Methodological Framework for the Review of Nutrient Reference Values

V3.5 October 2025

date of publication: 2025

authorship: National Health and Medical Research Council

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ISBN number

preferred citation for the guideline publication: NHMRC (2025) Methodological Framework for the Review of Nutrient Reference Values

Version

Year	Version	Comment
2015	v1.0	Australian Department of Health contracted Nous Consulting to develop a comprehensive report on the scoping and methodology underpinning the advice that future reviews of nutrients should be targeted. *Under this framework, NHMRC's role is through third party guideline approval.*
2020	v2.0	Updated during the pilot period to align with methodological updates and changes to the governance structure. *Under this framework, NHMRC's role is as project manager and author.*
2023	V3.0	Updated following feedback from evidence reviewers and the Steering Group Advisory Committee meeting on the 8 March 2023.
2023	V3.1	Updated following feedback from Steering Group Advisory Committee on the 21 November 2023.
Feb 2024	V3.2	Steering Group Advisory Committee comments incorporated
April 2024 & June 2024	V3.3	Steering Group Advisory Committee comments incorporated
May 2025	V3.4	Preparing for public consultation. Steering Group Advisory Committee comments incorporated, updates to age groupings and reference weights, upper level (UL) and uncertainty factor (UF) methodology, diagrams added with permission from authors, other edits for better clarity
October 2025	V3.5	Version for public consultation

Contents

Chapter 1: Introduction

1.1 Background

Nutrient Reference Values (NRVs) are a set of recommendations that estimate the nutritional requirements of population groups and/or individuals, based on the available scientific evidence (NHMRC 2006). NRVs detail the recommended amounts of macronutrients and micronutrients required for different ages and sexes to maintain nutritional adequacy and avoid toxicity and chronic disease. They are also used by a broad range of stakeholders for dietary modelling and/or food labelling and food formulation.

The 2006 NRVs for Australia and New Zealand (Aotearoa) were developed as a joint initiative of the Australian National Health and Medical Research Council (NHMRC), Australian Government Department of Health, Disability and Ageing (Department) and the New Zealand Ministry of Health (NZ Ministry). The 2006 NRVs apply to the general, community-dwelling population in Australia and New Zealand. They have not been developed to meet the specific nutritional requirements of individuals with various diseases or conditions such as pre-term infants, some people with specific genetic profiles or others requiring specific clinical advice and treatment.

The 2006 NRVs form an essential component of the suite of Australian and New Zealand public health nutrition resources. The relationship between these resources and how they each contribute to determining and setting public health nutrition recommendations is outlined in Figure 1.1.

In 2015, the Department and the NZ Ministry developed a methodological framework to underpin future reviews of priority NRVs. The methodological framework was piloted on a review of select fluoride and sodium NRVs, culminating in revised NRV recommendations for fluoride in November 2016, and sodium in July 2017.

In March 2018, the Department commissioned NHMRC to continue the priority driven review of nutrients.

This framework updates the 2015 methodological framework and includes developments in evidence review methods, international approaches to NRV development, and lessons learnt from NHMRC's ongoing NRV reviews. See Appendix A. for a more detailed timeline of the framework development.

1.2 Scope and objectives

This framework outlines the principles and processes underpinning the review of NRVs for Australia and New Zealand. This includes:

- identifying and prioritising NRVs for review
- scoping activities, including
    - assessment of the suitability of existing international NRVs for adoption or adaptation

    - appropriate methods for assessing micronutrient intake, status and relevant health outcomes
- reviewing the evidence for physiological requirements and the intake-status-health relationship to inform NRV development
- assessing the certainty of evidence
- estimating nutritional requirements based on the evidence
- developing revised NRV recommendations for Australia and New Zealand through a documented evidence-to-decision process.

For a comprehensive understanding of the process, this framework should be read in conjunction with the supplementary information sources referenced throughout – in particular, the detailed EURRECA—Evidence-Based Methodology for Deriving Micronutrient Recommendations upon which it is based (Dhonukshe-Rutten et al. 2013).

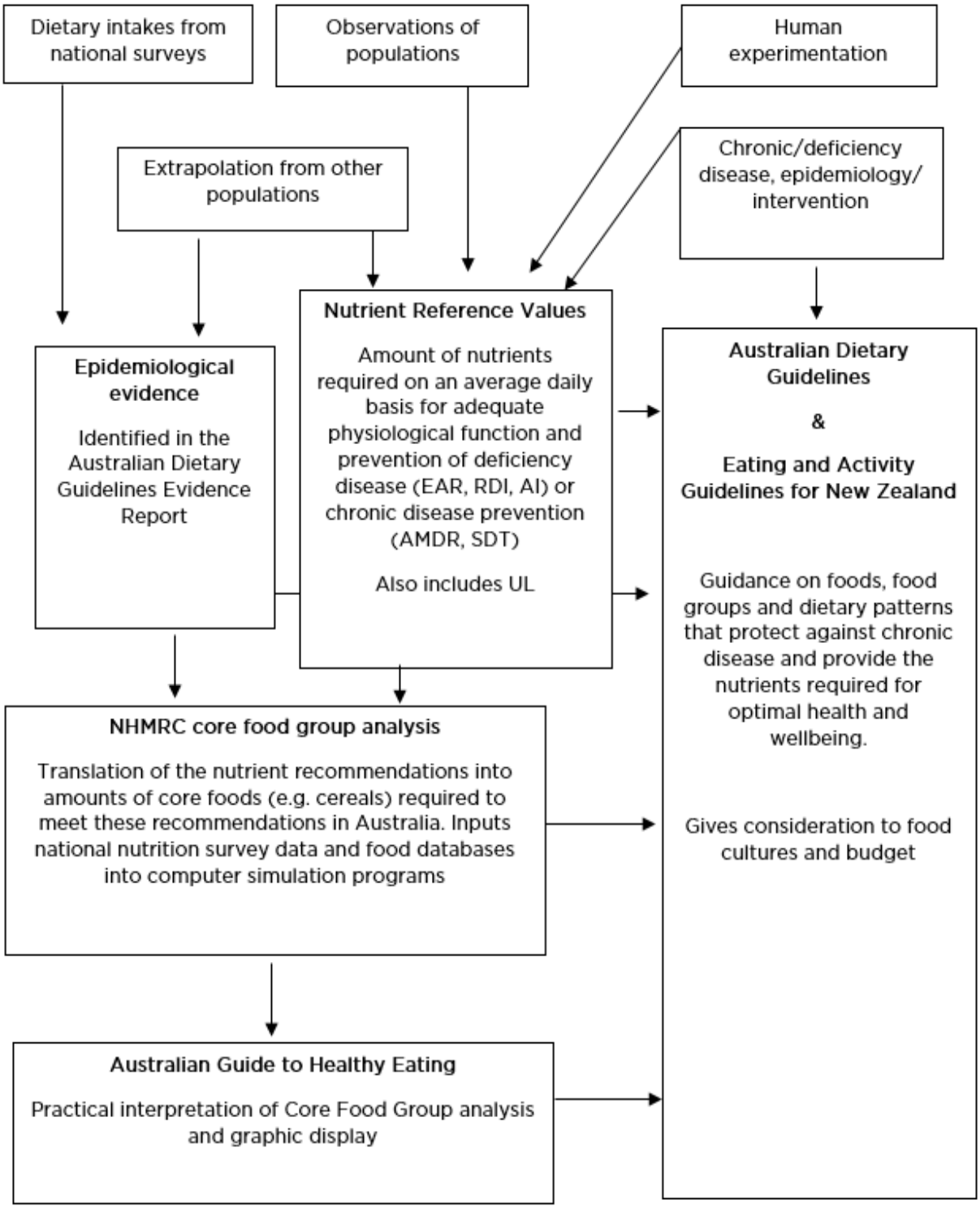

Figure 1.1 Public health nutrition resources in Australia and New Zealand

1.3 Process overview

An overview of the NRV update process is outlined in Figure 1.2 below. For more detailed information on any topic, refer to the relevant chapters outlined in the diagram.

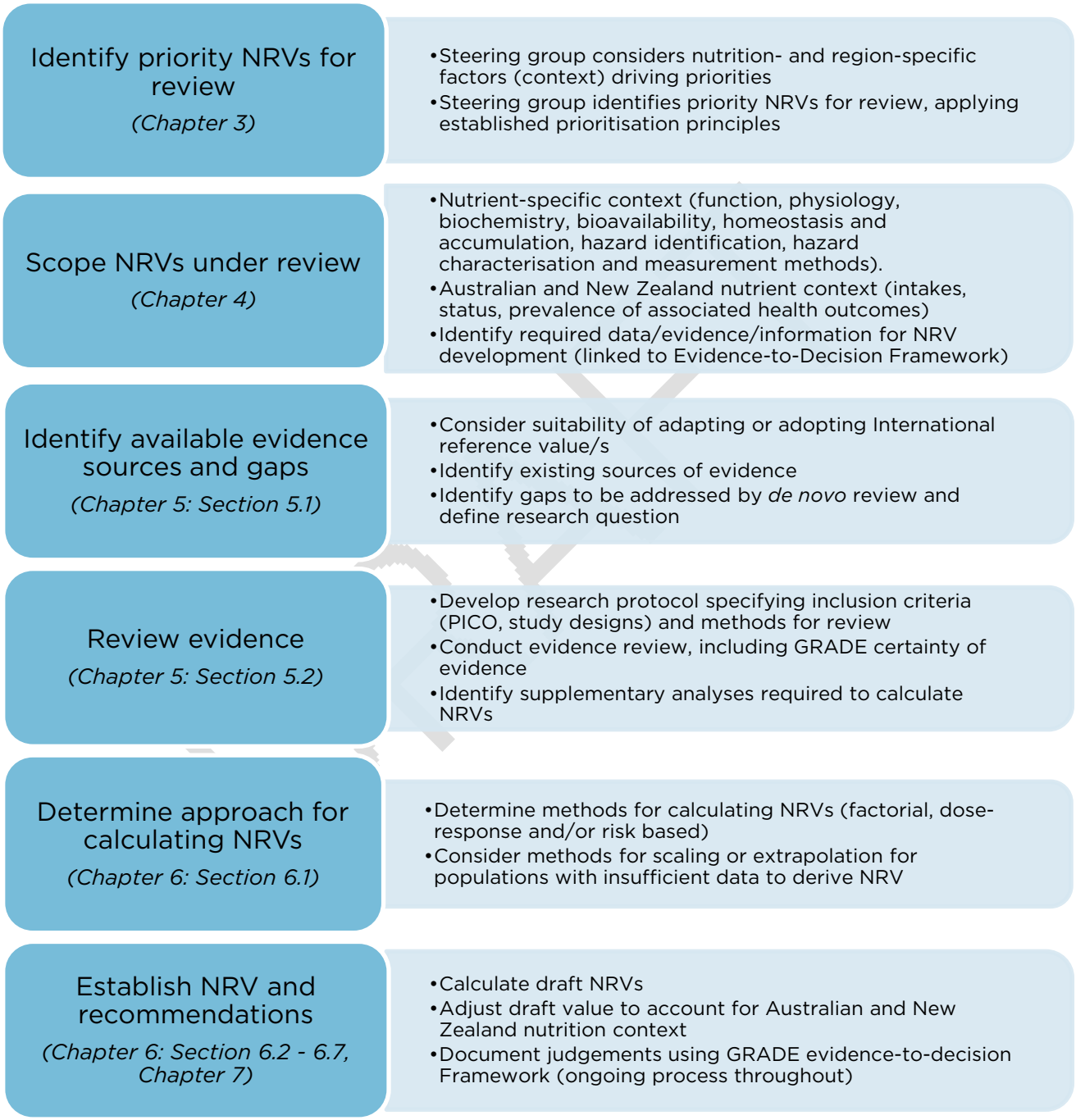

Figure 1.2 Procedural flowchart for NRV recommendation development

1.4 Key reference sources

There is an increasing focus on harmonising international efforts in NRV development, to maximise available resources and achieve efficiencies. Accordingly, this framework has been developed with reference to the following documents published by key international bodies:

- EURopean micronutrient RECommendations Aligned (EURRECA):
    - *EURRECA's Approach for Estimating Micronutrient Requirements (Matthys et al. 2011)*
    - *EURRECA—Principles and Future for Deriving Micronutrient Recommendations (Claessens et al. 2013)*
    - *EURRECA – Evidence-Based Methodology for Deriving Micronutrient Recommendations (Dhonukshe-Rutten et al. 2013)*
    - *EURRECA—Framework for Aligning Micronutrient Recommendations (Van't Veer et al. 2013)*
- US National Academies of Sciences, Engineering and Medicine:
    - *Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease (NASEM 2017)*
    - *Harmonization of Approaches to Nutrient Reference Values: Applications to Young Children and Women of Reproductive Age (NASEM 2018)*
    - *Defining Populations for Dietary Reference Intake Recommendations: A Letter Report (NASEM 2022)*
    - *Using Systematic Reviews to Support Future Dietary Reference Intakes (NASEM 2023)*
- European Food Safety Authority:
    - *Guidance for establishing and applying tolerable upper intake levels for vitamins and essential minerals (EFSA Panel on Nutrition Novel Foods and Food Allergens et al. 2024a)*
    - *Scientific Opinion on principles for deriving and applying Dietary Reference Values (EFSA Panel on Dietetic Products Nutrition and Allergies 2010)*
    - *Use of the benchmark dose approach in risk assessment (EFSA Scientific Committee et al. 2017)*
- Nordic Nutrition Recommendations 2022 - *The Nordic Nutrition Recommendations 2022 - principles and methodologies (Christensen et al. 2020)*

These documents present a detailed overview of the NRV development process and are referred to throughout the methodological framework as supplementary information sources. Complete references are available in the References section.

NHMRC guidelines must meet the NHMRC Standards for Guidelines (NHMRC 2016). As part of evidence informed guidelines NHMRC uses the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) approach. GRADE provides a structured framework for assessing the certainty of evidence and developing recommendations. The Framework uses the following documents on evidence synthesis and guideline development:

- NHMRC Guidelines for Guidelines (2016)
- Cochrane Handbook for Systematic Reviews of Interventions, Version 6.4 (updated August 2023) (Higgins et al. 2019)
- GRADE Book (Neumann et al. 2025)/GRADE Handbook (The GRADE Working Group 2024) and the Journal of Clinical Epidemiology GRADE Guidance series[1]
- WHO handbook for guideline development resources (WHO 2014).
- WHO Handbook for adaptation and guideline contextualisation (WHO 2023c)

1.5 Governance

1.5.1 Steering Group

A Steering Group, comprising representatives from NHMRC, the Department and NZ Ministry, is responsible for the strategic leadership, funding and resourcing elements of NRV updates. This includes priority setting for reviews of the NRVs and ensuring that NRVs are updated in a timely manner and reflect current scientific evidence.

1.5.2 NHMRC

Under the *National Health and Medical Research Council Act 1992* (NHMRC Act), the CEO of NHMRC is responsible for inquiring into and issuing guidelines on matters relating to the improvement of health and the prevention, diagnosis and treatment of disease. The CEO is advised by the Council of NHMRC (Council) and the various NHMRC Principal and Working Committees established under the NHMRC Act.

The CEO, Council and Committees are supported by the Office of NHMRC, who have responsibility for the ongoing project management of NRVs reviews.

1.5.3 Council and committees

1.5.3.1 Council of NHMRC

The Council of NHMRC is established under the NHMRC Act to advise the CEO and perform functions conferred on it. Revised NRVs will be reviewed by Council prior to public consultation. The final NRVs will also be presented to Council for consideration and to seek Council's recommendation for release by the CEO.

[1] https://www.sciencedirect.com/special-issue/10F8V3S0J7V

1.5.3.2 Section 39 Committees

The review of NRVs for Australia and New Zealand is supported by various committees established under Section 39 of the NHMRC Act. This includes an overarching Steering Group Advisory Committee (the Advisory Committee) and nutrient-specific expert working groups.

Committee membership aims to achieve representation across Australia and New Zealand, and to include a balance of early and mid-career experts to allow for continuity and succession planning.

1.5.3.2.1 Steering Group Advisory Committee

The role of the Advisory Committee is to provide independent technical expertise and strategic advice to NHMRC, and the Steering Group more broadly. It also guides the work of the nutrient-specific expert working groups.

Membership of the Advisory Committee aims to achieve representation across Australia and New Zealand, and comprises individuals with technical expertise in macronutrients, micronutrients, toxicology, public health, end user needs, nutrition methodology, research, chronic disease and/or nutrition.

1.5.3.2.2 Nutrient-specific expert working groups

For each NRV review, a nutrient-specific expert working group is established to provide advice and guidance to NHMRC on the review of the evidence, and support development of nutrient-specific NRVs in consultation with the Advisory Committee.

Membership of the expert working groups is representative of Australia and New Zealand and comprises individuals with expertise in the key areas of nutrition science, food and dietary patterns, population health, macronutrients, micronutrients, toxicity, end user needs, dietary modelling and review methodology. Expertise in Indigenous health (specifically Aboriginal and Torres Strait Islander, Māori and Pacific populations) and consumer issues should also be represented. Additional expertise may be sought where knowledge outside the composition of the expert working groups is required (i.e. public health, genomics, microbiology, agricultural science).

1.5.4 Governing standards for guideline development

The *2016 NHMRC Standards for Guidelines* and accompanying *Guidelines for Guidelines* handbook have been developed to support the production of high-quality guidelines that meet the 2016 NHMRC Standards. They are applicable to all guidelines containing recommendations for clinical practice, public and environmental health including the development of NRVs.

The Guidelines for Guidelines Handbook is advice designed to help guideline developers produce high quality guidelines that meet the 2016 NHMRC Standards for Guidelines.

1.5.5 Independent third-party review processes

1.5.5.1 Methodological review

For adopting/adapting international NRVs or the evidence underpinning them, seek expert methodological advice early in the scoping phase to help you decide on the best approach.

For evidence evaluations commissioned by NHMRC, independent methodological review is undertaken on both the research protocol and evidence evaluation report prior to finalisation. Methodological review assesses the rigour of the evidence review methods and examines whether the review has been undertaken in accordance with the specified methods. It also evaluates the quality and comprehensiveness of reporting and provides advice about whether the review's conclusions are supported by the body of evidence.

To assess the methodological rigour and reporting quality of systematic reviews, methodological review should apply a range of established tools, with an emphasis on tools that have been scientifically tested and validated. Examples of such tools include:

- A MeaSurement Tool to Assess systematic Reviews (AMSTAR II) (Shea et al. 2017)
- Risk of Bias in Systematic Reviews (ROBIS) (Whiting et al. 2016)
- Methodological Expectations of Cochrane Intervention Reviews (MECIR) guidance (which includes the use of GRADE) (Higgins et al. 2023)
- Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance, including the PRISMA 2020 Checklist (Page et al. 2021).

1.5.5.2 Expert review

Before finalisation of the guidelines, NHMRC undertakes independent expert review of the draft recommendations. The purpose of the independent expert review is to obtain feedback from individuals not otherwise involved in the guideline's development. Independent review will assess whether the appropriate evidence has been considered in developing the proposed NRVs, and whether the NRV recommendations accurately reflect the available scientific evidence. Reviewer's perspectives regarding the usability and acceptability of NRV recommendations, and consensus with international perspectives, is also of importance.

Independent expert review will be undertaken consistent with the NHMRC Guidelines for Guidelines.

1.5.6 Public consultation

The NHMRC Act requires that NHMRC undertake public consultation on draft guidelines before their final release, and that it consider any submissions received during consultation. Public consultation on proposed NRV recommendations will be undertaken prior to finalisation.

1.5.7 Managing interests

To ensure that decision making is free from bias or industry influence, members of the Advisory Committee and the Expert Working Groups will be required to adhere to NHMRC's *Policy on the Disclosure of Interests Requirements for Prospective and Appointed NHMRC Committee Members* and be consistent with NHMRC's Guidelines for Guidelines policy.

Declarations of interest are also sought from contractors prior to engagement, with any declared interests considered in accordance with NHMRC policies.

Chapter 2: Definition and summary of NRVs

2.1 Scope and applications of NRVs

The NRVs for Australia and New Zealand apply to the general, community dwelling population in Australia and New Zealand. They may not capture the specific nutritional requirements of individuals with various diseases or conditions such as pre-term infants, some people with specific genetic profiles or others requiring specific clinical advice and treatment.

The NRVs are developed to assist nutrition and health professionals assess the dietary requirements of individuals and groups. They may also be used by health professionals, researchers, policy makers, food legislators and the food industry for a range of purposes, including:

- Public health: used by policy makers, epidemiologists and researchers in the assessment, monitoring/surveillance and modelling of nutrient intake data to support the development and evaluation of diet-related health policies and guidelines
- Population sub-group health: used by dietitians and nutritionists to plan menus and by health professionals and researchers to assess the adequacy of nutrient intakes of groups in national, regional and other surveys
- Risk assessment: used for population group risk assessment of both nutrient deficiency and toxicity
- Regulation: used by Food Standards Australia New Zealand (FSANZ), the Therapeutic Goods Administration (TGA) and the NZ MoH for assessments underpinning regulatory decisions, including: (i) voluntary and mandatory food fortification (e.g. iodised salt in bread, thiamine and folic acid in wheat flour for bread making); (ii) food labelling standards and requirements; and (iii) nutrient supplements
- Food formulation: used by food manufacturers for formulation, fortification and product labelling as permitted by the Food Standards Code
- Individual health: used by health professionals (e.g. doctors, dietitians, nutritionists) for dietary planning and individual risk assessment
- Education and research: used in a range of education settings and academic research.

2.2 Overview of NRVs for Australia and New Zealand

The NRVs can be used to assess nutrient status or nutrient intake for individuals or populations. The most appropriate NRV to use varies depending on whether an assessment of individuals or groups is being conducted. NRVs fall into two broad categories, summarised in Table 2.1:

(i) Nutrient adequacy NRVs: aimed at maintaining function (adequate intake) and avoiding toxic effects

(ii) Chronic disease NRVs: aimed at optimising health and reducing chronic disease risk.

Table 2.1 Classification of Nutrient Reference Values (NRVs)

Nutrient Adequacy NRVs	Chronic Disease NRVs
Estimated Average Requirement (EAR)	Suggested Dietary Targets (SDT)
Recommended Dietary Intake (RDI)	Chronic Disease Risk Reduction (CDRR)
Upper Level of Intake (UL)	
Adequate Intake[2] (AI)	
Acceptable Macronutrient Distribution Range (AMDR)	

Each NRV is described in further detail in the Sections below. Whilst the various NRVs are expressed on a per day basis, they should apply to intakes assessed across a period of three to four days. This will allow for the determination of the actual average intake for each nutrient.

Where evidence allows, an EAR and RDI will be established to estimate nutritional requirements. In the absence of sufficient evidence, an AI will be calculated.

2.2.1 Estimated Average Requirement (EAR)

The EAR is a daily nutrient intake level estimated to meet the requirements of 50% of healthy individuals in the population for a particular life stage and/or sex.

Individuals: Applied to examine the probability that usual intake is inadequate.

Groups: Applied to estimate the prevalence of inadequate intakes within a population group.

2.2.2 Recommended Dietary Intake (RDI)

The RDI is a mean daily dietary intake[3] level that is sufficient to meet the nutrient requirements of nearly all (97.5%) healthy individuals of a particular life stage and/or sex.

Individuals: Applied to assess the intake of individuals. Usual intake at or above this level has a low probability of inadequacy.

Groups: Cannot be applied to assess intakes of groups.

[2] Adequate Intake describes current intake levels, not adequacy. Therefore, AI should not be relied upon to determine adequacy.

[3] The term 'mean daily dietary intake' refers to the usual intake for a population, or individual (RDI only), based on observations of mean nutrient intakes by a group of apparently healthy people who are maintaining a defined criterion of adequacy.

It is important to recognise that RDIs exceed the actual nutrient requirements of practically all healthy persons and are not synonymous with requirements. Although they provide a means of assessing the probability that individual members of a population are vulnerable to nutrient deficiency, RDIs cannot be used for the diagnosis of nutrient deficiency.

2.2.3 Upper Level of Intake (UL)

The relationship between level of nutrient intake and risk of adverse effects is non-linear (see Figure 2.1). The UL is the highest mean daily nutrient intake[4] level likely to pose no adverse (toxic) health effects to almost all individuals in the general population. As intake increases above the UL, the risk of toxic effects increases.

Individuals: Applied to determine an individual's risk of adverse effects from excessive nutrient intake.

Groups: Applied to determine a population's risk of adverse effects from excessive nutrient intake.

Where there is sufficient evidence, the UL is a NRV that is calculated based on toxicological adverse effects – that is, adverse events that occur at a distinct threshold that differentiates 'safe' and 'unsafe' intakes. To derive an UL that will be protective for the general population, an uncertainty factor (UF) can be applied (see section 6.3.1 to the reference point (RP). In general, the principles for the risk assessment of chemicals also apply to setting UL for nutrients. The risk assessment process includes hazard identification, hazard characterisation, intake assessment and risk characterisation. Where evidence is less certain, greater expert interpretation and judgement is required.

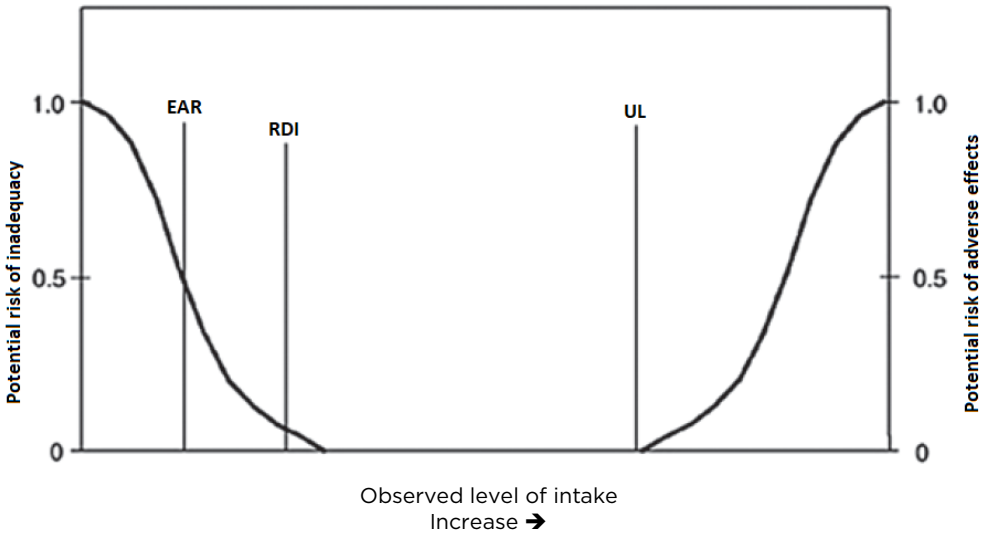

Figure 2.3 Relationship between risk of inadequacy and risk of adverse effects for nutrients (adapted from National Academy of Sciences (2018))

[4] The term 'mean daily nutrient intake' refers to the usual intake for a population, based on observations of mean nutrient intakes by a group of apparently healthy people who are maintaining a defined criterion of adequacy.

2.2.4 Adequate Intake (AI)

The AI is a mean daily nutrient intake[5] level, based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people. It is used when an EAR and RDI cannot be determined.

Individuals: Applied to determine the probability of inadequacy. Usual intake at or above this level has a low probability of inadequacy. When the AI is based on mean intakes of healthy populations, this assessment is made with less confidence.

Groups: Applied to determine the probability of inadequacy. Mean usual intake at or above this level implies a low prevalence of inadequate intakes. When the AI is based on mean intakes of healthy populations, this assessment is made with less confidence.

2.2.5 Suggested Dietary Target (SDT) and Chronic Disease Risk Reduction (CDRR)

The Suggested Dietary Target (SDT) refers to the average daily intake of nutrients from food and beverages that may contribute to a reduced risk of chronic disease. The SDT may be derived from either the mean or median of available intake data, depending on the strength and nature of the evidence. Where meta-analysis demonstrates a robust association between a nutrient and a primary health outcome, the SDT is typically based on the mean intake associated with the desirable health effect. Historically, SDTs in Australia and New Zealand have been set at the 90th percentile of intake.

The Chronic Disease Risk Reduction (CDRR) value represents the lowest level of intake for which there is sufficient strength of evidence to characterise a chronic disease risk reduction within an apparently healthy population (NASEM 2017). CDRRs may reflect either beneficial effects (e.g. increased fibre intake) or risk-reducing effects through decreased intake (e.g. reduced sodium) In line with international harmonisation efforts, this framework proposes the adoption of the CDRR approach for relevant nutrients

Application to individuals and population groups:

CDRR values are applied where a relationship between intakes of a nutrient and the chronic disease risk has been demonstrated. The suggested threshold value is based on evidence demonstrating at least moderate certainty of both a causal and an intake–response relationship between nutrient intake and chronic disease risk and is intended to inform recommendations for both individuals and population groups.

[5] The term 'mean daily nutrient intake' refers to the usual intake for a population, based on observations of mean nutrient intakes by a group of apparently healthy people who are maintaining a defined criterion of adequacy.

2.2.6 Acceptable Macronutrient Distribution Range (AMDR)

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.

2.3 International nutrient recommendations

The approach taken to categorising and naming nutrient recommendations for the NRVs for Australia and New Zealand is largely consistent with international approaches. Table 2.2 outlines the international approaches to nomenclature and classification of nutrient recommendations.

International nutrient recommendations have a range of potential applications in development of the Australian and New Zealand NRVs. This includes:

- as triggers for an NRV review and update, where other international reviews have identified new evidence and/or revised NRVs for a particular nutrient
- as potential sources of data on which to base NRV recommendations, including adapting or adopting NRVs set by other jurisdictions, or utilising systematic reviews undertaken by international bodies to inform development of Australian and New Zealand NRVs
- to benchmark draft NRV recommendations to explore consistency with contemporary NRV recommendations set by comparable international jurisdictions.

Table 2.2 Comparison of international nutrient terminology and categorisations

	Australia/ New Zealand	US-Canada	World Health Organization	UK (SACN)	European Food Safety Authority	EURRECA	Nordic Nutrition Recommendations
Values	***Nutrient Reference Values (NRV)***	*Dietary Reference Intake (DRI)*	*Human Vitamin and Mineral Requirements*	*Dietary Reference Values (DRV)*	*Dietary Reference Values (DRV)*	*Dietary Reference Values (DRVs)*	*Dietary reference value (DRV)*
Requirement	**Estimated average requirement (EAR)**	Estimated average requirement (EAR)	Estimated average requirement (EAR)	Estimated average requirement (EAR)	Average requirement (AR)	Estimated average requirement (EAR)	Average requirement (AR) provisional average requirement (Provisional AR)[6]
	Recommended dietary intake (RDI)	Recommended dietary allowance (RDA)	Recommended nutrient intake (RNI)	Reference nutrient intake (RNI)	Population reference intake (PRI)	Population reference intakes (PRI)	Recommended intake (RI)
	Adequate intake (AI)	Adequate intake (AI)	~	Safe intake (SI)	Adequate Intake (AI)	~	Adequate intake (AI)
Excess	**Upper level of intake (UL)**	Tolerable upper intake level (UL)	Upper tolerable nutrient intake level (UL)	Tolerable upper intake level (UL)	Tolerable upper intake levels (ULs) Safe level of intake when a UL cannot be established[7].	~	Tolerable Upper Intake Level, corresponds to Upper Intake Level and Upper Level (UL)
Optimum Health/ Chronic Disease Prevention	**Suggested dietary target (SDT)**	Chronic disease risk reduction intake (CDRR)	~	~	~	~	Chronic disease risk reduction intake (CDRR)
	Estimated energy requirement (EER)	~	Energy requirement (ER)	Estimated average requirement (energy) (EAR)	Average Requirements for energy intake (AR)	~	
	Acceptable macronutrient distribution range (AMDR)	Acceptable macronutrient distribution range (AMDR)				~	Recommended intake range of macronutrients

Adapted from King et al. (2007)

[6] The average daily nutrient intake level that is suggested to meet the requirements of half of the individuals in a particular life-stage group. The provisional AR, which is an approximation of AR, has larger uncertainty than AR. It is calculated by multiplying AI by a factor of 0.8. Can be used when an AR cannot be determined (NNR 2023).

[7] the highest level of intake for which there is reasonable confidence of the absence of adverse effects. Safe levels of intake have more limited applications than ULs. Intakes above the safe levels of intake do not necessarily mean that there is a risk of adverse effects, and these values cannot be used to characterise the proportion of the population at risk of adverse effects (European Food Safety Authority 2025).

Chapter 3: Prioritising NRVs for review

3.1 Identifying priority NRVs for review

The Steering Group is responsible for the ongoing monitoring of triggers for a new review, decision making, resourcing and ensuring nutrient reviews are conducted in a timely manner. In selecting and prioritising NRVs for review, consideration will be given to the relative priority, and resource requirements associated with potential updates, along with the available review resources at any given time.

An update of existing NRVs may be triggered via several mechanisms, including where:

- an update is identified as a priority for review by the Steering Group
- a recent, high quality systematic review is published, with implications for the currency or accuracy of related NRVs
- revised NRVs are set by comparable international jurisdictions, with implications for the currency or accuracy of related NRVs
- review is required to inform decisions about mandatory fortification programs.

If only one NRV for a particular nutrient is prioritised for review, consideration should be given to the impact of altering this value relative to other NRVs for that nutrient.

When considering several nutrients for update, factors such as associated health burden or health benefit should be considered relative to other potential nutrients for prioritisation (i.e. which nutrient has a higher associated health burden at a population level).

3.1.1 Prioritisation principles

The nutrient update prioritisation process is guided by the NRVs nutrient update prioritisation principles (see Appendix B). During the prioritisation process, the prioritisation principles are used to guide discussion and decision making, with the main points of discussion and reasons for decisions documented. This ensures a consistent and transparent process is followed.

The prioritisation principles are informed by those used in the review of the Australian Dietary Guidelines, drawing on prioritisation pathways from the Dietary Guidelines for Americans 2021–2025, the Nordic Nutrition Recommendations 2022, and Canada's Dietary Guidelines 2019. The principles also consider prioritisation criteria commonly used in the development of health practice guidelines (El-Harakeh et al. 2019).

The principles that guide prioritisation of NRVs for review are summarised below, and described in further detail in Appendix B:

- **Relevance** - will the NRVs prioritised for review apply to people of all ages and backgrounds in the general population, including people with common diet-related risk factors such as being overweight?

- **Importance** - is the information on the nutrient or NRV important to current public health priorities and to what degree?
- **Type of impact** – what type of impact could the nutrient or NRV have on public health including broader societal, economic or environmental impacts?
- **Degree of impact** - how significantly does the nutrient or NRV affect health, considering both the severity of related health outcomes and the size of the population likely to be impacted?
- **Evidence base** – are there likely to have been changes in the evidence base underpinning recommendations, or the food supply or dietary patterns that could impact nutrient intake?

3.1.2 Mandatory fortification programs

Review of mandatory fortification programs could trigger a review of NRVs. Mandatory fortification programs may be reviewed to assess if:

(i) there is still a need for fortification i.e. situational analysis conducted to determine current population intakes and nutrient status; and
(ii) there are any toxicity concerns that may require changes in ULs and fortification levels.

Before confirming a review is required, a cost-benefit analysis should be conducted to inform each review of the mandatory nutrient fortification program. This analysis should consider whether the likelihood of a NRV value changing due to the review justifies the investment of time and resources.

The review process should commence with horizon scanning for new evidence, international developments, or relevant changes in government policy that would warrant a nutrient review.

For more information on vitamins and mineral added to food:

Food Standards Australia New Zealand (2016) Vitamins and minerals added to food https://www.foodstandards.gov.au/consumer/food-fortification/vitamin-added

Chapter 4: Scoping NRVs for review

4.1 Understanding the context

Prior to commencing an NRV review, a comprehensive understanding of the nutrient, associated nutrition-related health outcomes and the associated Australian and New Zealand nutrition and public health context is essential. This context will enable identification of the required data/evidence/information to inform NRV development, and informs decisions about the scope, criteria and methods for evidence sources, and NRV development more broadly. Scoping should be informed by the best-available evidence and general population data, where relevant. To avoid duplication of existing research and maximise limited resources, scoping will typically be based on existing sources of data and evidence rather than a *de novo* review of the evidence.

The relationship between information gathered during the scoping and evidence-review stages of the project, and development of NRVs is shown in Figure 4.1.

4.1.1 Nutrition-specific context

An understanding of a macronutrient and micronutrient function, physiology and biochemistry and of the potential mechanisms underlying relationships between nutrient intake and adverse health effects is required. While the existing NRVs for Australia and New Zealand summarise the principal functions of micronutrients, and mechanisms underlying potential health effects, these descriptions should be revisited to ensure that they reflect current evidence.

Scoping the nutrient should aim to address the following questions, using the best available evidence:

- What is the nutrient's function, physiology and biochemistry? (literature review)
- What factors are known to impact on requirements or nutrient status (e.g. physical activity, height/weight, inflammatory factors)?
- What health outcomes are associated with insufficiency or excess of this nutrient? (literature review)
- What factors are known to impact on bioavailability of the nutrient? (literature review). Consider interactions with:
    - other nutrients
    - nutritional status
    - health status
    - genetics
    - gut microbiome
    - food matrix
    - medication use
    - inflammatory factors

- What is known to impact on availability of the nutrient? (literature review). Consider:
    - food (what is in the food supply or what is consumed?)
    - water
- Are there any other confounders or effect modifiers relevant to the nutrient or NRV under review? For example, environmental factors such as iodine usage as a sanitiser in dairy industry.

4.1.2 Country-specific context

Scoping must explore the Australian and New Zealand nutrition and public health context and understand how this intersects with the nutrient-specific factors identified above. Where relevant, decisions about country-specific context factors should be based on current population data. If current population data is unavailable, the best available data should be interpreted alongside other relevant evidence, such as current dietary patterns and food systems, to assess whether it likely reflects the population's present status.

Where other sources of evidence are used, consideration should be given to the generalisability of evidence to the Australian and New Zealand context.

Scoping the Australian and New Zealand context should aim to address the following questions:

- What are the current dietary intakes in Australia and New Zealand for this nutrient?
- What is the current nutritional status of the Australian and New Zealand populations?
- What are the public health implications of current population intakes/status?
    - Are there concerns about disease risk, maintaining function or avoiding toxicity?
    - Are there specific populations that require special consideration?
    - Does the current population intake/status have implications for bioavailability?
- Are there any considerations relating to the Australian and New Zealand food system for this nutrient?
- Are there any other factors that are likely to impact the calculation of an NRV for this nutrient?

Further information is outlined in:

- Dhonukshe-Rutten et al. (2013) EURRECA—evidence-based methodology for deriving micronutrient recommendations. *Critical reviews in food science and nutrition*, *53*(10):999-1040. https://doi.org/10.1080/10408398.2012.749209 - *Defining the Problem: Identifying the Nutrition-Related Health Problem (Activity 1, pp. 1000 – 1004)*
- NASEM (2017) *Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease*. The National Academies Press. https://doi.org/doi:10.17226/24828 - *pp. 76-77*

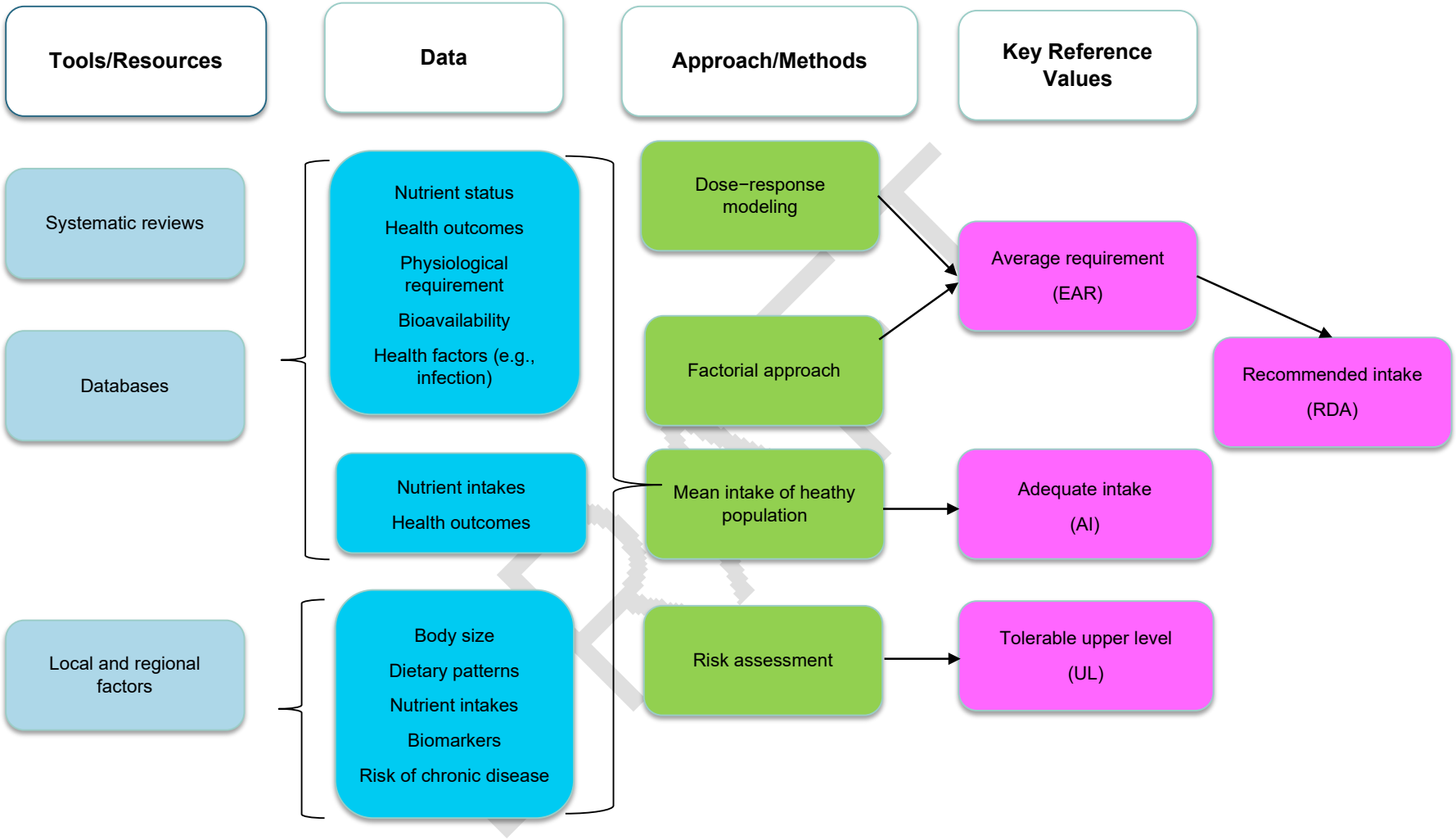

Figure 4.4 Specific inputs and their relationships to derive NRVs

adapted with permission from Yaktine et al. (2020)

4.2 Identifying evidence requirements to derive NRVs

NRVs can be calculated using several different approaches (see Chapter 6), each based on different data sources, including data on intake-status-health relationships (dose-response approach, risk assessment), physiological requirements (factorial approach), and bioavailability (factorial approach). The methods used to derive an NRV are determined by the availability of relevant data for each approach.

Ideally, all the above data would be available to support calculation of several values to be compared, to arrive at a final draft NRV. However, this is rarely the case in practice, and reviewers must identify the source of data that is most appropriate – and most likely to be available – for the purposes of developing a specific NRV or set of NRVs.

Research questions most likely to produce informative evidence should be prioritised to support NRV derivation.

Scoping steps may include:

- Reviewing evidence and findings from recent NRVs set by comparable international bodies
- Reviewing recent high quality systematic reviews on the intake-status-health relationship/s of interest
- Conducting a scoping review (depending on available resources)
- Considering sources of evidence for contextual factors

Questions to consider include:

- Does the existing evidence support the current NRV (when available) or is there a need for revision?
- Does existing evidence indicate that data on the intake-status-health relationship can be used to calculate the NRV of interest? If not, are any subsequent developments likely to have altered the evidence base such that an NRV can be calculated?
- Does existing evidence indicate that data on physiological requirements or adverse effects can be used to calculate the NRV of interest? If not, are any subsequent developments likely to have altered the evidence base such that an NRV can be calculated?

Based on the outcomes of scoping, a list of research questions to be addressed during the review should be developed. At this stage, consideration should also be given to whether any supplementary evidence will be required to inform contextual factors under the evidence-to-decision framework (See Chapter 7).

Further information is outlined in:

- NHMRC (2019c) *Guidelines for Guidelines: Forming the questions*. Canberra Retrieved from https://www.nhmrc.gov.au/guidelinesforguidelines/develop/forming-questions

- Dhonukshe-Rutten et al. (2013) EURRECA—evidence-based methodology for deriving micronutrient recommendations. *Critical reviews in food science and nutrition*, *53*(10):999-1040. https://doi.org/10.1080/10408398.2012.749209 - pp. 1016-1017

4.2.1 Identifying key inclusion and exclusion criteria

Before commencing an evidence review — or considering the appropriateness of existing guidance for adoption/adaption — the optimal methods and criteria for answering in scope research questions should be identified. This includes specifying the type of review (e.g. systematic review, literature review, scoping review), eligible study designs, and PI/ECO (Population, Intervention/Exposure, Comparator and Outcome) criteria. Defining these criteria provides a benchmark against which potentially usable sources (international NRV guidance, existing systematic reviews) can be assessed, or informs further research protocol development (for *de novo* reviews).

4.2.1.1 Study designs

NRVs are developed based on evidence from observational and experimental studies. In general, experimental studies are used to establish EAR (and RDI) whereas AIs and ULs are typically derived from observational studies.

The study designs eligible for inclusion will depend on the NRV being developed, and the expected body of evidence available. Inclusion of evidence from multiple sources assists in triangulating the evidence base and strengthens confidence in the assessment of outcomes.

Further information is outlined in:

- NASEM (2017) *Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease*. The National Academies Press. https://doi.org/doi:10.17226/24828 - pp. 268 – 274
- Beyerbach et al. (2022) Evaluating concordance of bodies of evidence from randomized controlled trials, dietary intake, and biomarkers of intake in cohort studies: a meta-epidemiological study. *Advances in Nutrition*, *13*(1), 48-65. https://doi.org/https://doi.org/10.1093/advances/nmab095
- Dhonukshe-Rutten et al. (2013) EURRECA-Evidence-based methodology for deriving micronutrient recommendations. *Crit Rev Food Sci Nutr*, *53*(10), 999-1040. https://doi.org/10.1080/10408398.2012.749209 - pp. 1016 – 1017

4.2.1.2 Population groups

The following population groups have been identified for NRVs:

- Adults (18 years and older)
- Older adults (65 years and older and/or 75 years and older)
- Pregnancy

- Lactation
- Children and adolescents (aged 1 year to 17 years)
- Infants (0 – 12 months)

To ensure that NRVs are consistent across nutrients, a data set with age range, reference weights has been developed for use across reviews (see Appendix C). This data set will be applied when preparing draft NRV values.

Most population groups specify the relevant age-range, and 'male' or 'female'. The distinction between male and female is based on sex rather than gender, as nutrient intake and metabolism are physiological processes that are impacted by hormones. The definitions of 'sex' and 'gender' used to make this distinction come from the NHMRC Statement on Sex, Gender, Variations of Sex Characteristics and Sexual Orientation in Health and Medical Research (2024), where 'sex' relates to biological characteristics (i.e. hormones, chromosomes, reproductive organs) and 'gender' is a social and cultural concept. People who are transgender, gender diverse or who have innate variations of sex characteristics may not identify with their sex recorded at birth and may at some point change the way they report their sex. For this reason, when NRVs are developed, it should be specified in the recommendations that 'male' and 'female' population groups refer to biological sex, and individuals who think this may not be relevant to them may need to consult a health practitioner who can consider their individual needs.

There may be other specific population groups that require additional consideration based on other attributes.

Subgroups of older adults and special population could include:

- Aboriginal and Torres Strait Islander people (aged 51+)
- Māori and Pacific Island people.

There may be additional functional requirements for some people which should considered when applying NRVs.

NRV recommendations are designed to be public health advice that applies to the general population. People who need nuanced advice on recommended nutrient intakes due to specific health conditions or other circumstances should seek individualised advice from a health professional. This message should be stated alongside all NRV recommendations.

4.2.1.2.1 Measuring intake and status

Methods for reliably measuring dietary intake and micronutrient status (biomarkers) must be identified, and acceptable (and unacceptable) methods reflected in review inclusion/exclusion criteria. Decisions about appropriate methods for intake assessment and micronutrient status should be based on evidence, to the extent possible within the available review resources.

An inclusive approach that allows for multiple acceptable measurement methods should be adopted, whilst maintaining minimum standards for accuracy and reliability. This will ensure that evidence for the intake-status-health relationship is sufficiently robust to guide NRV development, whilst allowing for the inclusion of a range of studies with differing methodological approaches in the review. Where measurement methods vary in their reliability, a hierarchy of measures may be developed and the impact of including less robust measurement methods explored in sensitivity analyses to assess how sensitive results are to different assumptions (Deeks et al. 2024).

Further information is outlined in:

- Dhonukshe-Rutten et al. (2013) EURRECA-Evidence-based methodology for deriving micronutrient recommendations. *Crit Rev Food Sci Nutr*, *53*(10), 999-1040. https://doi.org/10.1080/10408398.2012.749209 - pp. 1007 – 1012
- NASEM (2017) *Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease*. The National Academies Press. https://doi.org/doi:10.17226/24828 - pp. 75 – 76 and pp. 89 - 104

4.2.1.3 Outcomes/endpoints

The outcomes selected for inclusion in the evidence review will vary and may include:

- clinical indicators, such as signs of deficiency, altered body composition, impaired function, or increased morbidity
- biochemical markers of nutrient status or health outcomes (such as blood or urine levels)
- functional measures, such as bone health or hormone levels
- risk of developmental abnormalities
- risk of chronic disease outcomes

Typically, several outcomes will be used as indicators for setting NRVs, with a focus on the most sensitive end points for the NRV under development.

Outcomes selected should be critical or important to decision making (in accordance with GRADE approach (Grading of Recommendations, Assessment, Development, and Evaluations). Decisions about priority should consider the importance of an outcome for the purposes of setting NRVs – that is, with consideration given to the nutrient and country-specific context, along with the likely availability of evidence for that outcome. Adverse outcomes should also be considered.

Further guidance on outcome selection is available from:

- NASEM (2017) *Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease*. The National Academies Press. https://doi.org/doi:10.17226/24828 - pp. 107 – 125 and pp. 267 – 268 (relating to chronic disease outcome measures)
- Dhonukshe-Rutten et al. (2013) EURRECA-Evidence-based methodology for deriving micronutrient recommendations. *Crit Rev Food Sci Nutr*, *53*(10), 999-1040. https://doi.org/10.1080/10408398.2012.749209 - p. 1001

Chapter 5: Gathering evidence

5.1 Identifying available evidence sources and gaps

5.1.1 Adopting or adapting existing international NRVs

Methods to adopt or adapt existing NRVs set by comparable international jurisdictions are being prioritised. This will reduce duplication of effort and better direct resources towards gaps in the evidence base. If there is a recent NRV set by a comparable jurisdiction, the supporting evidence and documentation underpinning NRV development should be obtained and reviewed alongside any additional contextual information.

The committee should investigate the calculations and assumptions applied to the evidence and consider whether NRVs have been developed consistent with:

- the requirements outlined in this framework
- NHMRC Standards and accompanying Guidelines for Guidelines
- the specific requirements identified during scoping.

A template has been developed to guide decision making about the suitability of adopting/adapting existing NRVs and is provided at Appendix D. A guide to support decision making about the suitability of underpinning systematic reviews is provided at Appendix E.

If the evidence is appropriate to use, and the assumptions underpinning the calculations are generalisable to the Australian and New Zealand context, consideration can be given to adopting the value as the revised Australian and New Zealand NRV. If the committee considers that the underlying evidence is appropriate, but that different assumptions apply in deriving an NRV based on that evidence, consideration may be given to adapting the value to the Australian and New Zealand context. In both cases, an evidence-to-decision framework should be used for each population group to explain the committee's judgements during this process (see Section 7.3).

Where an international NRV has been deemed unsuitable to be adapted or adopted, consideration should be given to the extent to which any underpinning systematic reviews may be suitable for use – or can be updated for use – to inform the current NRV review. See Section and Appendix E for further information.

Further information is outlined in:

- NHMRC (2018) *Guidelines for Guidelines: Adopt, adapt or start from scratch* https://www.nhmrc.gov.au/guidelinesforguidelines/plan/adopt-adapt-or-start-scratch
- Klugar et al. (2024) GRADE guidance 39: using GRADE-ADOLOPMENT to adopt, adapt or create contextualized recommendations from source guidelines and evidence syntheses. *Journal of Clinical Epidemiology*, *174*, 111494. https://doi.org/10.1016/j.jclinepi.2024.111494

- The ADAPTE Collaboration (2009) The ADAPTE Collaboration. (2009). *The ADAPTE process: Resource toolkit for Guidelines Adaptation. Version 2.0.* http://www.g-i-n.net.
- Darzi et al. (2017) A methodological survey identified eight proposed frameworks for the adaptation of health related guidelines. *J Clin Epidemiol*, *86*, 3-10. https://doi.org/10.1016/j.jclinepi.2017.01.016

5.1.2 Using or updating existing systematic reviews

Using an existing review to address at least some questions relevant to the review is efficient and allows review resources to be concentrated on evidence gaps. Before commencing a de novo evidence review, consideration should be given to whether an existing, high-quality review has been published on the research question of interest.

Existing reviews may be identified for update to include evidence published since the review search date, or to undertake additional analysis or synthesis to support NRV development (e.g. subgroup analyses). In some cases, an existing review may only partially address the research question of interest, and a supplementary review of the evidence will be required to address gaps.

A guide to support decision making about the suitability of underpinning systematic reviews is provided at Appendix E.

Further guidance on using existing systematic reviews is included in:

- NASEM (2023) *Using Systematic Reviews to Support Future Dietary Reference Intakes: A Letter Report*. The National Academies Press. https://doi.org/https://doi.org/10.17226/27031
- NHMRC (2019d) *Guidelines for Guidelines: Identifying the evidence* https://www.nhmrc.gov.au/guidelinesforguidelines/develop/identifying-evidence .

5.2 Conducting a de novo evidence review

If no existing evidence reviews are identified as suitable for use or updating, a de novo evidence review should be undertaken to address key research questions of interest. Reviews should meet the NHMRC Standards and be guided by the Guidelines for Guidelines and associated third-party guidance and tools. This includes:

- Developing a detailed research protocol to be prospectively registered on an online review registry (e.g. PROSPERO)
- Conducting the evidence review in accordance with the protocol, with any deviations to be documented and a supporting rationale provided
- Documenting the review criteria, methods and findings in a comprehensive evidence evaluation report.

NHMRC's Guidelines for Guidelines (2019) provides detailed guidance on searching for evidence and the synthesis of evidence into appropriate categories for analysis. Relevant Guidelines for Guidelines modules include:

- Identifying the evidence | NHMRC
- Selecting studies and data extraction | NHMRC
- Synthesising evidence | NHMRC
- Assessing risk of bias | NHMRC
- Assessing certainty of evidence | NHMRC

Further guidance, specific to systematic reviews in nutrition, is available from:

- NASEM (2017) *Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease. The National Academies Press. https://doi.org/doi:10.17226/24828* - pp. 129-141 and pp. 165-166
- Arnesen et al. (2020) The Nordic Nutrition Recommendations 2022–handbook for qualified systematic reviews. *Food & Nutrition Research*, *64*, 4404. https://doi.org/10.29219/fnr

5.3 Developing GRADE evidence profiles

Evidence profiles are a recognised format to summarise the available information. An evidence profile should be developed for each research question used to inform NRV recommendations. For de novo evidence reviews, Evidence Profiles or Summary of Findings tables will be included in the final review report. Evidence from existing systematic reviews should be extracted and presented in this format, if this step has not been performed by the review authors.

Summarising comparable information will ensure that the committee has all the information it needs to inform its recommendations. This process will also provide an opportunity for the committee to identify any supplementary analyses required to calculate an NRV or inform decisions about recommendations.

Each profile should include:

- Some brief information on the question in a PI/ECOS (Population, Intervention/Exposure, Comparator, Outcome, Study design) or similar format.
- A list of the critical and important outcomes relevant to the question, including information on the time points at which outcomes are measured and tools/definitions used to measure the outcome. This list should include outcomes for which no evidence was found.
- Summary statistics for the point estimates from the meta-analyses, including, where possible both absolute risk (AR) and relative risk (RR) and confidence intervals (or for RCTs both mean difference (MD) and number needed to treat (NNT) or equivalent). More than one absolute effect may be reported for different populations with higher or lower levels of

risk, which can enable the guideline development group to assess the real world impact of its recommendations on different populations (Guyatt et al. 2013a; Guyatt et al. 2013b).

- Summary statements for any narrative or qualitative syntheses.
- Details of the GRADE assessment for level of certainty per outcome informed by the necessary sensitivity analyses, subgrouping and meta regressions, dose response testing and consideration of risk of bias within individual studies included in meta-analyses.
- The number of studies and participants contributing data to this outcome.
- Any additional important comments (Guyatt et al. 2011). If there is pooled data, it may be possible to undertake sensitivity analyses.

Further guidance on GRADE is available in:

- Neumann et al. (2025) *GRADE Book.* https://book.gradepro.org/
- The GRADE Working Group (2024) *GRADE Handbook* https://gdt.gradepro.org/app/handbook/handbook.html
- Journal of Clinical Epidemiology GRADE Guidance series. https://www.sciencedirect.com/special-issue/10F8V3S0J7V

Further guidance on sensitivity analysis is available in:

- Deeks et al. (2024) Chapter 10: Analysing data and undertaking meta-analyses [last updated November 2024]. In *Cochrane Handbook for Systematic Reviews of Interventions version 6.5*. https://www.cochrane.org/authors/handbooks-and-manuals/handbook/current/chapter-10#_Ref180060260

5.3.1 GRADE certainty of evidence

NHMRC has well-established standards and guidelines to support the application of the GRADE approach to evaluating certainty of evidence. The relevant module on assessing certainty of evidence is available in the Guidelines for Guidelines handbook (NHMRC 2019a).

NHMRC also acknowledges the GRADE approach has recognised challenges with assessing certainty of evidence from diverse sources including non-randomised studies, interpreting outcomes and identifying thresholds for decision-making that are particularly relevant public health guidelines (Boon et al. 2021).

Further information on the application of GRADE in the nutrition context is available in:

NASEM (2017) *Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease. The National Academies Press. https://doi.org/doi:10.17226/24828*
pp. 149-162, p 166 [GRADE certainty of evidence - general]

pp. 206 – 215 [GRADE certainty of evidence for intake-response relationships]

pp. 215 - 231 [GRADE EtD for NRVs]

Chapter 6: NRV calculation and recommendations

6.1 Determining the approach

Once the relevant evidence has been collated and synthesised, the approach for estimating nutritional requirements and deriving a draft NRV can be determined.

Key considerations when determining the approach include:

- the specific type of NRV being developed
- the specific nutrition-related health problem that the NRV review aims to address
- the availability and certainty of evidence for the relationship between dietary intakes and physiological function, nutritional status and health outcomes
- relevant factors that may impact on the NRV calculation, such as nutrient interactions, the food matrix and level of processing. Increasingly, the effect of the whole dietary pattern is considered to impact bioavailability and nutrient absorption (EFSA Panel on Nutrition Novel Foods and Food Allergens et al. 2024b).
- the need for scaling and extrapolation approaches to set NRVs for population groups where insufficient evidence is identified
- the impact of changes to height and weight on results and recommendations. A sensitivity analysis may be required to explore this.

Additional information may be required for development of specific NRVs, as identified below.

There are several approaches that may be used to estimate a draft NRV, depending on the above factors. These include:

- ***factorial approach:*** typically used for nutrients that are not metabolised (i.e. minerals because losses are more readily measurable as they are excreted in the same form as in the diet).
- ***dose-response approach:*** used to set an EAR or UL when there is a clear relationship between the intake of a nutrient and a metabolic or functional outcome.
- ***risk assessment approach:*** used to determine UL based on a risk assessment that considers traditional adverse event (toxicity) endpoints.

These approaches may also be used in combination with each other, where appropriate and supported by the available evidence (see Figure 6.2).

Draft NRV values must be supported with a rationale for the approach taken.

Further information is provided in:

- Dhonukshe-Rutten et al. (2013) EURRECA-Evidence-based methodology for deriving micronutrient recommendations. *Crit Rev Food Sci Nutr*, *53*(10), 999-1040. https://doi.org/10.1080/10408398.2012.749209 - pp. 1012 – 1023

- NASEM (2018) *Harmonization of Approaches to Nutrient Reference Values: Applications to Young Children and Women of Reproductive Age*. Washington, DC: The National Academies Press. https://doi.org/10.17226/25148 - Chapter 3.
- Gibson (2024). Principles of Nutritional Assessment. Nutrient Reference Values. https://nutritionalassessment.org/nrv/ 8a.23

6.1.1 Factorial approach

This approach measures the various (exchanges between) body pools to estimate losses and needs for maintenance and growth. The factorial approach is used in the absence of suitable biomarkers for the relationship between intake and status or health, or where scientific evidence for this relationship is lacking. It is also applied to derive requirements during periods of growth and development, such as during pregnancy or lactation.

At its core, the factorial approach calculates the estimated average requirement for replacement of obligatory losses (via faecal, urine, skin and other routes) and to support growth and development, accounting for the absorption efficiency from diet. The formula for estimating dietary requirements using the factorial approach is shown in Figure 6.1, taken from the EURRECA Framework (Dhonukshe-Rutten et al. 2013).

$$\text{Dietary Requirements} = \frac{\text{Sum of losses (faeces, urine, skin, menses etc)} + \text{Growth \& development requirements (foetus, pregnancy, lactation etc.)}}{\text{Bioavailability factor}}$$

Figure 6.5 Equation for calculating dietary requirements using factorial approach

When accounting for growth and development requirements, consideration may be given to:

- tissue deposition / accretion (including in fetal tissue, placenta or maternal tissue during pregnancy or lactation)
- requirements for breast milk production (e.g. breast milk concentration, daily volume).

Derivation of reference values for micronutrients through the factorial approach often requires application of a bioavailability factor to account for absorption from diet and convert the physiological requirement into a dietary intake value (Fairweather-Tait & Collings 2010).

For many nutrients, factors affecting bioavailability are not well established, so appropriate adjustments cannot be made. The adjustments required depend on usual dietary intake, the chemical form of the nutrient in the diet, and factors known to affect the absorption and metabolism of the nutrient. Fixed bioavailability factors may be applied, or adjusted as efficiency of absorption may vary with the dietary level of the nutrient, individual status or life-stage group(Gibson 2024).

Further information on the factorial approach can be found in:

- Dhonukshe-Rutten et al. (2013) EURRECA-Evidence-based methodology for deriving micronutrient recommendations. *Crit Rev Food Sci Nutr*, *53*(10), 999-1040. https://doi.org/10.1080/10408398.2012.749209 - pp. 1014–1016 and p. 1021
- NASEM (2018) *Harmonization of Approaches to Nutrient Reference Values: Applications to Young Children and Women of Reproductive Age. National Academies Press (US) https://doi.org/10.17226/25148 - pp. 55-56*
- FAO (2024) *Review of derivation methods for dietary intake reference values for older infants and young children – FAO request for scientific advice to develop general principles for the establishment of Codex nutrient reference values for older infants and young children.* Food and Agriculture Organization of the United Nations. https://doi.org/10.4060/cb9380en
- Fairweather-Tait and Collings (2010) Estimating the bioavailability factors needed for setting dietary reference values. *Int J Vitam Nutr Res*, *80*(4-5), 249-256. https://doi.org/10.1024/0300-9831/a000031

6.1.2 Dose response approach

Dose response testing can be based on data or meta-analyses from both intervention trials and prospective observational studies. The dose response is based on the prediction of a physiologically relevant outcome (e.g. measurement of an established micronutrient status biomarker; data or meta-analyses from prospective observational studies examining dietary intake; or assessment of clinical disease endpoints in relation to nutrient intake or status).

Estimation of the dose–response relationship requires testing at least two different intake levels. Very high doses—where 100% of the population achieves the target biomarker level—are of limited value, as they do not indicate how much the dose could be reduced while still achieving the same outcome. Conversely, testing a dose that results in only 20–30% of the population reaching repletion may require depletion–repletion studies, which differ physiologically from maintenance studies (where most participants are already replete). For example, iron absorption increases significantly during deficiency compared to repletion; however, only the absorption rate under replete conditions is relevant for estimating the Estimated Average Requirement (EAR).

This dose response approach provides evidence on optimal nutrition in relation to specific health outcomes and endpoints and is usually based on RCTs (e.g. intermediate health outcomes such as cardiometabolic risk factors) or prospective observational studies (e.g. disease occurrence and mortality). Ecological, cross-sectional and case-control studies are very rarely used due to the bias introduced in their study designs.

The dose response approach evaluates the associations between one or more of the following:

- Micronutrient or macronutrient intake and biomarkers of status (typically from RCTs)

- Micronutrient or macronutrient intake and health outcomes (typically from RCTs and cohort studies)
- Micronutrient or macronutrient status biomarkers and health outcomes (typically from cohort studies).

There are a range of suitable approaches for dose-response modelling (e.g. restricted cubic splines or fractional polynomials, depending on the available data and type of relationship being evaluated).

Further information about the dose-response approach is provided in:

- Dhonukshe-Rutten et al. (2013) EURRECA-Evidence-based methodology for deriving micronutrient recommendations. *Crit Rev Food Sci Nutr*, *53*(10), 999-1040. https://doi.org/10.1080/10408398.2012.749209 - pp. 1016–1017 and pp 1021–1022
- NASEM (2018) *Harmonization of Approaches to Nutrient Reference Values: Applications to Young Children and Women of Reproductive Age. National Academies Press (US)* *https://doi.org/10.17226/25148* - pp. 54-55
- NASEM (2017) *Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease. The National Academies Press. https://doi.org/doi:10.17226/24828* - pp. 196 – 206
- Greenland and Longnecker (1992) Methods for trend estimation from summarized dose-response data, with applications to meta-analysis. *American journal of epidemiology*, *135*(11), 1301-1309. https://doi.org/10.1093/oxfordjournals.aje.a116237

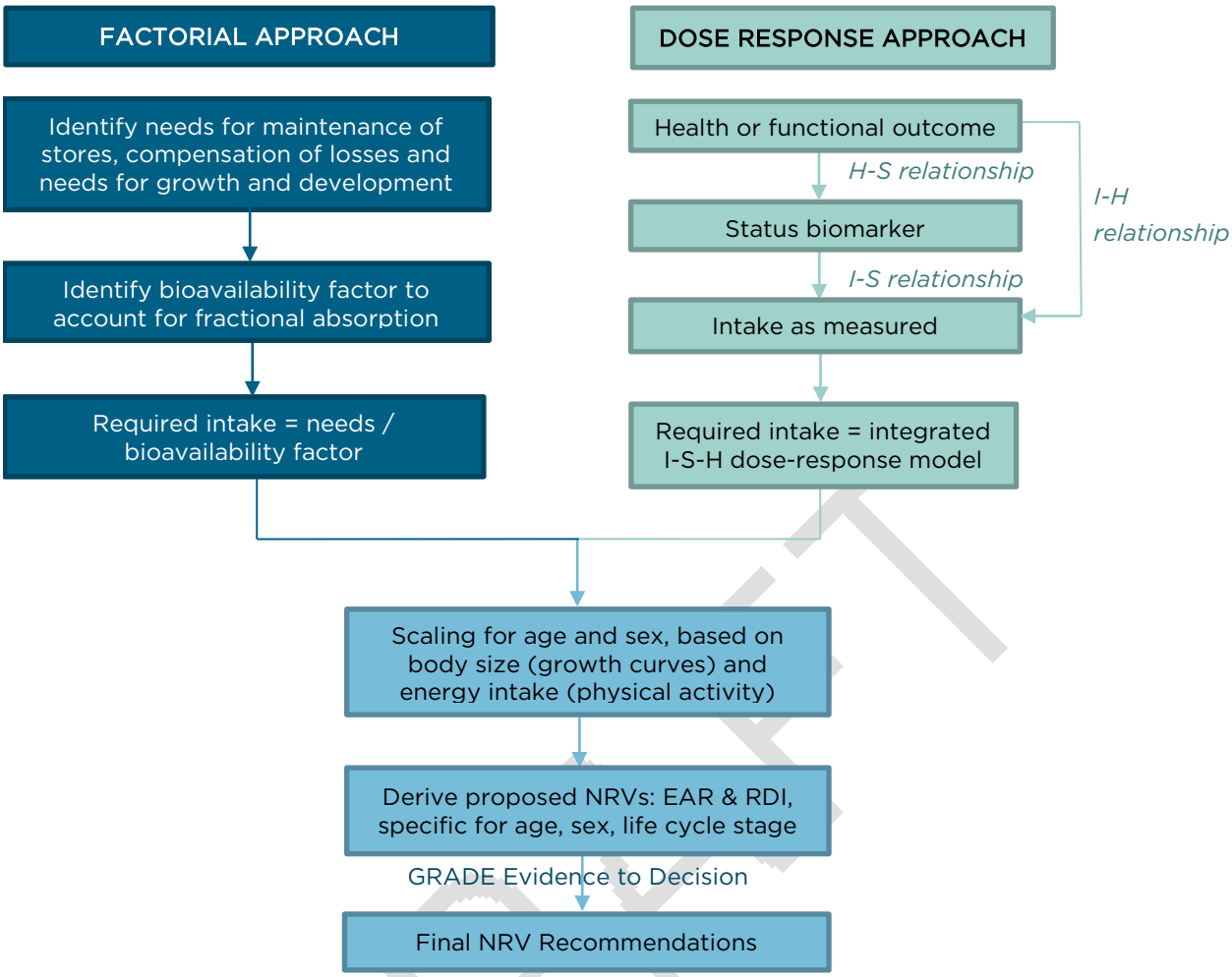

Figure 6.6 Diagram showing the factorial and dose response approaches to deriving NRVs, their respective inputs, and subsequent scaling and adjustments to arrive at final NRV recommendations specific for age, sex and life-cycle (Matthys et al. 2011).

Abbreviations: I, intake; H, health; S, status.

6.1.3 Risk assessment approach

The risk assessment approach can be used to derive a UL. Risk assessments are commonly used in toxicology to determine a reference value upon which to base recommendations. Due to inherent differences between nutrients and chemicals (the typical subject of risk assessments), the traditional risk assessment paradigm requires adjustment when used in deriving a nutrient UL. This requires a risk assessment process that weighs the benefits (i.e. nutritional requirements to meet physiological requirements) against toxicological effects associated with higher intakes.

Risk assessment comprises:

- hazard identification and characterisation
- exposure characterisation
- risk characterisation and establishment of reference values.

Further information on the use of risk assessment to derive ULs is available from:

- EFSA Panel on Nutrition Novel Foods and Food Allergens et al. (2024a) Guidance for establishing and applying tolerable upper intake levels for vitamins and essential minerals. *EFSA Journal*, *22*(11), e9052. https://doi.org/10.2903/j.efsa.2024.9052
- NASEM (2018) *Harmonization of Approaches to Nutrient Reference Values: Applications to Young Children and Women of Reproductive Age. National Academies Press (US)* *https://doi.org/10.17226/25148* - pp.79-81

6.2 Deriving draft nutrient adequacy recommendations

When the available evidence allows, the EAR and RDI should be derived based on:

- Factorial estimates (physiological requirements adjusted to reflect bioavailability), and/or
- Dose-response estimates for each of the associations between intake-status, status-health and intake-health (based on identified evidence), along with an integrated intake-status-health dose-response model, where data allows.

Where EAR/RDI cannot be calculated based on the available evidence, an Adequate Intake (AI) may be set, based on observed or experimentally determined nutrient intakes of apparently healthy populations.

Methods for calculating NRVs should be clearly described and documented alongside recommendations, to support transparency and facilitate international adaptation / adoption where relevant. This includes specifying the values used as inputs into any models or formulae, and from where those values have been obtained.

6.2.1 Estimated Average Requirements (EAR)

The EAR is the nutrient level adequate for 50% of the population (i.e. it is mean requirement).

EAR is calculated from studies that evaluate the relationship between nutrient dose and micronutrient status (i.e. deficiency). Studies that test a nutrient dose that leads to more or less than 50% of subjects having inadequate intake do not identify the EAR. However, a scaling could be derived based on the body of evidence using appropriate statistical methods which would allow the EAR to be calculated by determining the point at which there is a 50% chance of nutrient adequacy and a 50% chance of nutrient deficiency.

6.2.2 Recommended Dietary Intake (RDI)

The RDI indicates the intake levels of essential nutrients considered to be adequate to meet the known nutritional needs of nearly all healthy people. That is, the nutrient level is adequate for 97.5% of the population (if the requirement is normally distributed) because it is two standard deviations (SD) above the EAR (Figure 6.3).

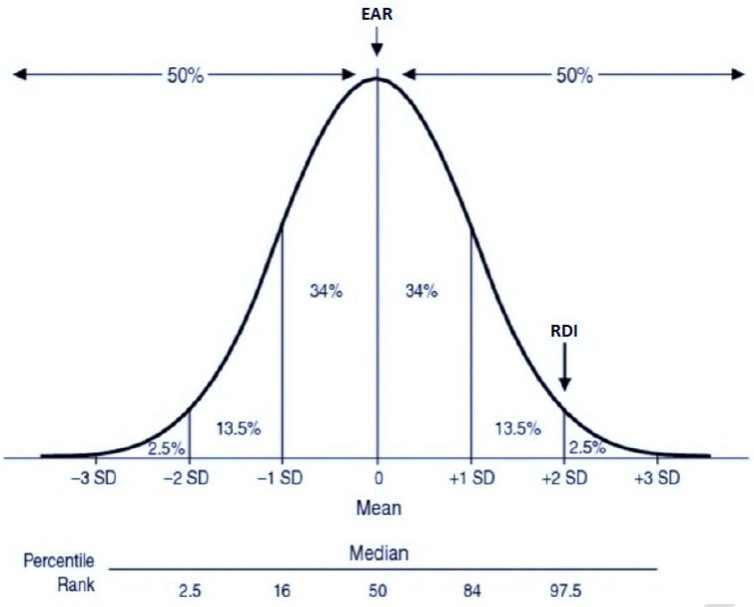

Figure 6.7 Calculation of Recommended Dietary Intake (RDI) as two standard deviations above the Estimated Average Requirement (EAR), covering 97.5% of the population.

The RDI is calculated from the EAR, based on individual variability in nutritional requirements within the population. Where there is sufficient data about the variability in requirements to calculate a standard deviation, the RDI can be calculated as:

RDI = EAR + 2SD of EAR

If data about variability in requirements are insufficient to calculate the SD, a coefficient of variation (CV) is used.

Unless there is available data to indicate that greater variation is probable for a particular nutrient, a CV of 10% is applied. The 10% is based on extensive data on variation in basal metabolic rate and protein requirements. Table 6.1 outlines the calculations required to determine RDIs using the CV.

Variability in requirements: RDI = EAR + 2CV

Table 6.1 Calculating RDIs using coefficient of variation values

CV	RDI Equation
10%	RDI = EAR x 1.2
15%	RDI = EAR x 1.3
20%	RDI = EAR x 1.4

For example, if the EAR for B12 for adults is 2.0µg/day, RDI = 2.0µg/day x 1.2 = 2.4µg/day

6.2.3 Adequate Intake (AI)

An AI is the average (mean) daily level of intake based on observed or experimentally determined approximations or estimates of nutrient intake, by a group (or groups) of apparently healthy people.

AI can be calculated based on:

- experimental evidence, or
- mean intake in the Australian/New Zealand population, where it can reasonably be assumed that the population is not deficient in that nutrient

While both the RDI and AI can be used as a goal for individual intake, there is significantly less certainty about the AI value as it depends to a greater degree on the judgement of the Expert Working Group. An AI might deviate significantly from and be numerically higher than an RDI, if the RDI could be determined.

Where AIs are based on mean population intakes of assumed healthy populations (e.g. derived from national nutrition survey data), the assessment of the adequacy for an individual or population is made with less confidence. The use of mean population intakes is not suitable for some nutrients where the current intake exceeds the Suggested Dietary Target, e.g. sodium.

This assumption means that any AIs should be set with great caution. Instances where AIs are relevant for assessing individual risk are infrequent due to issues with reliability. Rationale for setting AIs must be clearly outlined, and the evaluation of evidence process closely followed.

The AI for infants is nearly always set according to the mean amount of nutrient in human milk consumed daily by healthy, exclusively breastfed infants less than 6 months of age.

The equation for the AI of young infants is:

$$AI_{young\ infant} = Nutrient\ concentration_{mean}\ human\ milk\ x\ daily\ volume_{mean}\ human\ milk\ consumed/lost\ through\ lactation$$

Nutrient composition of human milk varies during lactation, between and within feeds and with maternal diet, as well as the sex and size of the infant. Nutrient composition data for human milk should be based on a representative sample of adequately nourished lactating women EFSA (2013).

Further information about deriving an AI is provided in:

- Dhonukshe-Rutten et al. (2013) EURRECA-Evidence-based methodology for deriving micronutrient recommendations. *Crit Rev Food Sci Nutr*, *53*(10), 999-1040. https://doi.org/10.1080/10408398.2012.749209
- FAO (2024) *Review of derivation methods for dietary intake reference values for older infants and young children – FAO request for scientific advice to develop general principles for the establishment of Codex nutrient reference values for older infants and young children.* Food and Agriculture Organization of the United Nations. https://doi.org/10.4060/cb9380en

6.3 Deriving Upper Levels (UL) of intake recommendations

Essential nutrients are vital for the normal functioning of the human body, but excess consumption can lead to adverse health effects. For this reason, an Upper Level (UL) value is set to provide guidance for health professionals, policy makers, regulators and consumers to manage the risk of excess intake (see Section 2.2.3 and Figure 2.1).The European Food Safety Authority (EFSA) defines the tolerable upper intake level (UL) as "the maximum level of total chronic daily intake of a nutrient (from all dietary sources) which is not expected to pose a risk of adverse health effects to humans"(EFSA Panel on Nutrition Novel Foods and Food Allergens et al. 2024a).

EFSA published draft international guidance on establishing ULs in 2022. The principles were piloted for 2-years and published in 2024.

EFSA's guidance outlines aspects related to the planning of the risk assessment (problem formulation and definition of methods) and its implementation (evidence retrieval, appraisal, synthesis, integration, development and application of uncertainty factors (UF)).

When deriving ULs, unless otherwise stated, intake from all sources including foods, food fortification, supplements, medicines and water should be considered. Where possible a UL should be based on strong scientific evidence and, in the interests of international harmonisation, developed following EFSA's guidance for establishing ULs. Where the evidence is less certain, interpretation and judgement from an expert working group or advisory committee may play a greater role in determining the final value.

Once a proposed UL value has been derived, contextual, practical, and other relevant factors should be considered through an evidence-to-decision process before finalising the value (see section 7.3). During this process an evidence-to-decision template is used to capture discussion, the rationale and any judgements or assumptions about the nutrient by the expert committee and is published alongside the value to ensure greater clarity and transparency. To ensure all relevant considerations are made for each population group, separate evidence-to-decision tables can be used where needed, or specific sections or questions can be added for populations with unique considerations.

Where a UL has recently been developed by another international jurisdiction, consideration should be given to adopting or adapting that value to the Australian and New Zealand context before initiating a de novo derivation process (see Section 5.1.1).

Members of the general population should be advised not to routinely exceed the UL. The absence of a UL for a nutrient likely reflects a lack of evidence rather than a lack of adverse effects and does not necessarily indicate that excessive intakes pose no risks.

Further information about deriving an UL is provided in:

- EFSA Panel on Nutrition Novel Foods and Food Allergens et al. (2024a) Guidance for establishing and applying tolerable upper intake levels for vitamins and essential minerals. *EFSA Journal*, *22*(11), e9052. https://doi.org/10.2903/j.efsa.2024.9052
- NASEM (2017) *Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease. The National Academies Press. https://doi.org/doi:10.17226/24828* - pp. 223-225, 239-242

6.3.1 Developing and applying uncertainty factors (UF)

To derive an upper level (UL) that will be protective for the general population, an uncertainty factor (UF) is applied to the reference point (RP) as follows:

$$UL = \frac{RP}{UF}$$

The application of an uncertainty factor (UF) aims to establish a UL that will be protective for the general population, while considering varying nutrient sensitivity within the population and the uncertainty associated with the body of evidence. The greater the level of uncertainty, the larger the uncertainty factor and the lower the UL.

In chemical risk assessment, when a RP comes from studies in humans, a default UF of 10 is used to account for inter-individual variability when further chemical-specific information on kinetics and/or dynamics is not available (EFSA Scientific Committee 2012). For nutrients, this default UF of 10 may be reduced based on one or more of the following:

- the size, quality and diversity of human studies available
    - is some of the inter-individual variability likely to be accounted for in the evidence-base?
- the severity and reversibility of the adverse health effects
    - are the effects mild and reversible, or biomarkers of a potential future effect?
- the availability of evidence on the toxicokinetics and toxicodynamics of the nutrient in humans.

Different jurisdictions have different conventions for setting UFs. If there is confidence that intake of the nutrient up to the RP identified in the evidence is not expected to pose a risk of adverse health effects for the general population, a UF of 1.0 is used, meaning the RP can be used as the UL. A default UF of 2 for extrapolation from sub-chronic to chronic exposure is applicable to toxicity studies in rodents. There is no default value for the extrapolation of exposure duration in human studies (EFSA 2024).

EFSA provides further guidance on default UFs for sources of variability or uncertainty in relation to exposure to chemicals that may be relevant to nutrients. These include the use of a Lowest Observed Adverse Effect level (LOAEL) in the absence of a No Observed Adverse Effect Level (NOAEL), extrapolation from animal studies to humans, or extrapolation from studies of short-term exposure when critical effects are expected from lower dose but longer-term exposure (EFSA Scientific Committee 2012).

Food Standards Australia New Zealand progression of Uncertainty Factors is usually done using *e*, the base of the natural logarithm, rounded off to a whole number based on a dose-response curve typically plotted on a semilog graph. If the default value of 10 is not justified for a particular Uncertainty Factor, the next lowest option is 3.0, a rounding-off of 2.718. If it is considered that the value is still not justifiable, the next step down is to a UF of 1.

When deriving a UL, determining what to use as the UF can be the most challenging, arbitrary, contentious, and sometimes least scientific aspect of the process (Australian Government

Department of Health & New Zealand Ministry of Health 2017). Expert judgement is needed to ensure that applying default UFs does not result in a UL that could cause nutrient deficiency or is impractical to implement in the real world (i.e. a UL that is too close to or overlapping recommended nutritional adequacy levels for the nutrient). A case-by-case approach is needed for each nutrient that also considers nutrient intake requirements, homeostatic mechanisms, balance of benefits and harms, values and preferences, cost-effectiveness and required resources, and other factors such as equity, feasibility and sustainability. The rationale for the chosen UF should be described alongside the NRV, and the considerations, discussion and decisions underpinning the chosen UF should be recorded during the evidence-to-decision process (Section 7.3).

Further information about uncertainty can be found in:

- EFSA Panel on Nutrition Novel Foods and Food Allergens et al. (2024a) Guidance for establishing and applying tolerable upper intake levels for vitamins and essential minerals. *EFSA Journal*, *22*(11), e9052. https://doi.org/10.2903/j.efsa.2024.9052
- EFSA Scientific Committee et al. (2018) Guidance on uncertainty analysis in scientific assessments. *EFSA Journal*, *16*(1), e05123. https://doi.org/10.2903/j.efsa.2018.5123
- EFSA et al. (2019) Guidance on communication of uncertainty in scientific assessments. *EFSA Journal*, *17*(1), e05520. https://doi.org/10.2903/j.efsa.2019.5520
- EFSA Scientific Committee (2012) Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data. *EFSA Journal*, *10*(3), 2579. https://doi.org/10.2903/j.efsa.2012.2579
- Dankovic et al. (2015) The scientific basis of uncertainty factors used in setting occupational exposure limits. *Journal of occupational and environmental hygiene*, *12*(sup1), S55-S68. https://doi.org/10.1080/15459624.2015.1060325

6.4 Suggested Dietary Target and Chronic Disease Risk Reduction

Diet-related chronic diseases develop over a long period of time and in a context where nutrients are consumed from a variety of foods within a dietary pattern. Thus, the extent to which scientific research can expose the relationship between chronic disease risk and a specific nutrient is often limited and will depend on several factors, including the reliability of the diet assessment.

Suggested Dietary Targets (SDTs) and Chronic Disease Risk Reduction levels (CDRR) aim to support the prevention of chronic disease. They relate only to nutrients for which there is a body of evidence which indicates a level of intake to reduce chronic disease risk within the apparently healthy population.

In Australia and New Zealand SDTs are set based on a daily average intake from food and beverages for certain nutrients that that may help in prevention of chronic disease using the 90th

percentile. Average intake may be based on the mean or median depending on the nutrient and available data.

Moving forward Australia and New Zealand will adopt the Chronic Disease Risk Reduction (CDRR) approach for specific nutrients where the evidence indicates moderate certainty of chronic disease risk reduction.

CDRRs should use chronic disease outcome/s as the desired endpoint when reviewing the evidence. Where a single nutrient is associated with several disease endpoints, a value should be determined for each. In the case of negative effects, such as sodium and hypertension, the CDRR should reflect the lowest level of intake for which there is significant strength of evidence to characterise chronic disease risk reduction. An overall CDRR should reflect the lowest intake value range for disease prevention for a particular population group. This value may represent an increase or decrease to known current consumption levels.

As the evidence base for chronic disease prevention is mainly developed from studies and health outcomes in adults, CDRR will generally apply only to adults. A CDRR for children and/or adolescents may be considered if the evidence is sufficient and the members of the nutrient-specific Expert Working Groups deem it reasonable and appropriate.

Further information on deriving CDRR can be found in :

- NASEM (2017) *Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease. The National Academies Press.* https://doi.org/doi:10.17226/24828 - pp. 279-290
- Yetley et al. (2017) Options for basing Dietary Reference Intakes (DRIs) on chronic disease endpoints: report from a joint US-/Canadian-sponsored working group. *The American journal of clinical nutrition, 105(1), 249S-285S.* https://doi.org/10.3945/ajcn.116.139097
- Yaktine and Ross (2019) Milestones in DRI development: what does the future hold? *Advances in Nutrition*, *10*(3), 537-545. https://doi.org/10.1093/advances/nmy121.

6.5 Acceptable Macronutrient Distribution Range (AMDR)

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.

There is evidence that a major imbalance in the relative proportions of macronutrients can increase risk of chronic disease (WHO 2023d). AMDR is not however linked to macronutrient quality (NASEM 2024).

AMDRs have not been identified for inclusion in recent reviews of the NRVs. NASEM (2024) noted that the approach to derive AMDRs is not consistent with current evidence-based standards. If macronutrients are prioritised, the review should consider the quality and strength of the evidence associated with chronic disease risk.

Consideration of the body of evidence, combined with dietary modelling to assess the effects of changes in macronutrients on micronutrients, should be considered for adults in Australia and New Zealand. Recommendations are for healthy people, and it is assumed that usual dietary intake will be at a level to maintain current healthy body weight.

As the evidence base for chronic disease prevention is mainly developed from studies and health outcomes in adults, AMDRs apply only to adults.

Further information on AMDR can be found in:

- WHO (2023a) Carbohydrate intake for adults and children: WHO guideline, World Health Organization.
- WHO (2023d) Total fat intake for the prevention of unhealthy weight gain in adults and children: WHO guideline, World Health Organization.
- WHO (2023b) Saturated fatty acid and trans-fatty acid intake for adults and children: WHO guideline, World Health Organization.
- NASEM (2024) Rethinking the Acceptable Macronutrient Distribution Range for the 21st Century: A Letter Report. Washington, DC: The National Academies Press. https://doi.org/10.17226/27957

6.6 Extrapolation and interpolation

NRVs will need to be set for population groups for which there is currently no experimental research data. Values may be set for these groups by extrapolation or interpolation of data from other populations. Extrapolation estimates values outside the range of known data while interpolation estimates values within the range of known data (i.e. to estimate values for a group in-between two groups for which data exists). Interpolation typically assumes a consistent change in nutrient requirements between groups for which data is available, with values derived using linear interpolation. In contrast with interpolation, extrapolation assumes that observations in one

group continue outside the observed range, increasing uncertainty in the estimate – particularly where linear extrapolation methods are used. For deriving infant and older infant NRVs interpolation is regarded as having greater uncertainty than extrapolation (FAO 2024).Interpolating or extrapolating data involves assumptions about how nutrient requirements change with age, size, body weight and other physiological factors such as life stage, body composition and metabolic rate. The accuracy of interpolated or extrapolated values is therefore dependant on the accuracy of these underlying assumptions.

Extrapolated NRVs should be biologically plausible and consistent with nutrient surveys of apparently healthy populations (FAO 2024).

6.6.1 Scaling

Scaling is a commonly used approach for extrapolating or interpolating NRVs for children and adolescents. NRVs can be scaled up for children and adolescents from infant values; or scaled down from adult values or older children.

Different methods of scaling can be applied, depending on the characteristics of the nutrient in question:

- isometric scaling assumes that linear / proportional relationships – relative to body weight - are preserved as size changes during growth or over time
- allometric scaling assumes that the metabolic rate of an organism is an exponential function of body weight.

The most appropriate scaling method should be determined based on:

- the available evidence for the population under consideration
- nutrient-specific context, including:
    - variation in requirements for pregnant or lactating women
    - differences in metabolism, toxicokinetics adaptive and homeostatic mechanisms between adults and children

If there is no clear rationale to select one method over another, the average of the methods can be used (FAO 2024) .

Expert Working Groups are responsible for ensuring that selected scaling methods are appropriate for each nutrient. All methods, assumptions and underlying scientific evidence should be clearly documented, along with a rationale for the selected method used for scaling.

When scaling, a mathematical formula is applied to calculate an NRV from a reference NRV based on various scaling parameters -typically, body weight. Other parameters such as body surface-area (BSA), energy or protein requirements (or intakes) can be used if they are more relevant to the function of the nutrient (FAO 2024). The scaling methods previously used to extrapolate reference values for a range of nutrients are listed in Appendix F. Scaling methods used internationally for NRVs for information.

When scaling, the general formula is:

$$Average\ value_{\ target\ group} = Average\ Value_{\ reference\ group}\ x\ (scaling\ factor)$$

In the context of NRVs, the average value is the AI, EAR, or UL depending on the NRVs being derived.

6.6.1.1 Scaling to derive Upper Level recommendations

In a 2023 EFSA workshop on human-to-human scaling approaches for the derivation of UL's, a decision tree was developed, outlining the considerations that need to be made when deciding on a scaling approach for setting an UL (Figure 6.4). It should be noted that this decision tree represents the views of the workshop participants on the day and does not necessarily reflect the views of the NDA panel (Foods et al. 2024).

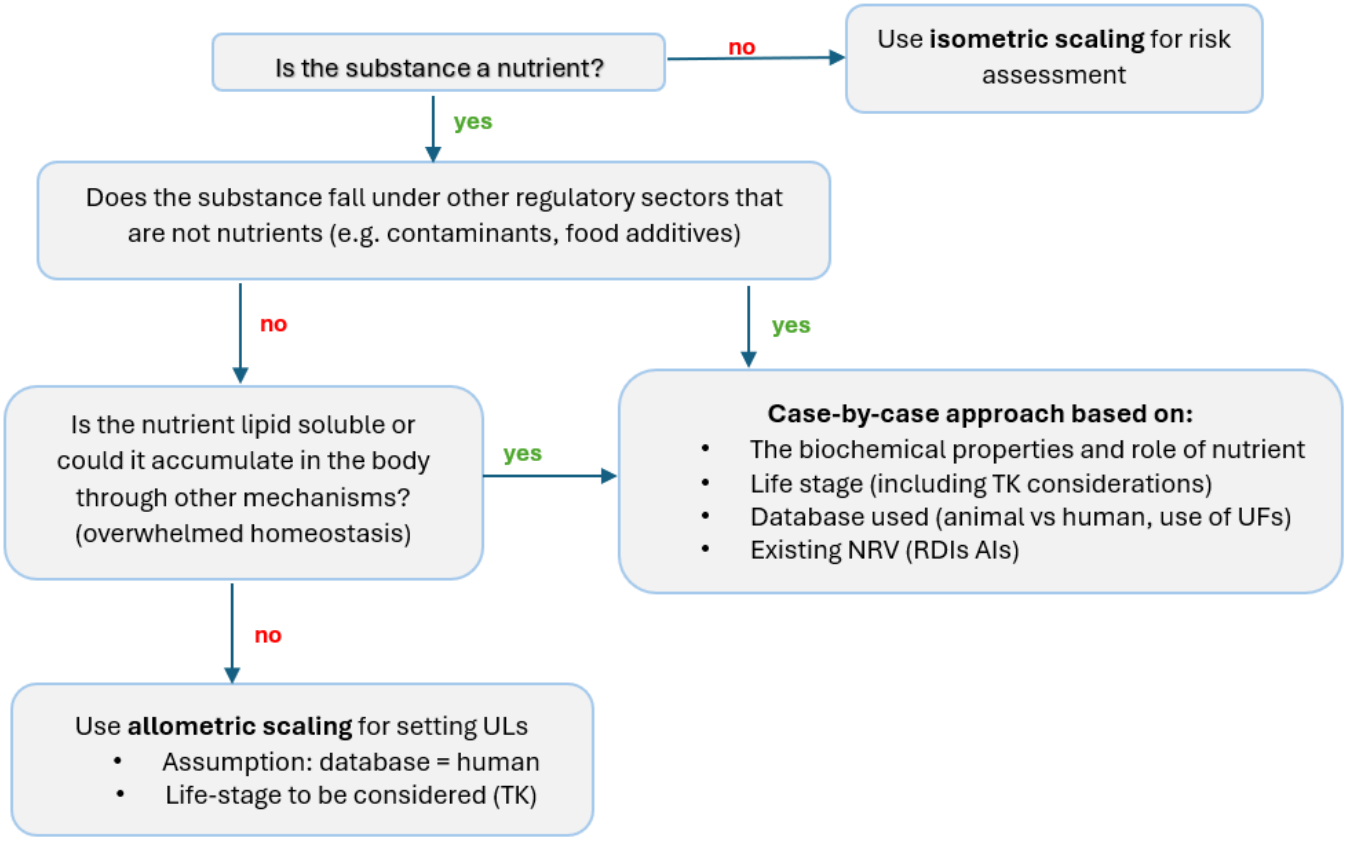

Figure 6.8 Decision tree for choosing a scaling approach for setting an UL.

Adapted with permission from (Foods et al. 2024)

TK, toxicokinetics.

Because scaling relies on assumptions, the resulting reference values for infants and children often carry greater uncertainty than those for adults. As a result, when scaling is used to estimate upper levels, the derived UL may be lower than the observed intakes in younger age groups, even when no adverse effects are evident.

6.6.1.2 Isometric scaling

Isometric scaling (i.e. proportional scaling) is used for data relating to less metabolically active body tissues, such as minerals in bone and electrolytes (FAO 2024). It should be applied for nutrients that are:

- homogenously distributed within the body, or
- distributed in specific sites (e.g. tissues or organs) where the proportional relationship to body mass is maintained as body size changes (NASEM 2018).

Depending on the method for scaling, corrections may be required to account for additional nutrient requirements to support growth (NASEM 2018) – see 6.6.2 Growth factors.

Typically, isometric scaling is undertaken based on body weight (EFSA Panel on Dietetic Products Nutrition and Allergies 2010; FAO 2024; NASEM 2018), using the following equation:

$$[EAR\ or\ AI]_{target\ group} = [EAR\ or\ AI]_{reference\ group}\ x\ (weight_{\ target\ group} / weight_{\ reference\ group})$$

For example, if scaling down from adults to younger children, the reference group would be 'adults' and the target group would be 'younger children'. Similarly, if scaling up from younger infants to older infants, the reference group would be 'younger infants' and the target group would be 'older infants'.

Reference body weights specific to the Australian and New Zealand populations have been developed from 'ideal' body weight data from the 2022-2024 Australian Health Surveys and the equivalent in New Zealand (Appendix C).

Note that this formula assumes a linear relationship between the requirements for the reference and target populations, proportionate to body weight. For some nutrients involved in growth and development, this formula may require adjustment to account for growth - see 6.6.2 Growth factors.

In contrast to the body weight approach adopted by other international bodies (EFSA Panel on Dietetic Products Nutrition and Allergies 2010; NASEM 2018), the EURECCA framework adopted an isometric scaling method based on BSA (body surface area) using the formula:

$$EAR_{child} = EAR_{adult} * \frac{BSA_{child}}{BSA_{adult}} = EAR_{Adult} * \sqrt{\frac{Weight_{child} * Height_{child}}{Weight_{adult} * Height_{adult}}}$$

In practice this method is used infrequently in nutrition, as there are also concerns about the reliability of BSA estimates particularly for children (Redlarski et al. 2016).

Occasionally, isometric scaling based on energy requirements may be used (e.g. sodium). However, the difference between BSA and energy intake-based equations are expected to be marginal as there are no reliable estimates of activity factors in each age group.

Isometric scaling has also been used to estimate requirements for nutrients in parallel, where nutrients have a shared function and robust data for one nutrient may be lacking. For example, EFSA used the calcium-to-phosphorus ratio to estimate phosphorus requirements based on calcium NRVs (EFSA Panel on Dietetic Products Nutrition and Allergies 2015). However, this approach is uncommon.

6.6.1.3 Allometric scaling

Allometric scaling should be undertaken when the relationship to body mass is not maintained as body size changes. In this case, body weight should be adjusted to derive a metabolic body weight that accounts for metabolic or surface area differences between age groups.

Metabolic weight has been defined as 0.75 power of body mass (weight) to adjust for metabolic differences between age groups. The 0.75 power is used to account for metabolically active tissue,

which is proportionally higher in infants (and possibly during high growth periods around puberty) than in adults (NASEM 2018). Reference body weights specific to the Australian and New Zealand populations have been developed from 'ideal' body weight data from the 2022-2024 Australian Health Surveys and the equivalent in New Zealand (Appendix C).

Metabolic weight 0.75 power of body mass (weight) should not be used for pregnancy.

Metabolic weight adjustment does not account for differences in adaptive and homeostatic mechanisms for nutrient absorption and elimination or differences in metabolism or synthesis of body tissue during growth.

Older people may have a lower lean body mass and metabolic activity than younger adults, compared with children who may have higher metabolic activity.

Allometric scaling expresses maintenance needs relative to metabolic body weight, and uses the formula:

$$EAR\ or\ AI_{\ target\ \ group} = EAR\ or\ AI_{reference\ \ group}\left(\frac{Weight_{target\ \ group}}{Weight_{reference\ \ group}}\right)^{0.75}$$

Further adjustment to account for growth requirements is typically required, particularly for scaling from adult values, as adult NRVs reflect maintenance needs only. See 6.6.2 Growth factors.

Further information about scaling approaches, can be found in:

- EFSA Panel on Dietetic Products, Nutrition, and Allergies (2010) Scientific Opinion on principles for deriving and applying Dietary Reference Values. *EFSA Journal, 8(3): 1458.* https://doi.org/10.2903/j.efsa.2010.1458 - Appendix 1 (pp 28-29)
- EFSA Panel on Nutrition Novel Foods and Food Allergens et al. (2024a) Guidance for establishing and applying tolerable upper intake levels for vitamins and essential minerals. *EFSA Journal*, *22*(11), e9052. https://doi.org/10.2903/j.efsa.2024.9052 - Annex A Workshop report on human-to-human scaling approaches for the derivation of tolerable upper intake levels
- NASEM. (2018). Harmonization of Approaches to Nutrient Reference Values: Applications to Young Children and Women of Reproductive Age. National Academies Press (US) https://doi.org/10.17226/25148 - pp. 60-61
- Atkinson (2007) *Background Paper: The DRI Development Process; Issues Related to Extrapolation and Interpolation.* The Development of DRIs 1994-2004: Lessons Learned and New Challenges, Workshop Summary, Washington DC. https://nap.nationalacademies.org/read/12086/chapter/9
- FAO (2024) *Review of derivation methods for dietary intake reference values for older infants and young children – FAO request for scientific advice to develop general principles for the establishment of Codex nutrient reference values for older infants and young children.* Food and Agriculture Organization of the United Nations. https://doi.org/10.4060/cb9380en

6.6.2 Growth factors

When NRVs are derived by scaling from adult requirements, the calculated result typically reflects maintenance needs only. Scaling approaches must therefore adjust for growth requirements by applying a growth factor. When scaling up from infants to older infants, a separate growth factor is not typically required because the reference AI for a growing young infant already accounts for growth requirements.

Growth factors are calculated based on estimated additional protein requirements for growth at the different ages and are presented at Appendix C.

When a growth factor is included in the scaling, the general formula becomes:

$$Average\ Value_{\ target\ group} = Average\ Value_{\ reference\ group} \times (scaling\ factor) \times (1 + growth\ factor)$$

6.7 Rounding and adjustments

Estimates from extrapolation and interpolation are inherently uncertain, and the range of calculated values should be reviewed to ensure differences between age groups are coherent (NASEM 2018). Where abrupt or significant changes are observed between age groups, consideration should be given to whether this change is appropriate (e.g. does it reflect a significant shift in requirements aligned with a particular life age/stage). NRVs should be adjusted – where necessary - to ensure appropriate consistency in recommendations across age groups. Where age groupings include children and adolescents of varying age and developmental stage, consideration should be given to whether it is most appropriate to round upwards or downwards to ensure that the needs of all children within an age grouping are met.

Any rounding and adjustment to draft values must be clearly communicated and the rationale included in the review documentation. Implications of any rounding must be considered.

6.8 Special considerations

6.8.1 Requirements for physiologically derived nutrients

Nutrients that are synthesised in the body, such as vitamin D and vitamin K, have both dietary and non-dietary sources. Review of these two nutrients requires consideration of whether NRVs should be set based on:

(i) physiological requirements of individuals (regardless of the source of intake), or

(ii) dietary requirements following consideration of the non-dietary contribution to the physiological intake.

Reviews of these nutrients should clearly identify the basis for setting nutrient values and ensure:

- Studies are consistent in focus i.e. they report on dietary or physiological requirements
- If values are developed based on dietary requirements, both physiological and dietary reference values are provided
- Recommendations clearly identify appropriate comparison and use of values. For example, it is inappropriate to compare population vitamin D intakes from a region that experiences high sunlight exposure with an AI that assumes minimal sunlight exposure.

Consideration should be given to development of an AI for vitamin D levels in Australia and New Zealand that considers varying sunshine exposure in all regions/populations.

Chapter 7: Developing NRV recommendations

7.1 Translating estimated nutritional requirements into NRV recommendations

The following documents and information are required to translate evidence into an NRV recommendation:

- current NRV for Australia and New Zealand
- rationale for updating
- description of the question and priority outcomes
- summary of the evidence from:
  - an evidence review from an international jurisdiction that underpins the NRV and/or
  - existing high-quality reviews (that meet NHMRC requirements) and/or
  - de novo evidence review
- intended approach for:
  - calculating NRV requirements (factorial approach, dose response or risk assessment)
  - scaling (including rationale for the selected scaling method)
  - calculations with assumptions
- contextual evidence including factors relating to:
  - nutrient requirements in the Australian and New Zealand context (e.g. dietary patterns, food system, population status and intakes)
  - comparison against international NRVs
  - equity and other social determinants.

7.2 Relevant contextual factors

7.2.1 Dietary patterns

7.2.1.1 Dietary patterns for adequacy

Recommended dietary patterns are based on the four Foundation Diets developed in *A Modelling System to Inform the Revision of the Australia Guide to Healthy Eating* (Dietitians Association of Australia et al. 2011). Evidence reviewers are not required to develop or adapt the Modelling

System. Evidence reviewers will check any draft values proposed meet the criteria of realistic and achievable for the Australian/New Zealand population using various data sources (NHMRC 2011).

As part of this work, evidence reviewers are requested to develop and propose draft NRVs based on the evidence. These draft values should then be compared with the results of relevant nutrient analysis of **current** dietary patterns in Australia[8] and New Zealand such as the Australia Physical Activity and Nutrition Survey 2011-12 (ABS 2014) to ensure the value is **realistic** and **achievable.**

7.2.1.2 Nutrient intake and Upper Level of Intake (UL)

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. Quantified risk estimates for the adverse health risks associated with different levels of nutrient intake are also required. When proposing draft UL values, validation of proposed ULs against actual population intakes requires consideration of supplement use.

For each defined sub-population of interest, consider all nutrient sources by combining the Foundation Diet intakes or survey data with supplements and drinking water. Determine the upper boundary of intakes that has not been associated with adverse outcomes in reliable studies.

7.2.2 Potential impacts

The implications should be discussed of any proposed draft value that:

- varies significantly from relevant nutrient content of current dietary patterns
- varies significantly from relevant nutrient content of recommended dietary patterns i.e. Foundation Diet Models
- varies significantly from existing values and the values of other comparable international jurisdictions
- impacts on regulation

7.2.3 International dietary reference values

Proposed NRVs should be contrasted with NRVs from comparable international jurisdictions. If final recommendations differ substantially to international values or the previous Australian value, Expert Working Groups should record the rationale for difference in findings. Rationale should also be included when final recommendations reflect existing values. All decisions regarding the basis of final NRV values will be clearly recorded and communicated to final end-users as per the GRADE process.

[8] Noting that currently there is no similar data set for the New Zealand population.

7.3 GRADE evidence-to-decision process

The GRADE evidence-to-decision (EtD) framework is guided by a set of criteria that consider the available scientific evidence, anticipated benefits and harms, stakeholder values and preferences, resource implications, equity, acceptability, and feasibility. For the development of NRVs, one EtD framework should be applied for each population group for each nutrient.

People consume whole foods rather than isolated nutrients, and that interactions between nutrients may need to be considered when deriving reference values. The considerations in the EtD framework will also be related to food sources and supply, food systems, dietary patterns and the public health situation in Australia and New Zealand.

The EtD template is used to capture discussion, the rationale and any judgements or assumptions about the nutrient by the expert committee throughout the development process. It is published alongside the value to convey the Committee's judgement of the evidence and how those judgements are reflected in the value. This ensures a transparent decision-making process and for future harmonisation efforts across jurisdictions.

If there are overarching issues that are important to the calculations of NRVs they should be reflected in the EtD framework.

The following framework has been adapted from templates available in the GRADEpro platform (https://www.gradepro.org/).

7.3.1 Evidence-to-decision template

Outline the background and context of nutrient in Australia, NZ and other relevant jurisdictions

What is the current NRV value in Australia and NZ and what was the evidence upon which it was based?

What is the current value in international jurisdictions? (benchmark against international and foundation diets)

What are the associated health implications of this nutrient?

Is this nutrient linked to other nutrients?

What is the rationale for prioritising this review?

- What evidence was used to decide priorities?

Why do you need an NRV for this nutrient?

What is the nutrient specific health issue you are trying to address in Australian and NZ?

What are the current dietary intakes in Australia and NZ?

- What assumptions are made about the dietary surveys?
    - What are the risks in those assumptions?
    - What are the associated mitigation strategies?

Who uses this NRV?

Summary of evidence

What does the current evidence base consist of?

Is there enough evidence to perform metanalysis? If not, how will the evidence be used to calculate the NRV?

Is there enough information to calculate an NRV from?

Comparison of calculated value

Does this revised value differ from the current value?

Is this value consistent with other comparable international jurisdictions. If not, can the differences be explained?

Is the new value sufficiently different from the old value to justify a change?

Is the underlying evidence certain enough to justify a change?

What is the impact of altering this value relative to other NRVs for the nutrient?

What are the consequences of not changing the NRV?

Was any rounding done to the figure?

What Uncertainty Factor (UF) was applied?

- What was the justification for the UF used?

Were there any other adjustments made to the value? (if so, why?)

Scaling method

Will scaling and extrapolation be needed for certain populations?

What methods were used to scale values for this specific population?

Evidence to decision

Criterion	Judgement factors
Balance of effects (Benefits and harms)	Do the benefits outweigh the harms for establishing the NRV at the proposed level? Is it acceptable to make the NRV recommendation if there are harms in one population but benefits in others? What proportion of the population should be covered by the NRV?
Certainty of the evidence	GRADE methodology (or similar) will be used to determine evidence certainty during the evidence review stage
Values and preferences	Is there uncertainty or variability in how much people value the outcome? How does the proposed NRV value relate to current dietary patterns? Do people have different views on harms and benefits associated with intakes of this nutrient that may influence values and preferences?
Cost effectiveness and	*This should be considered with context to available food sources.* What are the resource implications of the proposed NRV recommendation?

required resources	Are sources of this nutrient available in a cost-effective form (for instance through available food sources)?
	What are the implications for food/supplement industries?
	What are the implications for government/regulators?
	What are the implications for consumers?

Other factors to be considered by the Committee (equity, acceptability, feasibility, environmental sustainability). Sample questions to guide discussion are offered below:

Will there be some groups who are more advantaged or disadvantaged in meeting the NRV recommendation for this nutrient?

Is ingestion of this nutrient within the levels specified by the NRV acceptable to all stakeholders and populations?

With consideration to current dietary patterns is the specified value feasible to achieve?

Are there sustainability issues in obtaining this nutrient? I.e. from certain food sources?

Are there bioavailability considerations relevant to the Australian or New Zealand context?

What impact does intake within the level/s specified by the NRV have on other nutrient requirements?

Are there interactions of this nutrient with other nutrients?

Is specific public health advice required?

Further guidance on GRADE evidence-to-decision is available in:

- Neumann et al. (2025) *GRADE Book.* https://book.gradepro.org/
- The GRADE Working Group (2024) *GRADE Handbook* https://gdt.gradepro.org/app/handbook/handbook.html
- Journal of Clinical Epidemiology GRADE Guidance series. https://www.sciencedirect.com/special-issue/10F8V3S0J7V
- NHMRC Guidelines for Guidelines (2019) Evidence to decision making recommendations Evidence to decision | NHMRC
- Moberg et al. (2018) The GRADE Evidence to Decision (EtD) framework for health system and public health decisions. *Health Res Policy Sys* **16**, 45 https://doi.org/10.1186/s12961-018-0320-2 .

Glossary

ABS	Australian Bureau of Statistics
ADGs	Australian Dietary Guidelines
AI	Adequate Intake: The mean daily nutrient intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate (used when an EAR cannot be determined)
allometric	allometric scaling assumes that the metabolic rate of an organism is an exponential function of body weight
AMDR	Acceptable Macronutrient Distribution Range: 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.
AMSTAR II	A MeaSurement Tool to Assess Systematic Reviews II
AR	Average requirement: the level of (nutrient) intake that is adequate for half of the people in a population group, given a normal distribution of requirement (EFSA Panel on Dietetic Products Nutrition and Allergies 2010)
BSA	Body surface area
Department	Australian Government Department of Health, Disability and Ageing
CDRR	Chronic Disease Risk Reduction: lowest level of intake for which there is sufficient strength of evidence to characterise a chronic disease risk reduction within an apparently healthy population
EAR	Estimated Average Requirement: A daily nutrient level estimated to meet the requirements of half the healthy individuals in a sex[9] and particular life stage group. This also takes into account height, weight and physical activity levels.
EFSA	European Food Safety Authority
EURRECA	EURopean micronutrient RECommendations Aligned: Evidence-based methodology for deriving micronutrient recommendations
extrapolation	Scaling the NRVs for younger or older age groups either upwards or downwards.

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

factorial method	Derives requirements from the sum of estimates of nutrients intake for physiological maintenance and growth and nutrients lost from the body in faeces, urine, sweat and respiration
FAO	Food and Agriculture Organization of the United Nations
GRADE	Grading of Recommendations, Assessment, Development and Evaluation: an internationally recognised approach to rate the quality of evidence and the strength of recommendations and is considered the standard in guideline development
interpolation	Derive NRVs for an intervening group or groups when the NRVs for the two groups on either side are known. The NRVs for the intervening group or groups are estimated and smoothed between the NRVs of the two other groups using interpolation.
IOM	Institute of Medicine: a component of the US National Academy of Sciences that works outside the framework of government to provide evidence-based research and recommendations for public health and science policy.
isometric	isometric scaling assumes that proportional relationships – relative to body weight - are preserved as size changes during growth or over time
LOAEL	Lowest Observed Adverse Effect level: Lowest dose at which there is a measurable adverse effect from a test substance in a test subject or population.
MD	mean difference
Modelling System	The document, A Modelling System to inform the revision of the Australian Guide to Healthy Eating, was developed in 2011 and translates selected NRVs and healthy dietary patterns into dietary models, known as Foundation Diets. It describes the foods required to support positive health outcomes and the quantities needed to meet estimated nutrient requirements of groups of Australian individuals at different ages, sex, body size and activity. It also takes into consideration social and food cultures, promotion of health and wellbeing and the Australian food system while applying the best available scientific evidence. The nutrient composition of each Foundation Diet type – omnivore, rice-based, pasta-style and lacto-ovo vegetarian – is provided (NHMRC 2011)
NASEM	United States National Academy of Science Engineering and Medicine
NHMRC	National Health and Medical Research Council: Australia's peak body for supporting health and medical research; for developing health advice for the Australian community, health professionals and governments; and for providing advice on ethical behaviour in health care and in the conduct of health and medical research
NOAEL	No Observed Adverse Effect Level: Highest dose at which there is no measurable adverse effect from a test substance in a test subject or population

NOS	Newcastle Ottawa Scale. A risk of bias tool used to assess the quality of nonrandomised studies
NRV	Nutrient Reference Values: A set of nutritional recommendations, based on current scientific knowledge, used to assess the health status of populations and individuals.
NZ MInistry	New Zealand Ministry of Health
PI/ECOS	Population, Intervention/Exposure, Comparator, Outcome, Study design
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RDI	Recommended Dietary Intake: The mean daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97.5 per cent) healthy individuals of a particular life stage and sex.
RoB 2	Risk-of-bias tool. Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) is the recommended tool to assess the risk of bias in randomized trials included in Cochrane Reviews
ROBIS	Risk of bias in systematic reviews tool
SD	Standard Deviation
SDT	Suggested Dietary Target: A daily mean intake from food and beverages for certain nutrients that may help in the prevention of chronic disease.
UF	Uncertainty Factor
UL	Upper Level of Intake: The highest mean 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 risk of adverse effects increases

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Appendices

Appendix A. History of framework development

Table A.1: NRV development in Australia and New Zealand

Year	Activity
1991	NHMRC published *Recommended Dietary Intakes for use in Australia*
1997	Need to revise *Recommended Dietary Intakes for use in Australia* identified
1999	Scope of review agreed: • A joint review between Australia and New Zealand should be conducted • A set of nutrient recommendations should be developed using the terminology of NRVs • NRVs should be based on the US-Canadian DRIs and concurrent work being conducted in these countries.
2001	NHMRC commissioned to undertake a scoping study
2002	NHMRC commissioned to manage the joint Australian/New Zealand revision process.
2002 - 2004	40 priority nutrients reviewed
2005	Consultation of revised NRVs
2006	Nutrient Reference Values for Australia and New Zealand (2006) released
2011	Scoping study commissioned by the Department for undertaking a review of the NRVs. Recommended targeted reviews of priority nutrients
2015	Methodological Framework developed to guide nutrient reviews. Three priority nutrients identified: fluoride, sodium and iodine.
2016	Pilot nutrient review undertaken by Department in consultation with NZ Ministry and endorsed by the NHMRC addressing aspects of the NRVs for sodium and fluoride
2018	NHMRC appointed to finalise reviews of priority nutrients

Year	Activity
2019	Update to methodological framework and governance structure post pilot including age range clarification and ideal median weight data Commencement of sodium and iodine reviews Update to methodological framework with additional detail on scaling/ NRV derivation and adopt/adapt processes
2025	Update to methodological framework methods with inclusion of GRADE, updated age groups, reference weights, growth factors

Appendix B. NRV nutrient update prioritisation framework

In the February 2025 Steering Group Advisory Committee meeting, a draft prioritisation framework for selecting future nutrients to be updated was discussed. This document was finalised in March 2005.

This framework is based on *the Australian Dietary Guidelines review* *Prioritisation Process Report*. The principles were modelled on the prioritisation pathways used for development of the Dietary Guidelines for Americans 2021-2025, the Nordic Nutrition Recommendations 2022, and Canada's Dietary Guidelines 2019. The principles also consider prioritisation criteria commonly used in the development of health practice guidelines (El-Harakeh et al. 2019).

The Steering Group is responsible for the ongoing monitoring of triggers for a new review, decision making, resourcing and ensuring nutrient reviews are conducted in a timely manner. In selecting and prioritising NRVs for review, consideration will be given to the relative priority and resource requirements associated with potential updates, along with the available review resources at any given time.

An update of existing NRVs may be triggered via several mechanisms, including where:

- an update is identified as a priority for review by the Steering Group
- a recent, high quality systematic review is published, with implications for the currency or accuracy of related NRVs
- revised NRVs are set by comparable international jurisdictions, with implications for the currency or accuracy of related NRVs
- review is required to inform decisions about mandatory fortification programs.

If only one NRV for a particular nutrient is prioritised for review, consideration should be given to the impact of altering this value relative to other NRVs for that nutrient.

NRV update prioritisation framework

For each nutrient:

- time since last review
- is there new available evidence? (what kind?)
- Have any levels for this nutrient been updated internationally recently?

1. Relevance

NRVs prioritised for review will apply to people of all ages and backgrounds in the general population, including people with common diet-related risk factors such as being overweight.

Consider if the information on the NRV:

- relates to the Australian and New Zealand context
- is applicable to the general Australian and New Zealand populations
- is relevant to the promotion of health or prevention (rather than treatment or management) of a nutrition-related chronic disease or nutrition-related risk factors.
- suggests the current NRV may be inappropriate for the population based on significant new evidence.

2. Importance – importance to current public health priorities and to what degree.
Is the topic:

- of significant public health importance
- an emerging public health priority
- aligned with, or addressed Australian or New Zealand Government health priorities
- a long-standing issue or has the potential to change existing recommendations
- likely to change a recommendation and if so, would it result in significant public health improvement
- addressing an area of rapidly changing evidence
- an area of significant public interest, including in media
- an area of potential misinformation
- an area that could inform (and to what extent) national food and health policies and programs.

3. Type of impact - on public health including broader societal, economic or environmental impacts.
Does the nutrient:

- have an associated health burden
- have the potential to impact health outcomes
- have associated health consequences
- impact mortality, survival, longevity and life expectancy
- impact morbidity and disability
- impact disease burden or have the potential to reduce severity of disease
- relate to health biomarkers
- relate to food and dietary patterns
- address socioeconomic, demographic and cultural issues/needs
- relate to ethical sensitivities
- consider equity or human rights
- have societal impacts or impacts on non-health outcomes
- have environmental impacts
- have economic or financial impacts
- affect fortification of foods (reduce, increase, begin, stop fortification).

4. **Degree of impact –** including considering the magnitude of the issue and the size of the affected populations likely to be impacted.

Consider:

- the magnitude of the health burden associated with the topic
- the magnitude of the potential impact on health outcomes
- the degree to which a topic would impact financial, economic, environmental or societal areas.

Evidence base

- Is the evidence underpinning recommendations likely to have changed significantly since the previous values were derived?
- Is there new data available?
- Are there changes in food supply/dietary patterns that have the potential to significantly impact intake for this nutrient

Overarching questions:

- How often should reprioritisation happen?
- Should we consider all nutrient reference values for each nutrient every time?
- Factors such as associated health burden or health benefit should be considered relative to other potential nutrients for prioritisation (i.e. if fluoride and fibre are under consideration for prioritisation, one of these has a much higher associated health burden at a population level, so it should be prioritised above the other)

Other potential steps/approaches for selecting priority nutrients

- mapping exercise to look at recommended intake vs current intake to identify the largest gap/need (to see where we could achieve in health gains)
- for future NRV updates we initially consider adopting/adapting overseas values if relevant to make the most effective use of limited resources and avoid duplication of effort

– for example, EFSA has recently updated the ULs for vitamin A, vitamin B6, vitamin D, vitamin E, beta-carotene, iron, manganese, folate/folic acid, and selenium; WHO recently updated values for trans fats, carbohydrates and proteins.

Appendix C. Standardised age, height, weight and growth

C.1. Age groups

In 2025 the Department has included additional age groupings to reflect different educational and developmental stages. These groupings are the ones reported on by the Australian Bureau of Statistics in the National nutrition survey. NHMRC has also changed the way children's groups are expressed to clarify that the group includes up to the day before the next birthday.

Adults are considered to be 18-years and over, (previously 19+ years) and older adults are separated into the following groups: 50-64 years, 65-74 years, 75+ years (previously 51-70 years, 70+ years). There are also additional children's age groups (early years, primary school, adolescence) see Table C.1 for further details.

Table C.2.1 Comparison age groupings

<table>
<tr><th>NRV Age Groups</th><th>Additional Age groups for nutrition reporting</th></tr>
<tr><td colspan="2">INFANTS</td></tr>
<tr><td colspan="2">0 - 6 months</td></tr>
<tr><td colspan="2">7 - 12 months</td></tr>
<tr><td colspan="2">CHILDREN & ADOLESCENTS</td></tr>
<tr><td rowspan="2">1 to under 4 years</td><td>12 to under 24 months</td></tr>
<tr><td rowspan="2">2 to under 5 years (preschool)</td></tr>
<tr><td rowspan="2">4 to under 9 years</td></tr>
<tr><td rowspan="2">5 to under 12 (primary school)</td></tr>
<tr><td rowspan="2">9 to under 14years</td></tr>
<tr><td rowspan="2">12 to under 18 years (adolescence)</td></tr>
<tr><td>14 to under 18 years</td></tr>
<tr><td colspan="2">ADULTS</td></tr>
<tr><td colspan="2">18 to under 30 years</td></tr>
<tr><td colspan="2">30 to under 50 years</td></tr>
<tr><td colspan="2">50 to under 65 years</td></tr>
<tr><td colspan="2">65 to under 75 years</td></tr>
<tr><td colspan="2">75 years and over</td></tr>
</table>

The additional age groups will be added for future NRV updates. For nutrients where not all values are being updated (i.e. if only the UL is updated), consideration will be given to whether the age groups for the values not being updated can be converted to the additional age groupings without affecting the validity of the values.

C.2. Median heights

Australian median height data was provided by the Australian Bureau of Statistics (ABS) from the Australian National Health Survey 2022-24 (ABS 2022). This was compared to New Zealand data from the 2018-20 New Zealand Health Surveys (Ministry of Health 2019, 2022).

C.3. Reference bodyweights

For consistency across nutrients, 'ideal' body weight will be used to derive reference weights for updating NRVs for all nutrients, unless there is evidence that adipose tissue impacts requirements for a nutrient (i.e. vitamin D or zinc).

Reference body weights used for deriving and updating NRVs prior to 2025 are outlined in the Nutrient Reference Values for Australia and New Zealand (NHMRC 2006). From 2025 onwards, calculated 'ideal' weight will be used for the updated reference weights. These weights have been provided by the ABS (Attachment 1). This data was calculated from the Australian National Health Survey 2022-24 data (ABS 2022) using median heights from the 2022-24 National Health Survey and 'ideal' BMI. 'Ideal' BMI was calculated as follows: for adults, take the midpoint of the normal BMI range, this gives a BMI of 21.75. For children take the midpoint of the normal BMI range for each half-year age group (by sex where appropriate) (using whole years as boundaries) and average these (Cole et al. 2000; Cole et al. 2007). No adjustments were made for overweight and obesity. If nutrients under review are highly metabolically active in adipose tissue further consideration should be given to the difference between calculated reference body weights and measured body weights.

New Zealand height and weight data were provided by the NZ MoH. Data from the 2018-2020 Health Surveys were pooled to produce more robust estimates. 'Ideal' weight was not calculated for the New Zealand data as height measurements appeared very similar to Australian height measurements. This was confirmed by checking with several groups using the equation that the ABS used: ideal weight kg = ideal BMI * height in metres squared, using sex/age specific ideal BMI from ABS data. This single data set will be applied to all NRV reviews.

ABS will report nutrient intake data against reporting age groupings. For nutrients where age groupings have not been updated NRVs will be imputed from existing age groupings with weighted means.

As ABS does not collect data for infants under 2-years of age, for the 0-6 month, 7-12 month and 12 to under 24- infant age groups, reference body weight was calculated using the WHO Growth Standards (WHO Multicentre Growth Reference Study Group 2006). The following calculation process was used:

1. Weight-for-age (percentiles) data was extracted for boys and girls in each age group,
2. Mean and median of weight values for each sex was calculated,
3. Values calculated in step 2 were averaged.

Although the resulting values for infants are not calculated from weight data collected from the Australian and New Zealand population, this is the best available data for the purposes of NRV calculation.

Table C.3.1 NRV reference weights and their derivation methods.

Population	Age Group	Reference Weight (kg)			Source
		Persons	Females	Males	
Infants	0-6 months	6.1	5.8	6.4	Derived from WHO Child Growth Standards weight for age percentiles
	7- 12 months	8.7	8.3	9	
Children & Adolescents	1 to under 4 years	13.0	12.7	13.2	
	4 to under 9 years	22.4	22.3	23.0	Australian Bureau of Statistics (ideal body weights)*
	9 to under 14 years	40.7	40.4	41.1	
	14 to under 18 years	57.6	54.8	61.8	
Adults	18 to under 30 years	62.9	57.8	68.9	
	30 to under 50 years	62.1	57.8	67.4	
	50 to under 65 years	60.7	56.4	65.9	
	65 to under 75 years	59.2	55	64.3	
	75+ years	57.8	52.9	62.9	

*Attachment 1 Australian Ideal Bodyweight Dataset 2022 supplied by the ABS.

Alternate reporting age groupings

Population	Age Group	Reference Weight (kg)			Source
		Persons	Females	Males	
Infants	0-6 months	6.1	5.8	6.4	Derived from WHO Child Growth Standards weight for age percentiles
	7-12 months	8.7	8.3	9	
Children & Adolescents	12 to under 24	10.6	10.2	10.9	
	2 to under 5 years	15.9	15.7	16.1	Australian Bureau of Statistics (ideal body weights)*
	5 to under 12 years	28.6	29	28.7	
	12 to under 18 years	54.5	52.5	57.9	
Adults	18 to under 30 years	62.9	57.8	68.9	
	30 to under 50 years	62.1	57.8	67.4	
	50 to under 65 years	60.7	56.4	65.9	
	65 to under 75 years	59.2	55	64.3	
	75+ years	57.8	52.9	62.9	

*Attachment 1 Australian Ideal Bodyweight Dataset 2022-24 supplied by the ABS.

Table C.3.2 Weight-for-age percentiles derived from the World Health Organization (WHO) Child Growth Standards, used to calculate reference weights for children under two years of age.

Year:Month	Months	Median Weight	
		Girls	Boys
0:0	0	3.2	3.3
0:1	1	4.2	4.5
0:2	2	5.1	5.6
0:3	3	5.8	6.4
0:4	4	6.4	7
0:5	5	6.9	7.5
0:6	6	7.3	7.9
0:7	7	7.6	8.3
0:8	8	7.9	8.6
0:9	9	8.2	8.9
0:10	10	8.5	9.2
0:11	11	8.7	9.4
0:12	12	8.9	9.6
1:1	13	9.2	9.9
1:2	14	9.4	10.1
1:3	15	9.6	10.3
1:4	16	9.8	10.5
1:5	17	10	10.7
1:6	18	10.2	10.9
1:7	19	10.4	11.1
1:8	20	10.6	11.3
1:9	21	10.9	11.5
1:10	22	11.1	11.8
1:11	23	11.3	12

C.4. Growth factors

Growth factors were calculated as the proportional increase in protein requirement for growth relative to the maintenance requirement at the different ages (EFSA Panel on Dietetic Products Nutrition and Allergies 2012; NASEM 2018). The value for each age group corresponds to the mean of values for the years included

Table C.4.1 Growth Factor calculations

NRV Age Groupings

Age group (yrs)	Growth Factors		
	Girls[a]	**Boys**[a]	**Persons**[b]
0 - 12 months	0.57	0.57	0.57
1 to under 4 years	0.20	0.25	0.23
4 to under 9 years	0.08	0.09	0.09
9 to under 14 years	0.11	0.11	0.12
14 to under 18 years	0.04	0.08	0.06

Alternate reporting Age Groupings

Age group (yrs)	Growth Factors		
	Girls[a]	**Boys**[a]	**Persons**[b]
0 - 12 months	0.57	0.57	0.57
12 to under 24 months	0.44	0.44	0.44
2 to under 5 years (preschool)	0.12	0.12	0.12
5 to under 12 years (primary school age)	0.11	0.12	0.12
12 to under 18 years (adolescent)	0.06	0.09	0.07

(a) Derived from EFSA NDA Panel Growth Factors (EFSA Panel on Dietetic Products Nutrition and Allergies 2012) – see Table C.4.2

(b) Calculated as mean of Growth Factors for boys and girls

Table C.4.2 Source data underpinning Growth Factor calculations

Age (yrs)	Maintenance requirement (g protein/kg per day) (a) (A)	Growth requirement (g protein/kg per day) (a) (B)	Average Requirement for protein (g/kg per day) (a) (A+B)	Calculated growth factor (B/A)	Growth factor per age group (b)
Boys					
0.5	0.66	0.46	1.12	0.70	7-12 mo: 0.57
1	0.66	0.29	0.95	0.44	
2	0.66	0.13	0.79	0.20	12 to under 24 mo: 0.44
3	0.66	0.07	0.73	0.11	
4	0.66	0.03	0.69	0.05	1 to under 4 yrs: 0.25
5	0.66	0.03	0.69	0.05	
6	0.66	0.06	0.72	0.09	2 to under 5 yrs: 0.12
7	0.66	0.08	0.74	0.12	
8	0.66	0.09	0.75	0.14	4 to under 9 yrs 0.09
9	0.66	0.09	0.75	0.14	
10	0.66	0.09	0.75	0.14	5 to under 12 yrs: 0.12
11	0.66	0.09	0.75	0.14	
12	0.66	0.08	0.74	0.12	9 to under 14 yrs: 0.13
13	0.66	0.07	0.73	0.11	
14	0.66	0.06	0.72	0.09	12 to under 18 yrs: 0.09
15	0.66	0.06	0.72	0.09	
16	0.66	0.05	0.71	0.08	14 to under 18 yrs: 0.08
17	0.66	0.04	0.70	0.06	
Girls					
0.5	0.66	0.46	1.12	0.70	7 -12 mo 0.57
1	0.66	0.29	0.95	0.44	
2	0.66	0.13	0.79	0.20	12 to under 24 mo: 0.44
3	0.66	0.07	0.73	0.11	
4	0.66	0.03	0.69	0.05	1 to under 4 yrs: 0.2
5	0.66	0.03	0.69	0.05	
6	0.66	0.06	0.72	0.09	2 to under 5 yrs: 0.12
7	0.66	0.08	0.74	0.12	
8	0.66	0.09	0.75	0.14	4 to under 9 yrs: 0.08
9	0.66	0.09	0.75	0.14	
10	0.66	0.09	0.75	0.14	5 to under 12 yrs: 0.11
11	0.66	0.07	0.73	0.11	
12	0.66	0.06	0.72	0.09	9 to under 14 yrs: 0.11
13	0.66	0.05	0.71	0.08	
14	0.66	0.04	0.70	0.06	12 to under 18 yrs: 0.06
15	0.66	0.03	0.69	0.05	
16	0.66	0.02	0.68	0.03	14 to under 18 yrs: 0.04
17	0.66	0.01	0.67	0.02	

mo, months; yrs, years
(a): Data sources - (EFSA Panel on Dietetic Products Nutrition and Allergies 2012; NASEM 2018).

(b): The value for each age group corresponds to the mean of values for the years included.

Appendix D. Assessment criteria for adopting or adapting an NRV from other jurisdictions

The administrative and technical criteria for assessing preliminary suitability of existing nutrient reference values are outlined below. These criteria have been informed by NHMRC's Guidelines for Guidelines: Adopt, adapt or start from scratch (NHMRC 2018), GRADE-ADOLOPMENT (Klugar et al. 2024), and the ADAPTE process (The ADAPTE Collaboration 2009). International organisations whose processes have been assessed previously include EFSA, WHO, US NASEM, Germany-Austria-Switzerland D-A-CH. National reviews for chemical risk assessments from AVPMA and FSANZ may also be relevant. Reviews from other organisations could also be considered if their processes are consistent with NHMRC Standards for Guidelines.

The systematic literature review and evaluation should meet many of the criteria outlined in Table - Administrative and technical criteria for assessing the suitability of existing nutrient reference values. Literature search details (databases searched, search terms, date range, exclusion criteria, etc), exposure parameters used, mathematical algorithms, etc should be fully documented.

Study quality which impacts on overall certainty of the evidence should be discussed, at least for the principal study/studies used for NRV derivation. The quality of these pivotal studies should be evaluated to justify their selection for underpinning the NRVs.

Consideration of the Australian and New Zealand context should include:

- Is the nutrient an issue in Australian and New Zealand dietary patterns?
- Are exposure assumptions consistent with Australian and New Zealand practice?
- Is the scaling method used appropriate for Australian and New Zealand populations?

Administrative and technical criteria for assessing the suitability of existing nutrient reference values

Title/Reference of document being assessed:

Assessment made by ONHMRC: *(date assessed)*

NHMRC's preference is to review sources that have made their processes publicly available, however it is understood that some technical aspects of an organisations' development process may need to be requested from the developer.

1. Overall guidance/advice development process			
Criteria	Yes/No/NA	Comment	Page #
Are the administrative processes (e.g. the NRV development process and associated governance, principles and procedures) documented and publicly available?			
Are the key stages of the organisation's NRV development processes compatible with NHMRC processes? (i.e., relevant and useful, transparent, overseen by a guideline development group/committee, COI management, focussed on health-related outcomes, evidence informed, actionable recs, up to date and accessible)			
Was the work overseen by an expert advisory committee?			
Are potential conflicts of interest of committee members declared, managed and/or reported?			
Are funding sources declared?			
Was there public consultation on this work? if yes, is the public consultation documented and/or published?			

1. Overall guidance/advice development process			
Criteria	Yes/No/NA	Comment	Page #
Was the guidance/advice developed or updated recently?			

2. Evidence review parameters			
Criteria	Yes/No/NA	Comment	Page #
Are decisions about scope, definitions and evidence review parameters documented and publicly available?			
Were clinical/research questions articulated and PICO criteria outlined appropriate to the topic?			
Does the organisation use or adopt review findings or risk assessments from other organisations?			
• what process was used to critically assess these external findings?			
Did the organisation undertake their own systematic literature review?			
Has the evidence report been reviewed by experts independent from the review authors? (e.g. peer review or committee review)?			
Does the organisation use or undertake systematic literature review methods to identify and select data underpinning the advice?			
• are the methods used documented clearly?			
• are inclusion/exclusion criteria used to select or exclude certain studies from the review?			
• is justification of inclusion/exclusion criteria provided?			

3. Evidence search			
Criteria	Yes/No/NA	Comment	Page #
Are databases and other sources of evidence specified?			
Does the literature search cover at least more than one scientific database as well as additional sources (which may include government reports and grey literature)?			
Is the date range of the literature search specified and justified?			
Are search terms and/or search strings specified?			

4. Critical appraisal methods and tools			
Criteria	Yes/No/NA	Comment	Page #
Is risk of bias of individual studies assessed and taken into consideration?			
• if yes, what tools are used? if no, was any other method used to assess study quality?			
Does the organisation use a systematic or some other methodological approach to synthesise the evidence (i.e. to assess and summarise the information provided in the studies)?			
Does the organisation assess the overall certainty of the evidence and reach recommendations?			

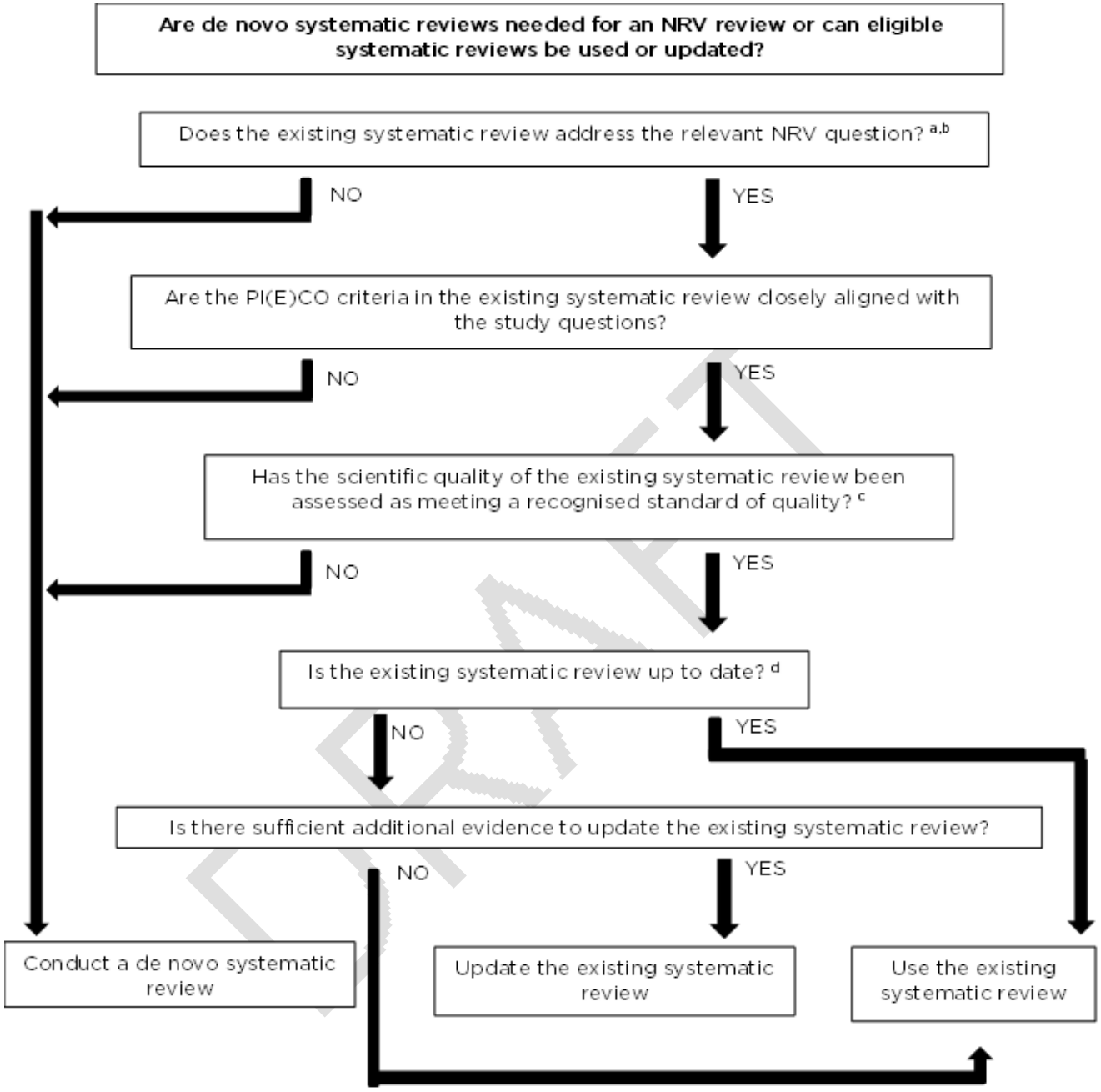
5. Derivation of nutrient reference values			
Criteria	Yes/No/NA	Comment	Page #
Is the method selected to calculate NRV(s) documented and justified? (factorial, dose response or risk assessment)			
Are the algorithms and calculations clearly documented and explained?			

5. Derivation of nutrient reference values			
Criteria	Yes/No/NA	Comment	Page #
Are the assumptions and reference data (intake, body weights for age groups etc) used for the calculations clearly documented and explained?			
Is there justification for the choice of uncertainty and safety factors?			
Is justification provided for any clinical/chronic endpoints selected as indictors/outcomes? (Details of endpoints to be provided in a supplementary table.)			
Is justification provided for the value selected for the reference point^? (including mechanistic evidence, health outcome data, key events, balance studies) ^ refence point is usually the baseline value to which any scaling and uncertainty factors are applied.			
Is the population group generalisable to the Australian and New Zealand population? - Where are the underlying studies from?			
If scaling was applied – was the method described, along with an appropriate rationale for the chosen method?			
• Is the method used appropriate for Australian and New Zealand populations?			
Are the processes used when expert judgement is applied documented and published? (Evidence-to-decision process used to obtain final conclusions).			

6. Suitability for adopting vs adapting			
Criteria	Yes/No/NA	Comment	Page #
How does the Australian and New Zealand context (e.g. food system, dietary patterns, intakes, status) compare with the jurisdiction in which the NRV under consideration was developed?			

- Overall conclusions

Appendix E. Decision guide for use/update of existing systematic reviews



Footnotes

a) A relevant NRV question would include specific NRVs to be addressed in the review such as setting a Tolerable Upper Intake Level (UL) vs. Chronic Disease Risk Reduction (CDRR) value.
b) This includes the process of setting the study questions and development of the PI(E)CO criteria.
c) For example, a recognised risk of bias tool for systematic reviews. Use the criteria outlined in *Table 1. Administrative and technical criteria for assessing the suitability of existing nutrient reference values* as a guide to assess whether recommended processes have been followed.
d) Is the review less than 5 years old?

Adapted with permission from National Academies of Sciences, Engineering, and Medicine. (2023). Using Systematic Reviews to Support Future Dietary Reference Intakes: A Letter Report. Washington, DC: The National Academies Press. https://doi.org/10.17226/27031

Appendix F. Scaling methods used internationally for NRVs

F.1. Background and Context

The following tables compile NRV derivation approaches from two international initiatives that addressed methodological harmonisation from different perspectives. The NASEM (2018) study focused on young children and women of reproductive age as part of North American efforts to standardise derivation methods globally. The (FAO 2024)report was commissioned to provide scientific advice for Codex Committee on Foods for Special Dietary Uses (CCNFSDU) on the details of nutrient reference values across six major scientific bodies for older infants and young children. While their differing analytical frameworks precluded direct synthesis, both reviews document the widespread reliance on extrapolation methods when direct evidence from target populations is unavailable. In addition, both reports emphasised the need for clearly reporting limitations and assumptions in NRV development. The NASEM (2018) data presented here in Tables F.4.1 & F.4.2 represent general scaling methodology from their technical appendix, while the FAO data in Tables F.5.1 & F.5.2 shows derivation methods used by different international organisations for specific nutrients in older infants (~6-12 months) and young children (~1-5 years).

F.2. Key Framework Differences

NASEM (2018): Technical reference documenting extrapolation and scaling methods used across nutrients and age groups.

(FAO 2024): Systematic analysis of derivation methods used by international organisations for older infants and young children. Table F.5.1 & F.5.2 focus on documenting which specific methods were used by each organisation.

F.3. Limitations and Considerations

Several important considerations apply:

- Both reviews found that extrapolation from other age groups is commonly used when direct research on target populations is unavailable.
- Final reference values depend on both the derivation method and the specific parameters used (such as body weights and growth factors).
- Estimated values carry forward any uncertainties from their original data sources.
- Some international organisations have “Not set” values for certain nutrients due to insufficient evidence.
- Extrapolation methods often result in lower confidence classifications when compared to direct evidence (FAO 2024)

F.4. NASEM (2018) Data

Tables F.4.1 and F.4.2 document the scaling methods using by NASEM (2018) for extrapolating nutrient reference values when direct evidence is insufficient. The data represents general methodology from their technical appendix showing which extrapolation approaches (allometric, isometric, growth factors) were applied to specific nutrients.

Table F.4.1 Mineral Derivation Methods – NASEM (2018)

Extrapolation methods used to derive NRVs when direct evidence is insufficient. Allometric scaling uses 0.75 exponent. AI: adequate intake; EAR: estimated average requirement; UL: upper level.

Nutrient	Extrapolation Method	Scaling Method		Growth Factor	Other Methodology
		Allometric	Isometric		
Choline	$AI_{adult} \rightarrow AI_{child}$	yes		yes	
	$AI_{0–6m} \rightarrow AI_{7–12m}$	yes		no	
Chromium	$EAR/AI_{adult} \rightarrow EAR/AI_{child}$	yes		yes	
	(no extrapolation for iodine EAR/AI for 1–3 y and 4–8 y old)	yes			
	$AI_{0–6m} \rightarrow AI_{7–12m}$			no	
Copper	$EAR/AI_{adult} \rightarrow EAR/AI_{child}$	yes		yes	
	(no extrapolation for iodine EAR/AI for 1–3 y and 4–8 y old)	yes			
	$AI_{0–6m} \rightarrow AI_{7–12m}$			no	
Fluoride	0.05 mg/kg/d	no	yes	no	
Iodine	$EAR/AI_{adult} \rightarrow EAR/AI_{child}$	yes		yes	
	(no extrapolation for iodine EAR/AI for 1–3 y and 4–8 y old)	yes			
	$AI_{0–6m} \rightarrow AI_{7–12m}$			no	
Iron	No extrapolation for 7–12m, 1–8y, 9–18 y				
Magnesium	$EAR_{10–15y} \rightarrow EAR_{1–3 \text{ and } 4–8y}$		yes	no	
	5mg/kg/d				
Manganese	$EAR_{adult} \rightarrow EAR_{child}$	yes		yes	
	$AI_{0–6m} \rightarrow AI_{7–12m}$	no		no	
Molybdenum	$EAR/AI_{adult} \rightarrow EAR/AI_{child}$	yes		yes	
	(no extrapolation for iodine EAR/AI for 1–3 y and 4–8 y old)	yes			
	$AI_{0–6m} \rightarrow AI_{7–12m}$			no	
Potassium	$AI_{adult} \rightarrow AI_{1–18y}$				AI child = AI adult × F F = energy intake child/ energy intake adult UL child = UL adult × F F= energy intake adult/ energy intake child
	$UL_{adult} \rightarrow UL_{child}$				
Selenium	$AI_{0–6m} \rightarrow AI_{7–12m}$	yes		no	
	$EAR_{adult} \rightarrow EAR_{child}$	yes		yes	
Sodium	Same as potassium				
Zinc					Factorial similar to allometric extrapolation from adult plus GF

Table F.4.2. Vitamin Derivation Methods – **NASEM (2018)**

Extrapolation methods used to derive NRVs when direct evidence is insufficient. Allometric scaling uses 0.75 exponent. AI: adequate intake; EAR: estimated average requirement; UL: upper level.

Nutrient	Extrapolation method	Scaling method		Growth Factor	Other methodology
		Allometric	Isometric		
Biotin	$AI_{0–6m}$→$AI_{7–12m}$, 1–18y, adult	yes		no	
Folate	$AI_{0–6m}$ →$AI_{7–12m}$	yes		no	
	EAR_{adult}→$AI_{7–12m}$	yes		yes	
	EAR_{adult}→EAR_{child}	yes		yes	
	UL_{adult} →UL_{child}	yes		no	
Niacin	EAR_{adult}→EAR_{child}	yes		yes	
	EAR_{adult}→$AI_{7–12m}$	yes		yes	
	UL_{adult} →UL_{child}	yes		no	
Pantothenic acid	adult→children	yes		yes	
	$AI_{0–6m}$→$AI_{7–12m}$	yes		no	
Riboflavin	EAR_{adult}→EAR_{child}	yes		yes	
	$AI_{0–6m}$ →$AI_{7–12m}$	yes		no	
Thiamin	EAR_{adult}→EAR_{child}	yes		yes	
	EAR_{adult}→$AI_{7–12m}$	yes		yes	
Vitamin A	EAR/AI_{adult}→EAR/AI_{child}	yes		yes	
	(no extrapolation for iodine EAR/AI for 1–3 y and 4–8 y old)	yes			
	$AI_{0–6m}$→$AI_{7–12m}$			no	
Vitamin B6	EAR_{adult}→EAR_{child}	yes		yes	
	$AI_{7–12m}$ from mean of extrapolations:	-		-	
	$AI_{0–6m}$ →$AI_{7–12m}$	yes		no	
	EAR_{adult}→$AI_{7–12m}$	yes		yes	
	UL_{adult} →UL_{child}	yes		no	
Vitamin B12	EAR_{adult}→EAR_{child}	yes		yes	
	EAR_{adult}→$AI_{7–12m}$	yes		yes	
Vitamin C	$AI_{0–6m}$ →$AI_{7–12m}$	yes		no	
	EAR_{adult}→EAR_{child}	no		no	
Vitamin D	adult→1–9y		yes	no	
Vitamin E	$AI_{0–6m}$ →$AI_{7–12m}$	yes		no	
	EAR_{adult}→EAR_{child}	yes		yes	
Vitamin K	$AI_{7–12m}$→$AI_{0–6m}$	yes		no	

F.5. FAO (2024) Data

The following tables show the derivation methods used by different international organisations for nutrient reference values in older infants (~6-12 months) and young children (~1-5 years), as documented in the FAO (2024) review.

Method Key:

- Factorial: The factorial summation of the various components involved in physiological growth, maintenance and loss
- Biomarker: The estimation of nutrient intake based on maintenance of a healthy plasma or urinary biomarker, or absence of deficiency disease in the target group
- Allometric (Up): Allometric scaling up from young infant reference values
- Allometric (Down): Allometric scaling down from adult reference values
- Isometric (Up): Isometric/linear scaling up from young infant reference values
- Isometric (Down: Isometric scaling down from adult reference values
- Linear (Down): Linear scaling down from adult reference values
- Linear (Unit): Linear scaling from unit measures
- Diet-based: Estimates of nutrient intake from diets of healthy older infants or young children
- Interpolate: Interpolation between reference values of younger and older age groups

F.5.1 Mineral Derivation Methods – FAO (2024)

Derivation methods used by international organisations for older infants and young children. Two methods listed = average of two methods used; * = multiple intake values for general population; ** = extrapolation parameter is product of body weight and dietary intake value energy.

Nutrient	Older infants (~6-12 months)						Young children (~1-5 years)					
	Australia and New Zealand (NHMRC/ MOH)	**Canada and USA (IOM)**	**Europe (EFSA)**	**WHO/ FAO**	**Japan (MHLW)**	**Nordic Countries (NCM)**	**Australia and New Zealand (NHMRC/ MOH)**	**Canada and USA (IOM)**	**Europe (EFSA)**	**WHO/FAO**	**Japan (MHLW)**	**Nordic Countries (NCM)**
Calcium	Diet-based	Diet-based	Isometric (Up)	Factorial	Diet-based	*Unknown*	Factorial	Factorial	Factorial	Interpolate	Factorial	Factorial
Copper	Diet-based	Diet-based	Allometric (Up), Diet-based	*Not set*	Diet-based	Allometric (Down)	Diet-based	Allometric (Down)	Diet-based	*Not set*	Allometric (Down)	Allometric (Down)
Iodine	Allometric (Up)	Allometric (Up)	Biomarker	Interpolate	Allometric (Up)	Isometric (Down)	Biomarker	Biomarker	Biomarker	Interpolate	Allometric (Down)	Isometric (Down)
Iron	Factorial						Factorial					
Magnesium	Diet-based	Diet-based	Isometric (Up), Diet-based	Interpolate	Diet-based	Linear (Unit)	Linear (Unit)	Linear (Unit)	Diet-based	Interpolate	Linear (Unit)	Linear (Unit)
Manganese	Allometric (Down), Diet-based	Allometric (Down), Diet-based	Isometric (Up) - (Linear (Down), Diet-based)	*Not set*	Diet-based	*Not set*	Diet-based	Diet-based	Linear (Down)	*Not set*	Allometric (Down)	*Not set*
Phosphorus	Diet-based	Diet-based	Linear (Down)	*Not set*	Diet-based	Linear (Down)	Factorial	Factorial	Linear (Down)	*Not set*	Diet-based	Linear (Down)
Potassium	Diet-based	Diet-based	Isometric (Down)	*Not set*	Diet-based	Isometric (Down)	Diet-based	Diet-based	Isometric (Down)	*Not set*	Allometric (Down)	Isometric (Down)
Selenium	Allometric (Up)	Allometric (Up), Diet-based	Isometric (Up)	Interpolate	Allometric (Up)	*	Allometric (Down)	Allometric (Down)	Isometric (Down)	Interpolate	Allometric (Down)	*Unknown*
Sodium	Allometric (Up)**	Diet-based	Isometric (Up)	*Not set*	Diet-based	*Not set*	Linear (Down)	Linear (Down)	Linear (Down)	*Not set*	*Not set*	*Not set*
Zinc	Factorial				Allometric (Up), Diet-based	Factorial	Factorial				Allometric (Down)	Factorial

F 5.2 Vitamin Derivation Methods – FAO (2024)

Derivation methods used by international organisations for older infants and young children. Two methods listed = average of two methods used; * = multiple intake values for general population; ** = extrapolation parameter is product of body weight and dietary intake value energy.

Nutrient	Older Infants (~6-12 months)						Young Children (~1-5 years)					
	Australia and New Zealand (NHMRC/ MOH)	**Canada and USA (IOM)**	**Europe (EFSA)**	**WHO/FAO**	**Japan (MHLW)**	**Nordic Countries (NCM)**	**Australia and New Zealand (NHMRC/ MOH)**	**Canada and USA (IOM)**	**Europe (EFSA)**	**WHO/FAO**	**Japan (MHLW)**	**Nordic Countries (NCM)**
Biotin	Allometric (Up)	Allometric (Up)	Allometric (Up)	Allometric (Up)	Allometric (Up, Down)	*Not set*	Allometric (Up)	Allometric (Up)	Diet-based	Allometric (Down)	Allometric (Down)	*Not set*
Folate	Allometric (Up, Down)	Allometric (Up, Down)	Allometric (Up)	Allometric (Up, Down)	Allometric (Up, Down)	Linear (Unit)	Allometric (Down)	Allometric (Down)	Allometric (Down)	Allometric (Down)	Allometric (Down)	Linear (Unit)
Niacin	Allometric (Down)	Allometric (Down)	Linear (Down)	Allometric (Up)	Allometric (Up, Down)	Linear (Down)	Allometric (Down)	Allometric (Down)	Linear (Down)	Allometric (Down)	Linear (Down)	Linear (Down)
Pantothenic acid	Allometric (Up)	Allometric (Up, Down)	Allometric (Up)	Allometric (Up)	Allometric (Up, Down)	*Not set*	Diet-based	Allometric (Down)	Diet-based	Allometric (Down)	Diet-based	*Not set*
Riboflavin	Allometric (Up, Down)	Allometric (Up, Down)	Allometric (Up)	Allometric (Up)	Allometric (Up, Down)	Linear (Down)	Allometric (Down)	Allometric (Down)	Allometric (Down)	Allometric (Down)	Linear (Down)	Linear (Down)
Thiamine	Allometric (Down)	Allometric (Down)	Linear (Down)	Allometric (Up)	Allometric (Up, Down)	Linear (Unit)	Allometric (Down)	Allometric (Down)	Linear (Down)	Allometric (Down)	Linear (Down)	Linear (Down)
Vitamin A	Diet-based	Allometric (Up), Diet-based	Factorial	Interpolate	Allometric (Up)	Allometric (Down)	Allometric (Down)	Allometric (Down)	Factorial	Interpolate	Factorial	Allometric (Down)
Vitamin B6	Allometric (Up)	Allometric (Up, Down)	Allometric (Up, Down)	Allometric (Up)	Allometric (Up, Down)	Linear (Down)	Allometric (Down)	Allometric (Down)	Allometric (Down)	Allometric (Down)	Linear (Down)	Linear (Down)
Vitamin B12	Allometric (Up)	Allometric (Up)	Allometric (Down)	Interpolate	Allometric (Up, Down)	Linear (Unit)	Allometric (Down)	Allometric (Down)	Allometric (Down)	Allometric (Down)	Allometric (Down)	Linear (Unit)
Vitamin C	Allometric (Up)	Allometric (Up), Diet-based	Biomarker	Interpolate	Allometric (Up, Down)	Isometric (Down)	Interpolate	Allometric (Down)	Linear (Down)	Interpolate	Allometric (Down)	Isometric (Down)
Vitamin D	Biomarker						Biomarker					
Vitamin E	Allometric (Up)	Allometric (Up)	Allometric (Up)	Interpolate	Allometric (Down)	Linear (Unit)	Diet-based	Allometric (Down)	Diet-based	Interpolate	Diet-based	Linear (Unit)
Vitamin K	Allometric (Up)	Allometric (Up)	Linear (Down)	Linear (Down)	Diet-based	*Not set*	Diet-based	Diet-based	Linear (Down)	Linear (Down)	Allometric (Down)	*Not set*