NUTS AND RISK OF CARDIOVASCULAR DISEASE

A systematic review and meta-analysis of the diet-disease relationship

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FOREWORD

The impact of nut consumption on health outcomes has been extensively investigated since the first known publication in 1992 of the pioneering Adventist Health Study, in which nut consumption was associated with a lower risk of coronary heart disease [1].

Since then, consistent evidence suggests that nuts are compelling cardioprotective foods. Several meta-analyses of large prospective cohort studies have shown that frequent nut consumption is inversely associated with a lower risk of cardiovascular disease (CVD) [2-5].

The most recent of these in 2019 [5], found a 15 per cent reduced risk of CVD, when comparing the highest and lowest nut intake categories.

These findings support an earlier systematic review and dose-response meta-analysis of 20 prospective cohort studies which found a 21 per cent reduced risk of CVD for a nut consumption dose of 28g (around one handful of nuts) per day, compared with low or no nut consumption [2].

Research conducted by my colleagues from Landmark Nutrition and the Smart Foods Centre at the University of Wollongong, on behalf of Nuts for Life in 2014, and updated in 2018, investigated the evidence on the effects of nut consumption on heart health for the purpose of self-substantiating a general-level health claim.

These two systematic review studies found that regular nut consumption improves several indicators of heart health, including total cholesterol, LDL-cholesterol and LDL-cholesterol to HDL-cholesterol ratio [6, 7].

Our most-recent review, from 2021, continues to build on this.

The results showed that, in the context of a healthy diet, regular nut consumption reduces the overall risk of CVD, by making positive changes to many biomarkers of CVD. These include total cholesterol, LDL-cholesterol, triglycerides, total cholesterol to HDL-cholesterol ratio, LDL-cholesterol to HDL-cholesterol ratio, apolipoprotein B, flow mediated dilation and endothelial function. At the same time, a significant increase in vascular cell adhesion-protein-1 was also found.

Nuts are nutrient-dense whole foods, rich in unsaturated fatty acids, plant protein, dietary fibre, vitamins, minerals, plant sterols and polyphenols.

Given this nutritional profile and the substantial body of evidence, a daily 30g handful of nuts, within the context of a healthy diet, should be considered in reducing the risk of CVD.

Our systematic literature review and meta-analysis forms part of an application by Nuts for Life to Food Standards Australia New Zealand (FSANZ) for a food-health relationship high-level health claim.

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The results showed that, in the context of a healthy diet, regular nut consumption reduces the overall risk of CVD.

EXECUTIVE SUMMARY

The evidence from the systematic review and meta-analysis indicates that, in the context of a healthy diet, regular nut consumption reduces the risk of cardiovascular disease (CVD), by positively impacting many biomarkers of CVD.

KEY FINDINGS:

- ✓ The consumption of nuts is beneficial in making positive changes to many biomarkers of CVD, creating an overall risk reduction.
- ✓ Nut consumption was associated with a significant decrease in:
  - Total cholesterol
  - LDL-cholesterol
  - Triglycerides
  - Total cholesterol to HDL-cholesterol ratio
  - LDL-cholesterol to HDL-cholesterol ratio
  - Apolipoprotein B
- ✓ Nut consumption was associated with a significant increase in:
  - Flow mediated dilation
  - Vascular cell adhesion-protein-1
- ✓ Nut consumption had no effect on HDL-cholesterol.
- ✓ Nut consumption tended to benefit other CVD biomarkers – including apolipoprotein A1, systolic and diastolic blood pressure, pulse wave velocity, and heart rate – although the findings were not significant.
- ✓ Moderately-consistent favourable associations were found for the risk of death from CVD and risk of CVD.
- ✓ The biological plausibility of the relationship between nut consumption and risk of CVD is supported by the literature – specifically, the favourable fatty acid and amino acid profiles, phytosterol and polyphenol contents, and antioxidant properties of nuts.
- ✓ Given the body of evidence, it is reasonable to suggest that 30g every day is an appropriate serving amount for nuts*.

**nuts refers to all tree nuts (excluding chestnuts) and peanuts*

Nuts do not simply display positive changes to one biomarker of CVD risk, but a range of biomarkers, to create an overall risk reduction.

Did you know?

A general level health claim, that nuts support heart health, as part of a healthy diet, has been available for use in Australia and New Zealand since 2015. This is based on clear and consistent evidence for a favourable effect of nuts on improved heart health, without an adverse effect on body weight.

INTRODUCTION

Cardiovascular disease (CVD) includes heart, stroke and blood vessel diseases.

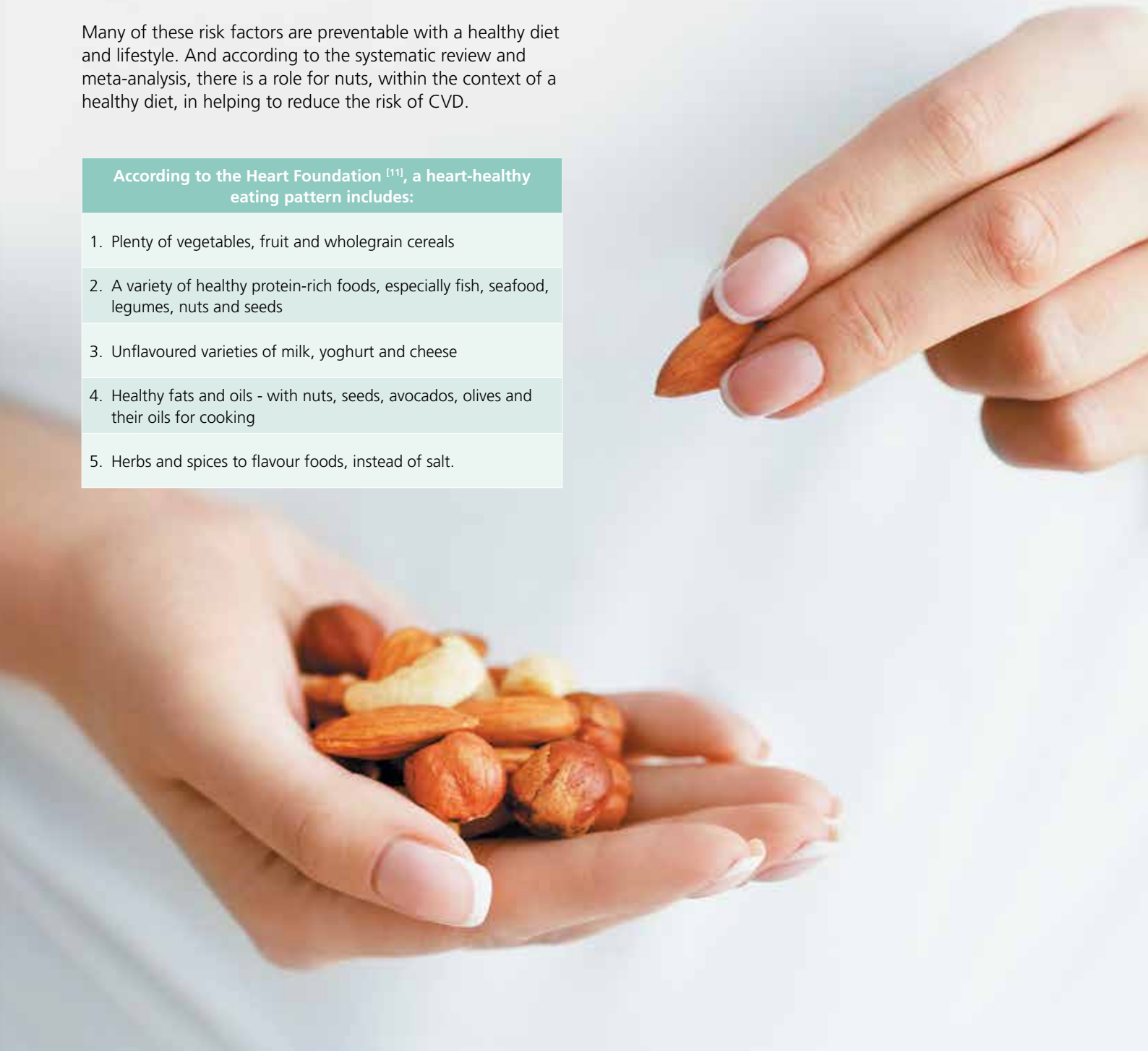
CVD is one of Australia's largest public health concerns, with three-quarters of Australians at risk of developing it [8]. CVD accounts for one in four of all deaths and claims the life of one person every 12 minutes [9]. It also costs the Australian economy $5 billion each year, more than any other disease[10].

Certain risk factors for CVD cannot be changed, such as sex, ethnicity, indigeneity and age. But some risk factors are modifiable, including poor diet, smoking, abnormal blood lipids, high blood pressure, overweight and obesity, and type 2 diabetes.

Many of these risk factors are preventable with a healthy diet and lifestyle. And according to the systematic review and meta-analysis, there is a role for nuts, within the context of a healthy diet, in helping to reduce the risk of CVD.

Cardiovascular disease affects more than four million Australians, or 16.6% of the population [12].

According to the Heart Foundation [11], a heart-healthy eating pattern includes:
1. Plenty of vegetables, fruit and wholegrain cereals
2. A variety of healthy protein-rich foods, especially fish, seafood, legumes, nuts and seeds
3. Unflavoured varieties of milk, yoghurt and cheese
4. Healthy fats and oils - with nuts, seeds, avocados, olives and their oils for cooking
5. Herbs and spices to flavour foods, instead of salt.



ABOUT THE RESEARCH

In 2021, Nuts for Life commissioned the University of Wollongong (UOW) to review the evidence on the relationship between nuts and risk of CVD. This work forms part of an application by Nuts for Life to Food Standards Australia New Zealand for a food-health relationship high-level health claim.

THE RESEARCH QUESTION:

'Does a greater consumption of nuts, or of specific types of nuts, result in reduced risk of cardiovascular disease, with no apparent adverse effect on body weight in humans?'

The review assessed whether nut consumption has a favourable impact on risk of CVD, defined as a:

- Reduction in: Total cholesterol (TC), LDL-cholesterol (LDL), triglycerides (TG), TG: HDL-cholesterol (HDL), TC: HDL, LDL: HDL, apolipoprotein B (ApoB), apolipoprotein A1 (ApoA1), systolic blood pressure (SBP), diastolic blood pressure (DBP), homocysteine, platelet aggregation, CVD mortality, CVD total incidence, CHD mortality, CHD total incidence, stroke mortality, stroke incidence, myocardial infarction (MI), heart failure (HF), atrial fibrillation (AF), heart rate, arterial stiffness (PWV), endothelial function (E-selectin, Intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion-protein-1 (VCAM-1), endothelin-1, augmentation index (AI)), intima-media thickness (IMT).
- Increase in: HDL, HDL: LDL, arterial compliance, plaque stability, endothelial function (flow mediated dilation (FMD), peripheral arterial tonometry (PAT), nitric oxide (NO)), heart rate variability, and peak systolic velocity.

MEDLINE, PubMed, CINAHL and Cochrane Central scientific databases were used to identify eligible studies, that were found to be published between 1992 and September 2021. A total of 182 studies (145 intervention trials and 37 observational studies) met the eligibility criteria (see Table 1).

The studies in the review:
182 studies (196 published papers)
From 25 countries (14 from Australia and New Zealand)
Published over a period of almost 30 years (from 1992 to 2021)

TABLE 1: PICOTS ELIGIBILITY CRITERIA FOR STUDY SELECTION

Population	Non-acutely ill individuals >2 years of age.
Intervention	Consumption of tree nuts (almond, Brazil nut, cashew, chestnut, hazelnut, macadamia, pecan, pine nut, pistachio, or walnut), mixed nuts or peanuts (including nut oils, nut powders and new genetic varieties of nuts), including as part of a portfolio of dietary changes where the effect of nut consumption on the health outcome could be isolated.
Comparator	Consumption of usual diet with no nuts or lower amounts of nuts.
Outcome	TC, LDL, HDL, TG, ApoB, ApoA1, SBP, DBP, homocysteine, PWV, Endothelial function (FMD, PAT, E-selectin, ICAM-1, VCAM-1, NO, endothelin-1, AI), peak systolic velocity, platelet aggregation, heart rate, heart rate variability, arterial compliance, endothelial vasodilator function, IMT, plaque stability, CVD mortality, CVD total incidence, CHD mortality, CHD total incidence, stroke mortality, stroke total incidence, total MI, non-fatal MI incidence, heart disease, HF, HF incidence, AF, and AF incidence.
Time	≥ 3 weeks.
Study design	Intervention trials with a control group (including randomised and non-randomised designs), prospective cohort studies, and case-control studies.

The majority of studies that met the eligibility criteria for study inclusion, investigated the consumption of either whole or ground nuts. All nut types were included in the evidence that was reviewed, but no studies were identified that looked specifically at chestnuts.

The term 'nuts' includes tree nuts (almonds, Brazil nuts, cashews, chestnuts, hazelnuts, macadamias, pecans, pine nuts, pistachios and walnuts), peanuts and mixed nuts.

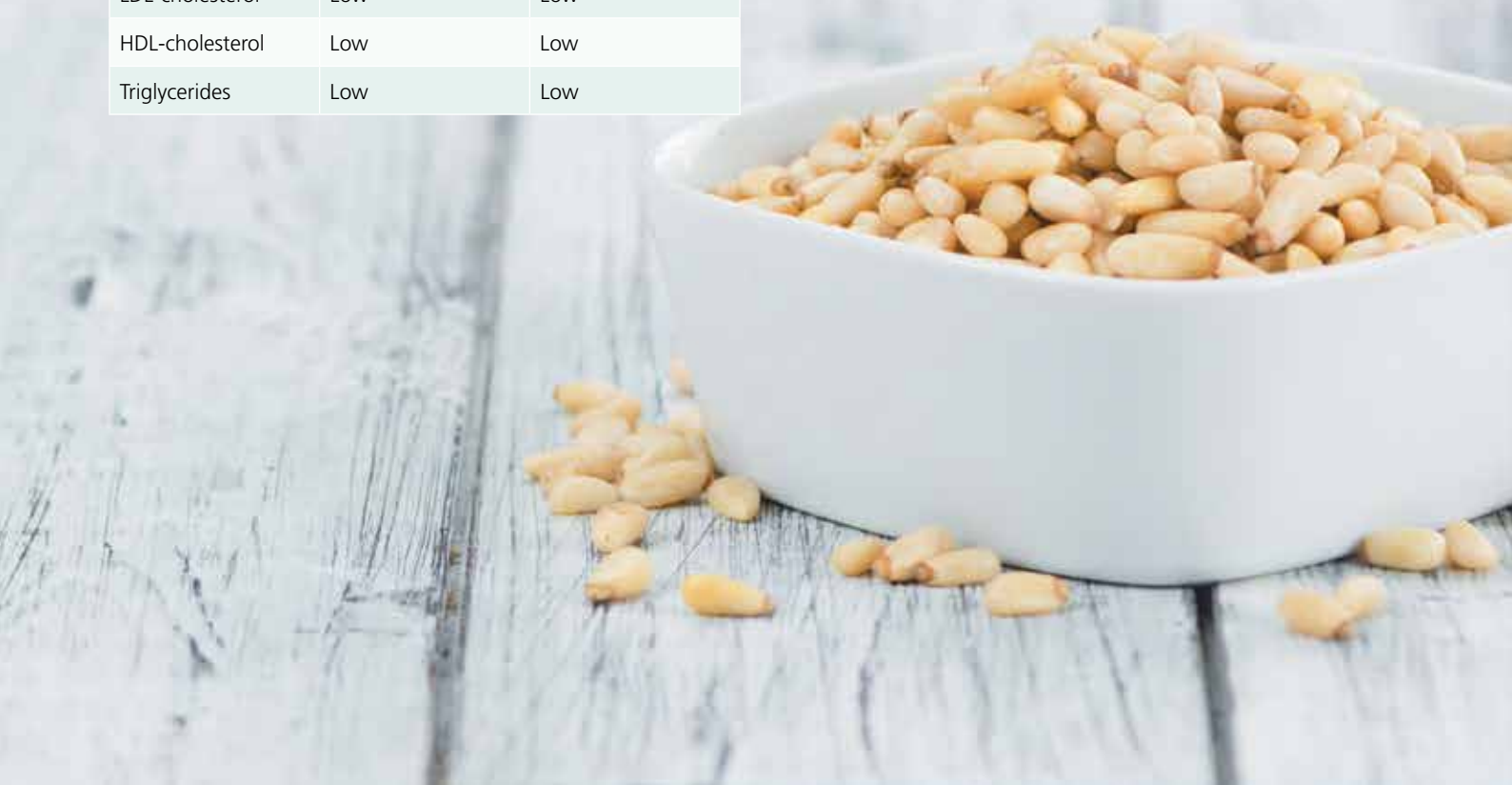
OBSERVATIONAL STUDY FINDINGS

Thirty-seven prospective cohort studies explored the link between nut consumption and cardiovascular endpoints, including total CVD, CHD, stroke, and death from these conditions. All were identified to be high-quality studies.

TABLE 2: CONSISTENCY OF EFFECTS FOR NUTS AND CARDIOVASCULAR DISEASE OUTCOMES IN OBSERVATIONAL STUDIES

Outcome of interest	Consistency rating on direction of favourable effect	Consistency rating on direction of favourable effect in higher quality studies
CVD mortality	Moderate	Moderate
Total CVD	Moderate	Moderate
CHD mortality	Low	Low
Total CHD	Low	Low
Stroke mortality	Low	Low
Total stroke	Low	Low
Hypertension	Low	Low
Non-fatal myocardial infarction	Low	Low
Heart failure	Low	Low
Atrial fibrillation	Low	Low
LDL-cholesterol	Low	Low
HDL-cholesterol	Low	Low
Triglycerides	Low	Low

> Moderately-consistent favourable associations were found for the risk of death from CVD (11 studies) and risk of CVD (3 studies) (see Table 2).



INTERVENTION STUDY FINDINGS

A total of 139 randomised controlled trials (RCTs), and six non-randomised trials were included. The majority of these (123 studies) were considered to be of high quality.

Intervention trials ranged from three weeks to 260 weeks in duration.

Nut doses varied across studies, ranging from 3g per day, to 168g per day, or as a set proportion of dietary energy.

Compared with control, nut consumption was associated with a significant decrease in:
• Total cholesterol
• LDL-cholesterol
• Triglycerides
• Total cholesterol to HDL-cholesterol ratio
• LDL-cholesterol to HDL-cholesterol ratio
• Apolipoprotein B.

The meta-analysis showed nut consumption was associated with a significant increase in flow mediated dilation and had no effect on HDL-cholesterol. In comparison, a significant increase in VCAM-1, which indicates poorer endothelial function, was also found (see Table 3).

There was also emerging evidence of a positive (though not significant) effect of nut consumption on other biomarkers of CVD risk, such as apolipoprotein A1 and pulse wave velocity. The evidence base for these biomarkers needs to be further established.

> “Nuts display positive changes to a range of biomarkers to create an overall CVD risk reduction.

TABLE 3: META-ANALYSIS OF INTERVENTION TRIALS				
Biomarker/outcome of interest	**Number of strata (analyses)**	**Number of participants**	**Effect estimate**	**Health effect of nut consumption**
LDL-cholesterol	126	9484	-0.11 [-0.14, -0.08]	Significant decrease
HDL-cholesterol	126	10099	0.00 [-0.01, 0.02]	No effect
Total cholesterol	127	9438	-0.14 [-0.18, -0.09]	Significant decrease
Triglycerides	122	9741	-0.05 [-0.08, -0.03]	Significant decrease
Triglyceride to HDL-cholesterol ratio	5	331	-0.13 [-0.44, 0.18]	Non-significant decrease
Total cholesterol to HDL-cholesterol ratio	51	3825	-0.15 [-0.24, -0.06]	Significant decrease
HDL to LDL-cholesterol ratio	3	211	-0.06 [-0.23, 0.11]	Non-significant decrease
LDL to HDL-cholesterol ratio	39	2527	-0.06 [-0.23, 0.11]	Significant decrease
Apolipoprotein B	40	3017	-2.90 [-4.33, -1.48]	Significant decrease
Apolipoprotein A1	33	2254	-1.04 [-2.62, 0.54]	Non-significant decrease
Systolic blood pressure	71	6514	-0.06 [-0.86, 0.74]	Non-significant decrease
Diastolic blood pressure	67	6205	-0.16 [-0.59, 0.28]	Non-significant decrease
Homocysteine	4	172	0.02 [-0.83, 0.88]	Non-significant increase
Pulse wave velocity	5	338	-0.03 [-0.27, 0.21	Non-significant decrease
Flow-mediated dilation	14	679	0.83 [0.18, 1.47]	Significant increase
Peripheral arterial tonometry	2	105	0.00 [-0.19, 0.20]	No effect
Heart rate	8	550	-0.09 [-1.11, 0.92]	Non-significant decrease
Heart rate variability	2	122	2.04 [-1.98, 6.06]	Non-significant increase
Endothelial function				
E-Selectin	6	291	-0.83 [-2.55, 0.88]	Non-significant decrease
ICAM-1	14	1102	-0.57 [-5.20, 4.06]	Non-significant decrease
VCAM-1	16	751	19.87 [4.89, 34.86]	Significant increase
Endothelin-1	4	212	0.02 [-0.12, 0.16]	Non-significant increase
Augmentation index	3	245	0.47 [-2.19, 3.13]	Non-significant increase

WHAT DOES THIS MEAN?

The high prevalence of CVD in Australia suggests a need to educate and support people on ways to manage their risk of this condition, especially as many CVD risk factors are preventable.

This current systematic review confirms there is a role for nuts, within the context of a healthy diet, in helping to reduce the risk of CVD.

The review findings support the current recommendations to consume 30g (around one handful) of nuts per day, as part of a healthy dietary pattern. Yet most Australians fall well short of this target.

A secondary analysis of the nationally-representative 2011-12 National Nutrition and Physical Activity Survey estimated the average (mean) nut consumption at just 4.6g/day, with just 2% of the population meeting the recommended daily amount [13].

These findings suggest that Australians must increase their nut intake to reap the heart-health benefits.

A well-recognised reason for this shortfall is concern around nuts' kilojoule and fat content and therefore their potential to cause weight gain – a risk factor for CVD. Yet, the evidence consistently shows that nut consumption does not adversely affect weight when consumed within a healthy diet [14-17], though the reason why is still being explored.

Previous systematic reviews have shown a positive effect of nuts on heart health, independent of body weight [6, 7]. This review upheld the relationship, while also addressing a wider range of biomarkers and disease endpoints.

We need to make it easier for Australians to adopt a heart-healthy eating pattern, and a powerful way to do this is through evidence-based health claims.

Establishing a food-health relationship high-level health claim for nuts and CVD could help to increase the consumption of nuts by both the Australian and the New Zealand populations.

Australians must increase their nut intake to meet the recommended 30g serving size.

Health professionals and dietary guideline messaging should recommend nuts for their cardiometabolic benefits without stipulations or concern of an adverse effect on weight control [14].

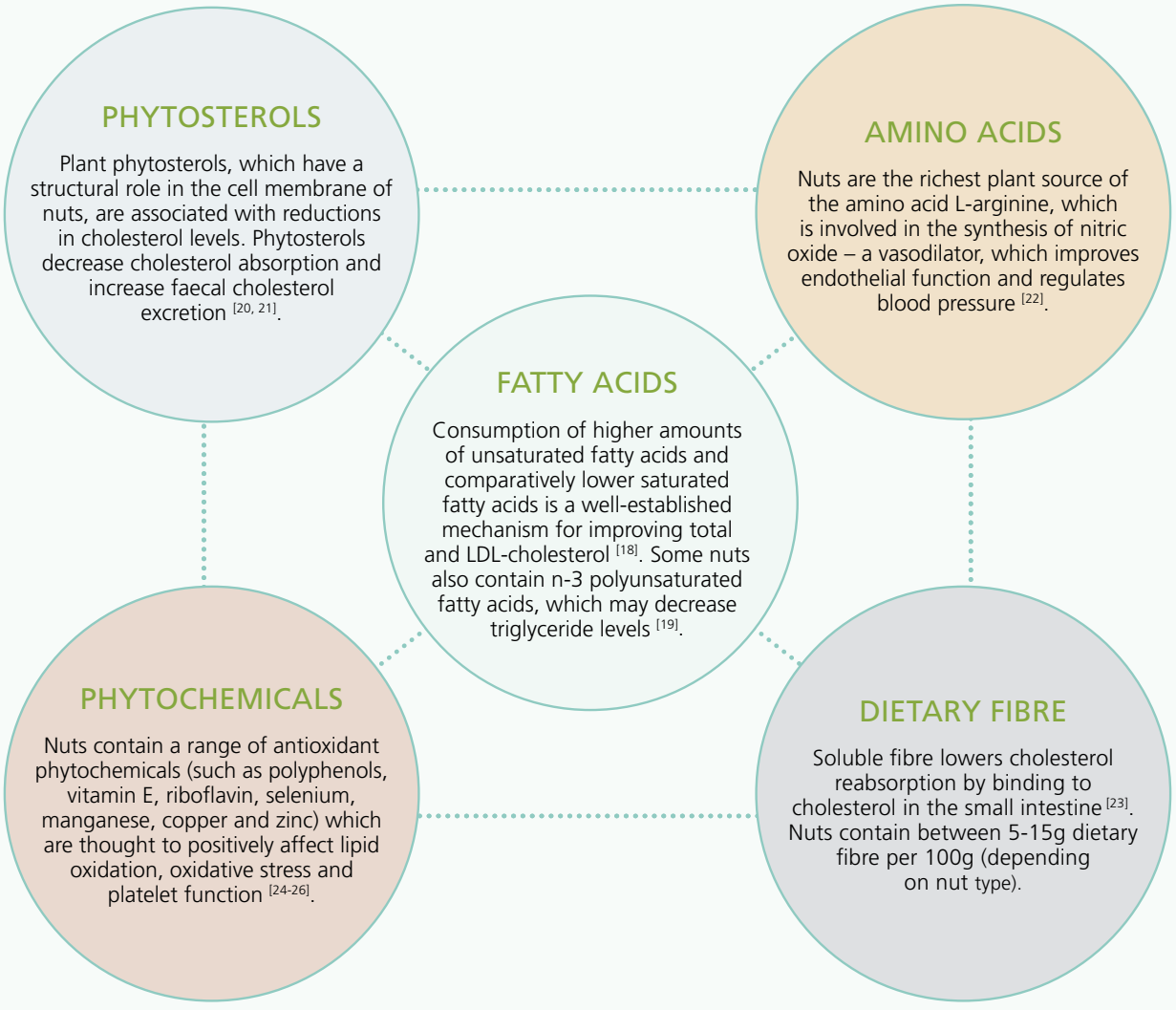
WHAT MAKES NUTS HEART HEALTHY?

The cardioprotective effect of nuts is likely due to their unique nutritional profile, and the synergistic effect of multiple bioactive components, within the food matrix.

Nuts have a unique fatty acid profile – with a high proportion of monounsaturated and/or polyunsaturated fatty acids (depending on nut type), relative to saturated fatty acids – which may, in part, explain their favourable effects on blood lipid profiles.

In addition, nuts are rich sources of phytosterols. And other components of nuts, including their amino acid profile, polyphenol properties and antioxidant content also play a role.

Component of nuts



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Nuts for Life is the health education initiative from the Australian tree nut industry. We are Australia's leading authority on the nutrition and health benefits of tree nuts. Our mission is to promote regular nut consumption by collating the latest evidence-based information, and informing Australians about the positive impact regular nut consumption can have on their health.

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