This finding was confirmed in a later randomised study (Vieth et al 2004) of inpatients with subclinical or marginal deficiency. Vieth et al (2001) felt that the earlier data of Narang et al (1984) may have been erroneous in dosage, citing concerns about lack of independent confirmation of the actual amount of vitamin D administered (there were no measures of serum 25(OH)D). There is also some animal evidence of oral vitamin D causing non-calcified atherosclerosis of large arteries (Taura et al 1979, Toda et al 1985), suggesting that a cautious approach should be taken to high dose vitamin D in people other than the elderly.

Taking all of this into account, the figure of 100 µg/day from Vieth's studies was adopted as the NOAEL and a UF of 1.2 was applied because of the inconsistencies in the studies and they were performed on relatively small number of subjects with pre-existing marginal vitamin D status. Vieth et al (2001) have themselves cautioned about the relatively small numbers in their studies.

The available data for pregnancy and lactation are inadequate to derive a figure different from that of other adults. There appears to be no increased sensitivity during these physiological states.

It should be noted that the intake of vitamin D via food would add to the vitamin D formed by exposure to sunlight.

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VITAMIN E

BACKGROUND

Vitamin E is the name given to a group of water-insoluble, plant-derived substances. There are eight naturally-occurring isomers and a number of semisynthetic or synthetic homologues. The naturally-occurring *d*- (or RRR) alpha-tocopherol is the most biologically active form and vitamin E activity is traditionally expressed in terms of equivalents of this isomer (mg alpha-tocopherol equivalents or α-TE). Other tocopherols such as gamma-tocopherol also have vitamin E activity. There are four tocopherol homologues (*d*-α-, *d*-β-, *d*-γ- and *d*-δ-) and four tocotrienols. Other forms of vitamin E occur in lower amounts in foods and are less active in animal bioassay. The usual form in supplements is synthetic *dl*- (or all-rac) α-tocopherol that consists of a mixture of active and inactive stereoisomers, because natural vitamin E from wheat germ oil is expensive. The equivalence of the various forms is shown below:

Form	Alternative name	mg α-tocopherol equivalence
d-α-tocopherol	RRR-α-tocopherol	1
d-α-tocopherol acetate	RRR-α-tocopherol acetate	0.91
d-α-tocopherol acid succinate	RRR-α-tocopherol acid succinate	0.81
dl-α-tocopherol	all-rac-α-tocopherol	0.74
dl-α-tocopherol acetate	all-rac-α-tocopherol	0.67
d-β-tocopherol	RRR-β-tocopherol	0.25–0.40
d-γ-tocopherol	RRR-γ-tocopherol	0.10
α-tocotrienol		0.25–0.30

The major role of vitamin E is to protect polyunsaturated fatty acids (PUFA) from oxidation. It acts as an anti-oxidant in the lipid phase of cell membranes. Vitamin E requirements have been reported to increase when intakes of PUFA are increased (Dam 1962, Horwitt 1962) and a ratio of at least 0.4 mg α-tocopherol per gram of PUFA has been recommended (Bieri & Evarts 1973, Horwitt 1974, Witting & Lee 1975). Most dietary sources of polyunsaturated fat are also relatively rich in vitamin E. However supplements of fish oils or other pure n-3 fatty acids may not provide the amount of vitamin E needed.

The activity vitamin E complements that of selenium-dependent glutathione peroxidase in protecting the membrane PUFAs from free radical damage. Although vitamin E is mainly located in cells and organelle membranes, its concentration may be very low, suggesting that after its reaction with free radicals it is rapidly regenerated, possibly by other antioxidants such as selenium, ubiquinols and vitamin C (Doba et al 1985, Niki et al 1982, Stoyanovsky et al 1995).

The main source of vitamin E is fats and oils. It is also found in some vegetables, in the fats of meat, poultry and fish and, to lesser degrees, in cereals and dairy foods. About half the tocopherol in wheat germ, sunflower, safflower, canola, olive and cottonseed oils is α-tocopherol but soybean and corn oils contain about 10 times as much γ-tocopherol as α-tocopherol. Most vitamin E is found in foods containing fat. Absorption requires micelle formation and chylomicron secretion in the gut (Muller et al 1974) together with biliary and pancreatic secretions. Efficiency of absorption is low, but the precise rate is unknown.

Vitamin E is transported in the blood by the plasma lipoproteins and erythrocytes. Tocopherols are carried from the gut to the liver in chylomicrons where they are incorporated as chylomicron remnants. Catabolism of chylomicrons takes place in the systemic circulation through the action of cellular lipoprotein lipase. Vitamin E can be transferred to high density lipoprotein (HDL) and then

to low density liopoprotein (LDL) and very low density lipoprotein (VLDL). Most α-tocopherol enters peripheral tissues within the intact lipoprotein through the LDL receptor pathway.

Although all tocopherol homologues are absorbed similarly, α-tocopherol predominates in blood and tissue as the binding proteins take it up preferentially. Plasma vitamin E and tissue concentrations vary little over a wide range of dietary intake and the brain is particularly resistant to depletion (Bourne & Clement 1991).

The main oxidation product of α-tocopherol is tocopheryl quinone which is conjugated to glucuronate and is excreted in bile or further degraded in the kidneys to α-tocopheronic acid before excretion in bile (Drevon 1991). Some may be excreted through the skin (Shiratori 1974).

Overt deficiency symptoms in normal individuals consuming diets low in vitamin E have never been described. It occurs only as a result of genetic abnormalities, fat malabsorption syndrome (Rader & Brewer 1993, Sokol 1993) or protein-energy malnutrition (Kalra et al 1998, Laditan & Ette 1982). The main symptom is a peripheral neuropathy. Other symptoms include spinocerebellar ataxia, skeletal myopathy and pigmented retinopathy (Sokol 1988).

In epidemiological studies, higher intakes of vitamin E have been related to reduction in cardiovascular disease risk (Gey et al 1991, Rimm & Stampfer 1993, Stampfer et al 1993), diabetic complications (Baynes 1991, Mullarkey et al 1990, Semenkovich & Heinecke 1997), certain cancers (Comstock et al 1997, Eichhlozer et al 1996, Yong et al 1997) and cataracts (Jacques & Chylack 1991, Knekt et al 1992, Leske et al 1991). Not all studies, however, have confirmed a relationship and clinical trials with supplements in high risk groups, have shown little benefit. Further discussion of these trials is given in the 'Chronic disease' section.

Indicators that have been used to estimate vitamin E requirements include lipid peroxidation markers, oxidation products of DNA or proteins, vitamin E metabolite excretion, vitamin E biokinetics, vitamin E deficiency symptoms, plasma α-tocopherol concentration, hydrogen peroxide-induced haemolysis or the relationship of vitamin E to chronic disease status. However, erythrocyte fragility studies have been the most widely used.

The US DRI review in 2000 used the data of Horwitt (1960, 1963). These same data had been used in setting the earlier US RDIs but were interpreted differently in 2000, leading to considerably increased recommendations. In the US DRI review of 2000, the amount of dietary vitamin E required to bring plasma α-tocopherol to a level where per cent haemolysis was low was used to estimate an EAR (Horwitt 1960, 1963). However, the interpretation of these data is problematic in relation to level of plasma α-tocopherol at which adverse effects are seen, as there were no data available for plasma α-tocopherol concentrations between 5 and 12 µmol/L. All four subjects below 6 µmol/L plasma α-tocopherol (range 2–5 µmol/L) had haemolysis of about 80% or above and all 6 subjects with concentrations between 12 and 22 µmol/L, had haemodialysis of 12% or less. There has been disagreement as to whether the 'adequacy' cut off should be midway between these two clusters or at the lowest point showing low haemolysis. The data are dichotomous, not continuous, thus preventing an accurate dose-response analysis. Changing the cut-off point makes a large difference to the estimated requirement. In addition, the authors of the key paper themselves expressed concern about the validity of the technique for assessing vitamin E requirements (Horwitt 1960, 1963, 2001).

Given these uncertainties, an AI rather than an EAR was set for vitamin E based on median population intakes in Australia and New Zealand – both healthy populations with no apparent vitamin E deficiency. Recommendations for infants were based on the median concentration in breast milk of healthy mothers.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	AI	Vitamin E (as α-tocopherol equivalents)
0–6 months	**4 mg /day**	
7–12 months	**5 mg /day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of vitamin E in breast milk of 4.9 mg/L (Boersma et al 1991, Chappell et al 1985, Jansson et al 1981, Lammi-Keefe et al 1985, 1990) and rounding. Two of these studies reported only α-tocopherol data but Boersma et al (1991) showed that the tocopherol content of breast milk is almost entirely comprised of α-tocopherol. For 7–12 months, the AI was extrapolated from younger infants on a body weight basis and rounded.

Children & adolescents	AI	Vitamin E (as α-tocopherol equivalents)
All		
1–3 yr	**5 mg/day**	
4–8 yr	**6 mg/day**	
Boys		
9–13 yr	**9 mg/day**	
14–18 yr	**10 mg/day**	
Girls		
9–13 yr	**8 mg/day**	
14–18 yr	**8 mg/day**	

***Rationale*:** As there are no specific data on which to base an EAR for children and adolescents, an AI was set based on the median intakes in Australia and New Zealand from the National Nutrition Surveys with rounding up to the nearest milligram (ABS 1998, MOH 1999, 2003).

Adults	AI	Vitamin E (as α-tocopherol equivalents)
Men		
19–30 yr	**10 mg/day**	
31–50 yr	**10 mg/day**	
51–70 yr	**10 mg/day**	
>70 yr	**10 mg/day**	
Women		
19–30 yr	**7 mg/day**	
31–50 yr	**7 mg/day**	
51–70 yr	**7 mg/day**	
>70 yr	**7 mg/day**	

***Rationale*:** As there are not sufficient data on which to base an EAR for adults, an AI was set based on the median intakes in Australia and New Zealand from the National Nutrition Surveys with rounding up to the nearest milligram (ABS 1998, MOH 1999). The values set for men and women were the highest median intake for any respective adult age band.

Pregnancy	**AI**	**Vitamin E (as α-tocopherol equivalents)**
14–18 yr	**8 mg/day**	
19–30 yr	**7 mg/day**	
31–50 yr	**7 mg/day**	

***Rationale*:** There is no evidence of increased needs for vitamin E in pregnancy, so the AI is set at that for the non-pregnant woman.

Lactation	**AI**	**Vitamin E (as α-tocopherol equivalents)**
14–18 yr	**12 mg/day**	
19–30 yr	**11 mg/day**	
31–50 yr	**11 mg/day**	

***Rationale*:** The AI for lactation is set at that for the non-lactating woman plus an allowance for the vitamin E secreted in milk.

UPPER LEVEL OF INTAKE - VITAMIN E - (as α-tocopherol equivalents)

Infants	
0–12 months	**Not possible to establish. Source of intake should be breast milk, formula and food only**
Children	
1–3 yr	**70 mg/day**
4–8 yr	**100 mg/day**
Boys	
9–13 yr	**180 mg/day**
14–18 yr	**250 mg/day**
Girls	
9–13 yr	**180 mg/day**
14–18 yr	**250 mg/day**
Adults 19+ yr	
Men	**300mg/day**
Women	**300mg/day**
Pregnancy	
All ages	**300 mg/day**
Lactation	
All ages	**300 mg/day**

***Rationale*:** In recent years, several clinical intervention trials have assessed the effects of high doses of vitamin E on chronic disease outcomes, including the CHAOS Heart trial which used 268–567 mg *d*-α-tocopherol/day (Stephens et al 1996), the GISSI study with 300 mg vitamin E as synthetic α-tocopherol (GISSI-Prevenzione Investigators 1999), the ATBC study using 55 mg *dl* α-tocopherol (ATBC 1994, Heinonen et al 1998), the HOPE study using 268 mg vitamin E (Yusuf et al 2000), the Primary Prevention Study using 300 mg/day synthetic α-tocopherol (Collaborative group of the Primary Prevention Study 2001) and the Heart Protection Study with 600 mg of vitamin E (Heart Protection Study Collaborative Group, 2002). In addition, there have been a number of experimental trials using supplements ranging from 540 to 970 mg *d*-α-TEs. With the exception of an increase in subarachnoid haemorrhaging in smoking hypertensives in the ATBC study (Leppanen et al 2000a,b), a non-significant increase in stroke (relative risk 1.17) in the HOPE study and a tendency to haemorrhage in aspirin users in the Primary Prevention Project, no adverse events have been recorded. However, most studies were not specifically designed to assess adverse events to Vitamin E alone.

Meydani et al (1998) undertook an experimental, dose-dependent study in 88 healthy volunteers aged >65 years, with one control group and three varying dose groups (equivalent to 34, 134 or 537 mg *d*-α-TEs), over 4 months. This study had the most comprehensive assessment of potential adverse events. There were no subjective side effects and no effects on glutathione peroxidase, superoxide dismutase, immunoglobulin, anti-DNA or anti-thyroglobulin antibodies, body weight, total plasma proteins, albumin, glucose, lipids or lipoprotein profile, total bilirubin, serum liver enzymes, blood count, platelet number, bleeding time, haemoglobin, haematocrit or urinary or serum creatinine. The NOAEL established from this study was 540 mg/day. A UF of 2 was applied to cover inter-individual differences in sensitivity. A larger UF was not considered necessary because data from a number of other less well controlled studies showed no adverse effects at considerably higher intakes. The UL for vitamin E was therefore established as 270 mg/day for adults and rounded to 300 mg/day. The ULs for other age groups were derived on a relative body weight basis.

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VITAMIN K

BACKGROUND

Vitamin K is the family name for a series of essential fat-soluble compounds needed for the chemical modification of a small group of proteins with calcium-binding properties (vitamin K dependent proteins or γ-carboxyglutamic acid-proteins, generally known as Gla proteins). The best-known role for vitamin K is the maintenance of normal blood coagulation. Use of anticoagulant drugs such as warfarin can affect vitamin K requirements. The vitamin K-dependent coagulation proteins that are made in the liver have both coagulant and anticoagulant properties. They include the coagulant factors II (prothrombin), VII, IX and X and the anticoagulant proteins C and S.

Vitamin K is involved in the post-translational modification of glutamate residues to γ-carboxyglutamate residues in the formation of the coagulation protein, prothrombin. The glutamate-containing (under-carboxylated) precursors of the vitamin K-dependent proteins are sometimes referred to as 'proteins induced by vitamin K absence' or 'PIVKA'. The glutamate precursor of prothrombin is called PIVKA-II. The vitamin K-dependent procoagulants are secreted from the liver as inactive forms. After the incorporation of Gla residues and in the presence of calcium ions they bind to the surface membrane phospholipids of platelets and endothelial cells where they form membrane-bound complexes with other cofactors. When coagulation is initiated, the inactive clotting factors are cleaved and activated.

Two other proteins containing γ carboxyglutamate residues are osteocalcin or bone Gla protein (with 3 Gla residues) produced by the osteoblasts and matrix Gla protein, or MGP, (with 5 Gla residues). Low vitamin K intakes are associated with undercarboxylated osteocalcin increases and have also been associated with increased rates of hip fracture in two cohort studies (Booth et al 2000, Feskanich et al 1999).

The only important molecular form of vitamin K in plants is phylloquinone (vitamin K_1) but bacteria can synthesise a family of compounds called menaquinones (vitamin K_2). The major dietary sources of vitamin K are green leafy vegetables such as kale, spinach, salad greens, cabbage, broccoli and brussel sprouts and certain plant oils such as soybean and canola oils (and to a lesser extent cottonseed and olive oils) and margarines and salad dressings made from them. Relatively large amounts of menaquinones can be found in some cheeses (Schurgers et al 1999).

There is little information about the bioavailability of phylloquinone from various foods. One study showed that its availability from a supplement was 25 times greater than that from spinach (Gijsbers et al 1996), although three times as much was absorbed when butter was added to the spinach. Another study showed that the availability from spinach, broccoli or romaine consumed as part of a meal was 80–84% lower than that from a supplement (Garber et al 1999). Overall, absorption from plant sources including plant oils (Booth et al 1999) seems to be no more than 20% of that from a supplement. Animal experiments have shown that high vitamin E intakes can antagonise the action of vitamin K (Rao & Mason 1975, Wooley 1945). Some effects have been seen in anticoagulated patients (Corrigan & Ulfers 1981), but no adverse effects have been shown in healthy humans.

Vitamin K deficiency causes a bleeding tendency through a lack of activity of the procoagulant proteins. A clinically significant deficiency is associated with an increase in prothrombin time (PT). Cases of dietary induced deficiency are rare, but may be associated with lipid malabsorption (Savage & Lindenbaum 1983). Experimentally induced deficiency occurred in 10 healthy subjects fed a diet containing less than 10 μg vitamin K/day (Udall 1965). Frick et al (1967) administered a parenteral nutrient solution to a small number of neomycin-treated adults for 4 weeks and observed prolonged prothrombin times (PTs) that responded to parenteral administration of phylloquinone. Frick et al (1967) concluded that requirements were between 0.30 and 1.05 μg/kg body weight. In more recent studies by Allison et al (1987) and Ferland et al (1993), healthy individuals eating diets containing 5–10 μg/day for two weeks showed no change in PT.

The biologic functions of vitamin K-dependent proteins produced in other tissues, notably osteocalcin and MGP are unclear. Evidence of a possible association of suboptimal vitamin K deficiency with increased risk of adverse outcomes for bone health and bone fracture is under investigation by a number of groups but the outcomes have not been clear cut to date (Binkley & Suttie 1995, Binkley et al 2002, Braam et al 2003, Schaafsma et al 2000, Shearer 1997, Vermeer et al 1995).

Various indicators for vitamin K requirements have been used, including PT, Factor VII, plasma and serum phylloquinone, urinary γ-carboxyglutamyl residues, undercarboxylated prothrombin and under-γ-carboxylated osteocalcin. Of these, only prothrombin has been associated with adverse clinical effects. Other indicators respond to dietary intake, but the physiological significance is unclear.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Vitamin K**
0–6 months	**2.0 µg/day**	
7–12 months	**2.5 µg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of vitamin K in breast milk, and rounding. The figure used for breast milk was 2.5 µg/L based on the studies of Canfield et al (1990, 1991), Greer et al (1991, 1997), Haroon et al (1982), Hogenbirk et al (1993) and Von Kries et al (1987).

The AI assumes that infants also receive prophylactic vitamin K at birth in amounts recommended in the *Joint Statement and Recommendations on Vitamin K administration to newborn infants to prevent vitamin K deficiency bleeding in infancy* from the NHMRC, Paediatric Division of the Royal Australasian College of Physicians, Royal Australian and New Zealand College of Obstetrics and Gynaecology, Royal Australian College of General Practitioners and Australian College of Midwives Inc (NHMRC et al 2000). In New Zealand, all babies receive such a supplement with parental consent.

Infant formula generally has much higher levels of phylloquinone than breast milk. Reported levels range from 50–100 µg/L (Greer 1995, Haroon et al 1982). The AI for older infants was derived from that of younger infants on a body weight basis.

Children & adolescents	**AI**	**Vitamin K**
All		
1–3 yr	**25 µg/day**	
4–8 yr	**35 µg/day**	
Boys		
9–13 yr	**45 µg/day**	
14–18 yr	**55 µg/day**	
Girls		
9–13 yr	**45 µg/day**	
14–18 yr	**55 µg/day**	

***Rationale*:** There are no data on which to set an EAR for children and adolescents, so an AI has been set based on median intakes from a re-analysis of the National Nutrition Survey of Australia, 1995 using the USDA nutrient data base, and rounding up.

Adults	AI	Vitamin K
Men		
19–30 yr	**70 µg/day**	
31–50 yr	**70 µg/day**	
51–70 yr	**70 µg/day**	
>70 yr	**70 µg/day**	
Women		
19–30 yr	**60 µg/day**	
31–50 yr	**60 µg/day**	
51–70 yr	**60 µg/day**	
>70 yr	**60 µg/day**	

***Rationale*:** There are not sufficient dose-response data to set an EAR for vitamin K in adults, so an AI has been set based on population median intakes from a reanalysis of the National Nutrition Survey of Australia, 1995, using the USDA data base. The AI is the highest median intake of any age group within the gender, rounded up. Experimental data indicate that these levels are well above the level needed to maintain a normal PT in otherwise healthy people and are in line with the intakes recommended by FAO:WHO (2001), the UK (1991) and the German/Austrian/Swiss Nutrition Societies (2002). They are, however, considerably lower than those recently recommended by the US (FNB:IOM 2001), based on median intakes in that country. Ferland et al (1993) found no difference in PT on dietary intakes of 10 µg/day or 80 µg/day in 32 subjects. Suttie et al (1998) found no change in PT during a depletion diet phase of 30–40 µg/day. Jones et al (1991) found that PT was in the normal range at a dietary intake of 40–60 µg/day and Bach et al (1996) found that PT was in the normal range in 18 people consuming about 70 µg/day in the baseline of their study. In general, changes in PT have only been seen at dietary intake levels well below 10 µg/day, although some changes in other indicators such as PIVKA II and plasma phylloquinone have been seen at intakes of 2–5 µg/day (Allison et al 1987).

Pregnancy	AI	Vitamin K
14–18 yr	**60 µg/day**	
19–30 yr	**60 µg/day**	
31–50 yr	**60 µg/day**	

***Rationale*:** There are no data to suggest that the vitamin K requirement in pregnancy differs from that of the non-pregnant woman. No additional amount in pregnancy has been recommended by the FAO: WHO, the US, the UK or European countries. Thus the AI is set at the level for non-pregnant women.

Lactation	AI	Vitamin K
14–18 yr	**60 µg/day**	
19–30 yr	**60 µg/day**	
31–50 yr	**60 µg/day**	

***Rationale*:** There are no data to suggest that the vitamin K requirement in lactation differs from that of the non-lactating woman. The vitamin K content of milk is relatively low and is little affected by maternal dietary intake in healthy women (Greer et al 1991). Thus the AI is set at the same level as for non-lactating women.

UPPER LEVEL OF INTAKE - VITAMIN K

There have been no ULs set for vitamin K.

***Rationale*:** No adverse effects have been associated with vitamin K consumption as food or supplements in humans or animals, so it is not possible to set a UL.

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MINERALS

CALCIUM

BACKGROUND

Calcium is required for the normal development and maintenance of the skeleton as well as for the proper functioning of neuromuscular and cardiac function. It is stored in the teeth and bones where it provides structure and strength. Low intakes of calcium have been associated with a condition of low bone density called osteoporosis which is quite common in western cultures and which often results in bone fracture. It is one of the major causes of morbidity amongst older Australians and New Zealanders, particularly postmenopausal women. Calcium intake throughout life is a major factor affecting the incidence of osteoporosis, however other factors, notably adequate vitamin D status and exercise, also play a role.

Bone mass increases by about sevenfold from birth to puberty and a further threefold during adolescence (Peacock 1991) and then remains stable until about age 50 in men and until the menopause in women. During the adolescent growth spurt, the required calcium retention is two to three times higher than that required for the development of peak bone mass which occurs at the same time as maximum height (Nordin et al 1979).

For approximately 5–10 years both during and after the climacteric and menopause (Heaney 1986), women lose bone more rapidly than men (2%–3% per year). Thereafter, the age-related loss in both sexes is about 0.5 to 1.0% per annum. All of the body's calcium reserve is stored in the skeleton. The size of the reserve is directly affected by the body's external calcium balance which depends on the relation between calcium intake and absorption on the one hand and losses of calcium through the skin, kidney and bowel on the other.

Until recently, the amount of dietary calcium needed to replace losses through sweat had not been included in estimates of calcium requirements. This omission accounts to a large extent for an apparent increase in calcium intake recommendations seen in the recent revisions of the FAO:WHO (2001) and US:Canadian (FNB:IOM 1997) recommendations and in the current revision of the Australian/New Zealand recommendations.

Calcium balance deteriorates at menopause when there is a decline in intestinal calcium absorption and/or an increase in urinary calcium excretion. In post menopausal women, there is evidence that a high calcium intake will slow the rate of bone loss and may reduce the risk of fracture (Cumming & Nevitt 1997, Dawson-Hughes et al 1990, Elders et al 1994, Nordin 1997, Prince et al 1995, Reid et al 1993, 1995) but it has been suggested that the improvement may attenuate over time (Mackerras & Lumley 1997).

A systematic review was also undertaken by Cumming & Nevitt (1997) of 14 studies of calcium supplements (including 4 RCTs), 18 studies of dietary calcium and hip fracture (no RCTs), and 5 studies of dietary calcium and other fracture sites (no RCTs). The 4 RCTs of calcium supplements (mean calcium dose 1,050 mg) found relative risk (RR) reductions of between 25% and 70%. Cochrane reviews by Shea et al (2003, 2004) also concluded that calcium supplementation had a small positive effect on bone density and a trend towards reduction in vertebral fractures but concluded that it was unclear if calcium reduces the incidence of non-vertebral fractures. However, one recent large intervention trial in 5,292 previously ambulatory elderly people who had already experienced a fracture showed no effect on the occurrence of further fractures of calcium and/or vitamin D supplements at levels of 1,000 mg calcium or 20 µg daily oral vitamin D3 alone or in combination (Grant et al 2005).

Calcium is found predominantly in milk and milk-based foods, with smaller amounts in bony fish, legumes and certain nuts, fortified soy beverages and breakfast cereals. Consumption of vegetarian diets may influence calcium needs because of their relatively high oxalate and phytate content, however, on balance, lacto-ovo-vegetarians appear to have similar calcium intakes to omnivores (Marsh et al 1980, Pedersen et al 1991, Reed et al 1994) and similar urinary excretion (Lloyd et al 1991, Tesar et al 1992).

Vegans have a lower calcium intake than vegetarians and omnivores (Larsson & Johansson 2002, New 2004), however one study by Kohlenberg-Mueller & Raschka (2003) has shown that both lactovegetarians and vegans can attain calcium balance. Intakes of calcium in adults in Australia and New Zealand average about 850 mg of which about 40% comes from non-milk sources.

For natural food sources of calcium, content is of equal or greater importance than bioavailability. The efficiency of calcium absorption varies across foods as calcium may be poorly absorbed from foods rich in oxalic acid (eg spinach, rhubarb, beans) or phytic acid (seeds, nuts, grains, certain raw beans and soy isolates). Absorption from soy milk can be, but is not always, as high as that from milk. Compared to milk, calcium absorption from dried beans is about 50% and from spinach, 10%.

Bioavailability from non-food sources (eg supplements) depends on the dosage and whether they are taken with a meal. In standardised studies of 250 mg calcium supplements given with a breakfast meal, absorption from supplements gave fractional absorption rates of 25–35% compared to a rate for calcium from milk of 29% (Heaney et al 1989, 1990, Miller et al 1988, Smith et al 1987). Efficiency of absorption of calcium from supplements is greatest at doses of 500 mg or less (Heaney et al 1975, 1988), but once the active transport mechanism is saturated, only 5–10% of additional calcium is absorbed.

Sodium intake can also affect calcium requirements as sodium and calcium excretion are linked in the kidney tubules (Nordin & Polley 1987, Matkovic et al 1995, O'Brien et al 1996, Devine et al 1995) – 2,300 mg of sodium takes out about 40 mg of calcium. The amount of protein in the diet can also affect calcium need. High intakes of protein increase urinary calcium excretion (Linkswiler et al 1981, Margen et al 1974) – each gram of protein takes out 1 mg of calcium. In contrast, diets that are particularly low in protein have also been shown to be of concern in terms of bone health, possibly due to lowered calcium absorption (Cooper et al 1996, Geinoz et al 1993, Hannan et al 2000, Kerstetter et al 2003a,b). The effect of protein on calcium retention is unclear (Delmas 1992, Walker & Linkswiler 1972).

Indicators that have been used to assess calcium requirements include balance studies, factorial estimates of requirements or assessment of changes in bone mineral density and bone mineral content. In setting the Australian and New Zealand recommendations, a balance approach used for the earlier Australian /New Zealand RDIs and used by FAO:WHO in their 2001 revision of *Human Vitamin and Mineral Requirements* (FAO:WHO 2001) was adopted. Other approaches, such as the various methods used by the US:Canadian DRI review (FNB:IOM 1997) give widely varying and inconsistent results, making interpretation problematic.

For adults, the results of 210 balance studies on normal individuals quoted in the FAO:WHO report were used to calculate calcium requirements. The estimate was based on the intake at which excreted calcium equals net absorbed calcium, adding an allowance for insensible losses. In postmenopausal women, allowance was made for an additional loss of calcium in urine.

The calcium requirements for other age/gender/physiological groups, for whom there were few balance studies, were estimated from the amount of calcium that each group must absorb in order to meet obligatory calcium losses, together with a consideration of their desirable calcium retention and then calculation of the intake required to provide this necessary rate of calcium absorption. The only exception to this was for infants in whom the concentration of calcium in breast milk formed the basis of recommendations.

1 mmol calcium = 40 mg calcium

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	AI	Calcium
0–6 months	**210 mg/day**	
7–12 months	**270 mg/day**	

***Rationale*:** The AI for 0–6 months was set by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of calcium in breast milk (264 mg/L) from 10 studies reviewed by Atkinson et al (1995), and rounding. Formula-fed babies require additional intakes in the vicinity of 350 mg/day as calcium is less bioavailable in formula. The AI for infants 7–12 months was set by adding an estimate for calcium from breast milk at this age, to an estimate of intake from supplementary foods. A breast milk volume of 0.60 L/day was assumed at older ages (Dewey et al 1984). The concentration of calcium in breast milk at this age averages 210 mg/L (Atkinson et al 1995). This gives a contribution of 126 mg/day from breast milk that is added to 140 mg/day from complementary foods (Abrams et al 1997, Specker et al 1997) and rounded, giving an AI of 270 mg/day.

Children & adolescents	EAR	RDI	Calcium
All			
1–3 yr	**360 mg/day**	**500 mg/day**	
4–8 yr	**520 mg/day**	**700 mg/day**	
Boys			
9–11 yr	**800 mg/day**	**1,000 mg/day**	
12–13 yr	**1,050 mg/day**	**1,300 mg/day**	
14–18 yr	**1,050 mg/day**	**1,300 mg/day**	
Girls			
9–11 yr	**800 mg/day**	**1,000 mg/day**	
12–13 yr	**1,050 mg/day**	**1,300 mg/day**	
14–18 yr	**1,050 mg/day**	**1,300 mg/day**	

***Rationale*:** The EAR for children 1–8 years was set by modelling the components of calcium requirements, including a component for skeletal growth (FAO:WHO 2001). Requirements were estimated from data on accumulation of whole-body calcium, which was converted to a daily rate of calcium accretion. This, together with consideration of urinary calcium losses, dermal losses and daily skeletal increments, gives an estimate of daily net absorbed calcium needs. For children 1–8 years, this results in a figure of about 220 mg. EARs were set for this age band based on the estimated amounts needed – 440 mg/day on average – to provide this level of absorbed calcium, assuming absorption rates of 1 SD above those of adults. A lower figure of 360 mg/day was applied to the younger age band as their requirements will be less and 520 mg/day to the older group, on an approximate body weight basis. The RDI was set assuming a CV of 15% for the EAR (as variation in the needs of children and adolescents are likely to be greater than for adults) and rounding, giving an RDI of 500 mg/day for 1–3 year-olds and 700 mg/day for 4–8 year-olds.

From 9–11 years of age, calcium accretion rates are similar to those in younger children with EARs being 800 mg/day, assuming absorption at 1 SD above that for adults. There is a striking increase in the rate of skeletal calcium accretion from 12 to 18 years of age (FAO:WHO 2001). For this age group, net absorbed calcium needs to be 440 mg. Assuming high calcium absorption (+2 SDs above that for adults) this requires an EAR of 1,046 mg/day. Assuming a CV of 15% for the EAR, this gives an RDI of 1,300 mg in the older adolescents. For children aged 9–11 years who have physically matured much earlier than average, the recommendations for 12–18 year-olds may be more appropriate.

Adults	EAR	RDI	Calcium
Men			
19–30 yr	**840 mg/day**	**1,000 mg/day**	
31–50 yr	**840 mg/day**	**1,000 mg/day**	
51–70 yr	**840 mg/day**	**1,000 mg/day**	
>70 yr	**1,100 mg/day**	**1,300 mg/day**	
Women			
19–30 yr	**840 mg/day**	**1,000 mg/day**	
31–50 yr	**840 mg/day**	**1,000 mg/day**	
51–70 yr	**1,100 mg/day**	**1,300 mg/day**	
>70 yr	**1,100 mg/day**	**1,300 mg/day**	

***Rationale*:** The EAR for adults was set by calculating calcium requirement as the intake at which excreted calcium equals net absorbed calcium, based on the results of 210 balance studies on 81 subjects (FAO:WHO 2001). This occurs at an intake of 520 mg/day to which losses through sweat must be added. Insensible losses of calcium have been estimated at 60 mg/day (Charles et al 1983, Hasling et al 1990). Taking the low absorption that occurs at about 500 mg/day into account, an additional intake of 320 mg is required to cover these losses, increasing the EAR to 840mg. At menopause, an additional 30 mg is lost in urine (Nordin et al 1999) and absorption probably decreases (Heaney et al 1989, Nordin 1997) raising the EAR to 1,100 mg. This gives an RDI of 1,000 mg/day for men and premenopausal women, and 1,300 mg for postmenopausal women (EAR+2SD = RDI), assuming a CV of 10% for the EAR.

Little is known about calcium metabolism in the elderly, but absorption is known to decrease with age in both sexes (Ebeling et al 1994, Morris et al 1991, Need et al 1998). Data for increased need at menopause are strong but those for older men are not. As a precaution, an additional average requirement of 250 mg/day is recommended, translating to an additional 300 mg for the RDI.

Pregnancy	EAR	RDI	Calcium
14–18 yr	**1,050 mg/day**	**1,300 mg/day**	
19–30 yr	**840 mg/day**	**1,000 mg/day**	
31–50 yr	**840 mg/day**	**1,000 mg/day**	

***Rationale*:** The EAR and RDI for pregnancy were based on the needs of the mother plus any additional allowance for the fetus and products of conception. The fetus retains about 25–30 g, mostly in the third trimester of pregnancy, but there is evidence that pregnancy is associated with increased calcium absorption (Cross et al 1995a, Heaney & Skillman 1971, Kent et al 1991, Kumar et al 1979). Significant increases in maternal calcium accretion, bone turnover and intestinal absorption early in pregnancy before fetal bone mineralisation have also been shown (Heaney & Skillman 1971, Purdie et al 1988).

Dietary calcium intake does not appear to influence changes in maternal bone mass in pregnancy (Raman et al 1978) and there is no relationship between the number of previous pregnancies and bone mineral density (Alderman et al 1986, Koetting & Warlaw 1988, Kreiger et al 19832, Walker & Linkswiler 1972, Wasnich et al 1983) or fracture risk (Johansson et al 1993). Indeed, some studies show a positive correlation between number of children born and radial bone mineral density or total body calcium (Aloia et al 1983) as well as reduction in the risk of hip fracture (Hoffman et al 1993).

These findings support the concept that maternal skeleton is not used for fetal calcium needs. The work of Prentice (2003) also confirms no additional need for calcium in pregnancy. The available information thus does not support the need for additional dietary intake in pregnancy as maternal adaptive mechanisms including enhanced efficiency of absorption more than meet the additional needs in the last trimester. The implication is that normal calcium intake is sufficient to meet the calcium requirement in the pregnant state.

Lactation	EAR	RDI	Calcium
14–18 yr	**1,050 mg/day**	**1,300 mg/day**	
19–30 yr	**840 mg/day**	**1,000 mg/day**	
31–50 yr	**840 mg/day**	**1,000 mg/day**	

***Rationale*:** During pregnancy, 210 mg calcium/day on average is secreted in milk. The primary source of this calcium appears to be from increased maternal bone resorption (Affinato et al 1996, Dobnig et al 1995, Kent et al 1990) which is independent of calcium intake (Cross et al 1995b, Sowers et al 1995, Specker et al 1994). This bone loss is replaced after weaning. There is no evidence that the calcium intake of lactating women should be increased above that of non-lactating women.

UPPER LEVEL OF INTAKE - CALCIUM

Infants	
0–12 months	**Not possible to establish**
Children and adolescents	
1–3 yr	**2,500 mg/day**
4–8 yr	**2,500 mg/day**
9–13 yr	**2,500 mg/day**
14–18 yr	**2,500 mg/day**
Adults 19+ yr	
Men	**2,500 mg/day**
Women	**2,500 mg/day**
Pregnancy	
14–18 yr	**2,500 mg/day**
19–50 yr	**2,500 mg/day**
Lactation	
14–18 yr	**2,500 mg/day**
19–50 yr	**2,500 mg/day**

***Rationale*:** Because of the inverse relationship between fractional calcium absorption and calcium intake, an additional intake of 1,000 mg added to a typical western diet would only increase calcium in urine by about 60 mg. Urinary calcium rises slowly with intake and risk of developing kidney stones (nephrolithiasis) from calcium supplements is therefore negligible. Toxic effects of calcium have only been seen when calcium is given in high doses as the carbonate as an antacid. The result is hypercalcaemia with renal calcification and renal failure and is known as the milk alkali syndrome or MAS (Burnett et al 1949).

Using MAS as the critically defined endpoint, a LOAEL of about 5 g can be identified for adults from 16 studies involving 26 subjects (FNB:IOM 1997).

A UF of 2 takes into account the potential for increased risk of high calcium intake, given the relatively common occurrence of kidney stones in Australia and New Zealand, the fact that hypercalciuria in people with renal stones has been shown to occur at intakes as low as 1,700 mg /day in men and 870 mg in women (Burtis et al 1974) and concern that calcium will interfere with absorption of other minerals such as zinc and iron in vulnerable populations. The UL is therefore set conservatively at 2,500 mg/day.

As there is little evidence for other age and physiological groups, this figure is used for all age and gender groups and physiological states, particularly in relation to the need to prevent interference with zinc and iron absorption.

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CHROMIUM

BACKGROUND

Chromium is involved in potentiating the action of insulin in vivo and in vitro (Mertz 1969, 1993, Mertz et al 1961) and several studies have shown beneficial effects of chromium on circulating glucose, insulin and lipids in humans, although not all studies were positive. These studies have been reviewed by Anderson (1997), Mertz (1993), Offenbacher et al (1997) and Stoecker (1996).

In man, chromium accumulates in liver, spleen, soft tissue and bone (Lim et al 1983). Research on chromium metabolism is limited by the lack of a good measure for establishing deficiency states in man. However, data from metabolic balance and urinary excretion studies suggest that only 0.4–2.5% of chromium is absorbed, the actual amount being determined by the environment of the gastrointestinal tract and ligands provided by foods (Clydesdale 1998).

Chromium is widely distributed through the food supply but the content within a given type of food can vary widely because of geochemical factors (Welch & Carey 1975).

Most ingested chromium is excreted unabsorbed in the faeces (Mertz 1969, Offenbacher et al 1986) whilst absorbed chromium is excreted mainly in the urine (Anderson et al 1983). Vitamin C appears to increase absorption (Davis et al 1995, Offenbacher 1994, Seaborn & Stoecker 1990). Animal experiments have shown that high phytate levels can reduce absorption (Chen et al 1973) although lower levels appear to have no effect (Keim et al 1987). There are no systematic data for humans. Animal experiments have shown that long-term consumption of some medicines can affect chromium absorption through affecting stomach acidity or gastrointestinal prostaglandins (Davis et al 1995, Kamath et al 1997). It has also been suggested that absorption may increase with chronic resistive exercise (Rubin et al 1998).

In man, diets very high in simple sugars (35% energy) have been shown to increase urinary chromium excretion (Kozlovsky et al 1986) which may be related to the insulinogenic actions of carbohydrates (Anderson et al 1990). Urinary excretion also appears to be increased by aerobic exercise (Anderson et al 1982, 1984, 1988).

Chromium deficiency is relatively rare but has been reported in patients on total parenteral nutrition (Brown et al 1986, Freund et al 1979, Jeejeebhoy et al 1977). It has been hypothesised that poor chromium status contributes to the incidence of impaired glucose tolerance and type II diabetes which has led to interest in a potential role for chromium supplements in type II diabetes. One Chinese study involved 180 subjects with type II diabetes being given placebo, 200 µg or 1,000 µg chromium as chromium picolinate for 4 months. The subjects showed decreased fasting and 2-hour insulins at two months at both supplement levels, with glycosylated haemoglobin and fasting and 2-hour glucose concentrations being lower in the higher supplement group only. The reduced glucose and insulin concentrations were maintained to 4 months and glycosylated haemoglobin in both dosage groups was also reduced (Anderson et al 1997).

Approaches to the estimation of chromium requirements have included balance studies (Bunker et al 1984, Offenbacher et al 1986), urinary chromium excretion (Anderson et al 1982, 1983, 1991, Anderson & Kozlovsky 1985, Paschal et al 1998), plasma chromium concentration (Anderson 1987, Veillon 1989) and blood glucose and insulin concentrations (Anderson et al 1991). However, none of these approaches has been found to be satisfactory (FNB:IOM 2001).

1 mmol chromium = 52 mg chromium

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Chromium**
0–6 months	**0.2 µg/day**	
7–12 months	**5.5 µg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of chromium in breast milk, and rounding. The figure for breast milk used was 0.25 µg/L based on the studies of Anderson et al (1993), Casey & Hambidge (1984), Casey et al (1985), Engelhardt et al (1990), and Mohamedshah et al (1998). The AI for 7–12 months was derived from consideration of the overall energy intake of infants of this age (3,530 kJ), the estimated contribution from breast milk (0.6 L/day at 0.25 µg/L = 0.15 µg chromium and 1,880 kJ), plus chromium from the amount of complementary foods needed to provide the additional 1,670 kJ using a chromium concentration of 3.2 µg/1,000 kJ (Anderson et al 1992). This gives a total chromium of 5.5 µg/day (0.15 µg from milk + 5.36 µg from foods).

Children & adolescents	**AI**	**Chromium**
All		
1–3 yr	**11 µg/day**	
4–8 yr	**15 µg/day**	
Boys		
9–13 yr	**25 µg/day**	
14–18 yr	**35 µg/day**	
Girls		
9–13 yr	**21 µg/day**	
14–18 yr	**25 µg/day**	

***Rationale*:** As there are limited data to set an EAR, AIs were set for children. In the absence of any data, the children's AIs were derived from the adult AIs on a body weight basis.

Adults	**AI**	**Chromium**
Men		
19–30 yr	**35 µg/day**	
31–50 yr	**35 µg/day**	
51–70 yr	**35 µg/day**	
>70 yr	**35 µg/day**	
Women		
19–30 yr	**25 µg/day**	
31–50 yr	**25 µg/day**	
51–70 yr	**25 µg/day**	
>70 yr	**25 µg/day**	

***Rationale*:** As there are limited data to set an EAR, an AI was set for adults. As there are no national intake data or food composition data available either for Australia or New Zealand for chromium, data from the FNB:IOM review (2001) were used to derive the AIs. The US estimates were based on analytical studies of 22 well-balanced adult diets designed by US nutritionists (Anderson et al 1992).

These studies gave an average chromium concentration of 3.21 µg/1,000 kJ food (range 2–5.7 µg/1,000 kJ). As there is some evidence that dietary intake data may have a tendency to underestimate actual intake (Mertz et al 1991), the average concentration in food was applied to the highest median intakes of energy for a given age group within the adult men or women, using intake data from the Australian (ABS 1998) and New Zealand (MOH 1999) National Nutrition Surveys.

Pregnancy	**AI**	**Chromium**
14–18 yr	**30 µg/day**	
19–30 yr	**30 µg/day**	
31–50 yr	**30 µg/day**	

***Rationale*:** Because of lack of data to establish the additional needs in pregnancy, the AI was extrapolated from the AIs for adolescent girls and women on the basis of an average weight gain of 16 kg in pregnancy for pregnancies with good outcomes (Carmichael et al 1997).

Lactation	**AI**	**Chromium**
14–18 yr	**45 µg/day**	
19–30 yr	**45 µg/day**	
31–50 yr	**45 µg/day**	

***Rationale*:** The AI for lactation was estimated from the intake necessary to replace chromium secreted in milk plus the AI for women. The amount needed to be absorbed is 0.252 µg/L x 0.78 L/day (200 ng/day). With absorption at 1%, an additional 20 µg/day is needed.

UPPER LEVEL OF INTAKE - CHROMIUM

The ULs for chromium are unknown as there are insufficient data.

A number of potential adverse effects of high chromium intakes in relation to renal failure, genotoxicity, carcinogenicity, hepatic dysfunction and reproductive function have been seen either in animal studies or in humans (Al-Hamood et al 1998, Bagchi et al 1997, Bataineh et al 1997, Cerulli et al 1988, Elbetieha & Al-Hamood 1997, Fristedt et al 1965, Kaufman et al 1970, Kusiak et al 1995, Loubieres et al 1999, Speetjens et al 1999, Stearns et al 1995, Wasser et al 1997). However, adequate human data on trivalent chromium are limited.

No adverse side effects were reported in a number of supplementation trials in which subjects received up to 1 mg chromium/day, mostly as picolinate, for several months (Flodin 1990, Hathcock 1997). These trials, however, were mainly studies of efficacy and not designed to find potential toxic effects. The limited data from all studies on subchronic, chronic and reproductive toxicity on soluble trivalent chromium salts do not give clear information on the dose-response relationship. Therefore, ULs cannot be derived.

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COPPER

BACKGROUND

Copper is a component of a number of metalloenzymes including diamine oxidase, monoamine oxidase, lysyl oxidase, ferroxidases, cytochrome *c* oxidase, dopamine beta monoxygenase, alpha-amidating monooxygenase and cupro/zinc superoxide dismutase.

Copper is widely distributed in foods with organ meats, seafood, nuts and seeds being major contributors. Wheat bran cereals and whole grain products are also good sources. Nearly two thirds of the body's copper is found in the skeleton and muscles but the liver is also important in maintaining plasma levels (Olivares & Uauy 1996, Turnlund et al 1998).

Copper is absorbed mainly in the small intestine although some absorption may also occur in the stomach. Absorption varies with copper intake, ranging from more than 50% at intakes below 1 mg/day to less than 20% for intakes above 5 mg/day (Turnlund 1998). The composition of the diet itself has little effect on bioavailability. However, very high levels of zinc or iron, generally taken as supplements, can affect absorption in adults and infants (Botash et al 1992, Lonnerdal & Hernell 1994, Morais et al 1994 Turnlund 1999). Excretion through bile is used to regulate copper balance. Urinary copper excretion is normally very low over a wide range of intakes.

Copper deficiency results in defects in connective tissue that lead to vascular and skeletal problems, and anaemia related to defective iron metabolism. It can also affect the central nervous system (Harris 1997, Turnlund 1999) and the immune and cardiovascular systems, notably in infants (Graham & Cordano 1969, Olivares & Uauy 1996, Turnlund, 1999). Frank copper deficiency is rare in humans but has been seen in certain circumstances in infants (Shaw 1992) and under conditions of total parenteral nutrition (Fujita et al 1989). Symptoms include normocytic, hyperchromic anaemia, leukopenia and neutropenia. Other studies have observed osteoporosis in copper-deficient infants and young children (Higuchi et al 1988) and heart beat irregularities (Milne 1998).

There is no single indicator for the assessment of requirements for copper in humans (FNB:IOM 2001). Serum copper, ceruloplasmin concentration, erythrocyte superoxide dismutase activity, platelet copper, cytochrome *c* oxidase activity, urinary copper, leucocyte copper concentration, lysyl oxidase activity, peptidyl glycine alpha-amidating mono-oxygenase activity, diamine oxidase activity, copper balance and factorial analysis have all been used, but they generally give inconsistent results.

1 mmol copper = 63.5 mg copper

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Copper**
0–6 months	**0.20 mg/day**	
7–12 months	**0.22 mg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of copper in breast milk, and rounding. The figure used for breast milk was 0.25 mg/L based on the studies of Biego et al (1998), Raiten et al (1998) and Rossipal & Krachler (1998) as outlined in the relevant FNB:IOM document (FNB:IOM 2001). The AI for 7–12 months was set by adding the average intake from human milk to a component for complementary foods. There are no data for copper intake of weaning foods in Australia or New Zealand. Data from the US NHANES survey (FNB:IOM 2001) showed that the median copper intake from weaning foods for children 7–12 months was 0.1 mg/day. At 7-12 months, human milk concentration is 0.20 mg/L or less, such that with a milk volume of 0.6 L, intake from milk is 0.12 mg/day. Thus, total intake is 0.22 mg/day.

Children & adolescents	AI	Copper
All		
1–3 yr	**0.7 mg/day**	
4–8 yr	**1.0 mg/day**	
Boys		
9–13 yr	**1.3 mg/day**	
14–18 yr	**1.5 mg/day**	
Girls		
9–13 yr	**1.1 mg/day**	
14–18 yr	**1.1 mg/day**	

***Rationale*:** As there are no data to set EARs, AIs for children were set using the median intakes from reanalyses using appropriate age-bands of the National Nutrition Surveys of Australia (ABS 1998) and New Zealand (MOH 1999, 2003) weighted on a population basis.

Adults	AI	Copper
Men		
19–30 yr	**1.7 mg/day**	
31–50 yr	**1.7 mg/day**	
51–70 yr	**1.7 mg/day**	
>70 yr	**1.7 mg/day**	
Women		
19–30 yr	**1.2 mg/day**	
31–50 yr	**1.2 mg/day**	
51–70 yr	**1.2 mg/day**	
>70 yr	**1.2 mg/day**	

***Rationale*:** It was felt that the small data sets – one in young men, one in men of mixed age and one in postmenopausal women – were insufficient to allow the setting of an EAR and an RDI. An AI was set based on median population intakes from the Australian (ABS 1998) and New Zealand (MOH 1999) National Dietary Surveys weighted on a population basis. As dietary data can underestimate intakes, the highest intake of the adult age groups for the men and women was used to set a figure for all adult males or females.

Pregnancy	AI	Copper
14–18 yr	**1.2 mg/day**	
19–30 yr	**1.3 mg/day**	
31–50 yr	**1.3 mg/day**	

***Rationale*:** There are no data on the needs for copper in pregnancy. Therefore an AI was derived based on the amounts of copper that must be accumulated during pregnancy to account for the fetus and products of pregnancy. Over the course of pregnancy, the additional requirement is about 0.067 mg absorbed copper/day (Widdowson & Dickerson, 1964) or 0.10 mg dietary copper/day. From the available data, it is not possible to assume that absorption efficiency increases in pregnancy to account for this; so 0.10 mg/day was added to the AI for non-pregnant, adolescent girls and women.

Lactation	AI	Copper
14–18 yr	**1.4 mg/day**	
19–30 yr	**1.5 mg/day**	
31–50 yr	**1.5 mg/day**	

***Rationale*:** There are no data to set an EAR for lactating women. The AI was set on the basis of the amount of copper required to replace copper secreted daily in human milk, equivalent to additional absorbed copper of 0.20 mg/day. At the level of the AI, copper bioavailability is about 65–75%, so an additional 0.30 mg/day copper needs to be consumed.

UPPER LEVEL OF INTAKE - COPPER

Infants	
0–12 months	**Not possible to establish. Source of intake should be milk, formula and food only**
Children and adolescents	
1–3 yr	**1 mg/day**
4–8 yr	**3 mg/day**
9–13 yr	**5 mg/day**
14–18 yr	**8 mg/day**
Adults+ 19 yr	
Men	**10 mg/day**
Women	**10 mg/day**
Pregnancy	
14–18 yr	**8 mg/day**
19–50 yr	**10 mg/day**
Lactation	
14–18 yr	**8 mg/day**
19–50 yr	**10 mg/day**

***Rationale*:** Human data relating to liver effects were used as the indicator outcome as described in FNB:IOM (2001). A NOAEL of 10 mg/day was identified from the work of Pratt et al (1985) who undertook a 12-week, double blind study in seven adults. Liver function tests were normal. A UF of 1 was applied, as there is no evidence from large international databases to indicate adverse effects at 10–12 mg copper/day in foods and because of the rarity of observed liver damage from copper exposure in humans with normal copper homeostasis. Thus, a UL of 10 mg/day from food and supplements was set for adults.

Given the lack of information, the ULs for children and adolescent were extrapolated from the adult figure on the basis of relative body weight, and rounded down. As there are no data about toxicity in pregnancy and lactation, the ULs for adolescent girls and adult women were also applied to the equivalent pregnant and lactating adolescent girls and women.

These ULs do not apply to individuals with Wilson's disease, Indian Childhood Cirrhosis or Idiopathic Copper Toxicosis.

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FLUORIDE

BACKGROUND

Fluoride is a normal constituent of the human body, involved in the mineralisation of both teeth and bones (Fairley et al 1983, Varughese & Moreno 1981). The fluoride concentration in bones and teeth is about 10,000 times that in body fluids and soft tissues (Bergmann & Bergmann 1991, 1995). Nearly 99% of the body's fluoride is bound strongly to calcified tissues. Fluoride in bone appears to exist in both rapidly- and slowly-exchangeable pools. Because of its role in the prevention of dental caries, fluoride has been classified as essential to human health (Bergmann & Bergmann 1991, FNB:IOM 1997).

Ingestion of fluoride in the pre-eruptive development of teeth has the effect of reducing caries due to uptake of fluoride by enamel crystallites and formation of fluorohydroxyapatite which is less soluble than hydroxyapatite (Brown et al 1977, Chow 1990). The post-eruptive effect on reducing caries is due to reduced acid production by bacteria and increased enamel remineralisation in acidogenic challenge (Bowden 1990, Hamilton 1990, Marquis 1995). Fluoride also has a unique ability to stimulate new bone formation and as such has been used as an experimental drug for the treatment of osteoporosis (Kleerekoper & Mendlovic 1993) although results have been variable depending on site assessed and the outcome measured (Kroger et al 1994, Riggs et al 1990, Sowers et al 1986, 1991).

Because of the low natural levels of fluoride in some water supplies and high levels of dental caries, many authorities worldwide, including Australia and New Zealand, have permitted, or instigated, fluoridation of water supplies. Although this has met some opposition, partly because of the potential health or dental effects that include fluorosis, the NHMRC concluded that a concentration of 1 mg/L secures most of the caries preventive effect available from fluoridated water, while maintaining minimal contribution of water fluoride to dental fluorosis in children and that there was no evidence of adverse health effects attributable to fluoride in communities exposed to a combination of fluoridated water (1 mg/L) and contemporary discretionary sources of fluoride (NHMRC 1991).

Not all Australian water supplies are fluoridated, notably those in parts of Queensland such as Brisbane. Concentrations in fluoridated areas are within the range identified by the NHMRC as safe and effective, varying from 0.6 mg/L in Darwin to 1.1 mg/L in Hobart. In New Zealand, the Ministry of Health (MOH) has recommended fluoridation of water supplies since the 1950s as the most effective and efficient way of preventing dental caries in communities receiving a reticulated water supply. In the Drinking Water Standards 2000, fluoridation is recommended at a level of 0.7–1.0 mg/L in drinking water. Around 85% of the New Zealand population is on what the government considers to be satisfactorily safe community water supplies in terms of fluoride content. Another 5% of the population are on community water supplies. Some of the larger centres without fluoridated water supplies currently are Whangarei, Tauranga, Wanganui, Napier, Nelson, Blenheim, Christchurch, Timaru and Oamaru.

The World Health Organization states in a review of chronic disease and diet that evidence that both locally applied and systemic fluoride are preventive for dental caries is convincing (WHO 2003).

One of the concerns expressed about fluoridation of the water supply relates to increasing rates of fluorosis in children seen in some communities over the same period as fluoridation has been practised. Dental fluorosis is a biomarker of over-exposure to fluoride among young children and results in a mottling of teeth. Recent research in Australia among children not exposed and exposed to water fluoridation indicated prevalences of 19% and 34%, respectively (Puzio et al 1993). However, Kumar et al (1989) have shown that the increases in fluorosis in other communities have been greater in areas with non-fluoridated water supplies and are likely to be due to increased intake of fluoride from supplements and ingestion from toothpaste and reconstituted infant formula (Osuji et al 1988, Pendrys & Stamm 1990).

Fluoride intake from most foods is low. Foods generally have concentrations well below 0.05 mg/100 g (Taves 1983). However, water in fluoridated areas, as well as beverages, teas, some marine fish and some infant formulas, especially those that are made or reconstituted with fluoridated water,

generally have higher concentrations. Other sources of fluoride include supplements and dental products. Water-soluble fluoride eg sodium fluoride, is nearly completely absorbed. The bioavailability may be reduced by the presence of calcium, magnesium, aluminium, iron or other cations. Absorbed fluoride is rapidly bound to the minerals in bones and teeth. Most of the non-retained or metabolic fluoride is excreted through the kidneys and the remainder via the intestines. In healthy young or middle-aged adults, about 50% of absorbed fluoride is retained and 50% excreted, but young children may retain as much as 80% (Eksterand et al 1994a,b).

Indicators used to assess the requirements for fluoride include prevalence of dental caries, measures of bone mineral content and fluoride balance studies.

1 mmol fluoride = 19 mg fluoride

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Fluoride**
0–6 months	**0.01 mg/day**	
7–12 months	**0.50 mg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of fluoride in breast milk of 0.013 mg/L (Dabeka et al 1986, FNB:IOM 1997) for mothers in areas with fluoridated water. Levels in formulas can vary widely depending on the concentration in the water used to reconstitute it. The AI for 0–6 months was based on extensive documentation about relationships between caries, water concentrations and fluoride intake (FNB:IOM 1997). A level of 0.05 mg/kg/day confers a high level of protection against caries and is not associated with unwanted health effects. Assuming a standard weight of 9 kg, this gives an AI of 0.5 mg/day. Infants living in non-fluoridated areas will not easily achieve the AI for fluoride, so supplements have been recommended based on life stage and level of water fluoridation.

***Special note*:** Australian data have shown that prolonged consumption of infant formulas reconstituted with optimally-fluoridated water beyond 12 months of age could result in excessive amounts of fluoride being ingested during development of the enamel of the anterior permanent teeth and therefore may be a risk factor for fluorosis of these teeth (Silva & Reynolds 1996).

The majority of Australian/New Zealand infant formula manufacturers now control the concentration of fluoride. It is also possible to reduce concentrations by preparing formula using non-fluoridated water such as rain, filtered or spring water from non-volcanic areas in its preparation.

Supplements may be necessary for older infants in non-fluoridated areas. However, it is likely that many older infants and younger children are already ingesting 0.4–0.6 mg fluoride per day from foods, beverages and toothpaste alone (Burt 1992). A study of 60, 11–13 month old New Zealand infants (Chowdhury et al 1990) showed that total intake including fluoride from tablets and toothpastes ranged from 0.093 to 1.299 mg fluoride/day in fluoridated areas and from 0.039 to 0.720 mg fluoride/day in non-fluoridated areas. The fluoride from the diet (food and drink) ranged from 0.089 to 0.549 mg day in the fluoridated areas, and 0.038 to 0.314 mg day in the non-fluoridated areas.

Children & adolescents	AI	Fluoride
All		
1–3 yr	**0.7 mg/day**	
4–8 yr	**1.0 mg/day**	
Boys		
9–13 yr	**2.0 mg/day**	
14–18 yr	**3.0 mg/day**	
Girls		
9–13 yr	**2.0 mg/day**	
14–18 yr	**3.0 mg/day**	

***Rationale*:** The AI for children is based on the requirement of 0.05 mg/kg body weight/day outlined above and adjusted for the standard body weights of 13 kg for 1–3 year olds, 22 kg for 4–8 year olds, 40 kg for 9–13 year olds, 64 kg for boys aged 14–18 years and 57 kg for 14–18 year-old girls. Supplements may be necessary for children in non-fluoridated areas, although the younger children (1–3 years) may already be getting much of their requirement from foods, beverages and toothpaste (Burt 1992).

Adults	AI	Fluoride
Men		
19–30 yr	**4 mg/day**	
31–50 yr	**4 mg/day**	
51–70 yr	**4 mg/day**	
>70 yr	**4 mg/day**	
Women		
19–30 yr	**3 mg/day**	
31–50 yr	**3 mg/day**	
51–70 yr	**3 mg/day**	
>70 yr	**3 mg/day**	

***Rationale*:** The AI for adults is based on the requirement of 0.05 mg/kg body weight/day outlined above and adjusted for the standard body weights of 76 kg for men and 61 kg for women.

Pregnancy	AI	Fluoride
14–18 yr	**3 mg/day**	
19–30 yr	**3 mg/day**	
31–50 yr	**3 mg/day**	

***Rationale*:** There is no evidence that requirements in pregnancy are greater than those of the non-pregnant woman.

Lactation	AI	Fluoride
14–18 yr	**3 mg/day**	
19–30 yr	**3 mg/day**	
31–50 yr	**3 mg/day**	

***Rationale*:** There are no studies of the metabolism of fluoride in pregnancy. Fluoride concentrations in milk are very low and fairly insensitive to differences in the fluoride concentration of maternal drinking water. The AI is not greater than that of women in the non-pregnant, non-lactating state.

UPPER LEVEL OF INTAKE - FLUORIDE

Infants	
0–6 months	**0.7 mg/day**
7–12 months	**0.9 mg/day**
Children and adolescents	
1–3 yr	**1.3 mg/day**
4–8 yr	**2.2 mg/day**
9–13 yr	**10.0 mg/day**
14–18 yr	**10.0 mg/day**
Adults 19+ yr	
Men	**10.0 mg/day**
Women	**10.0 mg/day**
Pregnancy	
All ages	**10.0 mg/day**
Lactation	
All ages	**10.0 mg/day**

***Rationale*:** The UL was set on the basis of moderate enamel fluorosis. A LOAEL of 0.10 mg/kg body weight for infants and children up to 8 years was set on the basis of community studies (Dean 1942, FNB:IOM 1997). A UF of 1 was applied, as the adverse effect is cosmetic rather than functional. For older children and adults, a NOAEL of 10 mg/day was derived based on data on the relationship between fluoride intake and skeletal fluorosis (FNB:IOM 1997, Leone et al 1954, 1955, McCauley & McClure 1954, Schlesinger et al 1956, Sowers et al 1986, Stevenson & Watson 1957). A UF of 1 was selected, as there are no signs of symptomatic skeletal fluorosis at this level of intake. No data exist to show increased susceptibility in pregnancy or lactation, so the same UL was adopted.

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IODINE

BACKGROUND

Iodine was one of the first trace elements to be identified as essential. In the 1920s it was shown to be an integral component of the thyroid hormone, thyroxine (T_4), required for normal growth and metabolism. Soon after, it was recognised as a component of 3,5,3'-tri-iodothyronine (T_3), a key regulator of important cell processes. The thyroid hormones are required for normal growth and development of tissues such as the central nervous system and have a broader role in maturation of the body as a whole. They are important for energy production and oxygen consumption in cells thereby helping to maintain the body's metabolic rate. Iodine occurs in tissues in both organic and organically bound forms. The iodine content of the adult body is approximately 15–20 mg, of which 70–80% is in the thyroid gland – which concentrates iodine (Freake 2000) – and the rest is in blood.

Once iodine is absorbed in the form of iodide and reaches the circulation, it is concentrated in the thyroid gland where it is converted to iodine and combined with tyrosine residues of thyroglobulin. The iodinated tyrosines are removed from the thyroglobulin by proteolytic enzymes and T_4 is released into the circulation (Kidd et al 1974). T_4 is inert until deiodinated either to T_3 (or reverse T_3, an inactive form of T_4). Deiodination requires selenocysteine as the active form of selenium in the iodothyronine deiodinases (Arthur & Beckett 1999). Regulation of thyroid hormone synthesis, release and action is complex. It involves the thyroid, pituitary, brain and peripheral tissues. Excess inorganic iodine is readily excreted in urine, with smaller amounts in faeces and sweat (Lamberg 1993).

Iodine in foods is in the inorganic iodide form and is easily absorbed in the stomach and upper small intestine (Sumar & Ismail 1997) as is supplemental iodine. Thus the amount of bioavailable iodine depends on the amount consumed rather than the chemical form or composition of the diet (Fairweather-Tait & Hurrell 1996). However, the utilisation of absorbed iodine is influenced by goitrogens. Goitrogens such as sulphur-containing thionamides found in brassica vegetables such as cabbage, broccoli and brussel sprouts can interfere with the synthesis of the thyroid hormones. They impair the binding of iodine to thyroglobulin and prevent oxidation of iodide by thyroid iodide peroxidase (Gaitan 1980). Foods containing goitrogenic cyanoglucosides such as sweet potato and maize release thiocyanate that competes with iodide, blocking its uptake by the thyroid (Gaitan 1980, Lamberg 1993).

The iodine content of most foods is low and can be affected by soil, irrigation and fertilisers. Losses can occur in cooking. Most soils in New Zealand are low in iodine resulting in low concentrations in locally grown foods. The major food sources are of marine origin. Processing aids such as calcium iodate, potassium iodate, potassium iodide and cuprous iodide act to increase the content of iodine in certain foods. Iodophores used by the dairy industry, which opportunistically enter the food supply, were the major, if not the prime, contributors to intake of iodine in Australia and New Zealand in the 1960s. However, controls introduced in the early 1970s saw changes in practices leading to reduced iodine in milk. As the use of iodised salt has also declined since that time, intakes of iodine have fallen in both Australia and New Zealand (Eastman 1999, Gunton et al 1999, Hynes et al 2004, Skeaff et al 2002, 2005, Thomson 2002, 2004).

Iodine deficiency results in a range of conditions collectively termed 'iodine deficiency disorders' (Hetzel et al 1990, Thomson 2002). In severe deficiency, these include major effects on the fetus, such as abortion or stillbirth, congenital anomalies, increased perinatal and infant mortality, neurological cretinism or mental deficiency with deaf mutism, spastic diplegia and squint, myxoedematous cretinism and dwarfism and psychomotor effects. In neonatal life, childhood or adulthood, iodine deficiency can lead to goitre or hypothyroidism as well as impaired mental and physical development.

Several indicators are used to assess iodine requirements, including urinary iodide excretion, thyroid hormones in plasma or serum, assessment of thyroid size and goitre rate, radioactive iodine uptake, balance studies and epidemiologic, population studies. Thyroid iodine accumulation and turnover is generally considered to be the best measure.

1 mmol iodine = 127 mg iodine

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Iodine**
0–6 months	**90 µg/day**	
7–12 months	**110 µg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of iodine in breast milk (115 µg/L), and rounding. The figure used for breast milk was that recommended by FAO:WHO (2001) which is also consistent with the study of Johnson et al (1990) in New Zealand. The AI for 7–12 months was extrapolated from that of younger infants using a metabolic weight ratio.

Children & adolescents	**EAR**	**RDI**	**Iodine**
All			
1–3 yr	**65 µg/day**	**90 µg/day**	
4–8 yr	**65 µg/day**	**90 µg/day**	
Boys			
9–13 yr	**75 µg/day**	**120 µg/day**	
14–18 yr	**95 µg/day**	**150 µg/day**	
Girls			
9–13 yr	**75 µg/day**	**120 µg/day**	
14–18 yr	**95 µg/day**	**150 µg/day**	

***Rationale*:** The EAR for children was based on balance studies for the age groups 1–3 years, 4–8 years and 14–18 years (Ingenbleek & Malvaux 1974, Malvaux et a 1969) and by extrapolation from adults using metabolic body weight ratios for 9–13 year olds. The RDI was set assuming a CV of 20% for the EAR from studies in adults (FNB:IOM 2001), and rounded.

Adults	**EAR**	**RDI**	**Iodine**
Men			
19–30 yr	**100 µg/day**	**150 µg/day**	
31–50 yr	**100 µg/day**	**150 µg/day**	
51–70 yr	**100 µg/day**	**150 µg/day**	
>70 yr	**100 µg/day**	**150 µg/day**	
Women			
19–30 yr	**100 µg/day**	**150 µg/day**	
31–50 yr	**100 µg/day**	**150 µg/day**	
51–70 yr	**100 µg/day**	**150 µg/day**	
>70 yr	**100 µg/day**	**150 µg/day**	

***Rationale*:** The EARs for adults were based on iodine balance studies indicating that iodine balance is achieved at intakes over 100 µg/day but not below 40 µg/day. From these data, particularly the iodine accumulation and turnover studies, and a New Zealand study in adults relating urinary iodide to thyroid volume (Thomson et al 2001) that indicated physiological requirements of 85–100 µg/day, a value of 100 µg/day was adopted for the EAR. The RDI was set assuming a CV of 20% for the EAR (FNB:IOM 2001), and rounded up to reflect the possible influence of natural goitrogens.

Pregnancy	**EAR**	**RDI**	**Iodine**
14–18 yr	**160 µg/day**	**220 µg/day**	
19–30 yr	**160 µg/day**	**220 µg/day**	
31–50 yr	**160 µg/day**	**220 µg/day**	

***Rationale*:** The EAR for pregnancy was based on data relating to the thyroid content of newborns, iodine balance studies and iodine supplementation studies in pregnancy (FNB:IOM 2001). The RDI was set assuming a CV of 20% for the EAR.

Lactation	**EAR**	**RDI**	**Iodine**
14–18 yr	**190 µg/day**	**270 µg/day**	
19–30 yr	**190 µg/day**	**270 µg/day**	
31–50 yr	**190 µg/day**	**270 µg/day**	

***Rationale*:** The EAR for lactation was based on the adult female needs (100 µg/day) and the replacement needs for iodine secreted in breast milk (90 µg/day). The RDI was set assuming a CV of 20% for the EAR.

UPPER LEVEL OF INTAKE - IODINE

Infants	
0–12 months	**Not possible to establish. Source of intake should be milk, formula and food only**
Children and adolescents	
1–3 yr	**200 µg/day**
4–8 yr	**300 µg/day**
9–13 yr	**600 µg/day**
14–18 yr	**900 µg/day**
Adults 19+ yr	
Men	**1,100 µg/day**
Women	**1,100 µg/day**
Pregnancy	
14–18 yr	**900 µg/day**
19–50 yr	**1,100 µg/day**
Lactation	
14–18 yr	**900 µg/day**
19–50 yr	**1,100 µg/day**

***Rationale*:** The first effect seen in iodine excess is challenged thyroid function by elevated TSH concentrations. This is the critical adverse effect (FNB:IOM 2001). Two studies of TSH concentrations after supplemental iodine showed increased TSH at 1,800 µg/day and 1,700 µg/day (Gardner et al 1988, Paul et al 1988) indicating a LOAEL of 1,700 µg/day. A UF of 1.5 is applied to derive a NOAEL that is the basis of the UL for adults. As there is little evidence for other age groups, ULs for children and adolescents were extrapolated from the adult recommendation on a metabolic body weight basis. The adult UL was also used for pregnancy and lactation as there was no evidence of increased sensitivity associated with these.

***Note*:** Individuals with thyroid disorders or a long history of iodine deficiency may still respond adversely at levels of intake below the UL.

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IRON

BACKGROUND

Iron is a component of a number of proteins including haemoglobin, myoglobin, cytochromes and enzymes involved in redox reactions. Haemoglobin is important for transport of oxygen to tissues throughout the body. Iron can exist in a range of oxidation states. The interconversion of these various oxidation states allows iron to bind reversibly to ligands such as oxygen, nitrogen and sulphur atoms. Almost two thirds of the body's iron is found in haemoglobin in circulating erythrocytes. About a quarter of the body's iron is found in readily metabolised stores as ferritin or haemosiderin in the liver and reticulo-endothelial system. The remaining iron is in the myoglobin of muscle tissue and a variety of enzymes necessary for oxidative metabolism and other cell functions.

The iron content of the body is highly conserved (Bothwell et al 1979). To achieve iron balance, adult men need to absorb about 1 mg/day and adult menstruating women about 1.5 mg/day, although this is highly variable. Towards the end of pregnancy, the absorption of 4–5 mg/day is necessary. Requirements are higher during periods of rapid growth in early childhood and adolescence.

Inadequate iron intake can lead to varying degrees of deficiency, from low iron stores (as indicated by low serum ferritin and a decrease in iron-binding capacity); to early iron deficiency (decreased serum transferrin saturation; increased erythrocyte protoporphyrin concentration and increased serum transferrin receptor) to iron-deficiency anaemia (low haemoglobin and haematocrit as well as reduced mean corpuscular haemoglobin and volume). These biochemical measures are used as the key indicators in setting the iron requirements.

Wholegrain cereals, meats, fish and poultry are the major contributors to iron intake in Australia and New Zealand, but the iron from plant sources is less bioavailable. The form in which iron is consumed will affect dietary intake requirements as not all dietary iron is equally available to the body. The factors that determine the proportion of iron absorbed from food are complex. They include the iron status of an individual, as well as the iron content and composition of a meal. Normal absorption may vary from 50% in breast milk to 10% or less in infant cereals. Iron in foods can come in two general forms – as haem or non-haem iron. Iron from animal food sources such as meat, fish and poultry may be either haem or non-haem whereas the iron in plant sources such grains and vegetables is non-haem. The haem form is more bioavailable to humans than the non-haem.

The presence of other nutrients such as vitamin C and organic acids such as citric, lactic or malic acid can increase the absorption of non-haem iron. Consumption of meat, fish and poultry can also increase non-haem iron absorption from plant foods consumed at the same time. In contrast, some other components of the food supply such as calcium, zinc or phytates (found in legumes, rice and other grains) can inhibit the absorption of both haem and non-haem iron, and polyphenols and vegetable protein can inhibit absorption of non-haem iron. High iron intakes can, in turn, affect the absorption of other nutrients such as zinc or calcium.

Functional indicators of iron deficiency may include reduced physical work capacity, delayed psychomotor development in infants, impaired cognitive function, impaired immunity and adverse pregnancy outcomes. However, as these are difficult to relate directly to a specific dietary intake, biochemical indices are generally used in estimating dietary requirements.

The distribution of iron requirements is skewed to the right and it is difficult to achieve a steady state with iron because it is highly conserved in the body. For these reasons, factorial modelling rather than the classical balance study method is used to determine the average requirements for the various age, gender and physiological states. This factorial modelling proposes daily physiological requirement for absorbed iron based on estimates of basal losses (obligatory losses through faeces, urine, sweat and exfoliation of skin) and, where relevant, menstrual losses and needs for iron accretion in periods of growth such as childhood, adolescence or pregnancy (FNB:IOM 2001). These accretion needs are estimated from known changes in blood volume, fetal and placental iron concentration and increases

in total body erythrocyte mass. The EARs are based on the need to maintain a normal, functional iron concentration, but only a small store (serum ferritin concentration of 15 μg/L).

1 mmol iron = 55.8 mg iron

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Iron**
0–6 months	**0.2 mg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of iron in breast milk (0.26 mg/L), and rounding (Butte et al 1987, Dewey & Lonnerdal 1983, Lipsman et al 1985, Picciano & Guthrie 1976, Vaughan et al 1979).

***Note*:** this recommendation relates to breast-fed babies. The iron in formula is much less bioavailable (generally only 10–20% as available as that in breast milk) (Fomon et al 1993, Lonnerdal et al 1981) so the intake in formula-fed infants will need to be significantly higher.

Infants	**EAR**	**RDI**	**Iron**
7–12 months	**7 mg/day**	**11 mg/day**	

Rationale: The EAR for 7–12 months was set by modelling the components of iron requirements, estimating the requirements for absorbed iron at the 50th centile with use of an upper limit of 10% iron absorption, and rounding. The RDI was set by modelling the components of iron requirements, estimating the requirement for absorbed iron at the 97.5th centile, with use of an upper limit of 10% absorption, and rounding.

Absorption is about 18% from a mixed western diet including animal foods and about 10% from a vegetarian diet; so vegetarian infants will need higher intakes.

Children & adolescents	**EAR**	**RDI**	**Iron**
All			
1–3 yr	**4 mg/day**	**9 mg/day**	
4–8 yr	**4 mg/day**	**10 mg/day**	
Boys			
9–13 yr	**6 mg/day**	**8 mg/day**	
14–18 yr	**8 mg/day**	**11 mg/day**	
Girls			
9–13 yr	**6 mg/day**	**8 mg/day**	
14–18 yr	**8 mg/day**	**15 mg/day**	

***Rationale*:** The EAR for children was set by modelling the components of iron requirements, estimating the requirements for absorbed iron at the 50th centile with use of an upper limit of 14% iron absorption for 1–3-year-olds and 18% at other ages, and rounding (FNB:IOM 2001). The RDI was set by modelling the components of iron requirements, estimating the requirement for absorbed iron at the 97.5th centile, with use of an upper limit of 14% absorption for 1–3-year-olds and 18% for other ages, and rounding.

In setting the EAR and RDI for girls, it was assumed that those younger than 14 years do not menstruate and that all girls 14 years and older do menstruate. The lower RDI for children aged 9–13 year compared to those aged 1–8 year despite the higher EAR reflects the very high variability in requirements within the younger age groups. Absorption is about 18% from a mixed western diet including animal foods and about 10% from a vegetarian diet; so vegetarians will need intakes about 80% higher.

Adults	**EAR**	**RDI**	**Iron**
Men			
19–30 yr	**6 mg/day**	**8 mg/day**	
31–50 yr	**6 mg/day**	**8 mg/day**	
51–70 yr	**6 mg/day**	**8 mg/day**	
>70 yr	**6 mg/day**	**8 mg/day**	
Women			
19–30 yr	**8 mg/day**	**18 mg/day**	
31–50 yr	**8 mg/day**	**18 mg/day**	
51–70 yr	**5 mg/day**	**8 mg/day**	
>70 yr	**5 mg/day**	**8 mg/day**	

***Rationale*:** The EARs for adults were set by modelling the components of iron requirements, estimating the requirements for absorbed iron at the 50th centile with use of an upper limit of 18% iron absorption, and rounding (FNB:IOM 2001). The RDI was set by modelling the components of iron requirements, estimating the requirement for absorbed iron at the 97.5th centile, with use of an upper limit of 18% iron absorption and rounding. The large difference between the EAR and the RDI in women aged from 19–50 years reflects high variability in needs related to variability in menstrual losses. In setting the EARs and RDIs for women, it was assumed that women over 50 years do not menstruate. Absorption is about 18% from a mixed western diet including animal foods and about 10% from a vegetarian diet; so vegetarians will need intakes about 80% higher.

Pregnancy	**EAR**	**RDI**	**Iron**
14–18 yr	**23 mg/day**	**27 mg/day**	
19–30 yr	**22 mg/day**	**27 mg/day**	
31–50 yr	**22 mg/day**	**27 mg/day**	

***Rationale*:** The EAR and RDI were established using estimates for the third trimester to build iron stores during the first trimester of pregnancy. The EAR was set by modelling the components of iron requirements for absorbed iron for the 50th centile and the RDI by modelling the 97.5th centile, and using an upper limit of 25% iron absorption, and rounding. Absorption is about 18% from a mixed western diet including animal foods and about 10% from a vegetarian diet; so vegetarians will need intakes about 80% higher.

Lactation	**EAR**	**RDI**	**Iron**
14–18 yr	**7.0 mg/day**	**10 mg/day**	
19–30 yr	**6.5 mg/day**	**9 mg/day**	
31–50 yr	**6.5 mg/day**	**9 mg/day**	

***Rationale*:** To estimate total iron requirement for lactation, iron secreted in milk and basal iron loss were added by simulated distribution (FNB:IOM 2001). An allowance for maternal growth needs was also made for adolescent mothers. The resultant distribution of iron need, assuming absorption of 18%, was used to estimate EARs and RDIs. The variability of requirement was based on basal needs modelled as for non-lactating women and milk secretion modelling with a CV of 30% for the EAR. These estimations assume that menstruation does not resume until after 6 months of exclusive breastfeeding. Absorption is about 18% from a mixed western diet including animal foods and about 10% from a vegetarian diet; so vegetarians will need intakes about 80% higher.

UPPER LEVEL OF INTAKE - IRON

Infants	
0–12 months	**20 mg/day**
Children and adolescents	
1–3 yr	**20 mg/day**
4–8 yr	**40 mg/day**
9–13 yr	**40 mg/day**
14–18 yr	**45 mg/day**
Adults 19+ yr	
Men	**45 mg/day**
Women	**45 mg/day**
Pregnancy	
14–18 yr	**45 mg/day**
19–50 yr	**45 mg/day**
Lactation	
14–18 yr	**45 mg/day**
19–50 yr	**45 mg/day**

***Rationale*:** Severity of toxicity is related to the amount of elemental iron absorbed and can range from gastrointestinal irritation to systemic toxicity. For adults, based on gastrointestinal symptoms, a LOAEL of 70 mg/day was set based on the level assessed as safe from the supplemental study of Frykman et al (1994) plus the median population dietary intakes (FNB:IOM 2001). Because of the self-limiting nature of the adverse outcomes, a relatively low UF of 1.5 was used to extrapolate from the LOAEL to the NOAEL, giving a UL of 45 mg/day after rounding. As data are limited for pregnancy and lactation, the same figure was applied to these groups.

For infants and young children, a UF of 3 was used to extrapolate from the LOAEL to the NOAEL based on potential adverse growth effects (Dewey et al 2002), giving a figure of 20 mg/day.

As the safety of excess supplemental non-haem iron in children from 4–18 years has not been studied, a UL of 40 mg/day was set for children aged 4–13 years and the adult UL of 45 mg was set for adolescents.

***Note*:** Up to 0.5% of the Caucasian population is homozygous for hereditary haemochromatosis and, as a result, particularly susceptible to iron overload, even at normal dietary iron intakes. Such individuals should avoid iron supplements and highly iron-fortified foods. The majority of homozygotes are not diagnosed or identified until sufficient iron has accumulated to produce adverse effects.

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MAGNESIUM

BACKGROUND

Magnesium is a cofactor for more than 300 enzyme systems (Wacker & Parisi 1968) and is involved in both aerobic and anaerobic energy generation and in glycolysis, either directly as an enzyme activator or as part of the Mg-ATP complex. Magnesium is required for mitochondria to carry out oxidative phosphorylation. It plays a role in regulating potassium fluxes and in the metabolism of calcium (Al-Ghamdi et al 1994, Classen 1984, Waterlow 1992,). The human body contains about 760 mg of magnesium at birth and 25 g in adulthood (Forbes 1987, Schroeder et al 1969, Widdowson et al 1951). Just over half the body's magnesium is found in bone, where it forms a surface constituent of the hydroxyapatite mineral component, and a further third is found in muscles and soft tissues (Heaton 1976, Webster 1987). The intracellular concentration is about ten times that of the extracellular fluid.

Magnesium is widely distributed in the food supply in both plant and animal foods. Most green vegetables, legumes, peas, beans and nuts are rich in magnesium, as are some shellfish and spices. Most unrefined cereals are reasonable sources, but highly refined flours, tubers, fruits, oils and fats contribute little. Between 50% and 90% of magnesium in breast milk or infant formula is absorbed (Lonnerdal, 1995, 1997). In adults on conventional diets, the efficiency of absorption varies greatly with magnesium content (Seelig 1982, Spencer et al 1980) ranging from 25% on high magnesium diets in one study to 75% on low magnesium diets (Schwartz et al 1984). The homeostatic capacity of the body to adapt to a wide range of intakes is thus high (Abrams et al 1997, Sojka et al 1997).

Magnesium is absorbed in the duodenum and ileum by both active and passive processes (Greger et al 1981). High fibre intakes (40–50 g/day) lower magnesium absorption, probably because of the magnesium-binding action of the phytate phosphorus associated with the fibre (Kelsay et al 1979, McCance & Widdowson 1942a,b). There is no consistent evidence that moderate increases in calcium, iron or manganese affect magnesium balance (Abrams et al 1997, Andon et al 1996, Lonnerdal 1995, Sojka et al 1997). However, high intakes of zinc at 142 mg/day reduce absorption (Spencer et al 1994b). Protein may also influence magnesium absorption. When protein intake is less than 30 g/day (Hunt & Schofield 1969), magnesium absorption decreases. When protein intake is greater than 94 g/day, renal magnesium excretion may increase (Mahalko et al 1983), although adaptation may occur.

The kidney plays a central role in magnesium homeostasis through active reabsorption that is influenced by the sodium load in the tubules and possibly acid-base balance (Quarme & Disks 1986). High dietary calcium intake (about 2,600 mg/day) with high sodium intake enhances magnesium output (Greger et al 1981), contributing to a shift to negative magnesium balance (Kesteloot & Joosens 1990, Quarme et al 1986).

Pathological effects of primary nutritional deficiency of magnesium occur only rarely in humans, unless low intakes are accompanied by prolonged diarrhoea or excessive urinary loss. The body is generally protected by the lability of serum magnesium. Most of the early signs of deficiency are neurologic or neuromuscular defects (Shils 1969, 1988) that may develop with time into anorexia, nausea, muscular weakness, lethargy, weight loss, hyper-irritability, hyper-excitability, muscular spasms, tetany and finally convulsions.

Hypocalcaemia also occurs in moderate to severe magnesium deficiency. Some studies have indicated that low magnesium status may be a risk for postmenopausal osteoporosis (Abraham & Grewal 1990, Reginster et al 1989, Sojka & Weaver 1995, Stendig-Lindberg et al 1993, Tucker et al 1995, Yano et al 1985), however others have not confirmed the link between low magnesium and risk of osteoporosis (Angus et al 1988, Freudenheim et al 1986). Sub-optimal magnesium status may be a factor in the aetiology of coronary heart disease and hypertension, but evidence is relatively sparse (Elwood 1994). Magnesium depletion has been shown to cause insulin resistance and impaired insulin secretion (Paolissa et al 1990), and magnesium supplements have been reported to improve glucose tolerance and insulin response in the elderly (Paolissa et al 1989, 1992).

Indicators used for estimating magnesium requirements have included serum magnesium, plasma ionised magnesium, intracellular magnesium, magnesium balance, estimates of tissue accretion in growth, magnesium tolerance tests and epidemiologic studies including meta-analysis. However, serum magnesium has not been properly validated as a reliable indicator of body magnesium status (Gartside & Glueck 1995). Plasma ionised magnesium may be an improvement on serum magnesium but requires further evaluation and the validity evidence for intracellular magnesium is limited. Magnesium balance is problematic if not carried out under close supervision, as magnesium in water can confound results, a factor that precluded the use of many early studies conducted in free-living situations or current studies where intakes were calculated, not analysed.

Accurate estimates of tissue accretion during growth throughout childhood are dependent on more extensive information about whole body mineral retention than are currently available, although there is some information for specific ages from cadaver data (Fomon & Nelson 1993, Koo & Tsang 1997). The magnesium tolerance test is an invasive procedure based on renal excretion of parenterally administered magnesium load. It is considered accurate for adults but not infants and children (Gullestad et al 1992, Ryzen et al 1985). The test requires normal renal handling and may be unreliable in diabetics or drug or alcohol users. It may also be affected by ageing of kidney tissue (Gullestad et al 1994). Epidemiological studies with meta-analysis may indicate relationships between magnesium intake and health outcomes.

1 mmol magnesium = 24.3 mg magnesium

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Magnesium**
0–6 months	**30 mg/day**	
7–12 months	**75 mg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of magnesium in breast milk (34 mg/L) from 10 studies reviewed by Atkinson et al (1995), and rounding (FNB:IOM 1997). Magnesium is somewhat less bioavailable in formula based on cow's milk but most formulas have higher magnesium content than found in human milk and should be adequate. The AI for 7–12 months was set by adding an estimate for magnesium from breast milk at this age to an estimate of intake from supplementary foods. A breast milk volume of 0.6 L/day (Dewey et al 1984, Heinig et al 1993) and the average magnesium concentration of breast milk of 34 mg/L (Atkinson et al 1995) gives a contribution of 20 mg/day from breast milk which is added to 55 mg/day from complementary foods (Specker et al 1997).

Children & adolescents	**EAR**	**RDI**	**Magnesium**
All			
1–3 yr	**65 mg/day**	**80 mg/day**	
4–8 yr	**110 mg/day**	**130 mg/day**	
Boys			
9–13 yr	**200 mg/day**	**240 mg/day**	
14–18 yr	**340 mg/day**	**410 mg/day**	
Girls			
9–13 yr	**200 mg/day**	**240 mg/day**	
14–18 yr	**300 mg/day**	**360 mg/day**	

***Rationale*:** In the absence of adequate balance and usual accretion data in children aged 1–8 years, data were interpolated from other groups based on body weight change and linear growth (FNB:IOM 1997) that indicate that a magnesium intake of 5 mg/kg a day meets most but not all the needs of those evaluated. This was the basis for the EAR for children 1–8 years. At 1–3 years, with a reference weight of 13 kg, the EAR is 65 mg. For 4–8 years with a reference weight of 22 kg, it is 110 mg/day.

The CV was assumed to be 10%, giving an RDI of 80 mg/day for 1–3 year olds and 130 mg/day for 4–8 year olds. The studies of Abrams et al (1997), Andon et al (1996), and Greger et al (1979) showed that the magnesium requirement per kilogram was the same for boys and girls at this age. Based on the reference weight of 40 kg for both boys and girls, this gives an EAR of 200 mg/day for each gender that, with a CV of 10% for the EAR gives RDIs of 240 mg/day.

The average magnesium requirement is slightly higher for older adolescents because of the increase in growth rate at this age (Abrams et al 1997, Andon et al 1996, Greger et al 1978, 1979, Schwartz et al 1973). The amount required is 5.3 mg/kg for both boys and girls, giving an EAR of 340 mg for boys aged 14–18 years with a standard weight 64 kg and 300 mg for girls aged 14–18 years with a standard weight of 57 kg. Assuming a CV of 10% for the EAR, this gives an RDIs for boys and girls of this age of 410 mg/day and 360 mg/day, respectively.

Adults	**EAR**	**RDI**	**Magnesium**
Men			
19–30 yr	**330 mg/day**	**400 mg/day**	
31–50 yr	**350 mg/day**	**420 mg/day**	
51–70 yr	**350 mg/day**	**420 mg/day**	
>70 yr	**350 mg/day**	**420 mg/day**	
Women			
19–30 yr	**255 mg/day**	**310 mg/day**	
31–50 yr	**265 mg/day**	**320 mg/day**	
51–70 yr	**265 mg/day**	**320 mg/day**	
>70 yr	**265 mg/day**	**320 mg/day**	

***Rationale*:** The EARs for adults were based on the assumption that the best indicator of adequacy currently available is the level that allows an individual to maintain total body magnesium over time (FNB:IOM 1997). Based primarily on the studies of Greger & Baier (1983), Kelsay & Prather (1983), Kelsay et al (1979), Lakshmanan et al (1984), Mahalko et al (1983), Schwartz et al (1986), Spencer et al (1994a) and Wisker et al (1991) the EARs for adult males are estimated to be 330 mg/day for ages 19–30 years and 350 mg/day at all other ages. Those for adult females are 255 mg/day at 19–30 years and 265 mg/day at all other ages. Assuming a CV of 10% for the EAR, the RDIs are 400 mg/day and 310 mg/day, respectively, for adult men and women aged 19–30 years and 420 mg/day and 320 mg/day, respectively, for men and women aged 31 and over.

Pregnancy	**EAR**	**RDI**	**Magnesium**
14–18 yr	**335 mg/day**	**400 mg/day**	
19–30 yr	**290 mg/day**	**350 mg/day**	
31–50 yr	**300 mg/day**	**360 mg/day**	

***Rationale*:** As there are no direct studies of needs in pregnancy, the EARs and RDIs for pregnancy were based on a consideration of the added lean body mass in pregnancy, assumed to be a mean of 7.5 kg (IOM 1991), a magnesium content of the additional lean body mass of 470 mg (Widdowson & Dickerson 1964) and an adjustment factor of 2.5 for a bioavailability of 40% (Abrams et al 1997). This gives an additional requirement of 35 mg in pregnancy (FNB:IOM 1997) as estimated from (7.5 kg/270 days) x 470 mg/kg x 2.5 = 33 mg, rounded to 35 mg. A CV of 10% for the EAR was assumed to derive the RDI.

Lactation	**EAR**	**RDI**	**Magnesium**
14–18 yr	**300 mg/day**	**360 mg/day**	
19–30 yr	**255 mg/day**	**310 mg/day**	
31–50 yr	**265 mg/day**	**320 mg/day**	

***Rationale*:** The EARs and RDIs for lactation were based on the results of one study of lactating women which showed no effect of lactation on magnesium balance (Dengel et al 1994) and another showing no difference in urinary magnesium between lactating and never-pregnant women consuming diets containing about 270 mg magnesium/day (Klein et al 1995). These studies and a third assessing the blood magnesium status of lactating women (Moser et al 1983) indicate that there is decreased urinary secretion and naturally increased bone resorption in lactation that is independent of diet and appears to provide the necessary additional magnesium without the need for increased dietary intake (FNB:IOM 1997). Thus the EAR and RDI for lactation are the same as for non-pregnant women.

UPPER LEVEL OF INTAKE - MAGNESIUM

(as a supplement)

Infants	
0–12 months	**Not possible to establish. Source of intake should be breast milk, formula and food only.**
Children and adolescents	
1–3 yr	**65 mg /day**
4–8 yr	**110 mg/day**
9–13 yr	**350 mg/day**
14–18 yr	**350 mg/day**
Adults 19+ yr	
Men	**350 mg/day**
Women	**350 mg/day**
Pregnancy	
14–18 yr	**350 mg/day**
19–50 yr	**350 mg/day**
Lactation	
14–18 yr	**350 mg/day**
19–50 yr	**350 mg/day**

***Rationale*:** There are few reports to assist in setting ULs for magnesium, as it has not been shown to produce toxic effects when ingested as naturally occurring magnesium in food. Diarrhoea was selected as the critical endpoint as it is the first sign of excess intake (FNB:IOM 1997). For children and adolescents 8 years and older and adults, a LOAEL of 360 mg of magnesium from non-food sources was established based on the results of Bashir et al (1993), supported by the findings of Fine et al (1991),

Marken et al (1989) and Ricci et al (1991). A UF of 1.0 was selected as diarrhoea is an adverse effect readily apparent to the sufferer. A UL of 350 mg from non-food sources was set for children over 8 years and adults including pregnant and lactating women. It was not possible to set a UL for supplements for infants on existing data, but the figure for children 1–8 years was set by extrapolation from older groups on a body weight basis at a level of 5 mg/kg/day.

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MANGANESE

BACKGROUND

Manganese is an essential element involved in formation of bone. It is also involved in the metabolism of carbohydrate, cholesterol and amino acids. Manganese metalloenzymes include manganese superoxide dismutase, arginase, phosphoenolpyruvate decarboxylase and glutamine synthetase.

Cereal products provide about one-third of the intake of manganese and beverages (tea) and vegetables are the other major contributors. Less than 5% of dietary manganese is absorbed (Davidsson et al 1988, Finley et al 1994). In excess, it can interfere with iron absorption (Finley 1999, Rossander-Hulten et al 1991).

Manganese is taken up from blood by the liver and transported by transferrin and possibly alpha$_2$-macroglobulin or albumin to other tissues (Davidsson et al 1989, Davis et al 1992, Rabin et al 1993). Retention can be affected by immediately prior intakes of manganese, calcium, iron and phosphorus (Freeland-Graves & Lin 1991, Greger 1998, Lutz et al 1993). Low ferritin levels are associated with increased manganese absorption, thus exerting a gender effect on manganese bioavailability (Finley 1999). Manganese is excreted rapidly into the gut through bile and lost primarily in faeces. Low bile excretion can therefore increase the potential for manganese toxicity. Urinary excretion is low and not related to diet (Davis & Greger 1992).

Manganese deficiency in animals is associated with impaired growth, reproductive function and glucose tolerance as well as changes in carbohydrate and lipid metabolism. It also interferes with skeletal development. Clinical deficiency in humans has not been associated with poor dietary intake in otherwise healthy individuals. Skin symptoms and lowering of cholesterol were also seen in one experimental depletion study in young men (Krishna et al 1966). Accidental overdose has been shown to result in symptoms such as scaly dermatitis, hypocholesterolaemia, hair depigmentation and reduced vitamin K-dependent clotting factors (Doisy 1973).

The indicators for estimating the requirement of manganese include balance and depletion studies, serum, plasma, blood or urinary manganese concentration, arginase activity and manganese superoxide dismutase activity. However, none of these is reliable or sensitive enough to be used for setting recommended intakes. Balance studies are problematic because of the rapid excretion of manganese into bile and because balance studies over short to moderate periods do not appear to give results proportional to manganese intakes (Greger 1998, 1999).

Serum, plasma, blood and urinary manganese measures seem highly variable over the normal range of consumption and largely insensitive to moderate dietary change (Davis & Greger 1992, Friedman et al 1987, Greger et al 1990). Arginase activity is affected by a number of factors, including high protein diet and liver disease. Ethanol and dietary polyunsaturated fats can affect manganese superoxide dismutase (Davis et al 1990, Dreosti et al 1982).

1 mmol manganese = 55 mg manganese

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Manganese**
0–6 months	**0.003 mg/day**	
7–12 months	**0.600 mg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of manganese in breast milk, and rounding (FNB:IOM 2001). The figure used for breast milk was 3.5 µg/L based on the studies of Anderson (1992), Aqulo et al (1996), Casey et al (1985, 1989) and Stastny et al (1984). The AI for 7–12 months was set using the estimates of Gibson & De Wolfe (1980) for average consumption of 6- and 12-month old babies of 0.071 and 0.080 mg/kg, respectively. Based on reference weights of 7 and 9 kg for these ages, the total intake from milk and complementary food would be 0.500 and 0.720 mg/day. The second method was to use body weight adjustment to extrapolate from adult data, giving a figure of 0.567 mg/day. Using these data, the AI was set at 0.600 mg/day.

The AI for infants of 7–12 months is much greater than that for 0–6 months as the concentration of manganese in breast milk (which is deemed to be the sole source of manganese for infants of 0–6 months) is much lower than in the foods included in the diets of older infants.

Children & adolescents	**AI**	**Manganese**
All		
1–3 yr	**2.0 mg/day**	
4–8 yr	**2.5 mg/day**	
Boys		
9–13 yr	**3.0 mg/day**	
14–18 yr	**3.5 mg/day**	
Girls		
9–13 yr	**2.5 mg/day**	
14–18 yr	**3.0 mg/day**	

***Rationale*:** As there are limited data to set an EAR, AIs for children were set using the median intakes from re-analyses using appropriate age bands of the National Nutrition Surveys of Australia (1998) and New Zealand (1999, 2003) weighted on a population basis and rounding to the nearest 0.5 mg.

Adults	**AI**	**Manganese**
Men		
19–30 yr	**5.5 mg/day**	
31–50 yr	**5.5 mg/day**	
51–70 yr	**5.5 mg/day**	
>70 yr	**5.5 mg/day**	
Women		
19–30 yr	**5 mg/day**	
31–50 yr	**5 mg/day**	
51–70 yr	**5 mg/day**	
>70 yr	**5 mg/day**	

***Rationale*:** As there are limited data to set EARs, AIs for adults were set using the median intakes from a re-analysis using appropriate age bands of the National Nutrition Surveys of Australia (1998) and New Zealand (1999, 2003) weighted on a population basis. As dietary assessment methods tend to underestimate intakes, the highest median intake value reported for the various adult age categories was used to set the AI for each gender, with rounding to the nearest 0.5 mg.

Pregnancy	AI	Manganese
14–18 yr	**5 mg/day**	
19–30 yr	**5 mg/day**	
31–50 yr	**5 mg/day**	

***Rationale*:** There are limited data about the need for manganese in pregnancy. Therefore the level was set at that for non-pregnant women

Lactation	AI	Manganese
14–18 yr	**5 mg/day**	
19–30 yr	**5 mg/day**	
31–50 yr	**5 mg/day**	

***Rationale*:** There are no data to set an EAR for lactating women. Only 3 µg manganese/day is secreted in human milk, so the AI for lactating women has been set at that for non-lactating women.

UPPER LEVEL OF INTAKE - MANGANESE

Manganese intake beyond that normally present in food and beverages could represent a health risk, but there are insufficient data to set a UL.

***Rationale*:** Manganese has low acute toxicity. Manganese is a known neurotoxin at high occupational levels of exposure by inhalation. However, it has also been suggested that exposure from lower levels in drinking water may result in more subtle neurological effects in human populations. The reported symptoms include muscle pain, fatigue, tremor, memory problems and impaired reflexes. Neurological effects have been reported at estimated intakes of 3.6–4.6 mg manganese from water, though comparable intakes have been negative in other studies. There were limitations with the human data and the non-availability of NOAELs for critical endpoints from animal studies produced a considerable degree of uncertainty. Therefore, in agreement with the European Commission (2002) no UL was set. The margin between oral effect levels in humans and experimental animals and the estimated intake from food is very low. Given the findings on neurotoxicity and the potential higher susceptibility of some subgroups in the general population, oral exposure to manganese beyond that normally present in food and beverages could represent a risk of adverse health effects without evidence of any health benefit. It should be noted that manganese from drinking water and supplements might be more bioavailable than that from food

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MOLYBDENUM

BACKGROUND

Molybdenum acts as a cofactor for the enzymes sulphite oxidase, xanthine oxidase and aldehyde oxidase. These enzymes are involved in catabolism of sulphur amino acids and heterocyclic compounds including purines and pyridines. No clear deficiency syndrome has been seen in animals even with major reductions in molybdoenzymes. Molybdenum is absorbed very efficiently over a wide range of intakes by passive transport and urinary excretion reflects intake (Turnlund et al 1995a,b).

Molybdenum is found in plant foods and reflects the soil content in which they grow. Legumes are major contributors of molybdenum in the western diet, as are grain products and nuts (Pennington & Jones 1987, Tsongas et al 1980). Animal foods, fruits and vegetables are low in molybdenum. Little is known about bioavailability from various foods. There are no data for Australia or New Zealand either for dietary or supplemental intake. One US study reports dietary intakes from 120–240 µg/day, averaging 180 µg/day (Tsongas et al 1980). The US Total Diet study showed dietary intakes of 76 µg/day for women and 109 µg/day men (Pennington & Jones 1987).

Deficiency has not been seen in otherwise healthy people. Evidence of essentiality relates to a specific genetic defect that prevents the synthesis of sulphite oxidase and can lead to severe neurological damage and to the demonstration of amino acid intolerance in a long-term parenterally fed patient where molybdenum was omitted from the feed (Abrumrad et al 1981, Johnson 1993). There is some limited and inconclusive epidemiological data that low intakes may be associated with increased incidence of oesophageal cancer (WHO 1996).

Plasma, serum or urinary concentrations of molybdenum or indicators can be used to assess requirements, as plasma levels are generally low and difficult to measure, and urinary measures alone do not reflect status. Molybdenum balance studies are therefore used to establish homeostasis and changes in body stores. Two such studies have been done in men (Turnlund et al 1995a,b), and one in pre-adolescent girls (Engel et al 1967).

1 mmol molybdenum = 96 mg molybdenum

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Molybdenum**
0–6 months	**2 µg/day (0.3µg/kg/day)**	
7–12 months	**3 µg/day (0.3µg/kg/day)**	

***Rationale*:** The AI for infants 0–6 months was based on the average volume of breast milk (0.78 L/day) and the average concentration of molybdenum in breast milk of 2 µg/L (Anderson 1992, Aqulio et al 1996, Biego et al 1998, Bougle et al 1988, FNB:IOM 2001, Krachler et al 1998, Rossipal & Krachler 1998). The AI for older infants was extrapolated using a body weight ratio from the AI for younger infants. Cow's milk contains more molybdenum (50 µg/L) than human milk, as does soy milk, but there are no data on bioavailability in cow's milk or infant formula.

Children & adolescents	EAR	RDI	Molybdenum
All			
1–3 yr	**13 µg/day**	**17 µg/day**	
4–8 yr	**17 µg/day**	**22 µg/day**	
Boys			
9–13 yr	**26 µg/day**	**34 µg/day**	
14–18 yr	**33 µg/day**	**43 µg/day**	
Girls			
9–13 yr	**26 µg/day**	**34 µg/day**	
14–18 yr	**33 µg/day**	**43 µg/day**	

***Rationale*:** There are no specific age-related data on which to base EARs for children and adolescents. The EARs are extrapolated from adult EARs on a metabolic body weight basis allowing for growth needs (FNB:IOM 2001). For this and all other age and gender groups, RDIs were set as the EAR plus twice the CVs, which were set at 15%.

Adults	EAR	RDI	Molybdenum
Men			
19–50 yr	**34 µg/day**	**45 µg/day**	
51–70 yr	**34 µg/day**	**45 µg/day**	
>70 yr	**34 µg/day**	**45 µg/day**	
Women			
19–50 yr	**34 µg/day**	**45 µg/day**	
51–70 yr	**34 µg/day**	**45 µg/day**	
>70 yr	**34 µg/day**	**45 µg/day**	

***Rationale*:** The adult EAR is based on the results of controlled balance studies in young men (Turnlund et al 1995a,b, FNB:IOM 2001) using an average bioavailability of 75%. As there are no data for older men and women, the same EAR was set for these groups. As the number of available studies was limited and subject numbers were low, RDIs were derived assuming a CV of 15% for the EAR.

Pregnancy	EAR	RDI	Molybdenum
14–18 yr	**40 µg/day**	**50 µg/day**	
19–30 yr	**40 µg/day**	**50 µg/day**	
31–50 yr	**40 µg/day**	**50 µg/day**	

***Rationale*:** There are no direct data for needs in pregnancy. The EAR was determined by extrapolating from the requirements for adolescent and adult women on a body weight basis, assuming an average additional 16 kg weight. The RDI was set using a CV of 15% for the EAR and rounding to the nearest 10 µg.

Lactation	EAR	RDI	Molybdenum
14–18 yr	**35 µg/day**	**50 µg/day**	
19–30 yr	**36 µg/day**	**50 µg/day**	
31–50 yr	**36 µg/day**	**50 µg/day**	

***Rationale*:** The EARs were based on that of the non-pregnant, non-lactating women plus the molybdenum intake required to replace molybdenum secreted in human milk. The RDI was set using a CV of 15% for the EAR and rounding to the nearest 10 µg.

UPPER LEVEL OF INTAKE - MOLYBDENUM

Infants	
0–12 months	**Not possible to estimate**
Children and adolescents	
1–3 yr	**300 µg/day**
4–8 yr	**600 µg/day**
9–13 yr	**1,100 µg/day**
14–18 yr	**1,700 µg/day**
Adults 19+ yr	
Men	**2,000 µg/day**
Women	**2,000 µg/day**
Pregnancy	
14–18 yr	**1,700 µg/day**
19–50 yr	**2,000 µg/day**
Lactation	
14–18 yr	**1,700 µg/day**
19–50 yr	**2,000 µg/day**

***Rationale*:** Toxic effects seen in animals have included decreased haemoglobin concentration, depression of growth, mild renal failure, diuresis and proteinuria, histological changes in kidney and liver and body weight loss. Other effects included impaired copper utilisation, prolonged oestrus cycle, failure to breed, decreased gestational weight gain, deaths in litters and adverse effects on embryogenesis (FNB:IOM 2001).

There are limited toxicity data in humans. The relevance to the general population of data on the effects of tetrathiomolybdate treatment on copper metabolism in subjects with Wilson's disease, a condition in which copper accumulates in the body (Brewer 2003, Goodman et al 2004), is unclear. The limited toxicity data may relate in part to the rapid excretion of molybdenum in urine, particularly at higher intake levels. One study of supplemental intakes up to 1.5 mg/day in humans showed no adverse effects on copper utilisation (Turnlund & Keyes 2000). There are limited and inconclusive data to suggest that high molybdenum intakes may be associated with increased dental caries.

Because of the limited human data, ULs were set on the basis of the most sensitive indicator in animals – the effect of molybdenum on reproduction and fetal development in rats and mice. These studies indicated a NOAEL of 0.9 mg/kg/day (Fungwe et al 1990). A UF of 30 was applied for extrapolation from animal to human data and for intraspecies differences to give a UL of 30 µg/kg/day for humans.

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PHOSPHORUS

BACKGROUND

Phosphorus is the second most abundant inorganic element in the body and is a part of many important compounds, including deoxyribonucleic acid (DNA), ribonucleic acid (RNA), (S)-2-amino-3-[5-tert-butyl-3-(phosphonomethoxy)-4-isoxazolyl]propionic acid (ATPO), adenosine diphosphate (ADP), phospholipids and sugar phosphates. Phosphorus as phosphate is a major buffer of acid in urine by virtue of its monovalent, divalent and trivalent forms. Phosphate helps to protect blood systemic acid/base balance, acts as a temporary store and transport mechanism for energy and helps in activating catalytic proteins. Eighty-five per cent of the body's phosphorus is in bone and the remainder is distributed through soft tissues (Diem 1970).

Inorganic phosphorus is only a tiny fraction of total body phosphorus but plays a critical role in blood and extracellular fluids. Phosphate enters the organic pool after absorption from the diet and resorption from bone. All urinary phosphorus and bone mineral phosphate are derived from the organic pool. Some phosphorus is absorbed with organic compounds such as peptides and lipids, but it is difficult to assess the relative amounts of inorganic and organic phosphorus consumed.

Phosphorus is widely distributed in natural foods and also found in food additives as phosphate salts, used in processing for retaining moisture, smoothness and binding. Most food sources are relatively bioavailable with the exception of plant seeds (beans, peas, cereals, nuts) that contain a special storage form of phosphate called phytic acid. Mammals are generally unable to hydrolyse and use phytate, although some foods also contain the enzyme phytase, as do colonic bacteria, which can release some phosphate from phytate. For adults, bioavailability estimates range from 55 to 70% (Lehmann 1996, Nordin 1989, Stanbury 1971).

Net phosphorus absorption is a linear function of phosphorus intake, indicating that diffusion is the main means of absorption. For infants, bioavailability is highest from human milk (85–90%), followed by cow's milk (72%) and soy formulas (about 59%). However, cow's milk and soy-based infant formulas generally contain substantially more phosphorus than human milk. As a result, phosphorus absorption for infants fed cow's milk and soy formulas appears to be almost twice that of infants fed human milk (Moya et al 1992).

Inadequate intakes or malabsorption of phosphorus as seen in vitamin D deficiency results in hypophosphataemia the symptoms of which include anorexia, anaemia, muscle weakness, bone pain, rickets, osteomalacia, general debility, increased susceptibility to infection, paresthesias, ataxia, confusion and possibly death (Lotz et al 1968). Phosphorus is so widespread in the food supply that dietary phosphorus deficiency is extremely rare, the exception being long-term, severe food restriction.

In the past, a great deal of emphasis was placed on the calcium:phosphorus ratio (Ca:P) of diets (Chinn 1981), particularly those of infants (Fomon & Nelson 1993). This is a useful concept during periods of rapid growth but has little relevance in adults when assessing requirements. Also, the ratio does not take into account differing bioavailabilities and adaptive responses of the two nutrients. In balance studies in human adults, Ca:P molar ratios ranging from 0.08 to 2.4 (a 30 fold range) had no effect on either calcium balance or absorption (Heaney & Recker 1982, Spencer et al 1965, 1978). For this reason, other indicators are now used to assess phosphorus requirements, including measurement of inorganic phosphorus in serum (serum P_i) or phosphorus balance.

As phosphorus intake directly affects serum P_i and because both hypo-and hyperphosphataemia directly cause dysfunction, serum P_i is seen as the best indicator of nutritional adequacy of phosphorus intake. Results of phosphorus balance studies can reflect changes occurring in the body in addition to dietary intake of phosphorus and, as such, are of limited use.

1 mmol phosphorus = 31 mg phosphorus

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Phosphorus**
0–6 months	**100 mg/day**	
7–12 months	**275 mg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of phosphorus in breast milk (124 mg/L) from 10 studies reviewed by Atkinson et al (1995), and rounding (FNB:IOM 1997). The AI for 7–12 months was set by adding an estimate for phosphorus from breast milk at this age to an estimate of intake from supplementary foods. A breast milk volume of 0.60 L/day (Dewey et al 1984, Heinig et al 1993) and the average concentration of phosphorus in breast milk at this age 124 mg/L (Atkinson et al 1995) give a contribution of 75 mg phosphorus/day from breast milk that is added to 200 mg/day from complementary foods (Specker et al 1997).

Children & adolescents	**EAR**	**RDI**	**Phosphorus**
All			
1–3 yr	**380 mg/day**	**460 mg/day**	
4–8 yr	**405 mg/day**	**500 mg/day**	
Boys			
9–13 yr	**1,055 mg/day**	**1,250 mg/day**	
14–18 yr	**1,055 mg/day**	**1,250 mg/day**	
Girls			
9–13 yr	**1,055 mg/day**	**1,250 mg/day**	
14–18 yr	**1,055 mg/day**	**1,250 mg/day**	

***Rationale*:** In the absence of data on serum P_i or phosphorus balance in children from 1–8 years, estimation of body accretion for these age groups was used on known tissue composition and growth rates (Fomon et al 1982, FNB:IOM 1997) using a conservative estimate of phosphorus absorption of 70%. The equation used was EAR = (accretion + urinary loss) divided by fractional absorption. This gave an EAR of 380 mg for children aged 1–3 years which, with an assumed CV of 10% for the EAR and rounding, gives an RDI of 460 mg/day. For children aged 4–8 years, the EAR and the RDI were estimated to be 405 mg/day and 500 mg/day, respectively. For 9–13 year olds, longitudinal data and a large cross-sectional database (Slemenda et al 1994) allowed estimation of phosphorus requirement from tissue accretion data using a factorial approach (FNB:IOM 1997) that was then also adopted for the 14–18-year-olds. The EAR for both age groups was set at 1,055 mg/day. Assuming a CV of 10% for the EAR and rounding gave an RDI of 1,250 mg.

Adults	EAR	RDI	Phosphorus
Men			
19–30 yr	**580 mg/day**	**1,000 mg/day**	
31–50 yr	**580 mg/day**	**1,000 mg/day**	
51–70 yr	**580 mg/day**	**1,000 mg/day**	
>70 yr	**580 mg/day**	**1,000 mg/day**	
Women			
19–30 yr	**580 mg/day**	**1,000 mg/day**	
31–50 yr	**580 mg/day**	**1,000 mg/day**	
51–70 yr	**580 mg/day**	**1,000 mg/day**	
>70 yr	**580 mg/day**	**1,000 mg/day**	

***Rationale*:** Using a graphical transformation technique (Nordin 1990, FNB:IOM 1997), the EAR for adults was based on average dietary intake of phosphorus required from a typical mixed diet to reach the lowest point of the normal range for serum P_i (Nordin 1976, 1989). The estimates assume an absorption efficiency of 62.5% (Heaney & Recker 1982, Stanbury 1971, Wilkinson 1976). By definition, at this level of intake, only half the population will achieve a P_i above the bottom of the normal range. A CV of 35% for the EAR was derived from consideration of the increase in ingested intake required to raise serum P_i from the bottom end of the normal range to a level of 3.1 mg/dL (1 mmol/L), the fasting level attained by most well nourished adults (Nordin 1976, 1989, FNB:IOM 1997) giving an RDI of 1,000 mg.

Pregnancy	EAR	RDI	Phosphorus
14–18 yr	**1,055 mg/day**	**1,250 mg/day**	
19–30 yr	**580 mg/day**	**1,000 mg/day**	
31–50 yr	**580 mg/day**	**1,000 mg/day**	

***Rationale*:** As there are no direct studies showing increased needs in pregnancy, the EAR and RDI were set at those of the non-pregnant state.

Lactation	EAR	RDI	Phosphorus
14–18 yr	**1,055 mg/day**	**1,250 mg/day**	
19–30 yr	**580 mg/day**	**1,000 mg/day**	
31–50 yr	**580 mg/day**	**1,000 mg/day**	

***Rationale*:** Increased bone resorption and decreased urinary excretion occurring independently of dietary intake provide the additional needs for milk production (Kent et al 1990, 1991) and thus there is no evidence of increased needs in lactation. Therefore the EAR and RDI are set at those of the non-pregnant state.

UPPER LEVEL OF INTAKE - PHOSPHORUS

Infants	
0–12 months	**Not possible to establish. Source of intake should be through naturally occurring food sources and formula only.**
Children and adolescents	
1–3 yr	**3,000 mg/day**
4–8 yr	**3,000 mg/day**
9–13 yr	**4,000 mg/day**
14–18 yr	**4,000 mg/day**
Adults	
19–70 yr	**4,000 mg/day**
>70 yrs	**3,000 mg/day**
Pregnancy	
14–50 yr	**3,500 mg/day**
Lactation	
14–50 yr	**4,000 mg/day**

***Rationale*:** The UL is set at the intake associated with the upper boundary of normal values of serum P_i. The upper boundaries are higher in infants than in adults and there is no evidence that intakes at the adult upper boundary cause harm. The higher boundaries in infants are obviously tissue-safe and assuming they approximate the upper normal human value, the corresponding ingested intake in an adult would be more than 10,000 mg/day. A NOAEL of 10,000 mg/day was therefore set (FNB:IOM 1997). Information concerning adverse effects in the area between normal P_i and levels associated with ectopic mineralisation is lacking. In keeping with pharmacokinetic practice when relationships between intake and blood level are known (Petley et al 1995), a UF of 2.5 was chosen, taking the UL for adults to 4,000 mg/day. For adults over 70 years, because of increased prevalence of kidney damage, a larger UF of 3.3 was applied, giving a UL of 3,000 mg/day. In pregnancy, absorption efficiency rises by about 15% so the UL was set 15% lower at 3,500 mg/day. In lactation, phosphorus metabolism is the same as in the non-pregnant state, so the UL stays at 4,000 mg/day.

For children, an upper level of intake of 3,000 mg/day was set by dividing the NOAEL for adults by an uncertainty factor of about 3.3 for potentially increased susceptibility related to smaller body size. For children, 9–18 years, the adult UL was applied as there was no evidence to suggest increased susceptibility.

No harm is known to result if dietary phosphorus intakes go above these limits, as may occur for some groups in the community, especially those with high energy intakes.

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POTASSIUM

BACKGROUND

Potassium is the major cation of intracellular fluid and an almost constant component of lean body tissues. A high intracellular concentration of potassium is maintained by the Na^+/K^+-ATPase pump. The movements of potassium out of cells and sodium into cells changes the electrical potential during depolarisation and repolarisation of nerve and muscle cells.

Leafy green vegetables, vine fruit such as tomatoes, cucumbers, zucchini, eggplant and pumpkin, and root vegetables are particularly good sources of potassium. It is also moderately abundant in beans and peas, tree fruits such as apples, oranges and bananas, milks and yoghurts and meats. In unprocessed foods, potassium occurs mainly with bicarbonate-generators like citrate. Potassium added during processing is generally as potassium chloride. About 85% of potassium is absorbed (Holbrook et al 1984).

Most of the ingested potassium (80–90%) is excreted in urine, the rest being excreted in faeces and sweat (Holbrook et al 1984, Pietinen 1982). Potassium filtered in the glomeruli of the kidney is mostly reabsorbed. The potassium in urine results from secretion into the cortical collecting duct under control of the hormone, aldosterone. High plasma levels of potassium stimulate release of aldosterone to increase the secretion of potassium.

Potassium requirements can be affected by climate and physical activity, the use of diuretics, and the intake of other electrolytes, notably sodium. Potassium blunts the effect of sodium chloride on blood pressure, mitigating salt sensitivity and lowering urinary calcium excretion (Whelton et al 1997). Given this interrelatedness, requirement for potassium depends to some extent on dietary sodium, however, the ideal sodium:potassium intake ratio is not sufficiently established to use in setting requirements.

It has been hypothesised that high protein-low potassium diets could induce a low-grade metabolic acidosis that could induce demineralisation of bone, osteoporosis and kidney stones (Barzel 1995, Lemann et al 1999) and epidemiological and metabolic studies have supported this suggestion (Maurer et al 2003, Morris et al 2001, New et al 1997, Sebastian et al 1994, Tucker et al 1999).

Potential indicators for potassium requirements include potassium balance, serum potassium and clinical endpoints, such as the levels required to avoid hypokalemia, high blood pressure, cardiovascular disease, bone demineralisation or kidney stones. However, dose-response trials are either not available for many of these endpoints, or are insufficient to estimate average requirements.

1 mmol potassium = 39 mg potassium

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Potassium**
0–6 months	**400 mg/day**	**(10 mmol)**
7–12 months	**700 mg/day**	**(18 mmol)**

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of potassium (500 mg/L), and rounding. For 7–12 months, an average breast milk volume of 0.6 L/day and concentration of 500 mg/L give an intake of 300 mg/day, to which is added 440 mg/day from complementary foods as determined by the US CSFII survey (FNB:IOM 2004).

Children & adolescents	AI	Potassium
All		
1–3 yr	**2,000 mg/day**	**(50 mmol)**
4–8 yr	**2,300 mg/day**	**(60 mmol)**
Boys		
9–13 yr	**3,000 mg/day**	**(76 mmol)**
14–18 yr	**3,600 mg/day**	**(92 mmol)**
Girls		
9–13 yr	**2,500 mg/day**	**(64 mmol)**
14–18 yr	**2,600 mg/day**	**(66 mmol)**

***Rationale*:** There is very little evidence about requirements in children. The recommendations are derived from the intakes from the appropriate age group data from the Australian (ABS 1998) and New Zealand (MOH 2003) National Nutrition Surveys on a population-weighted basis.

Adults	AI	Potassium
Men		
19–30 yr	**3,800 mg/day**	**(100 mmol)**
31–50 yr	**3,800 mg/day**	**(100 mmol)**
51–70 yr	**3,800 mg/day**	**(100 mmol)**
>70 yr	**3,800 mg/day**	**(100 mmol)**
Women		
19–30 yr	**2,800 mg/day**	**(72 mmol)**
31–50 yr	**2,800 mg/day**	**(72 mmol)**
51–70 yr	**2,800 mg/day**	**(72 mmol)**
>70 yr	**2,800 mg/day**	**(72 mmol)**

***Rationale*:** Whilst there are some experimental data on potassium intakes in relation to blunting of salt sensitivity (Morris et al 1999b) and some supportive epidemiological evidence on renal stones (Curhan et al 1993, 1997, Hirvonen et al 1999) these were considered insufficient basis for setting an AI as the sodium blunting experiment was carried out in males only and much of the key data related to salt sensitive African American males. The AI was therefore set at the highest median intake for the various age categories of adult males and females.

Pregnancy	AI	Potassium
14–18 yr	**2,800 mg/day**	**(72 mmol)**
19–30 yr	**2,800 mg/day**	**(72 mmol)**
31–50 yr	**2,800 mg/day**	**(72 mmol)**

***Rationale*:** Potassium accretion in pregnancy is small, so the AI is set at the same level as that for adult females.

Lactation	AI	Potassium
14–18 yr	**3,200 mg/day**	**(82 mmol)**
19–30 yr	**3,200 mg/day**	**(82 mmol)**
31–50 yr	**3,200 mg/day**	**(82 mmol)**

***Rationale*:** The lactation AI is set at that for adult females plus an allowance for potassium secreted in breast milk.

UPPER LEVEL OF INTAKE - POTASSIUM

No ULs have been set for potassium from dietary sources.

For infants 0–12 months, the source of intake should be breast milk, formula and food only. For children, adolescents and adults, including pregnant and lactating women, supplements should be taken only under medical supervision.

***Rationale*:** High potassium intakes can cause gastrointestinal discomfort and stress that may include ulceration and perforation (Lambert & Newman 1980, Leijonmarck & Raf 1985, Pietro & Davidson 1990, Sinar et al 1986). Arrhythmia can also arise from the resulting hyperkalaemia (Haddad & Strong 1975, Kallen et al 1976, Snyder et al 1975, Su et al 2001, Ray et al 1999, Wetli & Davis 1978).

However, in otherwise healthy people, there have been no reports of hyperkalaemia from acute or chronic ingestion of potassium naturally occurring in food, so a UL for foods has not been set.

Because of its well-documented potential for toxicity, supplemental potassium should only be provided under medical supervision. For infants, intake should be limited to potassium occurring in breast milk, formula and complementary foods.

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SELENIUM

BACKGROUND

Selenium functions as an antioxidant and in redox reactions and thyroid metabolism. It exerts its effects as a constituent of several selenoproteins of which there are at least 30 in mammalian systems. The most important are the glutathione peroxidases (GP_Xs), selenoprotein P, iodothyronine 5'-deiodinases and thioredoxin reductases (TrxRs).

Different forms of GP_X are found in the cytosol and membranes of cells in the gut, liver and colon and also in plasma. The cellular form (cGP_X) is thought to regulate intracellular concentrations of hydroperoxides formed during metabolism and to have a role in cellular antioxidant systems. It may also perform a storage role for selenium (Holben & Smith 1999).

The function of plasma GP_X is unknown. It may play an antioxidant role in kidney and be a secretory protein with antioxidant function in the extracellular space (Holben et al 1999). Gastrointestinal GP_X is found in rat gastrointestinal cells and human liver and colon. It may play a role in protecting against the adverse effects of hydroperoxides formed in the gut and liver. Phospholipid hydroperoxide GP_X reduces hydroperoxides formed in the metabolism of fatty acids, thereby reducing cell membrane peroxidation (Ursini et al 1985, Ursini & Bindoli 1987). It may also play a role in eicosanoid metabolism and regulation (Arthur & Beckett 1994).

Selenoprotein P is a selenocysteine-containing glycoprotein that may play an antioxidant role (Burk et al 1995) and a protective role against the endotoxin peroxynitrite (Mostert 2000). Iodothyronine 5'-deiodinases catalyse the conversion of thyroxine (T_4) to its active metabolite, triiodothyronine (T_3). Selenium deficiency increases plasma T_4 and decreases T_3. Low dietary intakes also result in the production of these deiodinases in preference to GP_X (Allan et al 1999). The TrxRs have a catalytic role in the NADPH-dependent reduction of thioredoxin (Mustacich & Powis 2000). They have a role as antioxidants and are important in a number of cellular functions including cell growth and transformation and recycling of ascorbic acid (vitamin C) from dehydroascorbic acid (Mustacich & Powis 2000). Several other selenium-containing enzymes have been identified in the muscle, sperm and prostate of animals, suggesting possible roles in muscle maintenance, fertility and protection against prostate cancer (Behne et al 1997, Calvin et al 1987, Vendeland et al 1993).

The potential role of selenium in cancer prevention has been assessed in humans. One prospective study of 34,000 men using a nested case-control study design showed that high selenium intakes were protective against prostate cancer (Yoshizawa et al 1998). However, few intervention studies have been done to date. One such study in China showed reduction in mortality from oesophageal cancer with a supplemental mixture of selenium, vitamin E and beta-carotene (Blot et al 1993).

A 10-year study of skin cancer in the US initially found no effect of supplemental selenium at 200 µg/day on basal cell or squamous cell skin cancer, but significant reduction in total cancer and cancers of the prostate, lung and colorectum (Clark et al 1996). However analyses of longer-term data showed that whilst selenium supplementation reduced total cancer incidence, it was not significantly associated with lung and colorectal cancer incidence (Duffield-Lillico et al 2002) and there was also an increase in squamous cell carcinoma and total non-melanoma skin cancer in supplemented subjects with relatively high baseline selenium (Duffield-Lillico et al 2003).

Selenium is found in a range of foods, the content of which varies with geographic sources of the food. Soil concentrations can range from <0.01 µg/g to >1,000 µg/g with plant food content reflecting this range. Variability of selenium levels is not so marked in animal foods. In Australia and New Zealand, the main dietary sources are seafood, poultry and eggs and, to a lesser extent, other muscle meats. The contribution of cereal products depends on the source. Much plant selenium is in the form of selenomethionine, selenocysteine or selenocysteine metabolites. Meats and seafood also contain selenoproteins with selenium in the form of selenocysteine. Low soil selenium levels in New Zealand mean that dietary intakes and selenium status are lower than in many other countries (Thomson 2004a).

Absorption of selenium – mostly selenomethionine and selenocysteine – from food is about 55–70% (Whanger 1998). Selenomethionine is absorbed mainly in the duodenum in the same way as methionine and is unaffected by selenium status. It is transported round the body in plasma albumin and red cell haemoglobin. Selenomethionine from food enters the methionine pool in the body and shares the fate of methionine until catabolised. The resulting free selenocysteine is further broken down to liberate a reduced form called selenide. Less is known about the absorption of other forms of selenium, although it is thought that both selenocysteine and selenate are well absorbed. Ingested selenate, selenocysteine and selenite are all metabolised directly to selenide. The selenide can be metabolised to selenophosphate, the precursor of selenocysteine in selenoproteins, or converted to excretory metabolites.

Excess selenium intake from selenate, selenite or selenocysteine is excreted in urine. The kidneys account for 50-60% of total excretion of selenium. There is also some faecal excretion of unabsorbed selenium and losses through skin, hair and, at high intakes, expired air.

Frank selenium deficiency results in a condition called Keshan Disease, an endemic cardiomyopathy occurring in low selenium areas of China that is responsive to sodium selenite supplementation (Keshan Disease Research Group 1979a,b). Keshan Disease results in cardiac enlargement, heart failure, arrythmias and premature death. It is associated with low selenium intake, low blood and hair levels and affects mostly children and women of childbearing age. Keshan Disease may occur at intakes of selenium of 20 µg/day or less, however, some features of the disease cannot be explained solely on the basis of low selenium status, so Keshan Disease is thought to depend on the presence of additional factors such as a virus, mineral imbalance or environmental toxins (Ge et al 1983, Yang & Xia 1995).

Other conditions such as Kashin-Beck disease, a cartilage condition, also occur in selenium-deficient areas (Yang et al 1988) although it has not been shown to respond to selenium supplementation. Selenium deficiency in conjunction with iodine-deficiency has also been reported to increase the risk of cretinism (Vanderpas et al 1992).

Indicators that have been used for assessing requirements include the existence of Keshan Disease, selenium in hair, nails and blood or GP_X and selenoproteins in blood. Whilst some countries base their minimum requirements on levels at which no Keshan Disease is evident in susceptible populations, most use measures of GP_X and other blood measures in response to varying intakes of selenium (Thomson 2004b).

1 mmol selenium = 79 mg selenium

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Selenium**
0–6 months	**12 µg/day**	
7–12 months	**15 µg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of selenium in breast milk of 15 µg/L based on the New Zealand and Australian studies of Cumming et al (1992), Daniels et al (2000) and Dolamore et al (1992), and rounding. The AI for 7–12 months was extrapolated from that of the younger infants on a metabolic weight basis.

Children & adolescents	EAR	RDI	Selenium
All			
1–3 yr	**20 µg/day**	**25 µg/day**	
4–8 yr	**25 µg/day**	**30 µg/day**	
Boys			
9–13 yr	**40 µg/day**	**50 µg/day**	
14–18 yr	**60 µg/day**	**70 µg/day**	
Girls			
9–13 yr	**40 µg/day**	**50 µg/day**	
14–18 yr	**50 µg/day**	**60 µg/day**	

***Rationale*:** The EAR for children was extrapolated from the adult data on a metabolic body weight basis, and rounded to the nearest 5 µg. The RDI was derived assuming a CV of 10% for the EAR. EARs and RDIs were estimated using the absolute data but rounded up to the nearest 5 µg for the final recommendations.

Adults	EAR	RDI	Selenium
Men			
19–30 yr	**60 µg/day**	**70 µg/day**	
31–50 yr	**60 µg/day**	**70 µg/day**	
51–70 yr	**60 µg/day**	**70 µg/day**	
>70 yr	**60 µg/day**	**70 µg/day**	
Women			
19–30 yr	**50 µg/day**	**60 µg/day**	
31–50 yr	**50 µg/day**	**60 µg/day**	
51–70 yr	**50 µg/day**	**60 µg/day**	
>70 yr	**50 µg/day**	**60 µg/day**	

***Rationale*:** The EARs for adults were based on the experimental data of Duffield et al (1999) and Xia et al (2005) assessing GP_X activity at various supplemental selenium intakes. The findings were corrected to the reference adult body weights. The RDI was set assuming a CV for the EAR of 10%. Both the EAR and RDI were rounded up to the nearest 5 µg for the final figure but the unrounded EAR was used to estimate the RDI before rounding.

Pregnancy	EAR	RDI	Selenium
14–18 yr	**55 µg/day**	**65 µg/day**	
19–30 yr	**55 µg/day**	**65 µg/day**	
31–50 yr	**55 µg/day**	**65 µg/day**	

***Rationale*:** Estimates from studies in New Zealand, Germany and Poland show additional requirements for fetal needs from 1–2 µg/day (Casey et al 1982, FAO:WHO 2001, Oster 1988, Zachara 2001). One US study indicated higher requirements in the order of 3–4 µg/day (Schroeder et al 1970) based on measures of skeletal muscle selenium, but this may reflect non-selective deposition of excess selenium in muscle tissues in a population with high selenium intake rather than skeletal muscle needs. Several countries assume that any additional requirement in pregnancy can be met by an adaptive increase in absorption (Netherlands Food and Nutrition Council 1989, Scientific Committee for Food EU 1993,

Department of Health 1991). An additional 2 µg/day was added to the EAR of adult women and rounded up to the nearest 5 µg. The RDI was set on the unrounded EAR assuming a CV of 10% and rounded up.

Lactation	**EAR**	**RDI**	**Selenium**
14–18 yr	**65 µg/day**	**75 µg/day**	
19–30 yr	**65 µg/day**	**75 µg/day**	
31–50 yr	**65 µg/day**	**75 µg/day**	

***Rationale*:** The EAR for lactation includes an allowance of 12 µg/day for selenium secreted in breast milk which is added to the mother's requirement. The RDI was set assuming a CV of 10% for the EAR. The EARs and RDIs were estimated using the absolute data but rounded up to the nearest 5 µg for the final recommendations.

UPPER LEVEL OF INTAKE - SELENIUM

Infants	
0–6 months	**45 µg/day**
7–12 months	**60 µg/day**
Children and adolescents	
1–3 yr	**90 µg/day**
4–8 yr	**150 µg/day**
9–13 yr	**280 µg/day**
14–18 yr	**400 µg/day**
Adults 19+ yr	
Men	**400 µg/day**
Women	**400 µg/day**
Pregnancy	
14–18 yr	**400 µg/day**
19–50 yr	**400 µg/day**
Lactation	
14–18 yr	**400 µg/day**
19–50 yr	**400 µg/day**

***Rationale*:** The UL relates to intakes from food and supplements. There are limited data about toxicity in humans but the most common outcomes are brittleness and loss of hair and nails (Yang et al 1983) as well as gastrointestinal disturbance, skin rash, fatigue, irritability and nervous system abnormalities (CDC 1984, Helzlsouer et al 1985, Yang et al 1983, 1989a). Studies from China (Yang et al 1983, 1989b,Yang & Zhou 1994) give a NOAEL for adults of 800 µg/day which was consistent with one US study (Longnecker et al 1991).

The Nutritional Prevention of Cancer Trial (Duffield-Lillico et al 2003) showed an increase in the risk of squamous cell carcinoma and total non-melanoma skin cancer with supplements of 200 µg/day among individuals at high risk of non-melanoma skin cancer. It is not known how this would relate to risk for the general public.

An UF of 2 is applied (FNB:IOM 2000) to protect sensitive individuals because of gaps in data and incomplete knowledge, bearing in mind that the toxic effect of selenium is not severe but may be irreversible. The UL is therefore set at 400 µg/day for all adults, as there are no data to suggest increased susceptibility during pregnancy and lactation.

The UL for young infants was based on the studies of Shearer & Hadjimarkos (1975) showing that a human milk concentrations of 60 µg/L was not associated with adverse effects. This gives a NOAEL of 47 µg/day (7 µg/kg body weight). A UF of 1 was applied, as there is no evidence that maternal intakes associated with human milk in this range cause toxicity for mothers or infants.

As there is no evidence of increased toxicity in older children and adolescents, the ULs for these groups were estimated on a body weight basis from the younger infant data using the level of 7 µg/kg body weight.

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SODIUM

BACKGROUND

Sodium is a cation needed to maintain extracellular volume and serum osmolality. Approximately 95% of the total sodium content of the body is found in extracellular fluid, being maintained outside the cell via the sodium/potassium-ATPase pump. Sodium is also important for maintaining the membrane potential of cells and for active transport of molecules across cell membranes. Absorption of sodium and chloride occurs primarily in the small intestine and is approximately 98% efficient across a wide range of intakes.

Sodium is found in most foods as sodium chloride, generally known as 'salt'. It is also present in the diet as sodium bicarbonate and as monosodium glutamate in processed foods. Sodium is also present in other food additives such as sodium phosphate, sodium carbonate and sodium benzoate. Sodium chloride, however, accounts for approximately 90% of the total sodium excreted in countries like Australia and New Zealand (Fregly 1984, Mattes & Donnelly 1991).

In industrialised countries, the majority of ingested sodium chloride is excreted in the urine, provided that sweating is not excessive (Holbrook et al 1984, Pitts 1974). Absorbed sodium and chloride remain in the extracellular compartments that include plasma and interstitial fluid. There are various systems and hormones that influence sodium balance, including the renin-angiotensin-aldosterone hormone system, the sympathetic nervous system, atrial natriuretic peptide, the kallikrein-kinin system, various intrarenal mechanisms, and other factors that regulate renal and medullary blood flow. In sodium and fluid balance, with minimal sweat losses, the amount of sodium excreted in urine roughly equals intake.

The Intersalt Cooperative Research Group (1988) found that the rate of sodium excretion ranges from less than 0.2 mmol of sodium/day in the Yanomamo Indians of Brazil to 242 mmol/day in Tianjin in China (Intersalt Cooperative Research Group 1988). Estimated intakes in Australia are about 150 mmol/day (Beard et al 1997, Notowidjojo & Truswell 1993). An almost identical figure has been found in New Zealand (Thomson & Colls 1998).

There many healthy populations with estimated intakes of less than 40 mmol/day (Intersalt Cooperative Research Group 1988). Survival at extremely low levels such as that of the Yanomamo reflects the ability to conserve sodium by reducing urine and sweat losses. With maximal adaptation, the smallest amount of sodium needed to replace losses is estimated to be no more than 0.18 g/day (8 mmol/day). However, a diet providing this level of sodium intake is unlikely to meet other dietary requirements in countries such as Australia and New Zealand.

Physical activity can potentially affect sodium chloride balance, mostly from increased losses in sweat. People who regularly undertake strenuous activity in the heat can lose substantial amounts of sodium. Loss of sodium in sweat is dependent on overall diet, sodium intake, sweating rate, hydration status and degree of acclimatisation to the heat (Allan & Wilson 1971, Allsopp et al 1998, Brouns 1991). Acclimatisation to the heat decreases the amount of sodium lost in sweat (Sawka & Montain 2002). Exposure to heat without exercise also alters the sodium concentration of sweat.

Other factors that can affect sodium needs include the intake of potassium (Liddle et al 1953) and calcium (Breslau et al 1982, Castenmiller et al 1985, McCarron et al 1981). Administration of potassium salts has been shown to increase urinary sodium excretion and a substantial body of evidence has documented that higher intakes of sodium result in increased urinary excretion of calcium.

The major adverse effect of increased sodium chloride intake is elevated blood pressure, a risk factor for cardiovascular and renal diseases. Blood pressure increases progressively in a dose-dependent relationship with sodium chloride excretion across the range seen in populations around the world. There has been a number of meta-analyses of the effect of reduction of sodium on diastolic and systolic blood pressure (Cutler et al 1997, Graudal et al 1998, Midgley et al 1996).

The strongest dose-response evidence comes from clinical trials that specifically examined the effects of at least three levels of sodium intake on blood pressure (Bruun et al 1990, Ferri et al 1996, Fuchs et al 1987, Johnson et al 2001, Kirkendall et al 1976, Luft et al 1979, MacGregor et al 1989, Sacks et al 2001, Sullivan et al 1980). The range of sodium intakes in these studies was 10 mmol/day to 1,500 mmol/day. Several trials included sodium intake levels close to 65 mmol/day and 100 mmol/day.

There is a well-recognised heterogeneity in the blood pressure response to changes in sodium chloride intake. People with hypertension, diabetes and chronic kidney disease and greater age tend to be more sensitive to the blood pressure raising effects of sodium chloride intake. Overweight also appears to increase susceptibility as demonstrated by He et al (1999) in a study of 14,407 participants with a 19-year follow up. In this study, relative risks for stroke and cardiovascular mortality were 1.89 and 1.61, respectively, for an increase in sodium intake of 100 mmol. However, the excess mortality was seen in overweight but not normal weight adults. Given the increasing level of overweight in the community, this is of particular importance. Genetic factors also influence the blood pressure response to sodium chloride. Sodium sensitivity is modifiable with the rise in blood pressure, being less on a diet high in potassium. In non-hypertensive individuals, a reduced sodium intake can decrease the risk of developing hypertension.

Indicators that have been used for assessing the need for sodium include sodium balance, serum or plasma sodium concentration, plasma renin activity, elevation in blood pressure, blood lipid concentrations and insulin resistance.

1 mmol sodium = 23 mg sodium
1 gram of sodium chloride (salt) contains 390 mg (17 mmol) of sodium

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Sodium**
0–6 months	**120 mg/day**	**(5.2 mmol)**
7–12 months	**170 mg/day**	**(7.4 mmol)**

***Rationale*:** The AI for 0–6 months was calculated by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of sodium of 160 mg/L from the studies of Dewey & Lonnerdal (1983), Gross et al (1980), Keenan et al (1982), Lemons et al (1982), Morriss et al (1986) and Picciano et al (1981). The AI for 7–12 months was extrapolated from that for 0–6 months from a consideration of metabolic body weights and relative energy requirements.

Children & adolescents	**AI**	**Sodium**
All		
1–3 yr	**200–400 mg/day**	**(9–17 mmol)**
4–8 yr	**300–600 mg/day**	**(13–26 mmol)**
9–13 yr	**400–800 mg/day**	**(17–34 mmol)**
14–18 yr	**460–920 mg/day**	**(20–40 mmol)**

***Rationale*:** There are not enough dose-response data to set an EAR for children and adolescents, so AIs have been set. There is no reason to expect that the sodium requirement of children ages 1 to 18 years would be fundamentally different from that of adults, given that maturation of kidneys is similar in normal children by 12 months of age (Seikaly & Arant 1992). The AIs for children and adolescents were derived from adult AIs based on relative energy intake.

Adults	AI	Sodium
Men	**460-920 mg/day**	**(20-40 mmol)**
Women	**460-920 mg/day**	**(20-40 mmol)**

***Rationale*:** As there are insufficient data from dose-response trials, an EAR could not be established, and thus a RDI could not be derived. An AI for adults for sodium was set at 460–920 mg/day (20–40 mmol/day) to ensure that basic requirements are met and to allow for adequate intakes of other nutrients. This AI may not apply to highly active individuals, such as endurance athletes or those undertaking highly physical work in hot conditions, who lose large amounts of sweat on a daily basis.

Pregnancy	AI	Sodium
14–18 yr	**460-920 mg/day**	**(20-40 mmol)**
19–30 yr	**460-920 mg/day**	**(20-40 mmol)**
31–50 yr	**460-920 mg/day**	**(20-40 mmol)**

***Rationale*:** During pregnancy there is a small increase in extracellular fluid, but as the AI for women was set generously, there should be no additional requirement in pregnancy.

Lactation	AI	Sodium
14–18 yr	**460-920 mg/day**	**(20-40 mmol)**
19–30 yr	**460-920 mg/day**	**(20-40 mmol)**
31–50 yr	**460-920 mg/day**	**(20-40 mmol)**

***Rationale*:** In lactation, there is a small increase in maternal extracellular fluids and some sodium is excreted in breast milk. However, these additional requirements are well within the additional margin added to the adult AI so there are no additional requirements.

UPPER LEVEL OF INTAKE - SODIUM

Infants		
0–12 months	**Not possible to establish. Source of intake should be through breast milk, formula and food only.**	
Children		
1–3 yr	**1,000 mg/day**	**(43 mmol)**
4–8 yr	**1,400 mg/day**	**(60 mmol)**
9–13 yr	**2,000 mg/day**	**(86 mmol)**
14–18 yr	**2,300 mg/day**	**(100 mmol)**
Adults 19+ yr		
Men	**2,300 mg/day**	**(100 mmol)**
Women	**2,300 mg/day**	**(100 mmol)**
Lactation		
All ages	**2,300 mg/day**	**(100 mmol)**

***Rationale*:** The adverse effects of higher levels of sodium intake on blood pressure provide the scientific rationale for setting the UL. Because the relationship between sodium intake and blood pressure is progressive and continuous, it is difficult to set a UL precisely. To complicate the analysis, other environmental factors (weight, exercise, potassium intake, overall dietary pattern and alcohol intake) and genetic factors also affect blood pressure. However, there is evidence of a population intake threshold for increased prevalence of hypertension.

For adults, a UL of 2,300 mg/day (100 mmol/day) is set on the basis of population studies showing low levels of hypertension (less than 2%) and no other observed adverse effects in communities with intakes below this level. The UL was also based on experimental studies such as the DASH-sodium trial that showed an additional systolic blood pressure reduction of 4.6 mmHg ($p < 0.001$) at intakes of 1,500 mg/day (65 mmol/day) compared to 2,500 mg/day (107 mmol/day) in people on the control diet. In this study, decreasing sodium intake by approximately 920 mg/day (40 mmol/day) caused a greater lowering of blood pressure when the starting sodium intake was at the intermediate level than when it was at a higher intake similar to the Australian/New Zealand average of about 6g/day. A NOAEL of 2,300 mg/day (100 mmol) was therefore adopted. However, this NOAEL was adopted in recognition of the fact that the considerable number of older and overweight people in the Australian and New Zealand population who have pre-existing hypertension will derive additional benefit from lowering intakes to 1,600mg/day (70 mmol). This level of 1,600 mg has thus been set as a Suggested Dietary Target for chronic disease prevention in line with WHO recommendations (WHO 2000) (see also 'Chronic disease' section).

A UF of 1 was applied as, by definition, there is no convincing evidence of harm in the general population at levels of intake of 100 mmol or less. There are no data to suggest increased susceptibility in pregnancy or lactation, so the UL is set at the same level as for adult women.

For infants, a UL could not be established because of insufficient data documenting the adverse effects of chronic over-consumption of sodium in this age group. The UL for children was extrapolated from the adult UL on an energy intake basis as numerous observational studies have documented that blood pressure tracks with age from childhood into the adult years (Bao et al 1995, Dekkers et al 2002, Gillman et al 1993, Van Lenthe et al 1994).

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ZINC

BACKGROUND

Zinc is a component of various enzymes that help maintain structural integrity of proteins and regulate gene expression. Zinc metalloenzymes include ribonucleic acid polymerases, alcohol dehydrogenase, carbonic anhydrase and alkaline phosphatase. The biological function of zinc can be catalytic, structural or regulatory. More than 85% of total body zinc is found in skeletal muscle and bone (King & Keen 1999).

Zinc is widely distributed in foods. Meats, fish and poultry are the major contributors to the diet but cereals and dairy foods also contribute substantial amounts. The presence of zinc in foods as a complex rather than as free ions affects its bioavailability. The environment within the gastrointestinal tract, which can be affected by other dietary constituents, markedly influences the solubility and absorptive efficiency of zinc (Cousins 1989, Lonnerdal 1989). The amount of protein in the diet is a factor contributing to the efficiency of zinc absorption as zinc binds to protein. Small changes in protein digestion may produce significant changes in zinc absorption (Sandstrom & Lonnerdal 1989). The markedly greater bioavailability of zinc from breast milk than from cow's milk is an example of how the lower protein digestibility of cow's milk influences zinc absorption (Roth & Kirchgessner 1985). In general, zinc absorption from a diet high in animal protein will be greater than from a diet rich in plant derived proteins (King & Keen 1999). The requirement for dietary zinc may be as much as 50% greater for vegetarians, particularly strict vegetarians whose major staples are grains and legumes and whose dietary phytate:zinc ratio exceeds 15:1.

Dietary intake of iron at levels found in some supplements can decrease zinc absorption, which is of particular concern in the management of pregnancy and lactation. High intakes of calcium have been shown to have a negative effect on zinc absorption in animal experiments, but human data are equivocal with calcium phosphate decreasing zinc absorption (Wood & Zheng 1997) and calcium as citrate-malate complex having no effect (McKenna et al 1997). Current data suggest that consumption of calcium-rich diets does not have a major effect on zinc absorption at an adequate intake level. There is also some evidence of potential interrelationship of zinc with copper and folate, but studies are limited. Regulation of zinc metabolism is achieved through a balance of absorption and secretion of reserves and involves adaptive mechanisms related to dietary zinc intake.

Zinc depletion in humans results in reduced endogenous zinc loss and increased efficiency of intestinal zinc absorption. While plasma zinc is only 1% of the body's total, its concentration is tightly regulated and is generally not affected by mild deficiency. Situations of stress, acute trauma and infection can lead to lower plasma zinc. Mild deficiency can result in impaired growth velocity, suboptimal pregnancy outcomes and impaired immune responses. Severe deficiency can result not only in growth impairment but also alopecia, diarrhoea, delayed sexual development and impotency, eye and skin lesions and impaired appetite.

Assessment of requirements is based on estimates of the minimal amount of absorbed zinc necessary to match total daily excretion of endogenous zinc (FNB:IOM 2001). Estimates are made using a factorial approach that involves calculation of both intestinal and non-intestinal losses (via the kidney, skin, semen and menstruation). Although urinary zinc losses decrease markedly with severe deficiency (Baer & King 1984), across a dietary intake range of 4–25 mg/day, urinary zinc (and non-intestinal losses in general) appears to be largely independent of dietary intake. Intestinal losses, however, correlate strongly to absorbed zinc.

To determine the dietary zinc requirement for a given age/gender group, it is necessary to define the relationship between absorption and intestinal losses and adjust by a constant for the non-intestinal losses in order to calculate the minimum quantity of absorbed zinc necessary to offset total endogenous losses. The factorial calculations used are based on metabolic/tracer studies in which participants are fed diets from which the bioavailability of zinc is likely to be representative of typical diets in Australia and New Zealand.

1 mmol zinc = 65.4 mg zinc

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Zinc**
0–6 months	**2.0 mg/day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of zinc in breast milk in the early months postpartum, and rounding. Concentrations of zinc in breast milk decline from approximately 4 mg/L at 2 weeks to 3 mg/L at 1 month, 2 mg/L at 2 months, 1.5 mg/L at 3 months and 1.2 mg/L at 6 months postpartum (Krebs et al 1995). The AI was set to match the zinc intake of infants in the early months (2.5 mg/L x 0.78 L/day). This estimate is also consistent with factorial estimates of requirements in infants aged 0–6 months fed breast milk (Krebs et al 1996, Krebs & Hambridge 1986). Although the absorption of zinc is higher from breast milk than from infant formula based on cow's milk or soy, these formulas generally have a much higher content of zinc than breast milk which compensates for the lower absorption efficiency (Lonnerdal et al 1988, Sandstrom et al 1983).

Infants	**EAR**	**RDI**	**Zinc**
7–12 months	**2.5 mg/day**	**3 mg/day**	

***Rationale*:** The EAR for 7–12 months was set by estimating the absorbable zinc required to replace endogenous zinc losses, extrapolating on a body weight basis from adult data and including considerations of growth needs, assuming an absorption of 30% (Davidsson et al 1996, Fairweather-Tait et al 1995) and making an allowance for growth. The RDI was set using a CV of 10% for the EAR and rounding, as information was not available on the SD of the requirement. Absorption is higher from animal foods than plants sources, so vegetarian infants, particularly strict vegetarians, will need higher intakes.

Children & adolescents	**EAR**	**RDI**	**Zinc**
All			
1–3 yr	**2.5 mg/day**	**3 mg/day**	
4–8 yr	**3.0 mg/day**	**4 mg/day**	
Boys			
9–13 yr	**5 mg/day**	**6 mg/day**	
14–18 yr	**11 mg/day**	**13 mg/day**	
Girls			
9–13 yr	**5 mg/day**	**6 mg/day**	
14–18 yr	**6 mg/day**	**7 mg/day**	

***Rationale*:** The absorbed zinc requirement was estimated by summing the estimated non-intestinal (urinary, integument, semen for men) and intestinal zinc losses to derive total endogenous losses. Endogenous losses for children were calculated using reference weights with an additional requirement for growth. The EAR was then estimated assuming an absorption of 24% for boys and 31% for girls (International Zinc Nutrition Consultative Group 2004), and rounding. The RDI was set on the unrounded EAR using a CV of 10% for the EAR and rounding, as information was not available on the SD of the requirement. Absorption is higher from animal foods than plants sources, so vegetarians, particularly strict vegetarians, will need intakes about 50% higher than those set.

Adults	**EAR**	**RDI**	**Zinc**
Men			
19–30 yr	**12 mg/day**	**14 mg/day**	
31–50 yr	**12 mg/day**	**14 mg/day**	
51–70 yr	**12 mg/day**	**14 mg/day**	
>70 yr	**12 mg/day**	**14 mg/day**	
Women			
19–30 yr	**6.5 mg/day**	**8 mg/day**	
31–50 yr	**6.5 mg/day**	**8 mg/day**	
51–70 yr	**6.5 mg/day**	**8 mg/day**	
>70 yr	**6.5 mg/day**	**8 mg/day**	

***Rationale*:** The absorbed zinc requirement was estimated by summing the estimated non-intestinal (urinary, integument, semen for men) and intestinal zinc losses to derive total endogenous losses. The EAR was then estimated assuming an absorption of 24% for men and 31% for women (IZiNCG 2004), and rounding. The RDI was set on the unrounded EAR using a CV of 10% for the EAR and rounding up, as information was not available on the SD of the requirement. Absorption is higher from animal foods than plants sources, so vegetarians, particularly strict vegetarians, will need intakes about 50% higher than those set.

Pregnancy	**EAR**	**RDI**	**Zinc**
14–18 yr	**8.5 mg/day**	**10 mg/day**	
19–30 yr	**9.0 mg/day**	**11 mg/day**	
31–50 yr	**9.0 mg/day**	**11 mg/day**	

***Rationale*:** The EAR was established by estimating the needs for the additional maternal and fetal tissues and adding this to the equivalent EAR for non-pregnant females. The figure used was based on late pregnancy estimates of zinc accumulation (the period of greatest need) to give a single recommendation throughout pregnancy. Zinc accumulation at this time averages 0.73 mg/day (Swanson & King 1987). Absorption in pregnancy is thought to be similar to that of non-pregnant women, so an absorption rate of 31% was used to estimate the additional requirement of 2.35 mg/day. Absorption is higher from animal foods than plant sources, so vegetarians, particularly strict vegetarians, will need intakes about 50% higher than those set.

***Note*:** For women taking high levels of iron supplements during pregnancy and lactation, the current EAR and thus RDI may not be adequate. There is some evidence that high levels of iron supplements prescribed to pregnant and lactating women may decrease zinc absorption (Fung et al 1997, Hambidge et al 1983, O'Brien et al 2000).

Lactation	EAR	RDI	Zinc
14–18 yr	**9 mg/day**	**11 mg/day**	
19–30 yr	**10 mg/day**	**12 mg/day**	
31–50 yr	**10 mg/day**	**12 mg/day**	

***Rationale*:** The lactation recommendation was based on consideration of the additional needs for milk production together with estimates of zinc released for use because of decreasing maternal blood volume (King & Turland 1989). This averages about 30 mg zinc that can be re-used. The average increased requirement for absorbed zinc is 1.35 mg/day. Absorption is about 42% in lactation (Fung et al 1997), giving an additional dietary zinc requirement of 3.2 mg/day. Absorption is higher from animal foods than plants sources, so vegetarians, particularly strict vegetarians, will need intakes about 50% higher than those set.

UPPER LEVEL OF INTAKE - ZINC

Infants	
0–6 months	**4 mg/day**
7–12 months	**5 mg/day**
Children and adolescents	
1–3 yr	**7 mg/day**
4–8 yr	**12 mg/day**
9–13 yr	**25 mg/day**
14–18 yr	**35 mg/day**
Adults 19+ yr	
Men	**40 mg/day**
Women	**40 mg/day**
Pregnancy	
14–18 yr	**35 mg/day**
19–50 yr	**40 mg/day**
Lactation	
14–18 yr	**35 mg/day**
19–50 yr	**40 mg/day**

***Rationale*:** There is no evidence of adverse effects from naturally occurring zinc in food. The UL applies to total zinc intake from food, water and supplements (including fortified food). Adverse events associated with chronic intake of supplemental zinc include suppression of immune response, decrease in high density lipoprotein (HDL) cholesterol and reduced copper status. The adverse effect of excess zinc on copper metabolism has been identified as the critical effect on which to base the UL. This is based on the consistency of findings (Fischer et al 1984, Samman & Roberts 1988, Yadrick et al 1989), the sensitivity of the marker used (erythrocyte copper-zinc superoxide dismutase) and the quality and completeness of the database for this endpoint. A LOAEL of 60 mg/day is based on the studies of Yadrick et al (1989) and is supported by other studies (Fischer et al 1984). A UF of 1.5 is applied to account for inter-individual variability in sensitivity and for extrapolation from LOAEL to NOAEL. As reduced copper status is rare in humans, a higher UF was unjustified. The adult UL was therefore set at 40 mg/day. There was inadequate data to justify a different UL for pregnancy and lactation and so the level is set at that for the equivalent non-pregnant women.

A study by Walravens & Hambridge (1976) of 68 infants, showed no adverse effects at a level of 5.8 mg zinc/L of infant formula fed for 6 months. This would translate to a NOAEL of 4.5 mg/day at 0.78 L milk per day. A UF of 1 was applied, given the length and quality of the study and the fact that there is no evidence of harm from intakes of formula at 5.8 mg zinc/L. Rounding down, a UL of 4 mg was therefore set for infants of 0–6 months. As there were no data for older children and adolescents, this figure was adjusted on a body weight basis, for older infants, children and adolescents and values rounded down. Lind et al (2003) showed in a double-blind RCT that plasma copper does not differ between infants receiving 10 mg zinc/day or placebo. However Bhandari et al (2002) reported lower copper levels in children of 6–12 month given 10 mg zinc/day and those of 1–2.5 years given 20 mg/day over 4 months.

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OPTIMISING DIETS FOR LOWERING CHRONIC DISEASE RISK

INTRODUCTION

Although Nutrient Reference Values (NRVs) are determined on the basis of needs for sustenance and avoidance of deficiency disease, it is obviously most beneficial if nutrient intakes are also compatible with intakes that may reduce chronic disease risk. Whilst there is an extensive and growing data base related to diet and chronic disease risk in humans, the population methodologies generally employed have a number of limitations in relation to identifying a specific level of intake that is optimal for reducing the risk of chronic disease.

The major tools used for associating food intake patterns and specific nutrients with chronic disease risk are:

- ***Ecologic studies*** in which national per capita food intakes are correlated with national health statistics relating to the incidence, prevalence and mortality of diseases.
- ***Case-control studies*** in which food intake patterns in individuals who have contracted a disease under study are gathered retrospectively and compared with the food intakes of appropriately chosen individuals who do not have the disease.
- ***Cohort studies*** in which food intake patterns in many study subjects are recorded while they are all free of the disease(s) of interest – and after an appropriate efflux of time (usually many years) the dietary patterns of those who develop disease(s) are compared with those who are still disease free.
- ***Intervention studies (randomised controlled trials, RCTs)*** in which subjects at (high) risk of the disease under study are randomly allocated to either a modified dietary/supplemental regimen or a control regimen – and the two study groups are compared with respect to their subsequent disease incidence or progression.

Evidence from individual studies may be supported by additional meta-analyses of a number of related studies that increase the power to detect associations and/or by systematic review of individual studies.

Ecologic studies provide the weakest evidence, since a diversity of other explanations may account for any observed association. The striking association between per capita consumption of fat and breast cancer mortality in women is a salutary example of a hypothesis generated by an ecologic study that could not be sustained in subsequent analytic studies. A case-control study is the most popular analytic tool for investigating chronic disease aetiology as it is easier to undertake (in terms of finance and time) than cohort studies or RCTs, but it is extremely vulnerable to biases arising from either inappropriate selection of control subjects, or from selective recall bias by case subjects of the foods they ate prior to the diagnosis of their condition.

While cohort studies are far less vulnerable to the problems of the case-control study, the huge numbers of study subjects required to ensure the future accrual of a sufficient number of 'cases' and the time required for the disease to develop has meant that very few cohort studies have ever been conducted. Finally, in a few instances, there has been sufficient confidence in the disease-preventive capacity of a specific food component or micronutrient to initiate an intervention trial. Modelled on the RCT, an intervention study provides the most reliable information for confirming a direct causal relationship between a dietary component and a chronic disease outcome. However, most interventions that have been undertaken to date have, for pragmatic reasons, involved use of supplements rather than dietary change. In many instances, supplement mixes (eg of antioxidant micronutrients) have been used and there is some evidence that mixes of micronutrients may be more effective than single nutrient approaches.

It is salutary to note, however, that at least in the case of the nutrient β-carotene, very promising data from both case-control and cohort studies indicating a protective effect for certain cancers was not confirmed in subsequent interventions studies and, indeed, indicated some potential harm. Earlier work had shown that dietary β-carotene could prevent DNA-damaging steps in the genesis of cancer, but intervention studies involving its use in people at high risk of cancer of the lung, colon and cervix either found no effect, or were discontinued due to the apparent impetus to progression of cancer in the study subjects. Recent work has shown similar concerns in relation to other nutrients given in supplemental form.

With these provisos in mind, there is some evidence that a range of nutrients could have benefits in chronic disease aetiology at levels above the RDI or AI. This is discussed in detail in the publications of the Food and Nutrition Board: Institute of Medicine as part of the reviews of the US:Canadian DRIs, notably those published in 1998, 2000 and 2002. It is not the purpose of this NRV review to revisit this extensive database of studies, but to acknowledge its existence and its complementarity to the NRV recommendations, and to summarise key findings from some of these studies and the intervention trials.

The nutrients for which higher than RDI and AI intakes have been linked to benefits for chronic disease risk include the antioxidant vitamins such as vitamin C, vitamin E and vitamin A (primarily its precursor, β-carotene) as well as selenium and nutrients such as folate, omega 3 fats and dietary fibre. These nutrients have been assessed in relation to heart disease and cancer as well as degenerative eye diseases such as cataract formation or macular degeneration, and conditions like Alzheimer's or cognitive decline.

The balance and type of macronutrients in the diet have also been studied extensively. The role of the various types of carbohydrates (starches, sugars, high vs low-glycaemic carbohydrates, resistant starch or RS, dietary fibres), fats (saturated, polyunsaturated, monounsaturated) and protein (animal, plant-based) have been variously assessed in relation to risk of conditions such as coronary heart disease (CHD), certain cancers, diabetes or insulin sensitivity and risk of obesity.

MICRONUTRIENTS AND DIETARY FIBRE

ANTIOXIDANT VITAMINS AND MINERALS

There have been many case-control and cohort studies assessing the relationship between antioxidant nutrients and chronic disease outcome mainly in relation to cancer and CHD. In addition, there are over 15 randomised, double-blind, placebo-controlled, intervention trials, some related to primary prevention and some secondary (FNB:IOM 2000). Some of these have tested single supplements while others have tested mixtures. Some have shown benefits for cancer (Blot et al 1993, Clark et al 1996, 1998) or aspects of heart disease (Stephen et al 1996). Some studies have shown no effect (GISSI 1999, Greenberg et al 1990, 1994, Hennekens et al 1996, Lee et al 1999, Stephen et al 1996) and some have reported negative effects (ATBC 1994, Omenn et al 1996), the latter generally associated with β-carotene. A brief summary is given below in relation to the individual key antioxidative micronutrients

VITAMIN A AND CAROTENOIDS

The antioxidant benefits of vitamin A relate primarily to its precursor, β-carotene. Many case-control studies and cohort studies have shown a relationship between β-carotene intake and cancer risk reduction. However, intervention trials have been disappointing. An intervention study for skin cancer (Greenberg et al 1990) showed no effect and neither did another for polyp prevention (Greenberg et al 1994). Trials in relation to cervical cancer, including some in Australia, have also shown no effect of vitamin A (Mackerras et al 1993, 1999). In fact, the CARET trial (Omenn et al 1996) on lung cancer produced an increased risk with 30 mg β-carotene administered together with retinyl palmitate, as well as an increase in total mortality, and the ATBC trial (1994) showed an 11% increase in risk of ischaemic heart disease with β-carotene and an 18% increase in lung cancer. The Linxian cancer intervention study (Blot et al 1993, 1995) included β-carotene with vitamin E and selenium and showed a 9% reduction in total mortality, a 23% reduction in cancer mortality and a 10% decrease in stroke with the supplement mix. Hennekens et al (1996) showed no effect on CVD or cancer in men receiving 50 mg supplements on alternate days and Lee et al (1999) saw no effect in women using the same dose. The carotenoid lycopene has been associated with reduction of risk in prostate cancer, but results are inconsistent (Giovannucci et al 1995a, Kristal & Cohen 2000).

Low levels of dietary or plasma carotenoids have also been associated with eye conditions. The existence or severity of cataracts has been linked to higher intakes of plasma carotenoids in some studies (Brown et al 1999, Hankinson et al 1992, Lyle et al 1999, Mares-Perlman et al 1995, Seddon et al 1994, Chasen-Taber et al, 1999) but not all (The Italian-American Cataract Study Group 1991, Vitale et al 1993). For many of the studies with positive results, effects were seen for some carotenoids but not others.

The carotenoids lutein and zeaxanthin have been associated with prevention of macular degeneration (Eye Disease Case-Control Study Group 1993, Hammond et al 1996, Seddon et al 1994, Snodderly 1995) but some studies have shown no effect (Mares-Perlman et al 1994). Mares-Perlman et al did, however, find an effect of increasing plasma lycopene. West et al (1994) also found a protective effect for plasma β-carotene and lycopene.

VITAMIN C

Several case-control and cohort studies have reported protection by vitamin C for cardiovascular disease and stroke (Enstrom et al 1992, Gale et al 1995, Khaw et al 2001, Knekt et al 1994, Nyyssonen et al 1997, Pandey et al 1995, Sahyoun et al 1996, Simon et al 1998). Other studies have shown no protective effect (Enstrom et al 1986, Kushi et al 1996b, Losonczy et al 1996, Rimm et al 1993).

Block (1991) has claimed that the epidemiologic evidence for vitamin C as being protective against cancer is strongly suggestive, but others claim it is not convincing (Ames et al 1995). From case-control and cohort studies, prevention has been claimed for a range of cancers including breast, cervical, colorectal, pancreatic, lung and gastric cancers (Bandera et al 1997, Bueno de Mesquita et al 1991, Fontham et al 1988, Freudenheimn et al 1990, Ghadirian et al 1991, Howe et al 1990, 1992, Knekt et al 1991, Kushi et al 1996a, Ocke et al 1997, Romney et al 1985, Shekelle et al 1981, Wassertheil-Smoller et al 1981, Yong et al 1997, Zatonski et al 1991). However, others have shown no such association (Graham et al 1992, Hinds et al 1984, Hunter et al 1993, Le Marchand et al 1989).

The few RCTs that have been conducted with vitamin C have proved disappointing (Heart Protection Study 2002, Ness et al 1999). Ness et al (1999) reported a meta-analysis of three trials with vitamin C supplements and cardiovascular disease in western populations (total of 1,034 subjects). There was no overall reduction in mortality with vitamin C supplementation, the relative risk being 1.08. The cancer intervention studies of Blot et al (1993) in China also showed no beneficial effect of vitamin C on cancer mortality rates, nor did the Polyp Prevention Trial of Greenberg et al (1994). The FNB:IOM, in its 2000 DRI review, concluded that data were not consistent enough to be able to identify a level of vitamin C that could be used for setting recommendations in relation to vitamin C and cancer.

Some studies of dietary vitamin C in relation to cataracts have shown benefits (Jacques & Chylack 1991, Leske et al 1991, Robertson et al 1989) and others have not (Hankinson et al 1992, Vitale et al 1993). However, in the study of Hankinson et al (1992), the use of supplement long term did relate to reduced risk. Asthma and cognitive function have also been assessed in relation to vitamin C intake. A recent Cochrane review of asthma concluded that there was no benefit of increased intakes of vitamin C. The results with cognition were mixed; with one showing no benefit (Jama et al 1996) and the other showing better memory performance (Perrig et al 1997).

VITAMIN E

Data related to the effects of vitamin E on chronic disease status are limited, but the strongest evidence is for CHD. A number of double-blind controlled trials assessing chronic disease outcome have been completed, including the Cambridge Heart Antioxidant Study (CHAOS) trial (Stephens et al 1996), the GISSI-Preventione Trial (1999) for CHD; the Health Outcomes Prevention Evaluation (HOPE) trial (Yusuf et al 2000) for heart disease and the Alpha-Tocopherol Beta-Carotene (ATBC) Cancer Prevention Study which also reported heart disease endpoints. Of the heart disease studies, only the CHAOS trial gave a positive result of a 77% decrease in risk of subsequent non-fatal myocardial infarction, but no benefit to cardiovascular mortality. The ATBC trial, which was undertaken in cigarette smokers, also reported a 50% increase in haemorrhagic stroke deaths with vitamin E, but no effect on lung cancer, the primary endpoint. The GISSI trial showed no effect with vitamin E, but did show an effect with omega-3 fats.

Two reviews that included meta-analyses of the data relating to vitamin E and CHD concluded that vitamin E has little effect on outcome. Eidelmann et al (2004) conducted a computerised search of the English-language literature from 1990 and found seven large-scale randomised trials of the effectiveness of vitamin E in the treatment and prevention of cardiovascular disease. Data were available on myocardial infarction, stroke, or cardiovascular death. Six of the seven trials showed no significant effect of vitamin E on cardiovascular disease. In a meta-analysis, vitamin E had neither a statistically significant nor a clinically important effect on any important cardiovascular event or its components, nonfatal myocardial infarction, or cardiovascular death. The authors concluded that the odds ratios and confidence intervals provided strong support for a lack of statistically significant or clinically important effects of vitamin E on cardiovascular disease. Shekelle et al (2004) also undertook a systematic review of placebo-controlled, RCTs, with a meta-analysis where justified, and concluded that there is good evidence that vitamin E supplementation neither beneficially or adversely affects cardiovascular outcomes.

Data in relation to vitamin E and cancer from epidemiological studies is limited. A study assessing intakes in the US NHANES I Epidemiological Follow-up study (Yong et al 1997) showed an inverse association in smokers and a prospective cohort study also found a weak inverse relationship with lung cancer (Comstock et al 1997). Two prospective cohort studies of breast cancer (Dorgan et al 1998, Verhoeven et al 1997) and one case-control study (van't Veer et al 1996) found no relationship with vitamin E status. A case-control study of prostate cancer showed no link (Andersson et al 1996) but an inverse association was found in one prospective study (Eichholzer et al 1996) although earlier cohort studies showed no association (Comstock et al 1992, Knekt et al 1988).

There have been few intervention trials of vitamin E and cancer. One study of heavy smokers showed no benefit for lung cancer but 34% lower incidence of prostate cancer (ATBC 1994, Heinonen et al 1998). Two small trials have shown no effects on mammary dysplasia or breast disease (Ernster et al 1985, London et al 1985) and no secondary polyp preventive effect was seen in five trials (Chen et al 1988, DeCosse et al 1989, Greenburg et al 1994, Hofstad et al 1998, McKeown-Eyssen et al 1988).

Vitamin E has also been investigated in relation to immune function (Ghalaut et al 1995, Meydani et al 1997) and cataracts (Jacques & Chylack 1991, Hankinson et al 1992, Knekt et al 1992, Leske et al 1991, Mares-Perlman et al 1994, Mohan et al 1989, Robertson et al 1989, Vitale et al 1993) with mixed results. The one intervention for cataracts showed no effect of 50 mg α-tocopherol/day (Teikari et al 1998).

SELENIUM

Selenium has been assessed in relation to both cancer and CHD. Selenium intakes greater than RDI have also been shown to improve immune function (Broome et al 2004).

Selenoproteins have an anticancer effect in cellular and animal experimentation and there are some indications of a protective role from human studies (Coombs 2005). One US study, using a nested case-control design within a cohort also showed that prostate cancer risk was lowered in those with higher toenail selenium levels (Yoshizawa et al 1998). However, there have been only three human intervention trials, one of which, in China, used a mixed supplement including selenium (Blot et al 1995). In this study, significantly lower total mortality occurred among those receiving supplementation with β-carotene, vitamin E and selenium. The reduction was mainly due to lower cancer rates, especially stomach cancer, with the reduced risk becoming apparent 1 to 2 years after the start of supplementation. A large trial in the US showed no effect of supplements of 200 μg/day on skin cancer risk (Clark et al 1996) but significant reduction in total cancer and cancers of the prostate, lung and colorectum. However, Duffield-Lillico et al (2003) analysed this study further and found that supplementation actually increased the risk of squamous cell carcinoma and total non melanoma. Another large trial assessing the effects of selenium on prostate cancer risk (SELECT) is underway in the US under the auspices of the National Cancer Insititute and should provide additional evidence about this relationship.

Some researchers suggest that intakes in the region of 100–200 μg/day resulting in plasma levels of about 120 μg/L, may be necessary to maximise cancer prevention (Combs 2005, Thomson 2004, Whanger 2004) but the data on long term effects of intakes at this level are currently limited.

The available data on selenium seem to suggest that men, and particularly male smokers, may benefit more than women from supplementation in terms of lowering cancer risk (Kocyigit et al 2001, Waters et al 2004).

Evidence for a protective role of selenium against cardiovascular disease (CVD) is conflicting. Two large studies in low selenium populations indicated that selenium was an independent risk factor for myocardial infarction (Salonen et al 1982, Suadicani et al 1992), but others have not found this (Rayman 2000). The data from some studies, but not all (Néve 1996), suggest there may be a threshold effect operating such that protection is only afforded those with prior low selenium status (Huttunen 1997, Salvini et al 1995, Suadicani et al 1992).

Protection, if it does occur, is likely to be related to an antioxidant effect on the oxidative modification of lipids and aggregation of platelets. In some studies, the effect is seen only in smokers, who are known to have lower blood selenium concentrations than non-smokers (Kay & Knight 1979, Thomas 1995). The status of other antioxidants such as vitamin E might also influence the outcome.

SUMMARY OF ANTIOXIDANTS AND CHRONIC DISEASE STATUS

Studies of the effects on antioxidant nutrients have shown some promising leads, such as the potential of selenium in prostate cancer prevention, but many intervention studies show little effect or even adverse effects. Case-control and cohort studies that initially identified the antioxidant micronutrients as having preventive potential generally compare people in the population consuming their everyday diets. These studies typically indicate that subjects at or above the top quintile of their population's intake generally have lower risk of a range of chronic diseases. This may relate to the nutrients of concern, but may also reflect more general benefits arising from consumption of the foods that contain these nutrients. As the 90th centile is the midpoint for the highest quintile, it may therefore be prudent for people to consume a diet which would provide these nutrients at levels currently equating to the 90th centile of intake in the population. A dietary approach rather than a supplemental one is encouraged to maintain nutrient balance and optimise benefits. The 90th centile of intake for vitamin C in Australia and New Zealand is about 220 mg/day for adult males and 190 mg/day for adult women. For vitamin E, the 90th centile of intake is about 19 mg for men and 14 mg for women. For vitamin A, the 90th centile of intake is 1,500 µg/day and for women, 1,220 µg/day and for β-carotene, the 90th centile is 5,800 µg/day for men and 5,000 µg/day for women.

There are no national selenium intake data for Australia and it is known that New Zealand is a low selenium country, so reference to the 90th centile of intake is probably not useful in this case.

FOLATE

Apart from its well known benefits in the prevention of neural tube defects in the fetus, folate is increasingly thought to play a role in reduction of chronic disease risk. In the cardiovascular area, this relates to its role in reducing the levels of plasma homocysteine, a key risk factor for increased CVD. Homocysteine is a sulphur-containing amino acid derived from enzymic transformations of the essential dietary amino acid, methionine. Interest in homocysteine stemmed initially from the observation that sufferers from a number of different rare genetic disorders, which all manifested themselves in elevated levels of circulating homocysteine, also had in common a greatly accelerated rate of atherosclerosis. This immediately begged the question of whether mild elevations of serum homocysteine were also associated with increased CVD – and increasingly it seems that the final answer is likely to be 'yes'.

In the last 20 to 30 years, numerous retrospective studies and prospective studies have demonstrated a relation between moderate homocysteinuria and premature vascular disease in the coronary, cerebral and peripheral arteries. Supplementation using folic acid with and without vitamin B_6 to reduce serum homocysteine levels has proved to be a successful strategy in some studies.

The randomised control trial of Venn et al (2002) showed that increasing dietary folate from 263 µg/day to 618 µg/day significantly increased serum folate by 37% and decreased homocysteine from 12–11 µmol/L over a 4-week period. The volunteers were healthy and in the 50–70 age group. These same researchers (Venn et al 2003) also showed in an RCT that supplementation of healthy subjects aged 40–60 years with either 100 µg/day folic acid or 100 µg/day L-5-methyltetrahydrofolate (MTHF) resulted in significant increments in plasma folate (52% and 34%, respectively) and red cell folate (31% and 23%, respectively), and a significant reduction in plasma homocysteine (–9.3% and –14.6%, respectively). MTHF was significantly more effective than folic acid in reducing plasma homocysteine.

Another such trial by van Oort et al (2003) showed that the minimum folic acid supplementation required for 90% optimal reduction in plasma homocysteine in healthy older adults, aged 50–75years, was 400 µg/day. This study investigated doses of folic acid ranging from 50 to 800 µg/day but failed to record the dietary intake of folate for the participants. The study of Tucker et al (2004) also showed that daily intake folic acid supplements, together with vitamins B_{12} and B_6 at US RDA levels in supplemented cereal, decreased homocysteine in healthy 50–85 year-olds from 7.9 to 7.5 µmol/L.

Schnyder et al (2001) showed in an intervention trial that plasma homocysteine was reduced from 11 to 7 µmol/L and coronary stenosis significantly reduced (compared to controls) after daily supplementation for six months with 1,000 µg folic acid, 400 µg vitamin B_{12} and 10 mg vitamin B_6 in patients who had undergone percutaneous coronary angioplasty.

Finally, in the prospective cohort component of the Nurses' Health Study, Rimm et al (1998) showed that those women with folate intakes in the top quintile (median 696µg folate/day) had 31% reduction in risk of developing CHD compared to those in the bottom quintile (median, 158 µg folate/day). The effect was strongest in those women who consumed more than one alcoholic drink per day, for whom the reduction in risk was 73%.

Elevated homocysteine levels have also been linked to increased fracture risk in older people. A prospective epidemiological study in older men and women (van Meurs et al 2004) showed that a homocysteine level in the highest age-specific quartile was associated with an increase by a factor of 1.9 in the risk of fracture. The associations between homocysteine levels and the risk of fracture appeared to be independent of bone mineral density and other potential risk factors for fracture. An increased homocysteine level appears to be a strong, and independent, risk factor for osteoporotic fractures in older men and women. The results of another prospective study (McLean et al 2004) also indicate that men and women in the highest quartile of plasma homocysteine had a greater risk of hip fracture than those in the lowest quartile; the risk was almost four times as high for men and 1.9 times as high for women. These findings suggest that the homocysteine concentration is an important risk factor for hip fracture in older persons.

The results of the cross-sectional study of Seshadri et al (2002) on the Framingham cohort also showed an increased relative risk for dementia and Alzheimer's disease with increasing plasma homocysteine. The risk for Alzheimer's disease for those with plasma homocysteine greater than 14 µmol/L was double compared to those with lower values. An increase in plasma homocysteine by 5 µmol/L increased the multivariate adjusted risk of Alzheimer's disease by 40%. Relationships between folate and mental function have also been reported for depression and affective state and for learning deficits (Goodwin et al 1983, Herbert 1962, Reynolds et al 1973, Shorvon et al 1980).

Pena et al (2004) in a randomised double-blind trial have also shown that 8 weeks of treatment with 5 mg folic acid improved endothelial cell function by 2.6% in children and adolescents with Type 1 diabetes. It is of interest to note, however, that this level of supplementation is well above the recommended UL for the general population.

Poor folate status is also thought to influence the risk of cancer and to enhance an underlying predisposition to cancer (Heimburger et al 1987, Mason & Levesque 1996). The mechanisms involved are believed to include the induction of DNA hypomethylation, increasing chromosomal fragility or diminished DNA repair, as well as secondary choline deficiency, a lessening of killer cell surveillance, mistakes in DNA synthesis and facilitation of tumorigenic virus metabolism (Kim et al 1997, Mason and Levesque 1996). However, not all studies have shown reduced cancer risk with improved folate status after confounding has been taken into account (Meenan et al 1996, Potischman et al 1991, Verrault et al 1989, Zeigler et al 1990, 1991).

Zhang et al (1999) showed that folate intake of greater than 300 µg/day was associated with a 25% reduction in breast cancer risk in those women from the Nurses' Health Study who consumed at least 15 g of alcohol per day. There are also data from two large well-controlled prospective studies showing a protective effect of higher folate intakes on adematous polyps (Giovannucci et al 1993) and cancer (Giovannucci et al 1995b). Thompson et al (2001) used a case-control design to demonstrate for the first time that supplementation with folate during pregnancy reduces the risk of acute lymphocytic leukaemia in the child by 60%.

Folate at higher than RDI levels has also been shown to lower DNA damage. In a randomised placebo controlled intervention in young Australian adults, Fenech et al (1998) showed that the intake of 700 µg folic acid with 7 µg vitamin B_{12} reduced the rate of chromosome damage in lymphocytes by 25% in those individuals with above average chromosome damage rates. No further protection was provided by increasing the intake to 2,000 µg folic acid and 20 µg vitamin B_{12}. This study indicated that intake of folate well above RDI is required to minimise chromosome damage (a risk factor for cancer) in 50% of the subjects studied who were otherwise not considered to be deficient by conventional criteria.

Intakes of folate in the Australian and New Zealand populations are currently significantly below the RDI proposed here, with median intakes of about 300 µg/day for men and 230 µg/day for women. The current 90th centile of intake of 416 µg/day in men is close to the new RDI and that of women (303 µg/day) close to the new EAR. The studies above indicate that an additional 100–400 µg/day over current intakes may be required to optimise homocysteine levels and reduce overall chronic disease risk and DNA damage.

CALCIUM AND VITAMIN D

Osteoporosis is a major public health problem in Australia and New Zealand. It can be considered both a deficiency and a chronic disease. The WHO concluded in its report on diet, nutrition and chronic disease that adequate calcium was important for osteoporosis prevention, at least in older populations, and that in countries with high incidence of osteoporotic fracture, a calcium intake of below 400–500 mg/day among older men and women is associated with increased fracture risk.

The WHO also found that adequate vitamin D status was a key factor in osteoporosis prevention. However, it is of interest to note that in contrast to the perceived role of calcium and vitamin D in osteoporosis prevention, one recent large intervention trial involving 5,292 previously ambulatory elderly people who had already experienced a fracture showed no effect of 20 µg daily oral vitamin D_3 or 1,000 mg calcium, alone or in combination, on occurrence of further fractures (Grant et al 2005).

The WHO also recognised that other nutrients and dietary factors may be important for long-term bone health, including high sodium intake, and, paradoxically, either low or high protein intake in the elderly (WHO 2003), as well as components associated with fruits and vegetables (such as vitamin K, phytoestrogens, potassium, magnesium and boron) and activity.

Calcium is also one of the nutrients (along with fluoride, the amount and frequency of free sugars, phosphorus and casein) thought to influence dental caries. The cariostatic nature of cheese has been demonstrated in several experimental studies and human observational and intervention studies (Kashket & dePaola 2002, Moynihan & Petersen 2004, Rugg-Gunn et al 1984). The cariostatic nature of milk has been demonstrated in animal studies (Bowen et al 1991, Reynolds & Johnson 1981), and Rugg-Gunn et al (1984) found an inverse relationship between the consumption of milk and caries increment in a study of adolescents in England.

Although the roles of calcium and vitamin D in optimising bone health have been known for some time, a wider role for these nutrients in chronic disease prevention has been proposed in recent years. There is evidence from both observational studies and clinical trials that calcium malnutrition and hypovitaminosis D are predisposing conditions for various common chronic diseases.

It has been proposed that deficits in calcium and vitamin D increase the risk of malignancies, particularly of colon, breast and the prostate gland. Early work on colon cancer and calcium was inconsistent and led the WHO (2003) to conclude that there were insufficient data to confirm a link between calcium and colon cancer. However, there have been a number of recent studies and re-analyses that support earlier claims of a link. In assessing the effects of calcium on colorectal cancer, Cho et al (2004) pooled the primary data from 10 cohort studies in five countries. The studies included 534,536 individuals, among whom 4,992 incident cases of colorectal cancer were diagnosed. Compared to the lowest consumption group (500 mg dietary calcium/day or less), the relative risk (RR) for those consuming 600–699 mg/day was 0.83 (not statistically different), for those consuming 700–799 mg/day it

was 0.79 and for those consuming 800–899 mg/day it increased to 0.89, which was also not statistically significant. The RR decreased to 0.79 for those consuming 900–1,099 mg/day and to 0.76 in those consuming 1,100–1,299 mg/day. The authors stated that a further regression analysis showed little additional protection of calcium above about 1,000 mg/day. When subjects were also classified into vitamin D tertiles, there was no significant effect of increasing calcium intake on colon cancer risk in those in the lowest two-thirds for vitamin D intake but there was an effect in those with the highest vitamin D status. This was despite there being no difference seen in colon cancer risk across the vitamin D tertiles themselves. The greatest effects were between those with the lowest compared with the highest combined vitamin D and calcium status.

Shaukat et al (2005) also undertook a systematic review and meta-analysis of RCTs of calcium supplementation in relation to recurrence of colon adenomas, the precursors of colon cancer. The authors statistically combined the data from the three trials that met strict eligibility criteria. The overall RR was 0.80. The results of this meta-analysis support a role for calcium supplements in preventing recurrent adenomas. Other studies or systematic reviews which support a role for calcium in preventing recurrent adenomas or abnormal colonic cell proliferation include Baron et al (1999), Holt et al (1998) and Weingarten et al (2004).

With respect to vitamin D, in addition to the study of Cho et al (2004), a review by Giovannucci (2005) of vitamin D and cancer concluded that there is substantial evidence that a higher 25(OH)D level obtained through increased sunlight exposure, dietary intake or supplement use inhibits colorectal cancer. He concluded for breast cancer that there was some promising data that were, however, too sparse to be definitive and for prostate cancer that whilst experimental evidence for an anti-cancer role of 25(OH)D is strong, epidemiologic data are not supportive. Some studies suggest that higher circulating 1,25(OH)(2)D may be more important than 25(OH)D for protection against aggressive, poorly-differentiated prostate cancer. Giovannucci (2005) suggests that a possible explanation for the disparate findings with prostate cancer is that these cancer cells may lose the ability to hydroxylate 25(OH)D to 1,25(OH)(2)D, and thus may rely on the circulation as the main source of 1,25(OH)(2)D. He further postulates that the suppression of circulating 1,25(OH)(2)D levels by calcium intake could explain why higher calcium and milk intakes appear to increase risk with advanced prostate cancer.

Calcium and vitamin D have also been purported to play a protective role in chronic inflammatory and autoimmune diseases such as insulin-dependent diabetes mellitus, inflammatory bowel disease and multiple sclerosis, as well as metabolic disorders including metabolic syndrome and hypertension (Peterlik & Cross 2005). Deficits in calcium and vitamin D affect a wide range of chronic diseases through attenuation of signal transduction from the ligand-activated vitamin D receptor and calcium-sensing receptor, causing perturbation of cellular functions in bone, kidney, intestine, mammary and prostate glands, endocrine pancreas, vascular endothelium, and, importantly, the immune system (Peterlik & Cross 2005).

Whilst the various studies mentioned suggest a protective effect for calcium and vitamin D for a number of chronic disease outcomes, the precise level of dietary intake that would afford protection is difficult to assess from the available studies, in part because many of the benefits are seen with calcium and vitamin D in combination. In many of these calcium and vitamin D studies, it is low intakes of calcium (well below the adult EARs of 840–1,100 mg or RDIs of 1,000–1,300 mg) that appear to increase RR rather than high intakes of well above the EARs and RDIs being protective. Further discussion on calcium and vitamin D in bone health is given in the relevant chapters.

For other nutrients, such as the antioxidants and dietary fibre, a suggested dietary target has been set at the level of the 90th centile of 'current intake' in Australia and New Zealand. The 90th centile of current daily intake for calcium in adults in Australia is 1,310 mg and for New Zealand, 779 mg. The EARs for adults are already set at 840–1,100 mg/day and the RDIs at 1,000–1,300 mg/day.

The 90th centile of vitamin D intake based on the NNS 1995 in Australia has been estimated at 5.5 µg a day, close to the AI of 5 µg/day for younger adults but below that of 10–15 µg for older adults. Dietary intake compared to the action of sunlight on skin, is also a relatively small contributor to vitamin D status other than for people with very limited access to sunlight. The recent National Surveys

in New Zealand did not assess vitamin D intakes but the data from the earlier National Survey in 1991 showed similar values to Australia (LINZ 1992).

For these reasons, no additional suggested dietary targets are set for calcium and vitamin D.

SODIUM

The evidence of an association between dietary salt intakes and blood pressure has been consistent in various study populations, including different ethnic groups. Relationships have been shown across a wide age range. Salt sensitivity increases with age and increased body weight, possibly linked to metabolic syndrome (Chen et al 1995, Mulrow et al 2002).

Several migration studies of population groups moving from rural areas with low salt intake to areas of high salt intake have reported subsequent increases in blood pressure in that group towards the level in the host population (He et al 1991, Poulter et al 1990). However such data are susceptible to confounding. The large International Study of Salt & Blood Pressure (Intersalt Co-operative Research Group, 1988) collected data on 24-hour urinary sodium excretion and blood pressure from more than 10,000 adults in 52 groups from 32 countries. Significant positive associations were found between sodium excretion and both systolic and diastolic blood pressures. However, when four centres that had very low salt intakes were removed from the analysis, the overall association was not statistically significant, although an association was found between salt intake and increase in blood pressure with age.

Elliot et al (1993, 1996) re-analysed the Intersalt data, adjusting for regression dilution caused by measurement errors, and found stronger associations but it has been suggested that the correction factors used may have been overestimated (Day 1997, Davey Smith & Phillips 1997).

A number of intervention studies have also been undertaken. One of the best of these in terms of design, length of intervention and subject numbers is the Dietary Approaches to Stop Hypertension (DASH) trial (Appel et al 1997). The DASH trial assessed the effects of dietary patterns on blood pressure in a group of about 460 normotensive and hypertensive adults. Subjects received a control diet low in fruit, vegetables and dairy products, with a fat content typical of the average US diet, for three weeks and were then randomised to receive one of three diets for eight weeks: the control diet, a diet rich in fruit and vegetables or a combination diet (the DASH diet) rich in fruit, vegetables and low-fat dairy products, and low in saturated and total fat. The salt content of each diet was similar and body weight, physical activity and alcohol were held constant throughout.

The trial showed that compared to a typical US diet, a diet rich in fruits, vegetables, and low-fat dairy products reduced mean blood pressure by 5.5/3.0 mmHg. The diet rich in fruit and vegetables produced a reduction of 2.8 mmHg in systolic blood pressure but not in diastolic blood pressure. In hypertensives, the DASH diet reduced blood pressure by 11.4/5.5 mmHg and in non-hypertensives, by 3.5/2.1 mmHg.

A follow-up DASH Sodium trial (Sacks et al 2001a) assessed the combined effect of the DASH diet and reduced salt intake. About 400 adults were randomly assigned to the control or DASH diet for three months. Each subject consumed their diet for 30 consecutive days at each of three levels of salt: high (3.6 g or 150 mmol sodium), intermediate (2.4 g or 100 mmol sodium) and low (1.2 g or 50 mmol sodium). The potassium intakes were greater on the DASH diet than in the controls, but were kept the same for all levels of salt intake at approximately 1.6 g potassium in the control diet and 3g in the DASH diet. Weight was stable throughout the study in all groups. Lowering salt intake reduced blood pressure by 6.7/3.5 mmHg on the control diet and by 3.0/1.6 mmHg on the DASH diet. The combined effects on blood pressure of the DASH diet and low salt intake were greater than either of the interventions alone and were 8.9/4.5 mmHg below the control diet at the high salt level. With this combination, mean systolic blood pressure was 11.5 mmHg lower in participants with hypertension, and 7.1 mmHg lower in participants without hypertension. The effects were observed in those with and without hypertension, in both sexes and across racial groups.

Concern has been expressed that the low sodium arm of the DASH trial was associated with an increase in the plasma levels of renin (Alderman 2001). In addition, McCarron (2001) claimed that it was the mineral intake from the DASH diet that was far more important than salt in determining blood pressure and that meaningful effects were only seen in hypertensive black females in the study. The authors argued, however, that diuretic therapy, which prevents CVD, also raises plasma renin and whilst accepting that susceptibility to salt may vary in the population, the effects were qualitatively similar among all subgroups (Sacks et al 2001b).

Another intervention trial, the Trials of Hypertension Prevention (TOHP) Phase II (TOHP Collaborative Research Group 1997) was a longitudinal study that assessed the effects of reduced salt intake and weight loss, either alone or in combination, on blood pressure. Participants in the study were moderately overweight with high normal blood pressures. At 6 months, sodium excretion was reduced by 1.8 g or 78 mmol in the salt reduction group and by 1.5 g or 64 mmol in the combined intervention group, achieving salt intake levels of 2.4 g/104 mmol sodium and 2.9 g/124 mmol sodium, respectively. Systolic and diastolic blood pressures were significantly lowered compared to controls by 2.9/1.6 mmHg in the salt reduction group, by 3.7/2.7 mmHg in the weight loss group and by 4.0/2.8 mmHg in the combined intervention group. However, effects were less at 36 months, with significant reduction in diastolic blood pressure only in the weight loss group. Systolic blood pressure reductions were small but significant for the salt reduction and the weight loss groups. Sodium excretion increased significantly over time and at 36 months there were only small but significant differences from the usual care group of 0.9 g or 40 mmol sodium/day for the salt reduction group and 0.6 g or 24 mmol sodium/day for the combined group. This reflected a decline in adherence to the protocol that also affected the blood pressure results, highlighting the difficulties of long-term compliance in a high salt environment.

The Trial of Nonpharmacologic Interventions in the Elderly (TONE) assessed the effects of salt reduction (target of 4.8 g salt/1.8 g or 80 mmol sodium) and weight loss, alone and combined, in older hypertensives whose blood pressures were controlled with one antihypertensive drug (Whelton et al 1998). Where both interventions were successful, more people were able to stop, and remain off, medication.

Several meta-analyses have been conducted pooling the results of randomised controlled intervention trials assessing the effect of salt reduction on hypertension (Alam & Johnson 1999, Cutler et al 1997, Ebrahim & Davey Smith 1998, Graudal et al 1998, Midgley et al 1996). Three concluded that decreases in blood pressure in response to sodium reduction are not sufficient to justify population-wide advice to lower salt intakes (Ebrahim & Davey Smith, 1998, Graudal et al 1998, Midgley et al 1996). However, these meta-analyses included short-term trials and trials assessing the effects of acute salt loading followed by severe depletion.

A meta-analysis by MacGregor and He (2002) that included only studies with modest salt reductions and a duration of at least four weeks (17 trials in hypertensives and 11 trials in normotensives) found significant reductions in blood pressure of 4.96/2.73 mmHg in hypertensives and 2.03/0.97 mmHg in normotensives and concluded that, on a population-wide basis, a modest reduction in salt intake for a period of four or more weeks has a significant effect on blood pressure in hypertensive and normotensive individuals.

A systematic review by Hooper et al (2002) that assessed the long-term effects of advice to reduce dietary salt in adults with and without hypertension (11 trials with follow-up from 6 months to 7 years) showed that at 6–12 months there were significant reductions of 2.5/1.2 mmHg in systolic and diastolic blood pressures but at 13–60 months, a significant reduction only remained for systolic blood pressure. Twenty-four-hour sodium excretion was reduced by 1.1 g or 48 mmol sodium/day at 6–12 months and by 0.8 g or 35.5 mmol sodium/day at 13–60 months.

On the basis of this evidence, a review in 2003 by the Scientific Advisory Committee on Nutrition in the UK concluded that a reduction in the dietary salt intake of the population would lower the blood pressure risk for the whole population and that a population-based approach is required to achieve a sustained reduction in salt intake.

This same review concluded that although clear effects of salt on blood pressure have been observed, the long-term effects on health and premature mortality outcomes are less certain. This may relate in part to the multiplicity of factors apart from sodium intake that can affect both blood pressure and its sequelae, such as stroke and CVD.

The development of hypertension has been shown to be related to a number of other dietary factors, notably lower intakes of potassium but also lower intakes of calcium, magnesium and possibly other micronutrients, as well as lower fruit and vegetable consumption (Appel et al 1997, John et al 2002, Margetts et al 1986) and higher alcohol consumption (Marmot et al 1994, Xin et al 2001). Other key factors include overweight and metabolic syndrome (Chen et al 1995, Mulrow et al 2002), lack of physical activity (Lesniak & Dubbert 2001, Whelton et al 2002) and genetic predisposition (Corvol et al 1999, Hunt et al 1998, Svetkey et al 2001).

POTASSIUM

Potassium can blunt the effect of sodium chloride on blood pressure, mitigating salt sensitivity and lowering urinary calcium excretion (Whelton et al 1997). Morris et al (1999) studied the effect of potassium on salt sensitivity and showed that sensitivity was blunted at 4.7 g/day in African American men and 2.7 g/day in white males. Given this interrelatedness, requirement for potassium depends to some extent on dietary sodium, however, the ideal sodium to potassium intake ratio is not yet clear.

Higher potassium intakes have also been related to decreasing risk of kidney stones in studies in western populations in the US and Finland. Curhan et al (1993, 1997) in the US showed the lowest rate of kidney stones in the highest quintile of intakes of potassium in their studies of both men and women (4.0 and 4.7 g/day, respectively) and Hirvonen et al (1999) in Finland showed that stones were reduced at the second quartile of intake (4.6 g/day) and that there were no further reductions at higher quartiles for men and women.

DIETARY FIBRE

Increasing dietary fibre intakes have been linked to lower rates of obesity, cardiovascular disease, diabetes and certain cancers.

Initially, dietary fibre was widely thought of as an inert bulking agent that lacked energy value and thus should have the potential to help in weight control. Methylcellulose, cellulose and other such unabsorbable materials have often been used as satiety agents for those attempting to restrict food intake. Guar supplements and other high fibre, high carbohydrate diets have been used with modest success by diabetic patients attempting to lose weight. It is thought that the small effects seen in these experimental situations might again relate to a satiating effect due to prolongation of absorption and a smoothing of blood glucose response after meals (Holt et al 1992, Jenkins 1988).

However, studies of weight loss using fibre supplements of various kinds have shown that weight loss is rarely sustained. Heaton et al (1976) could show no weight benefit in replacing white with wholemeal bread in a controlled trial and although increased faecal fat loss on high fibre diets was demonstrated by Jenkins (1988), the loss averaged only 7 g/day. However, the British Nutrition Foundation did conclude, in a 1990 report, that foods rich in non-starch polysaccharide (NSP) are useful in weight reduction, probably through the satiation effect and the fact that diets high in naturally occurring fibres are generally lower in fat (and thus energy) and may take longer to chew, thereby influencing meal size.

Dietary fibre intakes have also been linked to reduced risk of CHD, mainly through an effect on plasma cholesterol. The observation by Hardinge & Stare (1954) that complete vegetarians have lower serum cholesterol concentrations than non-vegetarians has been repeated in many subsequent studies. Furthermore, vegetarians typically have higher ratios of high density lipoprotein (HDL) cholesterol to total cholesterol than either lacto-ovo-vegetarians or nonvegetarians. Although these observations arise in part as a consequence of the reduced dietary intakes of saturated fats among vegetarians, subsequent

human trials have demonstrated lowered serum cholesterol concentrations in response to some, but not all, fibres or fibre-rich foods. It would appear that wheat bran, wheat wholemeal products and cellulose have no effect on serum cholesterol (Truswell & Beynen 1991, Truswell 2002). Pectin in large doses can affect a 10% reduction, oat bran and oat wholemeal products are capable of reductions of up to 23% (average 6%) and psyllium, 4% for total cholesterol and 7% for LDL cholesterol (Olson et al 1997). Most studies have found guar gum capable of reducing total serum cholesterol, but further studies to confirm the cholesterol-lowering effects reported for gum arabic, xantham gum, gum acacia, karaya gum and locust bean gum are needed (Truswell 1993).

A 1% reduction in serum cholesterol is generally considered to translate to a 2% reduction in CHD, suggesting substantial benefits from increased dietary fibre of the types described. Three major population studies have assessed the effects of dietary fibre on CHD risk. In the Health Professionals Follow-up study of men (Rimm et al 1996) there was a difference in fibre intake of 16.5 g/day between the highest (28.9 g/day) and lowest (12.4 g/day) intake groups and a RR for fatal heart disease of 0.45 and for total myocardial infarction of 0.59. The Nurses' Health Study (Wolk et al 1999) showed that the difference between the highest (22.9 g/day) and lowest (11.5 g/day) consumption groups of 11.4 g fibre/day equated to a RR of 0.77 for total CHD. In the Finnish men's study (Pietinen et al 1996), the highest consumption group (34.8 g/day) had an RR of 0.68 compared to the lowest consumers (16.1 g/day).

In relation to colon cancer, despite the wealth of experimental data in cell lines or animals models that provides convincing mechanisms and indicative protective effects of dietary fibre on colon cancer and one large human trial showing benefits (Bingham et al 2003), several other human studies have shown little benefit of higher fibre intakes on colon cancer or markers of the risk of colon cancer (Alberts 2002, MacLennan et al 1995, Schatzkin et al 2000). Fruits, vegetables and cereal grains are all good sources of dietary fibre. Nearly all studies of diet and colon cancer in humans have found decreased risks associated with high intakes of fruit and vegetables. However, whilst a number of studies have also reported reduced risks in association with high cereal grain intakes, a few studies have found an increased risk, which casts an element of doubt over the conclusion that the fibre component was responsible for the apparently protective effect almost universally found for fruit and vegetables (Byers 1995). It is possible that some of the confusion relates to the fact that RS was not accounted for in many early studies. International comparative studies show greater correlations between colon cancer and starch (and thus RS) intake across countries than with dietary fibre (Cassidy et al 1994).

Increased dietary fibre intakes have also been related to prevention of hormone-related cancers such as breast cancer. Pike et al (1993) argue strongly that international comparisons of breast cancer incidence are highly consistent with observed differences in circulating oestrogen levels. However, results from epidemiologic studies comparing the circulating levels of steroid hormones in newly diagnosed cases or high-risk groups with low-risk groups; or disease-free controls with hormone-related cancers, have been inconsistent. Breast cancer is the disease whose nutritional epidemiology has been studied most. Several case-control studies have reported decreased risks associated with fibre-rich diets (Baghurst & Rohan 1994, Lee et al 1991, Lubin et al 1986, van't Veer et al 1990). A Canadian cohort study observed a 32% reduction in breast cancer risk in the top quintile of fibre consumers relative to the bottom quintile (Rohan et al 1993), but two cohort studies in the US failed to observe the inverse relationship (Kushi et al 1992, Willett et al 1992). Dietary fibre is thought to exert its apparently protective effect through a reduction in circulating levels of oestrogen (Rose 1990). The exact mechanism by which this occurs remains uncertain. The WHO in its report on diet and chronic disease (WHO 2003) concluded that an effect of fibre on cancer risk was possible but data were insufficient.

Ecologic studies typically find an inverse association between fibre content of the diet and regional prevalence of diabetes (West 1974, West & Kalbfleisch 1971). However in a survey of two populations in Micronesia, one at high risk and one at low risk of developing Type 2 diabetes, estimates of dietary fibre intake were of no predictive value regarding the risk of subsequent diabetes (King et al 1984). The similarity of these populations with respect to many other factors raises the possibility that the association observed in ecologic studies may have arisen as a consequence of differences other than intakes of dietary fibre between the study populations.

Contemporary research on dietary fibre and diabetes is mostly focussed on the potential benefits of dietary fibre in the management (through glycaemic control) of both Type 1 and Type 2 diabetes. Diabetics exhibit substantially higher risks for CVD than their non-diabetic counterparts, and hyperinsulinaemia, insulin resistance and over-treatment of the diabetic with insulin have all been claimed to contribute to the development of a premature atherosclerosis (Venn & Mann 2004, Vinik & Wing 1992). Management procedures that reduce insulin requirements are therefore highly desirable.

High fibre foods typically slow absorption through an effect on gastric emptying and/or entrapment of material in the viscous digesta that result from high fibre intakes. An author of an early report which claimed that increased fibre intakes may be beneficial for diabetics (Jenkins et al 1976) concluded nearly twenty years later "*that the value of high fiber foods lies principally in their ability to prolong absorption in the small intestine*" and that... "*the effects on carbohydrate and lipid metabolism can be mimicked by reducing meal size and increasing meal frequency over an extended period of time*" (Jenkins et al 1995).

The intakes of dietary fibre that appear to bring meaningful chronic disease health benefits appear achievable through dietary change. The upper intakes from the three CHD risk studies (Pietinen et al 1996, Rimm et al 1996, Wolk et al 1999) that brought major improvements in cardiovascular risk were 29 g and 35 g/day for men and 23 g/day for women. Twenty-nine g/day is just under the current 70th centile of intake for males in Australia and New Zealand and 35 g equates to the 80th centile. For women, 23 g/day is just under the current 70th centile. Thus for people concerned with chronic disease risk, aiming to increase intakes towards the median intake of the highest current quintile of population intake (ie the 90th centile of 38 g/day for men and 28 g/day for women), would appear to be a prudent strategy to reduce chronic disease risk in a manner unlikely to lead to any adverse effects. Increasing intake through additional vegetables, legumes and fruits in the diet would also increase the intake of antioxidant vitamins and folate.

MACRONUTRIENT BALANCE

Unlike the micronutrients, the macronutrients (proteins, fats and carbohydrates) all contribute to dietary energy intake. Alcohol can also contribute to dietary energy. The effect of alcohol on health outcomes has been reviewed elsewhere and will not be revisited here except to say that alcohol intakes below about 5% of dietary energy are recommended (NHMRC 1999, 2003). For a given energy intake, increases in the proportion of one macronutrient necessarily involves a decrease in the proportion of one, or more, of the other macronutrients. Thus, for example, a high fat diet is usually relatively low in carbohydrate and vice versa and a high protein diet is relatively low in carbohydrate and/or fat.

There is a growing body of evidence that a major imbalance in the relative proportions of macronutrients can increase risk of chronic disease and may adversely affect micronutrient intake. However, the form of fat (eg saturated, polyunsaturated or monounsaturated or specific fatty acids) or carbohydrate (eg starches or sugars; high or low glycaemic) is also a major consideration in determining the optimal balance in terms of chronic disease risk. This has not always been given enough consideration in study design or interpretation.

There appears to be quite a wide range of relative intakes of proteins, carbohydrates and fats that are acceptable in terms of chronic disease risk. The risk of chronic disease (as well as the risk of inadequate micronutrient intake) may increase outside these ranges, but often data in free-living populations are limited at these extremes of intake. The Food and Nutrition Board of the Institute of Medicine in constructing the US:Canadian Dietary Reference Intakes (FNB:IOM 2002) called this range the Acceptable Macronutrient Distribution Range (AMDR). In their document, they extensively reviewed the current evidence, in terms of outcomes such as body weight maintenance, obesity, CHD and LDL oxidation, stroke, Type 2 diabetes, hyperinsulinaemia and glucose tolerance, metabolic syndrome, cancer, osteoporosis, renal failure, renal stones, inflammatory disorders and risk of nutrient inadequacy in adults, as well as some of these outcomes, plus birth weight and growth in relation to children. Much of the evidence is based on epidemiological studies with clinical endpoints but these studies generally show associations rather than causality and are often confounded by other factors that can affect chronic disease outcomes.

Randomised controlled trials, which provide the most conclusive evidence of causality, are often lacking in relation to optimising macronutrient profile. Studies of individual macronutrients are particularly prone to confounding by the other necessary changes to the diet (ie either the energy content changes in the control group and/or the proportion of other macronutrients). For example, in assessing the effects of a high carbohydrate diet on a specific endpoint, the test diet must be relatively low in fat and/or protein and/or vary in its energy content. If a benefit or adverse effect is seen, it is not immediately clear what is responsible for the observed outcome.

Given these limitations, an expert review of the evidence base described in the US:Canadian DRI review, together with consideration of papers published since the review, and dietary modelling to assess the effects of changes in macronutrients on micronutrients, was used to develop AMDRs for use with adults in Australia and New Zealand. It is important to remember that these recommendations are recommendations for otherwise healthy people and it is assumed that usual dietary intake will be at a level to maintain current body weight (ie these are not necessarily recommendations for optimal weight loss diets or for treatment or management of existing chronic disease conditions).

Dietary modelling involved two approaches. Firstly, an assessment was undertaken of 2-day adjusted, daily diets reported in the 1995 National Nutrition Survey for Australia (ABS 1998) in relation to macronutrient profile, energy intake and EARs (or a proportion of the AIs) for all nutrients except sodium, fluoride, biotin, selenium, choline, chromium, iodine and molybdenum, for which reliable analytical food data were not available. For modelling purposes, vitamin D was also excluded as much of this can be accessed through the action of sunlight on skin. For those nutrients where an AI was set, a value of 83% AI was used in modelling as this gave a rough equivalence to the relativity between the EAR and RDI (ie it is 2CV below the AI assuming a CV of 10% for the EAR, as used to derive RDIs where the variability in requirements is unknown). It is recognised that the National Nutrition Survey data were based on 24-hour recall and as such do not assess usual dietary intake in individuals.

In this instance, however, the data were being used only as examples of one-day intakes actually consumed by individuals in the community, albeit they may not be typical of the individual's usual intake (ie examples of real as opposed to simulated or designed daily intakes).

The second approach used linear programming to assess whether it was possible to design diets that conformed to the EARs and AIs as outlined above, for varying macronutrient and total energy intake profiles.

Where an RDI or AI had been set for one of the macronutrients (eg for protein or selected fatty acids), this has generally been used as the bottom end of the AMDR for that nutrient, unless dietary modelling showed this to be problematic.

PROTEIN

Low intakes of protein have been investigated in relation to impaired immune function and growth, as well as to low birth weight. Although protein malnutrition is uncommon in Australia and New Zealand, world wide, in conjunction with energy deficiency, it is responsible for more than half the deaths of young children (Pelletier et al 1995). In individuals with protein-energy malnutrition (PEM) immune responses are impaired (Keusch 1990), low intakes in pregnancy are correlated with a higher incidence of low birth weight (King 2000) and low intakes in early childhood result in stunting and wasting (Waterlow 1976).

In the US:Canadian Dietary Reference Intake review, the lower level of the AMDR was set at the level of the RDI (or Recommended Dietary Allowance in the US and Canada). This equates to about 10–11% of energy from protein. However, dietary modelling using linear modelling with commonly consumed foods, has shown that it is not possible to design diets based on commonly eaten foods at 10% energy from protein that reach the EARs for the micronutrients at energy intakes below about 15,000 kJ/day. Assessment of the one-day diets from the 1995 National Nutrition Survey of Australia (ABS 1998) confirmed this finding. Of the 10,852 adults in this survey, only six subjects with diets in the range of 10–11% energy on the day of the survey, conformed to their age/gender EARs. All were men and all had energy intakes in excess of 15,000 kJ/day. All but two had saturated fat intakes at 13% or above, the other two having added sugar intakes of 26 and 43% energy, which effectively diluted the per cent energy from protein. Both the analysis of the National Nutrition Survey and the linear modelling of diets indicated that protein intakes in the range of at least 15% energy from protein were required for most people to attain the EARs for micronutrients, especially at energy intakes below 15,000 kJ/day.

High protein intakes have been assessed in relation to a number of chronic diseases including cancer, renal disease, obesity, coronary artery disease and osteoporosis, however, the evidence is not convincing. In relation to cancer, no clear role for protein has emerged. For breast cancer, some studies have shown an effect (Hislop et al 1986, Lubin et al 1981, 1986, Toniolo et al 1994) while others have either shown none (Miller et al 1978, Phillips 1975) or a slight inverse effect (Decarli et al 1997). For other cancers such as lung (Lei et al 1996), oral and pharynx (Franceschi et al 1999), oesophageal (Gao et al 1994), and non-Hodgkin lymphoma (Chiu et al 1996, Ward et al 1994), no relationship was found. Indeed, Barbone et al (1993), Franceschi et al (1999) and Gao et al (1994) showed an inverse effect. High protein intake has, however, been shown to relate to upper digestive tract cancer (de Stephani et al 1999) and kidney cancer (Chow et al 1994).

Despite a clearly documented effect of protein on urinary calcium loss under controlled conditions, the evidence is inconsistent that within populations, individuals consuming self-selected diets with higher protein content have lower bone mass and/or increased fracture risk. This is hardly surprising since protein intake is only one of many factors, both dietary and non-dietary, that influence bone metabolism. Moreover, the assessment of many of these factors, including long term-dietary intake, in free-living individuals is not only difficult but also imprecise. Studies that address the influence of protein on bone status are included in the Appendix section. The general conclusion to be reached from

these studies is that both low and high protein intakes may be detrimental to bone health and that diets containing moderate levels of protein (1.0–1.5 g/kg) are probably optimal for bone health (Kerstetter et al 2003).

Heaney (1998) suggested that one reason why protein intake does not always adversely affect bone is because in self-selected diets, increased protein intake is often associated with increased calcium intake. In consequence, it is likely to be more informative to evaluate diets not on their protein content alone but on their calcium to protein ratio. On the basis of the 1997 US calcium recommendations for middle-aged women, Heaney proposed a ratio of calcium to protein (mg to g) of 20 to 1. In a review of data on protein intake and BMD and/or fracture risk in elderly women (Bell & Whiting 2002), however, mean calcium to protein ratios of 15–17:1 (mg:g) were associated with both increased and decreased fracture risk. A measure of net acid excretion, such as the dietary protein to potassium ratio (Frassetto et al 1998), is likely to be a better predictor of urinary acid excretion than protein intake per se. Whiting et al (2002) have also observed that not only protein, but also potassium and phosphorus were significant predictors of BMD in men with adequate calcium intakes. In 1995, except for children aged 2–8 years, 10% or less of the Australian population consumed diets with calcium to protein ratios of >15.0 and it is likely that the same is true for the population of New Zealand.

High protein intakes have also been investigated in relation to adverse renal outcomes. Elite Australian male athletes are known to have a daily protein intake over 1.5 g/kg (Burke et al 1991). In healthy male athletes who consumed long term daily protein intakes of up to 2.8 g protein/kg body weight, no negative effects on renal function were found, as indicated by glomerular filtration rate and by albumin and calcium excretion rates (Poortmans & Dellalieux 2000). In this Belgian study, the two groups of athletes investigated were body-builders and other well trained athletes with high and medium protein intake, respectively. The athletes underwent a 7-day nutrition record analysis as well as blood sample and urine collection to determine the potential renal consequences of a high protein diet. The body builders, who included protein supplements in their diet, on average consumed 16,335 ± 1,153 kJ/day and 169 ± 13 g of protein/day or 1.92 ± 0.13 g protein/kg/day. This group of trained athletes who consumed a high protein diet showed no evidence of short term renal stress. There is no published evidence that a diet containing up to 2.8 g protein/kg/day produces adverse effects on kidney metabolism in athletes. In addition, no known association of protein intake with progressive renal insufficiency has been determined (Brandle et al 1996).

Although in animal models, high protein diets have been shown to cause hyperlipidaemia and arteriosclerosis, there is no evidence of this in man. Indeed in the Nurses' cohort study, protein intake was found to be inversely related to risk of CVD. The range of actual protein intake was, however, limited (Hu et al 1999) and a moderate relative intake (in terms of per cent energy) appeared to be almost as beneficial as a high intake (above 25% energy) when compared to intakes below 15% of energy. A number of studies have shown protein to be more satiating than fat or carbohydrate, but some have shown a positive correlation between protein intake and body fatness, body mass index or skinfold thickness (Buemann et al 1995; Rolland-Cachera et al 1995). On the other hand, a 6 month randomised trial demonstrated that replacing carbohydrate with protein improved weight loss as part of a fat-reduced diet (Skov et al 1999).

In the US:Canadian DRI review, in the light of the lack of consistent data on the effect of protein on chronic disease, the upper level of the AMDR for protein was simply set "to complement the AMDR for fat and carbohydrate", giving an upper limit of 35% energy from protein. However, there is very limited information about the longer-term effects of diets in which protein provides >25% energy. Average usual intakes within the range 25-35% energy from protein are not reported in western populations, even in athletes. Reports of diets in which the per cent energy from protein is within this range tend to come from populations in Arctic regions, from pastoralists and hunter-gatherer groups, most frequently in circumstances under which energy intake is restricted (Speth 1989), rather than at times of ad libitum food intake.

In the laboratory study by McClellan et al (1930a,b) in which two men lived on a meat diet for a year without apparent ill effects (although calcium balance was negative), the per cent energy from protein ranged between 15 and 24%, except during a brief period when one of the men was asked to consume only lean meat (44% energy from protein). Within two days, this diet led to gastrointestinal disturbances, which resolved on resumption of the former diet. Similar symptoms are characteristic of the initial stages of 'rabbit poisoning' and were also seen briefly in two out of six subjects in whom nitrogen intake from a liquid formula diet was increased from 12 g to 36 g/day while energy intake remained constant but per cent energy from protein increased from about 10 to 30% (Oddoye & Margen 1979). Whether these symptoms would persist over the longer term is not known.

An analysis of the National Nutrition Survey of Australia showed that on the day of the survey, only 1.4% of subjects (n=152) had intakes at, or greater than, 30% protein and only 4.4% (n=480) were above 25% protein. Of those above 30% protein, none conformed to the EARs. Of those with protein intakes between 25 and 30% of energy, there were nine males who conformed to the EARs, with energy intakes ranging from 9,000-24,000 kJ/day (median 17,000 kJ/day) but all except one (at 15,000 kJ energy intake) also had saturated fat intakes well above 10% energy.

Linear modelling showed that it is possible to design diets of varying energy levels that conform to the EARs at protein intakes of 25–30% energy. However, given the lack of data about long term health effects of higher protein diets in largely sedentary western societies such as Australia and New Zealand, it would seem prudent to suggest an upper limit of 25% energy from protein for the general population, whilst recognising that for some highly active communities or certain individuals, higher intakes may be consistent with good health.

In conclusion, whilst diets as low as 10% of energy from protein will provide the protein required for maintenance and replacement of body tissues and for the necessary functional and structural proteins required by the body, intakes at or above 15% protein appear to be required for ensuring that the EARs for micronutrients are met, particularly for people with energy requirements below about 15,000 kJ/day. It should be remembered, however, that the EARs are average requirements that, by definition, will be more than is physiologically required by half the individuals in the population. Similarly, whilst some highly active, apparently healthy, populations living in Arctic regions or living as pastoralists or hunter-gatherers appear to have diets in the region of 30% protein or more, this population level of intake is not seen in any western, largely sedentary, societies such as Australia and New Zealand, so that potential long-term adverse effects in this lifestyle environment, are unknown. A Working Party convened by the FAO in 1997 recommended that protein intakes be limited to no more than 2 g/kg/day for the general population (Durnin et al 1999). This would equate to about 150 g/day of protein for the standard man and about 120 g/day for the standard woman or about 22–25% as energy using median population energy intakes. Until more is known about the long term effects of high protein diets in the context of the dominant lifestyles of western societies, a prudent upper level may therefore be 25% energy from protein, which is also equivalent to the current 95th centile of intake in Australia and New Zealand.

FATS

The recommendations for total fat and total carbohydrates in relation to their contribution to total dietary energy are intimately related, as it is generally the balance of fat and carbohydrates in diets that has been studied in relation to chronic disease outcomes.

The FNB:IOM (2002) review concluded that the optimal range for total fat was from 20–35% energy. At this level, the risk for obesity, CHD and diabetes could be minimised whilst allowing for sufficient intake of essential nutrients and keeping saturated fats at moderate levels. In making their assessment, the FNB:IOM (2002) looked not only at total amounts of fats but also at the various types of fats.

In assessing the role of total fat in relation to maintenance of body weight, Sonko et al (1994) concluded that 15% fat was too low to maintain body weight in women and Jequier (1999) showed that 18% fat is adequate, even with high physical activity. Some, apparently healthy Asian communities have been

reported to consume diets as low as 10% fat (Weisburger, 1988) but they also have short stature which may result from this low level of fat intake. For diets that are very low in total fat, the intake of essential fatty acids and fat-soluble vitamins (vitamins A, D, E and K) may also be compromised. Because of the types of foods that are often limited in very low fat diets (eg certain meats and dairy products), intakes of micronutrients such as zinc and iron as well as riboflavin, calcium and vitamin B_{12} may also be affected.

In the Australian National Nutrition Survey, only 7% of subjects had intakes on the day of the survey below 20% of energy from total fat, with only 2% being below 15% energy from fat. There were three men and one woman who had fat intakes from 19–21% who conformed to all of the EARs assessed. Three had energy intakes in the order of 8,000–9,000 kJ and one had an intake just above 15,000 kJ. In these subjects, protein intakes ranged from 17–22% of energy. Their saturated fat and added sugar intakes were also less than 10% energy. Dietary modelling also showed it was possible to design diets at 20% energy from total fat that would meet all other nutritional requirements. Below this level of energy from total fat it was more difficult to do so unless total energy intake was high. Considering all the above, a lower intake limit of 20% energy as fat seems prudent.

Epidemiological studies give mixed results in relation to whether high fat diets predispose to overweight or obesity and promote weight gain. However, intervention studies have shown that when fat intakes are relatively high, many individuals consume additional energy and gain weight, although this is often as much associated with changes in energy density in the diets as with fat per se (Glueck et al 1982, Lawton et al 1993, Lissner et al 1987, Poppit & Swann 1998, Poppitt et al 1998, Prosperi et al 1997, Stubbs et al 1995b, Thomas et al 1992, Tremblay et al 1989, 1991). Inappropriate weight gain can worsen the metabolic consequences of obesity, particularly the risk of CHD. High fat diets are often, although not always (eg Mediterranean diet), accompanied by high saturated fat intake and through this mechanism, can raise plasma LDL and further increase CHD risk. A meta-analysis of intervention studies by Yu-Poth et al (1999) showed that reduction in plasma cholesterol and LDL cholesterol was significantly correlated with reductions in per cent total fat, but that these also included a decrease in per cent saturated fat. Some case-control studies have shown an association between total fat and CHD risk, but it is difficult to disentangle the effects of the saturated fat. Consumption of diets high in fat (42 or 50%) has also been shown to increase blood concentration of the prothrombin markers, blood coagulation factor VII and activated factor VII (Bladbjerg et al 1994, Larsen et al 1997) which are related to increased risk of CHD.

Dietary modelling with commonly consumed foods shows that if all fat consumed is low in saturated fat (ie 20% of fat energy), a 35% fat diet would provide about 7% of total energy as saturated fat. Consuming a variety of fats will increase this level of saturated fatty acids. Thus if total fat exceeds about 35% of energy, for most people, it will be difficult to avoid high intakes of saturated fat.

Several studies have reported associations between higher fat intakes and increased insulin resistance as indicated by high fasting insulin concentrations, impaired glucose tolerance or impaired insulin sensitivity (Lovejoy & DiGirolamo 1992, Marshall et al 1991, Mayer et al 1993) as well as the development of Type 2 diabetes (West & Kalbfleisch 1971). However, other studies have not shown these associations (Coulston et al 1983, Liu et al 1983, Salmeron et al 2001). It is possible that the association seen in some studies was confounded by factors such as obesity and glycaemic index.

Epidemiological studies show inconsistent links between per cent energy from fat and cancer risk. One meta-analysis of 23 studies of breast cancer and fat gave RR values of 1.01 and 1.21 from cohort and case-control studies, respectively, for people with higher fat intakes. Howe et al (1997) could show no association between fat intake and colorectal cancer from a combined analysis of 13 case-control studies, and Smith-Warner et al (2002) could show no associations between intakes of total or specific types of fat and lung cancer risk among never, past, or current smokers. However, a meta-analysis by Huncharek & Kopelnick (2001) showed that high total fat intake was associated with a 24% increased risk of development of ovarian cancer across eight observational studies. With these conflicting results, it is difficult to use cancer outcome as a determinant for the UL.

Thus, in relation to its potential influence on body weight and its cardiovascular complications, and in agreement with the US:Canadian DRI review, a UL of 35% energy as fat, is recommended for the general population. This is approximately equivalent to the 60th centile of intakes reported in the latest Australian and New Zealand National Surveys for adults (ie at least 60% of subjects currently have intakes at or below 35% fat as energy).

In the Australian National Nutrition Survey, there were 40 people on the day of the survey who had fat intakes in the range of 34–36% energy who conformed to all of the EARs assessed. About 80% of these subjects were men with energy intakes ranging from 9,000–46,000 kJ/day on the day of survey. Only 8 subjects had energy intakes of less than 13,000 kJ/day and 12 had intakes over 19,000 kJ/day. Most of these subjects had saturated fats above 10% energy and protein intakes between 13% and 22% of energy. Added sugars were generally low. Dietary modelling showed it was possible to design diets that conformed to all the EARs within this range of per cent energy as fat but which also had acceptable levels of saturated fats. It is possible that a UL of 30% fat might bring additional benefits to some people, but the data delineating the benefits of 30% compared to 35% energy as fat are limited.

SATURATED AND *TRANS* FATTY ACIDS

Whilst the main focus of this section relates to the relative contribution of total fat to energy intake, it is widely acknowledged that the type of fat consumed is equally important in certain chronic disease conditions, notably heart disease.

There have been hundreds of studies of saturated fat intake in relation to serum cholesterol levels including both total cholesterol and LDL cholesterol. Regression analyses have shown that for each 1% increase in energy from saturated fats, serum LDL cholesterol will increase between 0.33 mmol/L and 0.045 mmol/L (Clarke et al 1997, Hegsted et al 1993, Mensink & Katan 1992). There is, in turn, a positive linear relationship between serum total and LDL cholesterol concentration and risk of CHD (Jousilahti et al 1998, Neaton & Wentworth 1992, Sorkin et al 1992, Stamler et al 1986, Weijenberger et al 1996). It has been estimated that a 10% reduction in serum cholesterol concentrations would reduce CHD mortality by 20% (Jousilahti et al 1998), although the studies on which these estimates were based were undertaken using pharmaceutical, not dietary, interventions. Whether dietary intervention would bring about equivalent lowering of CHD mortality is unknown.

Trans fatty acids (TFAs) are unsaturated fatty acids that have at least one double bond in the *trans* configuration. A *trans* double bond occurs between two carbon atoms that have changed geometry relative to the *cis* double bonds found most commonly in nature. The presence of a *trans*, relative to a *cis*, double bond results in acyl chains that can pack together more tightly, producing a fat with a higher melting point. TFAs are produced by partial hydrogenation of unsaturated oils during the manufacture of margarine and shortening but also occur naturally, in small amounts, in some ruminant animal foods. They have been shown to elevate LDL cholesterol and lower the beneficial HDL cholesterol (Aro et al 1997, Ascherio et al 1999, Judd et al 1994, 1998, Louheranta et al 1999, Muller et al 1998, Nestel et al 1992, Noakes & Clifton 1998, Seppanen-Laakso et al 1993, Sundram et al 1997). In a 20-year follow up of a large cohort of women *trans* fat intake was associated with an elevated risk of CHD (RR = 1.33, 95% CI: 1.07, 1.66; p(trend) = 0.01). The associations between intakes of *trans*-fat with CHD risk were most evident among women younger than age 65 years (Oh et al 2005).

There is good evidence that on a weight for weight basis, TFAs have a more adverse effect on CVD risk compared to saturated fatty acids (Ascherio et al 1999). However, quantitatively, dietary intake of TFA is substantially less than saturated fatty acid intake. The adipose tissue level of TFAs predicts heart disease even after adjustment for total cholesterol. It has been proposed that TFAs may adversely affect endothelial function as intake was positively related to concentrations of inflammatory markers (Lopez-Garcia et al 2005). The WHO in its report on diet, nutrition and chronic disease (WHO 2003) recommended that TFAs comprise no more than 1% of total dietary energy.

Whilst any increase in saturated and *trans* fats is associated with detrimental effects on markers of CHD risk, it would be impossible to consume a diet with no saturated fats that would provide all the other nutrient needs. Taking into account the nature of the food supply and the needs for fat in the diet, a combined limit of 8–10% of energy from saturated and *trans* fats together would be prudent.

N-3 AND N-6 FATTY ACIDS

Some fatty acids are essential in the diet and also have potential effects on the aetiology of chronic disease. These include some of the polyunsaturated n-6 and n-3 fatty acids, such as linoleic acid (LA), α-linolenic acid (ALA) and the long chain omega-3s (DHA, EPA and DPA).

Recent findings in large prospective cohort studies appear to confirm the earlier controlled intervention trials carried out in hospital-based populations (Dayton & Pearce 1969, Turpeinen et al 1979) that polyunsaturated fatty acids, predominantly LA, are associated with reduced incidence and mortality from CHD. A 15-year follow-up of Finnish men found energy-adjusted consumption of LA to be linked to reduced cardiovascular mortality (RR = 0.39) (Laaksonen et al 2005).

In the 20-year follow-up of the Nurses' Health Study that included a total of 5,672 women and 1,766 cases of clinical CHD, the RR attributable to polyunsaturated fat consumption was 0.75 (highest versus lowest quintile of intakes; $p > 0.001$) (Oh et al 2005). In this same cohort, the RR was even lower in overweight younger women (<65 years), and in those women who developed Type 2 diabetes or had Type 2 diabetes initially; the dietary polyunsaturated to saturated ratio was associated with significantly lower cardiovascular mortality over 18 years (Tanaescu et al 2004). These data are supported by evidence that plasma LA concentrations are inversely correlated with clinical CHD (Kris-Etherton et al 2004).

The lower end of the range of recommended intake for these fatty acids is set at the AI for each fatty acid type. The upper bound of recommended intake was set for linoleic acid and for alpha-linolenic acid at the current 90th centile of intake in the community expressed as per cent energy, as human data about additional benefits in relation to chronic disease outcome are currently limited for levels much in excess of these limits, and these levels of intake do not appear to cause harm. For n-6 fatty acids there is also some evidence from human studies showing that enrichment of lipoproteins and cell membranes with n-6 PUFA contributes to an adverse pro-oxidant state (Abbey et al 1993, Berry et al 1991, Bonanome et al 1992, Louheranta et al 1996, Reavan et al 1991, 1993, 1994), suggesting caution in recommending levels above 10% of dietary energy.

For LC n-3 fatty acids, an SDT was set at the 90th centile of intake. In the last decade, there has been an exponential rise in publications on health benefits of omega-3 PUFAs, particularly the longer chain omega-3s, EPA, DPA and DHA. Various expert groups have made consensus recommendations for consumption of ALA and/or the very long chain omega-3s, based on estimates of dietary requirement. Even though they may take account of the same body of published evidence, there is considerable variation between expert interpretations, consequent recommendations and their adoption by health authorities (Bahri et al 2002, BNF Task Force 1992, de-Deckere et al 1998, Department of Health 1994, FNB:IOM 2002, Health and Welfare Canada 1990, Health Council of the Netherlands 2001, Kris-Etherton et al 2002, Ministry of Health Labor and Welfare 1999, National Heart Foundation 1999, Nettleton 2003, NHMRC 1992, Nordic Council of Ministers 1996, Scientific Advisory Committee on Nutrition 2002, Simopoulos et al 1999, US FDA 2000, WHO 2003). It is apparent from the scientific literature that raising omega-3 intakes above current median levels (and thus above AI) may affords a wide range of health benefits. The evidence is strongest for reduction of CVD risk by EPA and DHA (WHO 2003).

The US Food and Drug Administration (US FDA 2000), when considering whether to allow an omega-3 health claim related to CHD, undertook a thorough evaluation of existing evidence for cardiovascular benefits of increased EPA and DHA consumption in humans. The evidence comprised epidemiological studies of fish consumption and intervention trials with EPA- or DHA-rich fish oil supplements. While the former were typically representative of a normal population, the latter were undertaken in subjects with pre-existing CVD. Hence, although there was strong overall evidence of benefit, the FDA originally

ruled that cardiovascular benefits of EPA and DHA had not been proven in a normal population. This limitation was expressed in the resultant health claim, which attributed decreased risk of CVD to consumption of fish but not specifically to its omega-3 content. Following recent revision, the claim now refers to omega-3 intake (US FDA 2003).

There is a lack of dose-response data relating EPA and DHA consumption to chronic disease health benefit. However, it is becoming increasingly common to relate the outcomes of epidemiological studies to estimates of EPA and DHA intakes or to plasma or erythrocyte EPA and DHA levels in each sector of the population, rather than to fish intakes. The Nurses' Health Study followed about 80,000 healthy women for up to 14 years and found that those in the highest quintile of EPA and DHA intake (about 480 mg/day) had a significantly lower risk of both CHD and thrombotic stroke (Hu et al 2002, Iso et al 2001). There was also a significantly lower risk of CHD at the highest (1.4 g/day) versus lowest (0.7 g/day) ALA intake (Hu et al 1999). This is consistent with the earlier MRFIT trial (about 13,000 men followed for 10.5 years) in which the risk of both CHD and total CVD were significantly lower at high ALA (1.6 g/day) and EPA and DHA (660 mg/day) intakes (Dolecek 1992).

The US Physicians' Health Study reported a reduction in sudden death in men consuming fish at least once weekly (90–160 mg EPA + DHA/day) (Albert et al 1998). Subsequent evaluation confirmed a tight inverse relationship between sudden death and blood EPA and DHA levels (Albert et al 2002). In contrast, the Health Professionals' Follow-Up Study reported no effect of EPA and DHA on CHD risk in men (Ascherio et al 1995). Re-analysis of this study, however, showed significant reduction of ischaemic stroke with increasing consumption of fish (He et al 2002).

Fish consumption has also been shown to counteract CV mortality in quintiles of a healthy aging population consuming at least 267 mg/day of EPA and DHA, whereas eating fish low in EPA and DHA gave no benefit (Mozaffarian et al 2003). The benefit correlated with increased plasma phospholipid EPA and DHA. The recent observation that heart rate is inversely correlated with both fish intake and erythrocyte DHA levels in about 10,000 healthy men (Dallongeville et al 2003) is consistent with an earlier study relating fish consumption and platelet DHA to heart rate variability (Christensen et al 1997) and a case-control study equating increased fish intake (an extra 0.2 g omega-3/day) with increased erythrocyte EPA and DHA levels and a 50% reduction in risk of primary cardiac arrest (Siscovick et al 1995).

The major epidemiological trials are supported by a rapidly increasing number of intervention trials reporting benefits of increased EPA and DHA consumption on both hard end-points and surrogate biomarkers for a variety of health conditions ranging from CVD to inflammatory disease, behavioural disorders and cancer. The most significant of these have been intervention trials post-myocardial infarction (MI) such as GISSI-P (GISSI-Prevenzione Investigators 1999) and DART (Burr et al 1989) showing reductions of CHD and particularly sudden death with fish oil supplementation. In the DART study, however, longer-term follow-up showed that the early reduction in all-cause mortality observed in those given fish oil advice was followed by an increased risk over the next 3 years, leading to the conclusion that the advice had no clear effect on coronary or all-cause mortality. The risk of stroke death was also increased in the fish oil advice group – the overall unadjusted hazard was 2.03 (Ness et al 2002).

Although one might expect that the dose needed to demonstrate significant benefit in a clinical trial would exceed the threshold intake for long-term efficacy, a substantial reduction of sudden death was achieved in the GISSI-P trial with only 850 mg EPA + DHA/day. This dose also reduced plasma triglycerides, the most consistent index of CV response to EPA and DHA. A subsequent post-MI intervention trial using a 4-fold higher dose of the same supplement failed to show a benefit (Nilsen et al 2001). However, this may have been due to the high habitual EPA and DHA consumption of the Norwegian subjects. Fish oil supplementation has also been shown to regress coronary artery disease (von Schacky et al 1999) and to stabilise atherosclerotic plaques (Thies et al 2003), but attempts to demonstrate prevention of restenosis following angioplasty have been inconclusive.

There is increasing awareness of the role of inflammatory mechanisms in the development of arterial disease (Osterud & Bjorklid 2003). While there is substantive evidence that omega-3 supplementation can counteract chronic inflammatory disorders such as rheumatoid arthritis, intervention trials have indicated the need for intakes well in excess of dietary levels (Calder 2001). However, plasma TNF (tumour necrosis factor) receptor levels are inversely related to dietary EPA and DHA intake (Pischon et al 2003) and recently it has been shown that inflammatory mediators, TNF and interleukin-6 (IL-6), may be suppressed at more modest intakes of EPA and DHA of about 0.3–1.0 g/day (Trebble et al 2003, Wallace et al 2003).

It would be unnecessarily repetitive to include an exhaustive review and appraisal of the evidence for the added health benefits of increased dietary EPA and DHA consumption. It is already the subject of numerous critical reviews, several of which have been published subsequent to the FNB:IOM (2002) report. These include the AHA Statement (Kris-Etherton et al 2002), a WHO report (WHO 2003) and a report by the Scientific Advisory Committee on Nutrition (2002). There have been several Cochrane reviews on relationships between fish oil, or n-3 fats, and asthma (Woods et al 2002), schizophrenia (Joy et al 2003), cystic fibrosis (Beckles et al 2002) and CVD (Hooper et al 2004). The latter is incomplete and the others are inconclusive. On the other hand, the WHO report, which classifies the quality of currently available evidence according to the NHMRC's preferred criteria, concludes that the relationship between EPA and DHA and cardiovascular disease is convincing (WHO 2003). In summary, there is increasing acceptance of evidence that, in populations with only modest intakes of EPA and DHA, increased dietary consumption could further improve health status.

Given this body of evidence and the modest intakes currently consumed in Australia and New Zealand, it would seem prudent to encourage increased consumption of LC n-3 fatty acids (DHA, EPA and DPA). Dietary intakes at the current 90th centile in the population would seem to provide potential benefit whilst being a safe level currently consumed by many Australians and New Zealanders. Rounding up to the nearest 10 mg, this equates to 610 mg/day for men and 430 mg/day for women. For men, the current 90th centile is close to the upper quintile from the MRFIT study which was associated with significantly less CVD (Dolecek 1992) and for women, the current 90th centile of intake is close to the level shown to produce benefit in the Nurses Health Study (Iso et al 2001).

This level is also consistent with the revised NHMRC *Dietary Guidelines for Australians* (NHMRC 2003) which recommend increasing the LC omega-3 fat intake to about 400 mg/day.
In this context, a total intake of 0.2% energy, or about 0.6 g/day for men and 0.4 g/day for women, is reasonable. It is also consistent with current National Heart Foundation advice (NHF 1999) to eat at least two fish meals per week (preferably oily fish) which is equivalent to about 430–570 mg/day.

CARBOHYDRATE

The AMDR for carbohydrate intake recommended by the FNB:IOM in adults and children is 45–65% of dietary energy intake (FNB:IOM 2002). The intakes were based on the IOM interpretation that there is an increased risk for CHD at high carbohydrate intakes (>65%) and increased risk of obesity with low carbohydrate, high fat intakes (<45%).

The FNB:IOM report did not consider in any great depth the nature of the carbohydrate when setting their AMDR. Added sugars were considered separately, otherwise the structure and polysaccharide composition of plant-based foods were not considered. Consideration of the nature of dietary carbohydrate is justified on the basis of associations with important chronic diseases such as Type 2 diabetes and CHD (Fung et al 2002, Jacobs et al 1998, Liu et al 2000, Meyer et al 2000). New occurrence of these diseases is more likely to be associated with the nature of carbohydrate, rather than percentage of daily energy intake provided by all carbohydrate-containing foods. The US:Canadian review used CHD and obesity as the limiting conditions when setting their upper and lower bounds of carbohydrate intake, respectively. However, it could be argued that consideration of aspects of optimal glucose metabolism, including the nature of dietary carbohydrate, may be of equal or greater relevance in the setting of an AMDR for carbohydrate. Insulin resistance and impaired glucose tolerance are major risk factors for Type 2 diabetes and CHD.

LOWER BOUND

The evidence reviewed by the FNB:IOM suggests that energy density, rather than a particular mix of fuels, leads to obesity. Although a high fat diet will be energy dense, the fat component alone will not lead to obesity unless energy is chronically consumed in excess of energy expenditure. This argument also applies to carbohydrates. In many western countries, the relative fat consumption (as a percentage of energy intake) has been declining over the last three decades (United States Department of Agriculture 1998). However, total fat consumption expressed as grams per day, has either remained relatively constant or dropped only slightly from the mid 1980s. The apparent discrepancy can be explained by an increasing energy intake due to higher carbohydrate intake. In Australia, between the 1983 and 1995 National Dietary Surveys (Cook et al 2001), total carbohydrate intake in adults increased by some 16–17%. About two-thirds of this increase was due to increased starch intake and one-third to sugar (both natural and added) intake. In children, between 1985 and 1995, total carbohydrate intake increased by about 20%, with starches increasing 18% and sugars about 20%. During this decade alone, the mean intake of non-alcoholic beverages (soft drinks, fruit and vegetable juices and mineral waters) for children rose nearly 50% in boys and 30% in girls.

The type of carbohydrate can markedly influence energy density of the diet. For example, it is easier to increase the energy density of the diet by consuming energy dense drinks with added carbohydrates compared to cereal foods, vegetables or fruits containing carbohydrates, because the extra energy intake from the former source is poorly compensated (Mattes 1996). In an experiment comparing drinks containing either sucrose or artificial sweeteners consumed by overweight people for 10 weeks, increases in body weight and fat mass occurred in the sucrose group compared with the artificial sweetener group (Raben et al 2002) as there was little or no energy compensation through reduction in intake of other energy sources.

Diets typified as low energy density contain a large amount of bulk in the form of fresh fruits, vegetables, whole grains and pulses and minimal fat, whereas a high energy-dense diet generally contains low bulk foods with higher sucrose and fat contents (Duncan et al 1983). In a crossover design, ad libitum daily energy intake on the low energy-dense diet was one-half of the energy intake on the high energy-dense diet. In a review of the effect of differing carbohydrate and fat intakes on energy balance, it was concluded that the lower energy density of carbohydrate foods on average is likely to lead to a lower ad libitum energy intake than a higher fat diet (Blundell & Stubs 1999). A dietary pattern typified as a 'white bread' diet (53.6% carbohydrate and 31.4% fat as a percentage of energy intake) was associated with a higher mean annual change in waist circumference compared with a 'healthy' diet (61.9% carbohydrate, 24.8% fat) in which the intake of white bread and refined grains was one-fifth (Newby et al 2003).

The FNB:IOM (2002) publication suggests that the lower limit of energy intake from carbohydrate should be 45%, leaving 55% of energy to come from protein and fat and possibly alcohol. Foods high in protein and fat are typically low bulk having a high energy density and energy intake from alcohol is poorly compensated. It is possible that the lower bound of 45% energy from carbohydrate may be too low to optimise reductions in energy intake associated with low energy-dense, high bulk foods, but the evidence is limited at this stage. However, the considerations described indicate that the form of carbohydrate is of key importance. Thus, for intakes at the lower end of the carbohydrate intake range, most of the carbohydrate has to be sourced from low energy-dense sources such as wholegrain cereals, vegetables, legumes and fruits, which are mostly low glycaemic index foods.

An analysis of the NNS survey showed that just under half of the population had intakes at or above 45% of energy as carbohydrate on the day of the survey. Dietary modelling also showed that it is possible to construct diets at 45% energy from carbohydrate that conform to the EARs for the nutrients assessed. About half the subjects from the NNS who conformed to all of the EARs assessed had carbohydrate intakes at or above 45% of energy.

UPPER BOUND

The rationale behind a high carbohydrate intake posing an increased risk for CHD is a worsening of the lipid profile (lower HDL and/or higher triglycerides) when comparing high and low carbohydrate diets. This effect is seen in some of the studies reviewed by the FNB:IOM (2002) with the effect being most pronounced when mono-unsaturated fatty acids formed a high proportion of the fat intake (Garg et al 1994, Grundy et al 1988). However, a high carbohydrate diet usually lowers total and LDL cholesterol concentrations relative to a high fat diet and, depending on the nature of the carbohydrate, improvements in the LDL:HDL ratio have been found with no raising of triglycerides compared with high fat diets (Turley et al 1998, Vidon et al 2001). It is difficult to judge the relevance of dietary-induced blood lipid changes on chronic disease because there are no clinical trials comparing a high carbohydrate diet with a high fat diet on coronary events (Sacks & Katan 2002). Even against the background of raised triglycerides whilst on high carbohydrate diets, flow-mediated vasodilation and LDL particle size did not differ from those with higher fat diets (de Roos et al 2001, Kasim-Karakas et al 1997).

Contrary to some of the studies discussed in the FNB:IOM DRIs review indicating that high carbohydrate diets may lower HDL or adversely affect triglycerides, there is some evidence that a high carbohydrate diet rich in complex carbohydrates derived from fruit, vegetables, grains and legumes may improve certain risk factors for heart disease. Further evidence that a consideration of the nature of carbohydrates is important in this context is found when considering the results of a study by Marckmann et al (2000) which showed that a high carbohydrate, high sucrose diet raised triglycerides compared with a high fat diet, whereas a high carbohydrate, low sucrose diet was associated with lower triglycerides. In the DASH trial, triglyceride concentrations were lowered in people having initially high concentrations after partial replacement of carbohydrates from a 'typical American' diet with fruit and vegetables (Obarzanek et al 2001). A meta-analysis of the effect of non-soya pulses on blood lipids found pulse consumption was associated with improved blood lipids including lower triglycerides and higher HDL cholesterol concentrations (Anderson & Major 2002). A change from a 70% carbohydrate diet to a 45% carbohydrate diet in South African prisoners resulted in a rise in serum triglycerides when the additional fat was butter or partially-hydrogenated oil and no change when sunflower seed oil was used (Antonis & Bersohn 1961). A switch back to a 70% carbohydrate diet resulted in a transient rise in triglycerides for 4–6 weeks followed by a gradual decline back to baseline levels. Unfortunately the nature of the carbohydrate portion of the diet was not well described. However, a diet high in unrefined foods, that provided about 68% of energy as carbohydrates lowered total cholesterol without changing triglycerides and improved fasting glucose concentrations, insulin sensitivity and glucose disposal (Fukagawa et al 1990).

It is clear that the nature of the fat and the carbohydrate content of the diet affect blood lipid profiles and glucose metabolism. Given these considerations, it is recommended that the upper bound of carbohydrate intake should be set at that required after the obligatory needs of fat and protein are met. In practice, using this approach and given the lower limit of 15% energy set for protein and 20% for fat, the upper bound would be 65%, the same as that recommended by the US:Canadian review, albeit arrived at using a somewhat different approach. The major difference between the two sets of recommendations lies in the emphasis placed in the Australian/New Zealand recommendation on the importance of the source of carbohydrate. Intakes of carbohydrate as high as 65% of energy or more from energy-dense, high glycaemic index sources may be detrimental to overall health. Data from the Third National Health and Examination Surveys (NHANES III) suggest that a high carbohydrate diet (>60% of energy intake) is associated with an elevated risk of metabolic syndrome in men (Park et al 2003). Unfortunately, there was no breakdown of the data by carbohydrate source that would have enabled an examination of the association between the metabolic syndrome and the nature of carbohydrate. Using the same database, Yang and colleagues found that the odds ratio for elevated serum C-peptide concentrations was reduced across quintiles of carbohydrate intake. Adjusting for total and added sugar intake strengthened the inverse association in men, suggesting that the nature of carbohydrate is important in the relationship between carbohydrate intake and elevated C-peptide concentrations (Yang et al 2003).

Presently, dietary recommendations from various countries separate the intakes of sucrose and other added sugars from total carbohydrate intake. There is no consensus as to how much can be included in a healthy diet. Evidence for a role of sucrose and other energy-containing sweeteners in adverse health conditions has been reviewed by the FNB:IOM (FNB:IOM 2002). These areas include behaviour, plasma lipids, CHD, obesity, nutrient density, physical activity, cancer, insulin sensitivity and Type 2 diabetes. Studies of the relationship between added sugars and the various categories listed above is ongoing. The FNB:IOM did not discuss a possible relationship between added sugar-sweetened drinks and bone health in children and adults through the avoidance of more nutrient-dense drinks. Familial conditioning suggests that maternal milk consumption predicts a trade-off between milk and soft drink consumption in the diets of young girls (Fisher et al 2000). Consumption of sweetened soft drinks was associated with a lower consumption of milk and calcium in Spanish children (Rodriguez-Artalejo et al 2003). Women with low milk intake during childhood and adolescence have less bone mass in adulthood and greater risk of fracture (Kalkwarf et al 2003). In another study, high fruit and vegetable intake was associated with higher bone mineral density compared with high intakes of candy (Tucker et al 2002).

The role of added sugars in the aetiology of disease and dental caries has been reviewed in some detail by WHO report on Diet and Chronic Diseases (WHO 2003). The WHO together with a number of countries such as the UK and Germany recommended equal or less than 10% of energy from added sugars, whilst the FNB: IOM document sets the limit at 25% of energy. Dental caries is often identified as the limiting factor in terms of an upper intake of cariogenic sweeteners, even in an era of fluoride exposure. There is no reason to suspect that the cariogenicity of sucrose and other sugars differs according to an individuals' energy intake. Thus, the dietary intake of sucrose and other cariogenic sugars might best be expressed as an absolute intake (grams per day) rather than as a proportion of energy intake. Indeed form and frequency of consumption also seem to be key indicators of adverse cariogenic outcome. The UL is likely to be less in children with primary dentition than it is for adults. The possible effect of sucrose and high fructose corn syrups in the aetiology of other diseases needs a more thorough review. These sweeteners cannot be treated as just another carbohydrate, because the fructose moiety imparts its own metabolic effect associated with elevated blood triglycerides and impaired glucose tolerance (Vrana & Fabry 1983).

Finally, the impact of sucrose intake on nutrient adequacy may differ between the US and Australia and New Zealand due to differing fortification policies. An example is folate, the intake of which declined strongly as added sugar intake increased in Australian adults (Baghurst et al 1992). This relationship is likely to be less pronounced in the US as certain cereal-based sugary foods such as cakes, biscuits and snack bars are made with folate-fortified flour. Of those who conformed to all of the EARs assessed in the NNS survey, 60% had added sugar intakes at or below 10% energy on the day of the survey and a further 23% had intakes between 11 and 15% of energy.

In summary, one of the key issues in relation to the AMDR recommendations for carbohydrate is that 'carbohydrate' is not a homogenous entity. Many epidemiological and dietary intervention studies refer to 'high carbohydrate' or 'low carbohydrate' diets with little or no description of the nature of the carbohydrate. Apart from considerations related to simple or added sugars, food structure, carbohydrate source and processing can all affect the physiological effects of carbohydrates and the amounts that can be consumed to optimise overall nutrient status and reduce chronic disease risk.

SUMMARY OF RECOMMENDATIONS TO REDUCE CHRONIC DISEASE RISK

TABLE 1. SUGGESTED DIETARY TARGETS (SDT) TO REDUCE CHRONIC DISEASE RISK – MICRONUTRIENTS, DIETARY FIBRE AND LC N-3 FATS

Nutrient	Suggested Dietary Target[a] (intake per day on average)	Comments
Vitamin A	Vitamin A: Men 1,500 µg Women 1,220 µg Carotenes: Men 5,800 µg Women 5,000 µg	The suggested dietary target is equivalent to the 90th centile of intake in the Australian and New Zealand populations, to be attained by replacing nutrient-poor, energy-dense foods and drinks with plenty of red-yellow vegetables and fruits, moderate amounts of reduced-fat dairy foods and small amounts of vegetable oils.
Vitamin C	Men 220 mg Women 190 mg	Equivalent to the 90th centile of intake in the Australian and New Zealand populations, to be attained by replacing nutrient-poor, energy-dense foods and drinks with plenty of vegetables, legumes and fruit.
Vitamin E	Men 19 mg Women 14 mg	Equivalent to the 90th centile of intake in the Australian and New Zealand populations, to be attained by including some poly- or monounsaturated fats and oils and replacing nutrient-poor, energy-dense foods and drinks with plenty of vegetables and moderate amounts of lean meat, poultry, fish, reduced-fat dairy foods and wholegrain cereals.
Selenium	No specific figure can be set. There is some evidence of potential benefit for certain cancers but adverse effects for others.	There are no available population intake data for Australia. New Zealand is a known low selenium area, thus recommendations based on centiles of population intakes are inappropriate. Selenium-rich foods include seafood, poultry and eggs and to a lesser extent, other muscle meats. The content in plant foods depends on the soil in which they were grown.
Folate	An additional 100–400 µg DFE over current intakes (ie a total of about 300–600 µg DFE) may be required to optimise homocysteine levels and reduce overall chronic disease risk and DNA damage.	Current population intakes are well below the new recommended intakes. Increased consumption through replacement of nutrient-poor, energy-dense foods and drinks with folate-rich foods such as vegetables and fruits and wholegrain cereals is recommended as the primary strategy. Dairy foods can also help with folate absorption but reduced fat varieties should be chosen. It should be noted that fortified foods contain folic acid which has almost twice the potency of naturally occurring food folates.

(continued)

TABLE 1 (CONT'D). SUGGESTED DIETARY TARGETS (SDT) TO REDUCE CHRONIC DISEASE RISK – MICRONUTRIENTS, DIETARY FIBRE AND LC N-3 FATS

Nutrient	Suggested Dietary Target[a] (intake per day on average)	Comments
Sodium/ potassium	Sodium: Men 1,600 mg 70 mmol Women 1,600 mg 70 mmol Potassium: Men 4,700 mg 120 mmol Women 4,700mg 120 mmol	Whilst a UL of 2,300 mg (100 mmol)/day was set for the general population, it is recognised that additional preventive health benefits (in terms of maintaining optimal blood pressure over the lifespan and thus reducing stroke and heart disease) may accrue if sodium intakes are further reduced to about 1,600 mg/day (70 mmol) in line with WHO recommendations. Reducing intakes to this level may also bring immediate benefit to older and overweight members of the community with pre-existing hypertension. As potassium can blunt the effect of sodium on blood pressure, intakes at the 90th centile of current population intake may help to mitigate the effects of sodium on blood pressure until intakes of sodium can be lowered. At the level of 4,700 mg/day for potassium there is also evidence of protection against renal stones. Increased potassium intake should be through greater consumption of fruits and vegetables.
Dietary Fibre	Men 38 g Women 28 g	Upper level at 90th centile of intake for reduction in CHD risk. Increased intakes should be through replacement of nutrient-poor, energy-dense foods and drinks and plenty of vegetables, fruits and wholegrain cereals.
LC n-3 fats (DHA:EPA: DPA)	Men 610 mg Women 430 mg	The suggested dietary target is equivalent to the 90th centile of intake in the Australian/New Zealand population to be attained by replacing energy-dense, low nutrient foods and drinks with LC n-3-rich foods such as fish such as tuna, salmon and mackerel, lean beef or low energy density, LC n-3-enriched foods.

a For most nutrients, unless otherwise noted, this is based on the 90th centile of current population intake.

TABLE 2. ACCEPTABLE MACRONUTRIENT DISTRIBUTION RANGES FOR MACRONUTRIENTS TO REDUCE CHRONIC DISEASE RISK WHILST STILL ENSURING ADEQUATE MICRONUTRIENT STATUS

Nutrient	Lower end of recommended intake range	Upper end of recommended intake range	Comments
Protein	15% of energy	25% of energy	On average, only 10% of energy is required to cover physiological needs, but this level is insufficient to allow for EARs for micronutrients when consuming foods commonly eaten in Australia and New Zealand. Intakes in some highly active communities (eg hunter-gatherers, Arctic, pastoralists) are as high as 30% with no apparent adverse health. No predominantly sedentary western societies have intakes at this level from which to assess potential adverse outcomes. Thus, a prudent UL of 25% of energy has been set.
Fat	20% of energy	35% of energy	The lower end of the range is determined by the amount required to sustain body weight and to allow for intakes of EARs of micronutrients. Some communities, notably some Asian groups, have average fat intakes below this level, but members of these groups are often smaller in stature and their overall nutrient status is not always known. The upper level was set in relation to risk of obesity and CVD, bearing in mind that high fat diets are often high in saturated fat, a known risk factor for heart disease, and are also often energy dense, increasing a propensity to over-consumption of energy. Saturated and trans fats together should be limited to no more than 10% of energy.
Linoleic acid (n-6 fat)	As per relevant age/gender AI: Equates to 4-5% dietary energy	90th centile of population intake: Equates to 10% of dietary energy	Based on intakes to help optimise chronic disease risk, notably CHD. There is some animal-based evidence that intakes up to 15% could be acceptable, but human evidence is limited. 10% as energy equates to about the 90th centile of current population intakes.
α-linolenic acid (n-3 fat)	As per relevant age/gender AI: Equates to 0.4–0.5% dietary energy	90th centile of population intake: Equates to 1% dietary energy	Based on intakes to help optimise chronic disease risk, notably CHD.
Carbohydrate	45% of energy (predominantly from low energy density and/or low glycaemic index foods)	65%of energy (predominantly from low energy density and/or low glycaemic index food sources)	The upper bound carbohydrate recommendations were set so as to accommodate the essential requirements for fat (20%) and protein (15%). It is of importance to note that the types of carbohydrates consumed are of paramount importance in relation to their health effects.

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SUMMARY TABLES OF NRVs FOR ENERGY, MACRONUTRIENTS AND MICRONUTRIENTS

TABLE 1. ESTIMATED ENERGY REQUIREMENTS (EERs) OF INFANTS AND YOUNG CHILDREN

Age (months)	Reference weight (kg)		EER (kJ/day)	
	Boys	Girls	Boys	Girls
1	4.4	4.2	2,000	1,800
2	5.3	4.9	2,400	2,100
3	6.0	5.5	2,400	2,200
4	6.7	6.1	2,400	2,200
5	7.3	6.7	2,500	2,300
6	7.9	7.2	2,700	2,500
7	8.4	7.7	2,800	2,500
8	8.9	8.1	3,000	2,700
9	9.3	8.5	3,100	2,800
10	9.7	8.9	3,300	3,000
11	10.0	9.2	3,400	3,100
12	10.3	9.5	3,500	3,200
15	11.1	10.3	3,800	3,500
18	11.7	11.0	4,000	3,800
21	12.2	11.6	4,200	4,000
24	12.7	12.1	4,400	4,200

Adapted from FNB:IOM (2002). Reference weights from Kuczmarski et al (2000)

TABLE 2. ESTIMATED ENERGY REQUIREMENTS (EERs) FOR CHILDREN AND ADOLESCENTS USING BMR PREDICTED FROM WEIGHT, HEIGHT AND AGE

Age Guide[a] Years	Reference weight[b] kg	Reference height m	BMR[c] MJ/day	PAL 1.2[d] Bed rest	PAL 1.4[d] Very sedentary	PAL 1.6[d] Light	PAL 1.8[d] Moderate	PAL 2.0[d] Heavy	PAL 2.2[d] Vigorous
Boys									
3	14.3	0.95	3.4	4.2	4.9	5.6	6.3	6.9	7.6
4	16.2	1.02	3.6	4.4	5.2	5.9	6.6	7.3	8.1
5	18.4	1.09	3.8	4.7	5.5	6.2	7.0	7.8	8.5
6	20.7	1.15	4.1	5.0	5.8	6.6	7.4	8.2	9.0
7	23.1	1.22	4.3	5.2	6.1	7.0	7.8	8.7	9.5
8	25.6	1.28	4.5	5.5	6.4	7.3	8.2	9.2	10.1
9	28.6	1.34	4.8	5.9	6.8	7.8	8.8	9.7	10.7
10	31.9	1.39	5.1	6.3	7.3	8.3	9.3	10.4	11.4
11	35.9	1.44	5.4	6.6	7.7	8.8	9.9	11.0	12.0
12	40.5	1.49	5.8	7.0	8.2	9.3	10.5	11.6	12.8
13	45.6	1.56	6.2	7.5	8.7	10.0	11.2	12.4	13.6
14	51.0	1.64	6.6	8.0	9.3	10.6	11.9	13.2	14.6
15	56.3	1.70	7.0	8.5	9.9	11.2	12.6	14.0	15.4
16	60.9	1.74	7.3	8.9	10.3	11.8	13.2	14.7	16.2
17	64.6	1.75	7.6	9.2	10.7	12.2	13.7	15.2	16.7
18	67.2	1.76	7.7	9.4	10.9	12.5	14.0	15.6	17.1

(Continued)

[a] The height and/or weight to age ratio may differ markedly in some ethnic groups. In this case, if BMI is in the acceptable range, it would be more relevant to use body weight as the main guide to current energy needs

[b] Reference weights from Kuczmarski et al (2000). See also FNB:IOM (2002)

[c] Estimated using Schofield (1985) equations for weight, height and age group 3–10, 10–18.

[d] PALs (Physical Activity Levels) incorporate relevant growth factor for age

TABLE 2. (CONT'D) ESTIMATED ENERGY REQUIREMENTS (EERs) FOR CHILDREN AND ADOLESCENTS USING BMR PREDICTED FROM WEIGHT, HEIGHT AND AGE

Age Guide[a] Years	Reference weight[b] kg	Reference height m	BMR[c] MJ/day	PAL 1.2[d] Bed rest	PAL 1.4[d] Very sedentary	PAL 1.6[d] Light	PAL 1.8[d] Moderate	PAL 2.0[d] Heavy	PAL 2.2[d] Vigorous
Girls									
3	13.9	0.94	3.2	3.9	4.5	5.3	5.8	6.4	7.1
4	15.8	1.01	3.4	4.1	4.8	5.5	6.1	6.8	7.5
5	17.9	1.08	3.6	4.4	5.1	5.7	6.5	7.2	7.9
6	20.2	1.15	3.8	4.6	5.4	6.1	6.9	7.6	8.4
7	22.8	1.21	4.0	4.9	5.7	6.5	7.3	8.1	8.9
8	25.6	1.28	4.2	5.2	6.0	6.9	7.7	8.6	9.4
9	29.0	1.33	4.5	5.5	6.4	7.3	8.2	9.1	10.0
10	32.9	1.38	4.7	5.7	6.7	7.6	8.5	9.5	10.4
11	37.2	1.44	4.9	6.0	7.0	8.0	9.0	10.0	11.0
12	41.6	1.51	5.2	6.4	7.4	8.5	9.5	10.6	11.6
13	45.8	1.57	5.5	6.7	7.8	8.9	10.0	11.1	12.2
14	49.4	1.60	5.7	6.9	8.1	9.2	10.3	11.5	12.6
15	52.0	1.62	5.8	7.1	8.2	9.4	10.6	11.7	12.9
16	53.9	1.63	5.9	7.2	8.4	9.5	10.7	11.9	13.1
17	55.1	1.63	5.9	7.2	8.4	9.6	10.8	12.0	13.2
18	56.2	1.63	6.0	7.3	8.5	9.7	10.9	12.1	13.3

[a] The height and/or weight to age ratio may differ markedly in some ethnic groups. In this case, if BMI is in the acceptable range, it would be more relevant to use body weight as the main guide to current energy needs

[b] Reference weights from Kuczmarski et al (2000). See also FNB:IOM (2002)

[c] Estimated using Schofield (1985) equations for weight, height and age group 3–10, 10–18.

[d] PALs (Physical Activity Levels) incorporate relevant growth factor for age

TABLE 3. ESTIMATED ENERGY REQUIREMENTS OF ADULTS USING PREDICTED BMR X PAL

Age yr	BMI = 22.0[a]		BMR MJ/d	Physical activity level (PAL)[b] Males MJ/day						BMR MJ/d	Physical activity level (PAL)[b] Females MJ/day					
	Ht (m)	Wt (kg)	Male	1.2	1.4	1.6	1.8	2.0	2.2	Female	1.2	1.4	1.6	1.8	2.0	2.2
19-30	1.5	49.5	–	–	–	–	–	–	–	5.2	6.1	7.1	8.2	9.2	10.2	11.2
	1.6	56.3	6.4	7.7	9.0	10.3	11.6	12.9	14.2	5.6	6.6	7.7	8.8	9.9	11.1	12.2
	1.7	63.6	6.9	8.3	9.7	11.0	12.4	13.8	15.2	6.0	7.2	8.4	9.6	10.8	12.0	13.2
	1.8	71.3	7.4	8.9	10.3	11.8	13.3	14.8	16.3	6.5	7.7	9.0	10.3	11.6	12.9	14.2
	1.9	79.4	7.9	9.5	11.1	12.6	14.2	15.8	17.4	7.0	8.4	9.7	11.1	12.5	13.9	15.3
	2.0	88.0	8.4	10.1	11.8	13.5	15.2	16.9	18.6	–	–	–	–	–	–	–
31-50	1.5	49.5	–	–	–	–	–	–	–	5.2	6.3	7.3	8.4	9.4	10.4	11.5
	1.6	56.3	6.4	7.6	8.9	10.2	11.4	12.7	14.0	5.5	6.5	7.6	8.7	9.8	10.9	12.0
	1.7	63.6	6.7	8.0	9.4	10.7	12.1	13.4	14.8	5.7	6.8	8.0	9.1	10.3	11.4	12.5
	1.8	71.3	7.1	8.5	9.9	11.3	12.7	14.2	15.6	6.0	7.2	8.3	9.5	10.7	11.9	13.1
	1.9	79.4	7.5	9.0	10.4	11.9	13.4	14.9	16.4	6.2	7.5	8.7	10.0	11.2	12.5	13.7
	2.0	88.0	7.9	9.5	11.0	12.6	14.2	15.8	17.3	_	_	_	–	–	–	–
51-70	1.5	49.5	–	–	–	–	–	–	–	4.9	6.0	6.9	7.9	8.9	9.8	10.9
	1.6	56.3	5.8	7.0	8.2	9.3	10.4	11.5	12.7	5.2	6.2	7.3	8.3	9.3	10.4	11.4
	1.7	63.6	6.1	7.3	8.6	9.8	11.1	12.3	13.6	5.4	6.5	7.6	8.7	9.8	10.7	12.0
	1.8	71.3	6.5	7.8	9.1	10.4	11.7	13.1	14.4	5.7	6.9	8.0	9.1	10.3	11.4	12.6
	1.9	79.4	6.9	8.3	9.6	11.1	12.4	13.8	15.2	6.0	7.2	8.4	9.6	10.8	12.0	13.2
	2.0	88.0	7.3	8.8	10.2	11.7	13.2	14.7	16.1	–	–	–	–	–	–	–
>70	1.5	49.5	–	–	–	–	–	–	–	4.6	5.6	6.5	7.4	8.3	9.3	10.2
	1.6	56.3	5.2	6.3	7.3	8.3	9.4	10.4	11.5	4.9	5.9	6.9	7.8	8.8	9.8	10.8
	1.7	63.6	5.6	6.7	7.8	8.9	10.0	11.2	12.3	5.2	6.2	7.2	8.3	9.3	10.3	11.4
	1.8	71.3	6.0	7.1	8.3	9.5	10.7	11.9	13.1	5.5	6.6	7.7	8.7	9.8	10.9	12.0
	1.9	79.4	6.4	7.6	8.9	10.2	11.4	12.7	14.0	5.8	6.9	8.1	9.2	10.4	11.5	12.7
	2.0	88.0	6.8	8.1	9.5	10.8	12.2	13.5	14.9	–	–	–	–	–	–	–

[a] A BMI of 22.0 is approximately the mid point of the WHO (1998) healthy weight range (BMI 18.5–24.9)

[b] Physical activity level (PAL) of 1.2 (bed rest) to 2.2 (very active or heavy occupational work).
PALs of 1.75 and above are consistent with good health. PALs below 1.4 are not compatible with moving around freely or earning a living.
PALs above 2.5 are difficult to maintain for long periods.

Note: the original Schofield equations from which these tables were derived (Schofield 1985) used 60+ years as the upper age category. For people aged 51–70 years, the estimates were derived by averaging those for the younger (19–30 years) and older (>70 years) adults.

TABLE 4. NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: MACRONUTRIENTS AND WATER

Age group & gender		Protein			Dietary fats[a]						Carbohydrate		Dietary fibre		Total water[b] (figure in brackets is fluid component only)	
					Linoleic (n-6)		α-linolenic (n-3)		LC n-3 (DHA/EPA/DPA)							
		g/day			g/day		g/day		mg/day		g/day		g/day		L/day	
		AI		*UL*	*AI*	*UL*	*AI*	*UL*	*AI*	*UL*	*AI*	*UL*	*AI*	*UL*	*AI*	*UL*
Infants[c]	0–6 mo.	10		BM	4.4	BM	0.5[a]	BM	–	NP	60	BM	NP	NP	0.7 (0.7)	NP
	7–12 mo.	14		BF	4.6	BF	0.5[a]	BF	–	NP	95	BF	NP	NP	0.8 (0.6)	NP
		EAR	*RDI*	*UL*												
Children	1–3 yr	12	14	NP	5	NP	0.5	NP	40	3,000	NO AI OR UL SET FOR OTHER AGES AS DATA ON ESSENTIALITY ARE INSUFFICIENT		14	NP	1.4 (1.0)	NP
	4–8 yr	16	20	NP	8	NP	0.8	NP	55	3,000			18	NP	1.6 (1.2)	NP
Boys	9–13 yr	31	40	NP	10	NP	1.0	NP	70	3,000			24	NP	2.2 (1.6)	NP
	14–18 yr	49	65	NP	12	NP	1.2	NP	125	3,000			28	NP	2.7 (1.9)	NP
Girls	9–13 yr	24	35	NP	8	NP	0.8	NP	70	3,000			20	NP	1.9 (1.4)	NP
	14–18 yr	35	45	NP	8	NP	0.8	NP	85	3,000			22	NP	2.2 (1.6)	NP

(Continued)

Abbreviations: AI adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, Upper Level of Intake

[a] Recommendation for total n-6 and total n-3; total fat AI also set at 30–31 g/day for infants

[b] Total water includes water from foods and fluids

[c] AI recommendations for infants are based on amounts in breast milk

[d] In 2nd and 3rd trimesters only

TABLE 4. (CONT'D) NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: MACRONUTRIENTS AND WATER

Age group & gender		Protein g/day			Dietary fats[a] Linoleic (n-6) g/day		α-linolenic (n-3) g/day		LC n-3 (DHA/EPA/DPA) mg/day		Carbohydrate g/day	Dietary fibre g/day		Total water[b] (figure in brackets is fluid component only) L/day	
		EAR	*RDI*	*UL*	*AI*	*UL*	*AI*	*UL*	*AI*	*UL*	*AI UL*	*AI*	*UL*	*AI*	*UL*
Men	19–30 yr	52	64	NP	13	NP	1.3	NP	160	3,000	NO AI OR UL SET FOR OTHER AGES AS DATA ON ESSENTIALITY ARE INSUFFICIENT	30	NP	3.4 (2.6)	NP
	31–50 yr	52	64	NP	13	NP	1.3	NP	160	3,000		30	NP	3.4 (2.6)	NP
	51–70 yr	52	64	NP	13	NP	1.3	NP	160	3,000		30	NP	3.4 (2.6)	NP
	>70 yr	65	81	NP	13	NP	1.3	NP	160	3,000		30	NP	3.4 (2.6)	NP
Women	19–30 yr	37	46	NP	8	NP	0.8	NP	90	3,000		25	NP	2.8 (2.1)	NP
	31–50 yr	37	46	NP	8	NP	0.8	NP	90	3,000		25	NP	2.8 (2.1)	NP
	51–70 yr	37	46	NP	8	NP	0.8	NP	90	3,000		25	NP	2.8 (2.1)	NP
	>70 yr	46	57	NP	8	NP	0.8	NP	90	3,000		25	NP	2.8 (2.1)	NP
Pregnancy	14–18 yr	47[d]	58[d]	NP	10	NP	1.0	NP	110	3,000		25	NP	2.4 (1.8)	NP
	19–30 yr	49[d]	60[d]	NP	10	NP	1.0	NP	115	3,000		28	NP	3.1 (2.3)	NP
	31–50 yr	49[d]	60[d]	NP	10	NP	1.0	NP	115	3,000		28	NP	3.1 (2.3)	NP
Lactation	14–18 yr	51	63	NP	12	NP	1.2	NP	140	3,000		27	NP	2.9 (2.3)	NP
	19–30 yr	54	67	NP	12	NP	1.2	NP	145	3,000		30	NP	3.5 (2.6)	NP
	31–50 yr	54	67	NP	12	NP	1.2	NP	145	3,000		30	NP	3.5 (2.6)	NP

Abbreviations: AI adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary
intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, Upper Level of Intake

[a] Recommendation for total n-6 and total n-3; total fat AI also set at 30–31 g/day for infants

[b] Total water includes water from foods as well as fluids

[c] AI recommendations for infants are based on amounts in breast milk

[d] In 2nd and 3rd trimesters only

TABLE 5. NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: B VITAMINS

Age group & gender		Thiamin mg/day			Riboflavin mg/day			Niacin[a] mg/day niacin equivalents			Vitamin B6 mg/day			Vitamin B12 µg/day			Folate[b] as dietary folate equivs µg/day			Pantothenic acid mg/day		Biotin µg/day	
		AI		*UL*	*AI*		*UL*	*AI*		*UL*	*AI*		*UL*[c]	*AI*		*UL*	*AI*		*UL*	*AI*	*UL*	*AI*	*UL*
Infants[d]	0–6 mo.	0.2		NP	0.3		BM	2		BM	0.1		BM	0.4		BM	65		BM	1.7	BM	5	BM
	7–12 mo.	0.3		NP	0.4		B/F	4		B/F	0.3		B/F	0.5		B/F	80		B/F	2.2	B/F	6	B/F
		EAR	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*AI*	*UL*	*AI*	*UL*
Children	1–3 yr	0.4	0.5	NP	0.4	0.5	NP	5	6	10	0.4	0.5	15	0.7	0.9	NP	120	150	300	3.5	NP	8	NP
	4–8 yr	0.5	0.6	NP	0.5	0.6	NP	6	8	15	0.5	0.6	20	1.0	1.2	NP	160	200	400	4.0	NP	12	NP
Boys	9–13 yr	0.7	0.9	NP	0.8	0.9	NP	9	12	20	0.8	1.0	30	1.5	1.8	NP	250	300	600	5.0	NP	20	NP
	14–18 yr	1.0	1.2	NP	1.1	1.3	NP	12	16	30	1.1	1.3	40	2.0	2.4	NP	330	400	800	6.0	NP	30	NP
Girls	9–13 yr	0.7	0.9	NP	0.8	0.9	NP	9	12	20	0.8	1.0	30	1.5	1.8	NP	250	300	600	4.0	NP	20	NP
	14–18 yr	0.9	1.1	NP	0.9	1.1	NP	11	14	30	1.0	1.2	40	2.0	2.4	NP	330	400	800	4.0	NP	25	NP

(Continued)

Abbreviations: AI adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, upper level of intake

[a] The UL for niacin refers to nicotinic acid. For supplemental nicotinamide, the UL is 900 mg/day for men and non-pregnant women, 150 mg/day for 1–3 yr-olds, 250 mg/day for 4–8 yr-olds; 500 mg/day for 9–13 yr-olds and 750 mg/day for 14–18 yr-olds. It is not possible to set a UL for nicotinamide for infancy (intake should be only breast milk, formula or foods) or pregnancy and lactation (source should be food only)

[b] For folate, the UL is for intake from fortified foods and supplements as folic acid

[c] For vitamin B_6, the UL is set for pyridoxine

[d] All infant AIs are based on milk concentrations in healthy women and average volumes

[e] This is for dietary intake. For pregnant women, it does not include the additional supplemental folic acid required to prevent neural tube defects

TABLE 5. (CONT'D) NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: B VITAMINS

Age group & gender		Thiamin mg/day			Riboflavin mg/day			Niacin[a] mg/day niacin equivalents			Vitamin B6 mg/day			Vitamin B12 µg/day			Folate[b] as dietary folate equivs µg/day			Pantothenic acid mg/day		Biotin µg/day	
		EAR	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*[e]	*RDI*[e]	*UL*	*AI*	*UL*	*AI*	*UL*
Men	19–30 yr	1.0	1.2	NP	1.1	1.3	NP	12	16	35	1.1	1.3	50	2.0	2.4	NP	320	400	1,000	6.0	NP	30	NP
	31–50 yr	1.0	1.2	NP	1.1	1.3	NP	12	16	35	1.1	1.3	50	2.0	2.4	NP	320	400	1,000	6.0	NP	30	NP
	51–70 yr	1.0	1.2	NP	1.1	1.3	NP	12	16	35	1.4	1.7	50	2.0	2.4	NP	320	400	1,000	6.0	NP	30	NP
	>70 yr	1.0	1.2	NP	1.3	1.6	NP	12	16	35	1.4	1.7	50	2.0	2.4	NP	320	400	1,000	6.0	NP	30	NP
Women	19–30 yr	0.9	1.1	NP	0.9	1.1	NP	11	14	35	1.1	1.3	50	2.0	2.4	NP	320	400	1,000	4.0	NP	25	NP
	31–50 yr	0.9	1.1	NP	0.9	1.1	NP	11	14	35	1.1	1.3	50	2.0	2.4	NP	320	400	1,000	4.0	NP	25	NP
	51–70 yr	0.9	1.1	NP	0.9	1.1	NP	11	14	35	1.3	1.5	50	2.0	2.4	NP	320	400	1,000	4.0	NP	25	NP
	>70 yr	0.9	1.1	NP	1.1	1.3	NP	11	14	35	1.3	1.5	50	2.0	2.4	NP	320	400	1,000	4.0	NP	25	NP
Pregnancy	14–18 yr	1.2	1.4	NP	1.2	1.4	NP	14	18	30	1.6	1.9	40	2.2	2.6	NP	520	600	800	5.0	NP	30	NP
	19–30 yr	1.2	1.4	NP	1.2	1.4	NP	14	18	35	1.6	1.9	50	2.2	2.6	NP	520	600	1,000	5.0	NP	30	NP
	31–50 yr	1.2	1.4	NP	1.2	1.4	NP	14	18	35	1.6	1.9	50	2.2	2.6	NP	520	600	1,000	5.0	NP	30	NP
Lactation	14-18 yr	1.2	1.4	NP	1.3	1.6	NP	13	17	30	1.7	2.0	40	2.4	2.8	NP	450	500	800	6.0	NP	35	NP
	19-30 yr	1.2	1.4	NP	1.3	1.6	NP	13	17	35	1.7	2.0	50	2.4	2.8	NP	450	500	1,000	6.0	NP	35	NP
	31-50 yr	1.2	1.4	NP	1.3	1.6	NP	13	17	35	1.7	2.0	50	2.4	2.8	NP	450	500	1,000	6.0	NP	35	NP

Abbreviations: AI adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, upper level of intake

[a] The UL for niacin refers to nicotinic acid. For supplemental nicotinamide, the UL is 900 mg/day for men and non-pregnant women, 150 mg/day for 1–3 yr-olds, 250 mg/day for 4–8 yr-olds; 500 mg/day for 9–13 yr-olds and 750 mg/day for 14–18 yr-olds. It is not possible to set a UL for nicotinamide for infancy (intake should be only breast milk, formula or foods) or pregnancy and lactation (source should be food only)

[b] For folate, the UL is for intake from fortified foods and supplements as folic acid

[c] For vitamin B_6, the UL is set for pyridoxine

[d] All infant AIs are based on milk concentrations in healthy women and average volumes

[e] This is for dietary intake. For pregnant women, it does not include the additional supplemental folic acid required to prevent neural tube defects

TABLE 6. NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: VITAMINS A, C, D, E AND K AND CHOLINE

Age group & gender		Vitamin A (retinol equivalents) µg/day			Vitamin C mg/day			Vitamin D µg/day		Vitamin E (α-tocopherol equivalents[a]) mg/day		Vitamin K µg/day		Choline mg/day	
		AI		*UL*[b]	*AI*		*UL*[c]	*AI*	*UL*	*AI*	*UL*	*AI*	*UL*	*AI*	*UL*
Infants[d]	0–6 mo.	250 (as retinol)		600	25		BM	5	25	4	BM	2.0	BM	125	BM
	7–12 mo.	430		600	30		B/F	5	25	5	B/F	2.5	B/F	150	B/F
		EAR	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*AI*	*UL*	*AI*	*UL*	*AI*	*UL*	*AI*	*UL*
Children	1–3 yr	210	300	600	25	35	NP	5	80	5	70	25	NP	200	1,000
	4–8 yr	275	400	900	25	35	NP	5	80	6	100	35	NP	250	1,000
Boys	9–13 yr	445	600	1,700	28	40	NP	5	80	9	180	45	NP	375	1,000
	14–18 yr	630	900	2,800	28	40	NP	5	80	10	250	55	NP	550	3,000
Girls	9–13 yr	420	600	1,700	28	40	NP	5	80	8	180	45	NP	375	1,000
	14–18 yr	485	700	2,800	28	40	NP	5	80	8	250	55	NP	400	3,000

(Continued)

Abbreviations: AI, adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, upper level of intake

[a] One α-tocopherol equivalent is equal to 1 mg RRR α-(or *d*-α-) tocopherol, 2mg β-tocopherol, 10mg γ tocopherol or 3 mg α-tocotrienol. The relevant figure for synthetic all-rac-α-tocopherols (*dl*-α-tocopherol) is 14 mg

[b] A UL cannot be established for supplemental β-carotene use and is not required for food use

[c] Not possible to establish a UL for vitamin C from available data, but 1,000 mg/day would be a prudent limit

[d] All infant AIs are based on milk concentrations in healthy women and average volumes

TABLE 6. (CONT'D) NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: VITAMINS A, C, D, E AND K AND CHOLINE

Age group & gender		Vitamin A (retinol equivalents) µg/day			Vitamin C mg/day			Vitamin D µg/day		Vitamin E (α-tocopherol equivalents[a]) mg/day		Vitamin K µg/day		Choline mg/day	
		EAR	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*AI*	*UL*	*AI*	*UL*	*AI*	*UL*	*AI*	*UL*
Men	19–30 yr	625	900	3,000	30	45	NP	5	80	10	300	70	NP	550	3,500
	31–50 yr	625	900	3,000	30	45	NP	5	80	10	300	70	NP	550	3,500
	51–70 yr	625	900	3,000	30	45	NP	10	80	10	300	70	NP	550	3,500
	>70 yr	625	900	3,000	30	45	NP	15	80	10	300	70	NP	550	3,500
Women	19–30 yr	500	700	3,000	30	45	NP	5	80	7	300	60	NP	425	3,500
	31–50 yr	500	700	3,000	30	45	NP	5	80	7	300	60	NP	425	3,500
	51–70 yr	500	700	3,000	30	45	NP	10	80	7	300	60	NP	425	3,500
	>70 yr	500	700	3,000	30	45	NP	15	80	7	300	60	NP	425	3,500
Pregnancy	14–18 yr	530	700	2,800	38	55	NP	5	80	8	300	60	NP	415	3,000
	19–30 yr	550	800	3,000	40	60	NP	5	80	7	300	60	NP	440	3,500
	31–50 yr	550	800	3,000	40	60	NP	5	80	7	300	60	NP	440	3,500
Lactation	14–18 yr	780	1,100	2,800	58	80	NP	5	80	12	300	60	NP	525	3,000
	19–30 yr	800	1,100	3,000	60	85	NP	5	80	11	300	60	NP	550	3,500
	31–50 yr	800	1,100	3,000	60	85	NP	5	80	11	300	60	NP	550	3,500

Abbreviations: AI, adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, upper level of intake

[a] One α-tocopherol equivalent is equal to 1 mg RRR α- (or d-α-) tocopherol, 2mg β-tocopherol, 10mg γ tocopherol or 3 mg α-tocotrienol. The relevant figure for synthetic all-rac- α-tocopherols (*dl*-α-tocopherol) is 14 mg

[b] A UL cannot be established for supplemental beta-carotene use and is not required for food use

[c] Not possible to establish a UL for vitamin C from available data, but 1,000 mg/day would be a prudent limit

[d] All infant AIs are based on milk concentrations in healthy women and average volumes

TABLE 7. NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: MINERALS – CALCIUM, PHOSPHORUS, ZINC AND IRON

Age group & gender		Calcium[a] mg/day			Phosphorus mg/day			Zinc mg/day			Iron mg/day		
		AI		*UL*	*AI*		*UL*	*AI*		*UL*	*AI*		*UL*
Infants	0–6 mo.	210		BM	100		BM	2.0		4	0.2		20
	7–12 mo.	270		B/F	275		B/F	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*
								2.5	3.0	5	7	11.0	20
		EAR	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*
Children	1–3 yr	360	500	2,500	380	460	3,000	2.5	3	7	4	9	20
	4–8 yr	520	700	2,500	405	500	3,000	3.0	4	12	4	10	40
Boys	9–13 yr	800–1,050	1,000–1,300	2,500	1,055	1,250	4,000	5.0	6	25	6	8	40
	14–18 yr	1,050	1,300	2,500	1,055	1,250	4,000	11.0	13	35	8	11	45
Girls	9–13 yr	800–1,050	1,000–1,300	2,500	1,055	1,250	4,000	5.0	6	25	6	8	40
	14–18 yr	1,050	1,300	2,500	1,055	1,250	4,000	6.0	7	35	8	15	45

(Continued)

Abbreviations: AI, adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, upper level of intake

[a] For calcium, there are separate recommendations for children aged 9–11 years and 12–13 years because of growth needs. 9–11 year-olds who are growing and maturing at much greater rates than average may need the intakes recommended for 12–13 year-olds

TABLE 7. (CONT'D) NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: MINERALS – CALCIUM, PHOSPHORUS, ZINC AND IRON

Age group & gender		Calcium[a] mg/day			Phosphorus mg/day			Zinc mg/day			Iron mg/day		
		EAR	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*
Men	19–30 yr	840	1,000	2,500	580	1,000	4,000	12.0	14	40	6	8	45
	31–50 yr	840	1,000	2,500	580	1,000	4,000	12.0	14	40	6	8	45
	51–70 yr	840	1,000	2,500	580	1,000	4,000	12.0	14	40	6	8	45
	>70 yr	1,100	1,300	2,500	580	1,000	3,000	12.0	14	40	6	8	45
Women	19–30 yr	840	1,000	2,500	580	1,000	4,000	6.5	8	40	8	18	45
	31–50 yr	840	1,000	2,500	580	1,000	4,000	6.5	8	40	8	18	45
	51–70 yr	1,100	1,300	2,500	580	1,000	4,000	6.5	8	40	5	8	45
	>70 yr	1,100	1,300	2,500	580	1,000	3,000	6.5	8	40	5	8	45
Pregnancy	14–18 yr	1,050	1,300	2,500	1,055	1,250	3,500	8.5	10	35	23	27	45
	19–30 yr	840	1,000	2,500	580	1,000	3,500	9.0	11	40	22	27	45
	31–50 yr	840	1,000	2,500	580	1,000	3,500	9.0	11	40	22	27	45
Lactation	14–18 yr	1,050	1,300	2,500	1,055	1,250	4,000	9.0	11	35	7	10	45
	19–30 yr	840	1,000	2,500	580	1,000	4,000	10.0	12	40	6.5	9	45
	31–50 yr	840	1,000	2,500	580	1,000	4,000	10.0	12	40	6.5	9	45

Abbreviations: AI, adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, upper level of intake

[a] For calcium, there are separate recommendations for children aged 9–11 years and 12–13 years because of growth needs. 9–11 year-olds who are growing and maturing at much greater rates than average may need the intakes recommended for 12–13 year-olds

TABLE 8. NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: MINERALS – MAGNESIUM, IODINE, SELENIUM AND MOLYBDENUM

Age group & gender		Magnesium mg/day			Iodine µg/day			Selenium µg/day			Molybdenum µg/day		
		AI		*UL*[a]	*AI*		*UL*	*AI*		*UL*	*AI*		*UL*
Infants	0–6 mo.	30		BM	90		BM	12		45	2		BM
	7–12 mo.	75		B/F	110		B/F	15		60	3		B/F
		EAR	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*
Children	1–3 yr	65	80	65	65	90	200	20	25	90	13	17	300
	4–8 yr	110	130	110	65	90	300	25	30	150	17	22	600
Boys	9–13 yr	200	240	350	75	120	600	40	50	280	26	34	1,100
	14–18 yr	340	410	350	95	150	900	60	70	400	33	43	1,700
Girls	9–13 yr	200	240	350	75	120	600	40	50	280	26	34	1,100
	14–18 yr	300	360	350	95	150	900	50	60	400	33	43	1,700

(Continued)

Abbreviations: AI, adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, upper level of intake

[a] Note that all of the ULs listed for magnesium refer to supplements

TABLE 8. (CONT'D) NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: MINERALS – MAGNESIUM, IODINE, SELENIUM AND MOLYBDENUM

Age group & gender		Magnesium mg/day			Iodine µg/day			Selenium µg/day			Molybdenum µg/day		
		EAR	*RDI*	*UL*[a]	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*	*EAR*	*RDI*	*UL*
Men	**19–30 yr**	330	400	350	100	150	1,100	60	70	400	34	45	2,000
	31–50 yr	350	420	350	100	150	1,100	60	70	400	34	45	2,000
	51–70 yr	350	420	350	100	150	1,100	60	70	400	34	45	2,000
	>70 yr	350	420	350	100	150	1,100	60	70	400	34	45	2,000
Women	**19–30 yr**	255	310	350	100	150	1,100	50	60	400	34	45	2,000
	31–50 yr	265	320	350	100	150	1,100	50	60	400	34	45	2,000
	51–70 yr	265	320	350	100	150	1,100	50	60	400	34	45	2,000
	>70 yr	265	320	350	100	150	1,100	50	60	400	34	45	2,000
Pregnancy	**14–18 yr**	335	400	350	160	220	900	55	65	400	40	50	1,700
	19–30 yr	290	350	350	160	220	1,100	55	65	400	40	50	2,000
	31–50 yr	300	360	350	160	220	1,100	55	65	400	40	50	2,000
Lactation	**14–18 yr**	300	360	350	190	270	900	65	75	400	35	50	1,700
	19–30 yr	255	310	350	190	270	1,100	65	75	400	36	50	2,000
	31–50 yr	265	320	350	190	270	1,100	65	75	400	36	50	2,000

Abbreviations: AI, adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, upper level of intake

[a] Note that all of the ULs listed for magnesium refer to supplements

TABLE 9. NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: MINERALS – COPPER, CHROMIUM, MANGANESE, FLUORIDE, SODIUM AND POTASSIUM

Age/gender group		Copper mg/day		Chromium µg/day		Manganese mg/day		Fluoride mg/day		Sodium mg/day[a]		Potassium mg/day	
		AI	*UL*	*AI*	*UL*	*AI*	*UL*[b]	*AI*	*UL*	*AI*	*UL*[c]	*AI*	*UL*[d]
Infants	0–6 mo.	0.20	BM	0.2	NP	0.003	BM	0.01	0.7	120	NP	400	NP
	7–12 mo.	0.22	B/F	5.5	NP	0.600	B/F	0.50	0.9	170	NP	700	NP
Children	1–3 yr	0.7	1	11	NP	2.0	NP	0.7	1.3	200–400	1,000	2,000	NP
	4–8 yr	1.0	3	15	NP	2.5	NP	1.0	2.2	300–600	1,400	2,300	NP
Boys	9–13 yr	1.3	5	25	NP	3.0	NP	2.0	10	400–800	2,000	3,000	NP
	14–18 yr	1.5	8	35	NP	3.5	NP	3.0	10	460–920	2,300	3,600	NP
Girls	9–13 yr	1.1	5	21	NP	2.5	NP	2.0	10	400–800	2,000	2,500	NP
	14–18 yr	1.1	8	24	NP	3.0	NP	3.0	10	460–920	2,300	2,600	NP

(Continued)

Abbreviations: AI, adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, upper level of intake

[a] 920 mg sodium/day is equivalent to 40 mmol/day; 2,300 mg sodium/day is equivalent to 100 mmol/day

[b] Intake of manganese beyond that normally found in food and beverages could represent a health risk, but there are insufficient data to set a UL

[c] A level of no more than 1,600 mg sodium/day (70 mmol) is recommended for older, overweight hypertensives and for those wishing to maintain low blood pressure over the lifespan

[d] For potassium, supplements should be taken only under medical supervision

TABLE 9. (CONT'D) NUTRIENT REFERENCE VALUES FOR AUSTRALIA AND NEW ZEALAND: MINERALS – COPPER, CHROMIUM, MANGANESE, FLUORIDE, SODIUM AND POTASSIUM

Age/gender group		Copper mg/day		Chromium µg/day		Manganese mg/day		Fluoride mg/day		Sodium mg/day[a]		Potassium mg/day	
		AI	*UL*	*AI*	*UL*	*AI*	*UL*[b]	*AI*	*UL*	*AI*	*UL*[c]	*AI*	*UL*[d]
Men	19–30 yr	1.7	10	35	NP	5.5	NP	4.0	10	460–920	2,300	3,800	NP
	31–50 yr	1.7	10	35	NP	5.5	NP	4.0	10	460–920	2,300	3,800	NP
	51–70 yr	1.7	10	35	NP	5.5	NP	4.0	10	460–920	2,300	3,800	NP
	>70 yr	1.7	10	35	NP	5.5	NP	4.0	10	460–920	2,300	3,800	NP
Women	19–30 yr	1.2	10	25	NP	5.0	NP	3.0	10	460–920	2,300	2,800	NP
	31–50 yr	1.2	10	25	NP	5.0	NP	3.0	10	460–920	2,300	2,800	NP
	51–70 yr	1.2	10	25	NP	5.0	NP	3.0	10	460–920	2,300	2,800	NP
	>70 yr	1.2	10	25	NP	5.0	NP	3.0	10	460–920	2,300	2,800	NP
Pregnancy	14–18 yr	1.2	8	30	NP	5.0	NP	3.0	10	460–920	2,300	2,800	NP
	19–30 yr	1.3	10	30	NP	5.0	NP	3.0	10	460–920	2,300	2,800	NP
	31–50 yr	1.3	10	30	NP	5.0	NP	3.0	10	460–920	2,300	2,800	NP
Lactation	14–18 yr	1.4	8	45	NP	5.0	NP	3.0	10	460–920	2,300	3,200	NP
	19–30 yr	1.5	10	45	NP	5.0	NP	3.0	10	460–920	2,300	3,200	NP
	31–50 yr	1.5	10	45	NP	5.0	NP	3.0	10	460–920	2,300	3,200	NP

Abbreviations: AI, adequate intake; BM, amount normally received from breast milk; B/F, amount in breast milk and food; EAR, estimated average requirement; RDI, recommended dietary intake; NP, not possible to set – may be insufficient evidence or no clear level for adverse effects; UL, upper level of intake

[a] 920 mg sodium/day is equivalent to 40 mmol/day; 2,300 mg/day sodium is equivalent to 100 mmol/day

[b] Intake of manganese beyond that normally found in food and beverages could represent a health risk, but there are insufficient data to set a UL

[c] A level of no more than 1,600 mg sodium/day (70 mmol) is recommended for older, overweight hypertensives and for those wishing to maintain low blood pressure over the lifespan

[d] For potassium, supplements should be taken only under medical supervision

APPENDIX I

TERMS OF REFERENCE, MEMBERSHIP OF WORKING PARTY AND EXPERT REVIEWERS

TERMS OF REFERENCE

The Working Party developed the NRVs with input from many expert reviewers, in keeping with the following terms of reference established by the NHMRC.

In developing a set of new recommendations for Australia and New Zealand, the Working Party will:

- Oversee the review of the 1991 ***Recommended dietary intakes for use in Australia*** adopted as the current New Zealand RDIs;
- Ensure that the recommendations are based on best available scientific evidence;
- Base the review on a consideration of the processes and recommendations of the recent revision in the United States:Canadian Dietary Reference Intakes taking into account any unique aspects of the populations in Australia and New Zealand including environmental, geographical, physiological, ethnic and cultural factors of both countries;
- Consider new scientific evidence and other recent recommendations from countries such as the UK, the European Union countries or FAO:WHO;
- Follow processes and standards acceptable to the Commonwealth Department of Health and Ageing, the New Zealand Ministry of Health, including its obligations under the Treaty of Waitangi, and the National Health and Medical Research Council, including liaison with SIGNAL; and
- Report to the Commonwealth Department of Health and Ageing (Population Health Division) and to the New Zealand Ministry of Health through the Health Advisory Committee and the National Health and Medical Research Council.

MEMBERS OF THE WORKING PARTY

Dr Katrine Baghurst (Chair)
CSIRO Health Sciences and Nutrition, Adelaide

Ms Elizabeth Aitken
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We are also grateful for the help of Ms Letitia White of Commonwealth Department of Health and Ageing and Dr Ruth Richards and Ms Mary-Louise Hannah of the NZ Ministry of Health during the process.

EXPERT REVIEWERS

The following people undertook from one to three expert reviews of nutrients according to the pro-forma included in the Evidence Appendix. The expert reviews were used by the Working Party in their decision process but the Working Party takes final responsibility for the recommendations. We are very grateful for the input of the following reviewers:

Dr Jane Allen
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We are grateful to the New Zealand Government for funding and making available two expert reviews of selenium and iodine (Thomson & Patterson 2001, Thomson 2002) as part of the review process.

We are also grateful to the Australian Nutrition Trust for funding and making available three evidence-based reviews of the selenium, calcium and vitamin D recommendations from several overseas countries (Flight & Baghurst 2003a,b,c) and for funding the nutrient modelling exercise that was also used as a cross-check for the recommendations relating to the balance of macro- and micronutrients. We also thank Dr Peter Baghurst of the Women's and Children's Hospital, Adelaide and Ms Sally Record of CSIRO Health Sciences & Nutrition for assisting with the dietary modelling, Dr Jason Armfield of the University of Adelaide for additional assistance with the fluoride reference values and Dr Erika Turkstra and Dr Peter Abbott from FSANZ for specialist discussions on the ULs.

APPENDIX 2

PROCESSES FOR PREPARING NUTRIENT REFERENCE VALUES

THE ASSESSMENT PROCESS

Reviewers completed a pro-forma that asked them to assess the suitability of the US:Canadian DRI recommendations for adoption in Australia and New Zealand, taking into consideration:

- the completeness and currency of the evidence base
- the interpretation of the evidence
- the selection of indicators for estimating requirements
- the justifiability of recommendations for various age and gender categories
- whether the needs of special groups were considered, including vegetarians, formula-fed versus breast-fed babies, cultural and racial groups, cigarette smokers, oral contraceptive users, those with high alcohol use or drug use, athletes, tropical dwellers or any other special group
- interactions with other nutrients or non-nutrients including the issue of bioavailability
- whether the effect of other factors had been considered (socio-economic status of study populations, customary intake of other competing nutrients or interfering/enhancing factors, lifestyle characteristics such as physical labour, prevalence of disease, climatic effects etc)
- whether dietary patterns of Australia and New Zealand were sufficiently different from those of the US:Canada to affect any of the recommendations (particularly relevant to the AI and AMDR recommendations)
- whether the UL was adequately addressed and whether it was appropriate for Australia and New Zealand
- whether there was evidence for a protective effect for chronic disease at levels of intake higher than RDI levels of intake
- whether there was evidence for a chronic disease-promoting effect of higher than RDI levels
- whether they had any other considerations that they wished to raise that would affect recommendations for Australia and New Zealand
- recommendations from other countries such as the UK, European countries or bodies such as the FAO:WHO or European Commission.

They were asked to provide an evidence-based assessment of the key papers used in the US:Canadian DRI review to derive the recommendations and to provide an analysis of any key missing papers or key papers published since the DRI review of that nutrient, using the NHMRC levels of evidence (see below) where possible or relevant.

Finally, they were asked to state whether they thought that Australia and New Zealand should adopt, adopt with minor changes, adopt with substantial changes, or reject, the US and Canadian recommendations in terms of their suitability for use in Australia and New Zealand, and to summarise their overall recommendations.

The expert reviews and recommendations together with the US:Canadian DRI reviews and those of other countries and health bodies were then considered by members of the Working Party who made the recommendations contained herein. The evidence tables and rationales for variation from the recommendations of the US:Canadian DRI reviews have been published separately as an Evidence Appendix to this report.

THE EVIDENCE BASE

There are several initiatives underway around the world to develop an evidence-based approach to nutrition and health issues. This has generally been in response to the need for proof in relation to health claims for food components (ANZFA 2000, Codex Alimentarius Commission 2000, Truswell 2001, US FDA 1999). A set of proposed levels of evidence for food or health claims has been developed by Food Standards Australia and New Zealand (formerly Australian New Zealand Food Authority), which is similar to, but somewhat broader in scope than, the set of NHMRC levels of evidence which was primarily designed for the development of clinical guidelines.

It was felt that the 1999 NHMRC designation of levels of evidence for clinical practice was applicable to assessing the evidence base for the development of the NRVs. Although the NHMRC system of evidence assessment has flexibility in the assignment of evidence levels to accommodate the type of question being asked (eg whether the question relates to the effectiveness of intervention or prevalence), a single set of evidence levels was used as the basis of the evidence assessment for clarity (see below).

The NHMRC's Levels of Evidence:	
I	Evidence obtained from a systematic review of all relevant randomised controlled trials.
II	Evidence obtained from at least one properly designed randomised controlled trial.
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.
IV	Evidence obtained from case series, either post-test or pre-test/post-test.

Source: *A Guide to the Development, Implementation and Evaluation of Clinical Practice Guidelines* (NHMRC 1999).

There are six levels of evidence. Level I is based on a systematic review of all relevant RCTs. Level II is based on evidence obtained from at least one properly designed RCT. With the possible exception of calcium, there are few Level I or Level II nutrient intervention trials that assess adequacy of nutrient intake in relation to deficiency states, although a number of nutrient-supplement trials have been undertaken in relation to chronic disease aetiology.

Some of the studies used to set nutrient requirements fall within Level III or Level IV, that include cohort studies, case-control studies and comparative ecological studies with historical controls or case series. However, much of the evidence comes from animal or human experimental studies that do not fall within these categories, or observational or cross-sectional survey data (eg all the recommendations for infants aged 0–6 months are based on the composition of milk from healthy mothers and a significant amount of the evidence for the UL comes from individual case reports of excessive intakes related to accidentally high intakes or special conditions such as parenteral feeding).

The NRVs were developed from a process of comprehensive, rather than systematic, review of the literature. A summary of the search strategies and key evidence used to set recommendations is provided in the Evidence Appendix.

The NHMRC states that "a decision should be made about what is feasible and appropriate in a given situation and the extent to which reasonable standards have been met by the available body of evidence". Although the NRVs are evidence-based where possible, there are generally very limited data on which to base recommendations. Life-stage and gender were considered to the extent possible

during assessment of the literature, but for many nutrients and for many age, gender and life-stage categories, requirements had to be estimated from one category on the basis of metabolic body weight, energy requirements, potentially decreased absorptive capacity, activity levels, additional needs for fetal growth or production of breast milk etc rather than being derived directly from experimental data.

Apart from studies of frank deficiency disease, few studies address the effects of inadequate intake on specific health indicators. While the recommendations are often given as single rounded numbers, it is acknowledged that these values may imply a precision not fully justified by the available human data. Nevertheless, the values recommended represent our best attempt to identify the requirements of the various age, gender and life-stage groups.

It is also recognised that the requirements for some nutrients can be affected by the intake of other nutrients and that health outcomes are often the result of an interplay between various nutrients (and/or other non-nutritional factors), rather than the effect of any single nutrient. Where known interactions exist, these have been taken into account in assessment of the data.

In his introduction to the publication of the 1981–1989 RDIs for Australia (Truswell et al 1990) Truswell wrote

No one who hasn't been responsible for producing RDI figures can realise how short we are of adequate original, numerical data. As we worked through 21 nutrients in 9 years, time and again we have said "we just don't know the answer to that question", or "if only several countries would collaborate in research to give us a proper picture of the distribution of numbers about that" and, of course, "what a pity we have no Australian (New Zealand) data on this".

In the 20 or so years since the previous RDIs were determined, new studies have been added to the data base. However, the available numerical data remain extremely limited for most nutrients, such that for some, we are forced to rely on one or two limited studies from which to derive the estimates. The limitations on data are particularly obvious for infants, children and adolescents, as most experimentation is carried out on adult populations. These limitations need to be borne in mind when applying the resulting reference values to the assessment of dietary adequacy for individuals or groups.

THE CONSULTATION PROCESS

After the Working Party had made its initial deliberations, the draft recommendations were submitted for public consultation in Australia and New Zealand between December 2004 and March 2005, allowing three months for consultation. Notification in Australia was published in the *Commonwealth Government Gazette* and on the NHMRC website as well as through direct notification of key bodies. The NZ Government ensured notification of key bodies and the public.

Copies of draft documents and supporting information were made available free of charge from the Office of NHMRC and on the NHMRC website. In addition, notices were included in other publications and media such as newspapers and radio. During the submission period, two workshops were held in each of Australia and New Zealand with health professionals, representatives of the food industry and end-users. They included consideration of optimal methods for dissemination, including electronic access. Each of these workshops was attended by 40–60 stakeholders.

Sixty-four submissions were received and considered by the Working Party in May 2005. The document was amended where relevant in response to the submissions, independently reviewed and assessed against the NHMRC criteria for guideline development. The document was technically edited before final submission to the NHMRC and Australian and New Zealand Governments for approval.

DISSEMINATION AND IMPLEMENTATION

Upon endorsement of the *Nutrient Reference Values for Australia and New Zealand* by the NHMRC, the Australian Government Department of Health and Ageing and the New Zealand Ministry of Health will manage the adoption of the NRVs through appropriate Government processes in their respective countries.

Media releases, including a question and answer section, will be issued in Australia and New Zealand. The main report, evidence appendix and summary report will be made available on the NHMRC and Ministry of Health websites.

Notification of availability of the final report and details of how to access both electronic and hard copies will be sent to all expert reviewers, those who made submissions regarding the December 2004 consultation draft and attendees at the consultation workshops in both countries.

The Australian Government Department of Health and Ageing and the New Zealand Ministry of Health will then:

- advertise release of, and prepare articles about, the *Nutrient Reference Values for Australia and New Zealand* in their own newsletters ands relevent publications and those of various stakeholder groups
- prepare presentations on the new NRVs for conferences and seminars
- introduce a program of progressive review and updating of existing nutrition documents and health professional education materials that include, or are based on, the NRVs
- advocate the use of the NRVs outside the lead ministries, including to the wider health sector, other government agencies, the education sector, non-government organisations, food industry groups, dietitians and nutritionists.

In keeping with the NHMRC publications review policy, it is expected that the process of reviewing the NRVs will commence within five years of endorsement of the publication by the NHMRC.

SUBMISSIONS IN THE CONSULTATION PROCESS

From Australia

Professor Cres Eastman	Institute of Clinical Pathology and Medical Research
Professor Stewart Truswell	University of Sydney
Dr Stephen Corbett	Sydney West Area Health Service
Ms Jen Savenake	Tasmanian Department of Health and Human Services
Mr Peter Liu	DSM Nutritional Products Australia Pty Ltd
Ms Barbara Eden	National Heart Foundation of Australia
Ms Gemma McLeod	Fremantle Hospital
Mrs Jenni Cooper	H.J. Heinz Company Australia Ltd
Ms Alison Stewart	Southern Health
Dr Beverley Wood	-
Mr Philip Juffs, Ms Helen Porteous	Princess Alexandra Hospital
Ms Trish Guy	Sanitarium Health Food Company
Ms Adrienne Mouritz	-
Mr Bill Shrapnel	Shrapnel Nutrition Consulting Pty Ltd

Dr Jeanette Fielding	Wyeth Australia Pty Ltd
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Ms Ingrid Coles-Rutishauser	-
Dr Trevor Beard	Menzies Research Institute
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Dr David Roberts	Australian Food And Grocery Council
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Dr Denise Robinson	NSW Health
Ms Judith Myers	Royal Children's Hospital
A/Professor David Colquhoun	The University of Queensland
Ms Wendy Morgan	Innovations and Solutions
Mr Terry Slevin	The Cancer Council Australia
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Ms Helen Wallwork	New Zealand Dietetic Association
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A/Professor Murray Skeaff	University of Otago

From the United Kingdom

Mr Stephen Taylor	Frenchay Hospital

APPENDIX 3

GLOSSARY AND ABBREVIATIONS

ABS	Australian Bureau of Statistics
ADP	Adenosine diphosphate
AMD	Age-related macular degeneration
Adverse effect	Any significant alteration in the structure or function of the human organism or any impairment of a physiologically important function that could lead to a health effect that is adverse.
AI	Adequate intake
ALA	Alpha-linolenic acid
AMDR	Acceptable macronutrient distribution range
ANZFA	Australia New Zealand Food Authority (now known as FSANZ)
ATBC	Alpha-tocopherol, beta-carotene cancer prevention trial
ATP	Adenosine triphosphate
ATPO	(S)-2-amino-3-[5-tert-butyl-3-(phosphonomethoxy)-4-isoxazolyl] propionic acid
AUS	Australia
Bioavailability	The accessibility of a nutrient to participate in metabolic and/or physiological processes including considerations of intestinal absorption
BMD	Bone mineral density
BMI	Body mass index; wt/ht^2 (kg/m^2)
BMR	Basal metabolic rate
Ca	Calcium
CARET	Carotene and Retinol Efficacy Trial
CDHAC	Commonwealth Department of Health and Aged Care (now known as Commonwealth Department of Health and Ageing)
CHD	Coronary heart disease
CI	Confidence interval
CNS	Central nervous system
CoA	Coenzyme A
COMA	Committee on Medical Aspects of Food Policy
CSFII	Continuing Survey of Food Intakes by Individuals
CSIRO	Commonwealth Scientific and Industrial Research Organisation
CV	Coefficient of variation
CVD	Cardiovascular disease
D-A-CH	D(Germany)- A (Austria) –CH (Switzerland)
DART	Diet and Reinfarction Trial
DASH	Dietary approaches to stop hypertension
DEER	Desirable estimated energy requirement
DFE	Dietary folate equivalents

DHA	22:6 docosahexaenoic fatty acid
DLW	doubly-labelled water
DNA	Deoxyribonucleic acid
DPA	22:5 docosapentaenoic fatty acid
DRI	Dietary reference intakes
DSIR	Department of Scientific and Industrial Research
EAR	Estimated average requirement
EC	European Commission
EER	Estimated energy requirement
EERM	Estimated energy requirement for maintenance
EGRAC	Erythrocyte glutathione reductase activity coefficient
EPA	20:5 eicosapentaenoic fatty acid
EU	European Union
g	grams
GISSI	Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico
FAO	Food and Agricultural Organization of the United Nations
FAD	Flavin adenine dinucleotide
Fe	Iron
FMN	Flavin mononucleotide
FNB:IOM	Food and Nutrition Board: Institute of Medicine
FSANZ	Food Standards Australia New Zealand
GP_X	Selenium-dependent glutathione peroxidases
HDL	High density lipoprotein
HOPE	Heart outcomes prevention evaluation
IHD	Ischaemic heart disease
IF	Intrinsic factor
IZiNCG	International Zinc Nutrition Consultative Group
Kashin-Beck	Human cartilage disease found in low selenium intake areas in Asia
kg	kilogram
kJ	kilojoule
LA	Linoleic acid
LC(n-3)	Long chain (n-3)
LDL	Low density lipoprotein
LINZ	Life in New Zealand
LOAEL	Lowest observed adverse effect level
MCV	Mean cell volume
Mg	Magnesium

mg	milligram
Mg-ATP	Magnesium-adenosine triphosphate
µg	microgram
MJ	Megajoule
MMA	Methylmalonic acid
Mn	Manganese
MOH	Ministry of Health
Mo	Molybdenum
MRFIT	Multiple Risk Factor Intervention Trial
MTHF	Methylenetetrahydrofolate
MTHFR	Methylenetetrahydrofolate reductase
Na/K	Sodium/potassium
NAD	Nicotinamide adenine dinucleotide
NADP	Nicotinamide adenine dinucleotide phosphate
ng	Nanograms
NE	Niacin equivalents
NHMRC	National Health and Medical Research Council
NHANES	National Health and Nutrition Examination Survey
Ni	Nickel
NNS	National Nutrition Survey (of Australia or New Zealand as indicated in the text)
NOAEL	No observed adverse effect leve
NRV	Nutrient Reference Values
NP	Not possible to set (due to insufficient evidence or no clear level for adverse effects)
NSP	Non-starch polysaccharide
NTD	Neural tube defect
NZ	New Zealand
P	Phosphorus
PAL	Physical activity level
PEM	Protein energy malnutrition
P*i*	Serum phosphorus (inorganic phosphate)
PIVKA	Proteins induced by vitamin K absence
PLP	Pyridoxal phosphate
PMP	Pyridoxamine phosphate
PN	Pyridoxine
PNP	Pyridoxine phosphate
PT	Prothrombin time
PTH	Parathyroid hormone

PUFA	Polyunsaturated fatty acids
RDI	Recommended dietary intake
RE	Retinol equivalents
RNA	Ribonucleic acid
RR	Relative risk
RS	Resistant starch
SD	Standard deviation
SDT	Suggested dietary target
T_4	Thyroxine
α-TE	alpha-tocopherol equivalent
TEE	Total energy expenditure
TFA	*Trans* fatty acid
THF	Tetrahydrofolate
TNF	Tumour necrosis factor
$T_{rx}R$	Thioredoxin reductases
UF	Uncertainty factor
UK	United Kingdom
UL	Upper level of intake
US	United States of America
VLDL	Very low density lipoprotein
WHO	World Health Organization of the United Nations
Zn	Zinc

The National Health and Medical Research Council

The National Health and Medical Research Council (NHMRC) was established in 1936 and is now a statutory body within the portfolio of the Australian Government Minister for Health and Ageing, operating under the *National Health and Medical Research Council Act 1992 (*NHMRC Act*)*. The NHMRC advises the Australian community and the Australian Government, and State and Territory governments on standards of individual and public health, and supports research to improve those standards.

The NHMRC Act provides four statutory obligations:

- to raise the standard of individual and public health throughout Australia;
- to foster development of consistent health standards between the states and territories;
- to foster medical research and training and public health research and training throughout Australia; and
- to foster consideration of ethical issues relating to health.

The NHMRC also has statutory obligations under the *Prohibition of Human Cloning Act 2002* (PHC Act) and the *Research Involving Human Embryos Act 2002* (RIHE Act).

The activities of the NHMRC translate into four major outputs: health and medical research; health policy and advice; health ethics; and the regulation of research involving donated IVF embryos, including monitoring compliance with the ban on human cloning and certain other activities. A regular publishing program ensures that Council's recommendations are widely available to governments, the community, scientific, industrial and education groups. The Council publishes in the following areas:

- Aged Care
- Blood and Blood Products
- Cancer
- Cardiovascular Health
- Child Health
- Clinical Practice Guidelines – Standards for Developers – Topics
- Communicable Diseases, Vaccinations and Infection Control
- Diabetes
- Drug and Substance Abuse
- Environmental Health
- Ethics in Research–Animal
- Ethics in Research–Human
- Genetics and Gene Technology
- Health Procedures
- Health Promotion
- Human Cloning and Embryo Research
- Indigenous Health
- Injury including Sports Injury
- Men's Health
- Mental Health
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