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Translating the scientific evidence for apples and pears into health messages

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For Horticulture Innovation Australia Ltd (Hort Innovation)

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Reference

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Abbreviations

BMI	Body mass index
CABI	The Centre for Biosciences and Agriculture International
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
DAPP	Dried apple peel powder
FSANZ	Food Standards Australia New Zealand
FSTA	Food Science Technology Australian
GI	Glycaemic index
HDL-C	High density lipoprotein cholesterol
LDL-C	Low density lipoprotein cholesterol
NHMRC	National Health and Medical Research Council
NIP	Nutrition information panel
OR	Odds ratio
TC	Total cholesterol
WoS CC	Web of Science Core Collections

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Executive summary

Background

Hort Innovation is developing communication and marketing programs to increase awareness of the health benefits of Australian apples and pears and hence increase demand and sales of apples and pears. CSIRO has previously completed a comprehensive scientific literature report on apples in 2010 and a subsequent comprehensive scientific literature report on the health and nutrition properties of pears in 2015. Following on from this, a set of next steps was identified.

Aims of the current report

- Identify new and emerging research on the health benefits of apples to update the Apple Review undertaken in January 2010;
- Compile a list of health claims/messages that can immediately be made for apples and pears that comply to the FSANZ standard code 1.2.7;
- Make recommendations for further actions Hort Innovation could undertake, in order to make health claims that would differentiate apples and pears from other fruit.

Literature review update on apples

An updated literature review of the human health benefits of apples identified 122 new studies published since 2010. The greatest number of studies were in the areas of cardiovascular risk (34 studies), cancer (17 studies, various types) and diabetes (13 studies).

Seventy-one studies were conducted in animals and 51 studies were in humans, of these 22 were intervention studies while the remainder (29 studies) were observational (can only determine associations, not cause-and-effect).

The largest body of evidence from human intervention studies was identified in cardiovascular disease risk with a total of 21 human intervention studies across the 2010 and 2016 reviews. Human intervention studies are considered the most convincing level of evidence for demonstrating a causative link between a food or food property and a health outcome and hence are necessary to support a general or high level health claim. Five human intervention studies were also identified in the area of satiety and weight management.

The studies published between 2010-2016 lend further support to the conclusions made in the 2010 Apple Report, particularly for the positive effects of apples and apple components on cholesterol lowering, improving satiety (i.e. lowering appetite) and aiding in weight control.

Nutrition and health claims

Food Standards Australia and New Zealand (FSANZ) are the Government body responsible for developing and administering the Australia New Zealand Food Standards Code (the Code). In January of 2016, Standard 1.2.7- Nutrition, Health and Related Claims came into force, which sets the requirements for making nutrition content or health claims on a food label or in an advertisement. The Code was reviewed to identify the pre-approved nutrition and health claims which can be made for apples and pears, without requiring further substantiation through a systematic literature review process.

Fourteen pre-approved nutrition content claims, 4 pre-approved general level health claims and 4 pre-approved high level health claims were identified that could be used for apples and pears immediately without requiring further substantiation. Consideration needs to be given towards the wording and presentation of these to create compelling marketing messages for apples and pears.

Recommendations

A number of recommendations were made for possible marketing messages for apples and pears. These include:

- Consideration of a general level health claim on apples and heart health.
- Consideration of clinical trial/s on the digestive health effects of pears. Positive findings from such trial/s could support a self-substantiated health claim linking pears to digestive heath.
- Use of the identified pre-approved nutrition content and health claims which do not require further investment in research and substantiation.
- Continuing to update the apple and pear reviews to monitor for future research, which strengthens the evidence for particular health conditions.

1 Introduction

1.1 Project background and scope

In 2010 CSIRO completed an extensive scientific literature review of the evidence related to the benefits of apples to human health [1]. Following on from this, CSIRO completed a comprehensive scientific literature report on the health and nutrition properties of pears in 2015 [2].

Hort Innovation is developing communication and marketing programs to increase awareness of the health benefits of Australian apples and pears and hence increase demand and sales of apples and pears.

APAL and CSIRO held a half-day workshop on 27 April in Melbourne to discuss and identify the next steps of how CSIRO can assist in achieving this goal. The following needs were identified: Updating of the 2010 apple scientific report; and a list of specific nutritional and health messages for apples and pear that comply with the Food Standard Australia New Zealand (FSANZ) code on Nutrition, Health and Related Claims (Standard 1.2.7).

1.2 Aim and objectives

To assist with the development of their communication and marketing plans to promote the health benefits of apples and pears by:

- Identifying new and emerging research on the health benefits of apples published since January 2010;
- Compiling a list of health claims/messages that can immediately be made for apples and pears that comply to the FSANZ standard code 1.2.7;
- Making recommendations on further actions needed before other health claims can be made that differentiate apples and pears from other fruit (e.g. a health claims dossier / further clinical research may be needed).

2 Updated scientific literature review of the benefits of apples for human health

2.1 Aims and objectives

The aim of the updated literature review on apples was to identify new and emerging research on the health benefits of apples published since January 2010. The following objectives were set:

- To undertake a comprehensive literature search of scientific journal databases from January 2010 to 4 August 2016 to identify all studies that investigated the effects of apples and apple components (e.g. whole apples, apple peel, apple juice, apple extract, apple puree) on any health/functional outcomes. Studies on individual bioactive components normally found in apples, but not directly from apples, were not included.

- To review the abstracts (only) of the studies that identify new and emerging research on the health benefits of apples and to determine whether the new evidence changes or strengthens previous conclusions in the 2010 Apple Report.

2.2 Literature search strategy

A comprehensive systematic literature search of relevant databases was performed during the period 3 to 4 August 2016 by a librarian experienced with systematic literature reviews.

Search terms were developed to capture articles on topics that were identified in the previous 2010 Apple Review as well as capturing new areas of research that have emerged since 2010.

Table 1. Search terms

Search terms
Apple OR apples AND
health OR wellbeing OR cancer OR diabetes OR metabolic OR hypertension OR inflammation OR asthma OR allergy OR brain OR alzheimers OR "DNA damage" OR "energy intake" OR satiety OR ulceration OR inflammation OR injury OR muscular OR muscle OR arthritis OR neurodegenerative OR neurodegeneration OR weight OR "heart disease" OR "cardiovascular disease" OR "digestive health" OR "gut health" OR "antioxidant activity" OR ageing OR cognition OR "bone health”

Inclusion and exclusion

Animal and human studies were included. *In vitro* (“test tube”) studies were not included because results from these studies cannot be extrapolated to humans and information from these studies are less informative and equivocal. Anti-oxidant capacity of foods measured *in vitro* does not predict *in vivo* antioxidant capacity. This could be explained by the fact that most polyphenols in food are incompletely absorbed in humans and they undergo extensive modification during metabolism reaching the circulation and tissues in lower levels and in different forms than is present in the food source [3]. Studies that measured compositional data e.g. polyphenol content were also excluded when they were not relating it to a specific health effect.

Studies on whole apples, apple peel, apple juice, apple extracts or apple puree were all included, whereas studies on apple cider, or extracts found in apple but not of apple origin were excluded.

To ensure full coverage of the literature a range of databases were searched including;

- PubMed/Medline
- Scopus
- Agricola
- Food Science Technology Abstracts (FSTA)
- The Centre for Biosciences and Agriculture International (CABI)

- Web of Science Core Collection (WoS CC)

2.3 Results

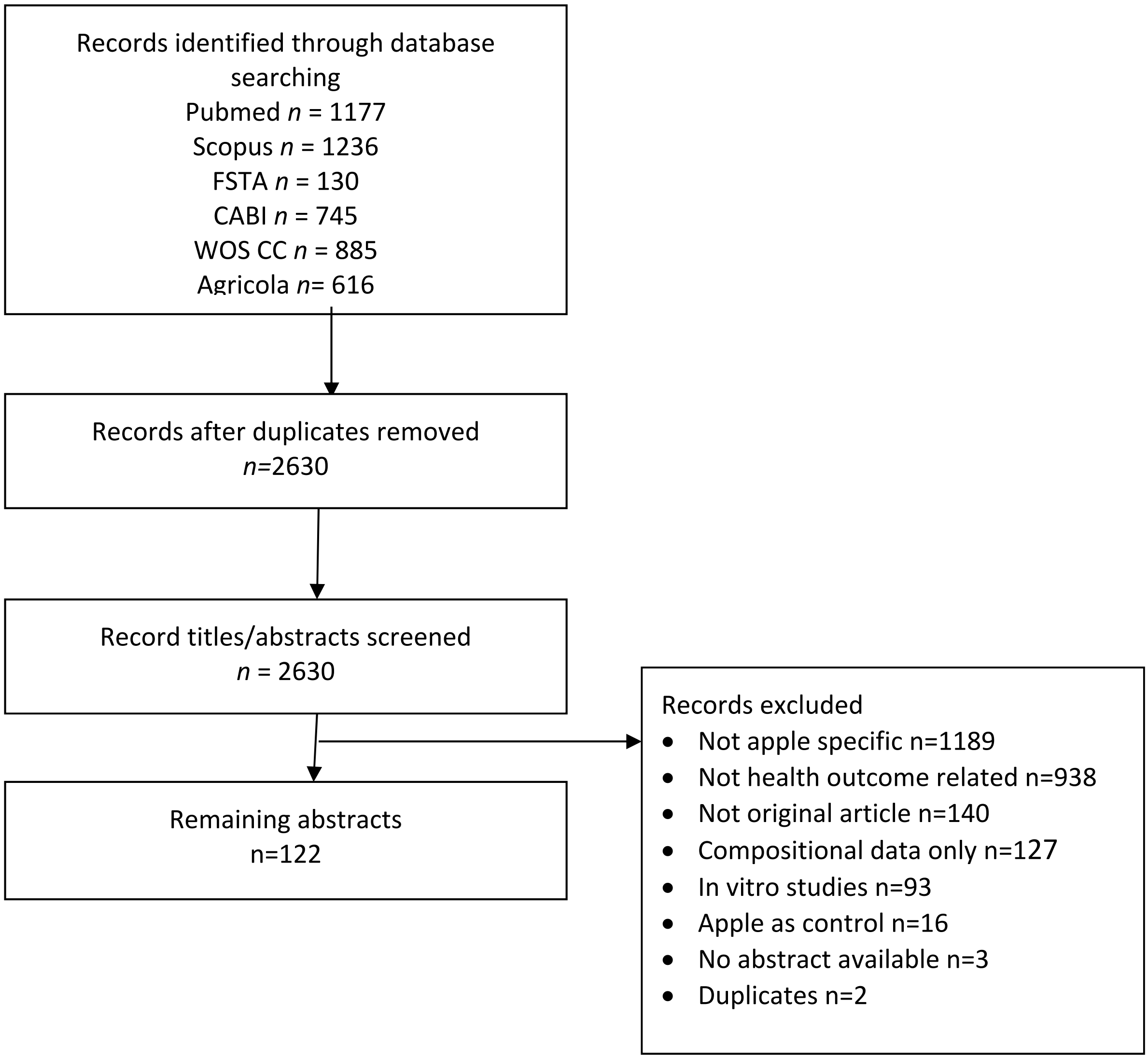

Figure 1. Search results

2.4 New findings

Results are summarised below, organised under the subject headings previously presented in the 2010 Apple Review. It is important to note that this information has been gleaned from abstracts only rather than full text review of the papers, hence statements about study quality are not included and papers require further review and interpretation to draw conclusions on study results. For each health condition the updated evidence has been presented along with a short summary from the 2010 Apple Review to highlight the changes in evidence since the previous review.

2.4.1 Allergy

2010 summary: Apple varieties differ in their allergenic potential to apple allergic individuals (usually those allergic to birch pollen). Apple allergens also differ between seasons. Apple polyphenols may help alleviate some of the symptoms such as sneezing. This effect has been noted with apple polyphenol amounts able to be consumed in 1 apple. However, further research in humans is needed to confirm this effect.
2016 update: Two observational studies were identified [4, 5] looking at correlations between apple intake and allergy. Miyake et al [4] looked at maternal intake of vegetables, fruit, and antioxidants during pregnancy and risk of wheeze and eczema in the offspring and Rosenlund et al [5] investigated the association between current fruit or vegetable intake and allergic disease in 8-year-old Swedish children. Neither study found significant associations between apple intake (maternal or child) and allergy or allergy symptoms after adjusting for confounding variables.

There is no conclusive evidence on the effect of apple intake on allergy incidence or symptoms.

2.4.2 Asthma

2010 summary: Based on food frequency questionnaire protocols, apples have been reported to be associated with lower incidence of asthma and bronchial hyper reactivity. However, to establish causation, human clinical trials are needed.

2016 update: No human clinical trials have been published. Only one new study [6] was identified since 2010 and this observational study provided conflicting results with the previous evidence. DeChristopher et al [6] found children consuming apple juice (≥5 times/week vs ≤1 time/month) were more than twice as likely to have asthma (Odds ratio [OR] 2.43, P=0.035). The authors' concluded that these results support the hypothesis that excess free fructose in apple juice (and other free fructose containing beverages) increases the in situ intestinal formation of advanced glycation end products, which may be absorbed and play a role in asthma.

The evidence on apples and asthma incidence are inconsistent and hence no conclusions can be drawn on this subject.

2.4.3 Arthritis

2010 summary: There is no conclusive evidence of increased rheumatoid arthritis from consumption of apples by humans.

2016 update: One small human pilot study [7] and one animal study [8] on apple peel extracts in arthritis were identified. The pilot human study looked at the effect of consuming dried apple peel powder for 12 weeks and the animal study looked at the acute anti-inflammatory effects of methyl ursolate extracted from apple peels. Both studies found that the apple peel intervention had positive effects on arthritis symptoms, showing improvements in range of motion and pain in humans [7] and a reduction in paw edema in the animal model [8].

While no conclusions can be drawn from the limited available evidence, this represents an area of interest worth monitoring for larger human research studies.

2.4.4 Brain health/cognition

2010 summary: No mention was made of the effects of apples on brain health or cognition.

2016 update: Two human intervention studies investigating apple and cognition were identified [9, 10]. Bondonno et al. [9] compared the acute effects of apple, apple + spinach vs. a control (low flavonoid apple and rice milk) on nitric oxide status, cognitive function and mood. Nitric oxide plays an important role in enhancing blood flow to different tissues in the body. While an increase on nitric oxide status was observed with both apples and apples + spinach, this did not result in any changes in cognitive function or mood. The other study [10] was a pilot study (n=21) investigating the effect of daily administration of apple juice for a month to an institutionalised population with Alzheimers disease (AD). They found no effects in ratings on the Dementia Rating Scale or Activities of Daily Living score. However caregivers reported a significant (27%) improvement in behavioural and psychotic symptoms as measured by the Neuropsychiatric Inventory. This study provides preliminary evidence that apple juice supplementation may attenuate mood decline in AD, but further research is needed.

Three animal studies also looked at the effect of apple consumption on brain health or cognition [11-13]. Cheng et al [11] found apple polyphenol extract was protective against aluminium-induced cognitive impairment in rats and Tsukhara et al [13] found apple peel and flesh improved cognition and emotion in mice whose ovaries had been removed. Finally, Keddy et al [12] found that apple peel from Northern Spy apples had neuroprotective and anti-inflammatory effects in a mouse model of hypoxic-ischaemic brain injury (i.e. stroke).

It is difficult to draw any conclusions in the area of brain health and cognition due to the heterogeneity of the study populations and outcomes of interest. It would be of interest to monitor further human studies in the brain health and cognition area.

2.4.5 Cancer

2010 summary: The previous report reviewed the evidence for the relationship of apples and a range of cancers including bladder, breast, colorectal, endometrial and ovarian, lung and prostate cancer. At this time there was no consistent evidence of associations between these cancer types and apple consumption.

2016 update: Seven human observational studies were identified looking at a range of cancer types (breast [14], prostate [15], pancreatic [16], colorectal [17, 18], non-Hodgkin's lymphoma [19] and all cause cancer mortality [20]) and associations with consumption of apples. All of the studies identified found apple consumption was associated with a reduced risk of cancer incidence or cancer mortality, however due to the observational nature of these studies, causation cannot be inferred.

Ten animal studies were identified [21-30]. The majority of these (7) focused on tumour prevention in colon cancer models, while two studies also looked at effects on oral cancers. While most studies used extracts from apple (e.g. polysaccharides) one study fed whole apples [26]. In general, most studies in animal models suggest that apples and apple extracts may have chemo preventative effects.

New evidence from seven observational studies support the conclusions in the 2010 report of an inverse association between apple intake and cancer, but no evidence is available from human studies to prove a causative link between apple consumption and reduced cancer risk. It is important to note, apples are a commonly consumed fruit across the world, and regular apple consumers may reflect an overall healthier diet and therefore reduced cancer risk.

2.4.6 Cardiovascular disease risk

2010 summary: Whole apples and apple polyphenol supplements (in capsules, approximating polyphenol content in 3 apples) have been shown to reduce total cholesterol and low density lipoprotein cholesterol (LDL-C) levels by 5-8%. Contradictory results have been reported on the effect of apple fibre on total cholesterol and LDL-C levels. In contrast, the consumption of apple juice (375 - 720 ml/day) has no effect on plasma cholesterol levels and may result in adverse effects on plasma triglyceride levels.

2016 update: *Eleven human intervention studies [31-41], 5 observational studies [42-46] and 16 animal studies [47-62] were identified.*

The observational studies showed that greater intake of apples (combined with pears in some studies) was associated with reduced risk of stroke [44, 46], hypertension [43], acute coronary syndrome [45] and abdominal aortic calcification scores (marker of sub-clinical atherosclerotic vascular disease) [42].

Similar to the 2010 summary, we found evidence from human intervention studies of beneficial effects of apples and their extracts on some markers of cardiovascular health. The only adverse effects we identified were from Haghighatjoo et al who showed an increase in triglyceride levels when hyperlipidaemic men consumed 300g of whole apples a day over 8 weeks compared to control diets; total cholesterol, LDL-C, HDL-C and oxidative stress markers were not affected [36]. Velliquette et al found no beneficial effects on postprandial triglyceride levels after consuming apple peel extract over a 7-day period [40].

The other human intervention studies demonstrated a range of improvements to markers of cardiovascular health from consuming whole apples, dried apples, apple pomace (residue after extraction of juice from apple; rich source of polyphenols and pectin) and cloudy apple juice, but no effect of clear apple juice. Bondonno et al found apples enhanced endothelial function (increased the elasticity of blood vessels) and lowered systolic blood pressure acutely. The authors concluded that this was likely due to the flavonoid content of apples [33]. Chai et al looked at the effect of postmenopausal women consuming 75g of dried apple per day (equal to about two medium-sized apples) compared with dried plum (control) over a year [34]. Women who consumed dried apple lost 1.5 kg body weight, although the weight loss was not significantly different from control. In the women who consumed the dried apple, total cholesterol and LDL-C dropped 14% and 23% respectively, but this was only significantly different from the control group at 6 months. Both dried apple and dried plum resulted in significant improvements in inflammatory (CRP) and oxidative stress (lipid hydroperoxide) markers. Fatima et al also found a LDL-C lowering effect of adding whole apples (250 g/day) over a 6 month period compared to a habitual control diet [35]. Ravn-Haren et al compared the effect of consuming whole apple (550 g/day), apple pomace (22 g/day), cloudy apple juice (500 ml/day), clear juice (500 ml/day) and no supplement for 4 weeks in crossover study. They reported trends towards lower LDL-C in all (whole apple 6.7%, apple pomace 7.9%, cloudy apple juice 2.2%) but the clear juice had the negative effect of increased LDL-C by 6.9%. This suggests the fibre component of apples may be necessary for their likely cholesterol-lowering effect. HDL-C, triglycerides, blood pressure, inflammation (measured by hs-CRP), glucose metabolism or gut microbiota were not affected [38]. Zhao et al found an apple a day over a 4 week period lowered a marker of atherosclerosis (oxidized LDL/beta$_2$-glycoprotein I complex) in healthy middle aged adults. Capsules of apple polyphenol extract also improved this marker of atherosclerosis, but not as much as the whole apple [41].

Alvarez-Parrila et al found that smoking habit affected the antioxidant and lipid lowering capacity of consuming fruit. In smokers the consumption of 1 apple, 1 pear and 200ml orange juice per day for 26 days lowered total cholesterol and LDL-C levels, but antioxidant capacity was unchanged compared to baseline levels. While in non-smokers TC, HDL-C and LDL-C as well as antioxidant capacity improved, compared to baseline levels [31].

A few of the intervention studies we identified were focussed on elucidating the potential mechanisms of how apples affect cardiovascular disease risk factors. Auclair et al set out to determine whether it is the polyphenols in apples that are responsible for the cardiovascular benefits [32]. Participants with high cholesterol consumed 40 g/day of freeze-dried apples, either polyphenol rich (1.43 g polyphenols/day) or polyphenol-poor (0.21 g polyphenols/day) for 4 weeks in a randomized cross-over trial. Neither of the interventions affected endothelial function, lipid levels, homocysteine or antioxidant capacity. Rago et al analysed blood samples obtained from the study by Ravn-Haren et al [38], discussed above, to investigate whether supplementation of whole apple or processed apple products affect the human plasma metabolome (the small-molecule chemicals found within a biological sample which reflects the interaction between an organism's genome and its environment). They showed that whole apple and apple pomace had stronger modifying effects on plasma metabolome than cloudy or clear apple juice. Changes in metabolomic profiles suggested that apples and apple pomace could beneficially affect cholesterol levels, insulin sensitivity and gut microbial functionality by several mechanism [37]. Soriano-Moldonado compared two cloudy apple juices with different polyphenol and vitamin C contents and found that combining vitamin C with the polyphenols from apple juice showed a trend towards mild improvements in cardiometabolic markers, including markers of antioxidant status, glucose metabolism, lipid profile and inflammation, as compared with apple polyphenols alone [39].

The 16 animal studies [47-51] [52-62] investigated the effect of apples and apple extracts on cardiovascular disease risk factors. There was an overall suggestion that apple and apple components, e.g. apple pectin, polyphenols, flavonols and homogenate (blended apple) improve lipid metabolism [47-50, 52-58, 61, 62], improve glucose control [47, 50, 62] and lower the production of inflammatory cells and markers [57, 60].

Overall, the studies lend further support to the 2010 conclusions that whole apples and their extracts reduce total cholesterol and LDL-cholesterol levels. In fact out of the 5 human intervention studies that assessed the effects of apples on lipid levels [32, 34-36, 38], 3 showed improvements in total cholesterol and LDL-C levels (6.7 – 23%) with dried apple [34], whole apple [35, 38], apple pomace and cloudy juice [38]. There is further evidence suggesting that the fibre in apples mediates this cholesterol lowering effect. Indeed clear apple juice does not produce this outcome and may in fact worsen lipid profiles [38]. Evidence is emerging for favourable effects of apple and apple products on short term changes in blood pressure and endothelial function; a normal functioning endothelial [i.e. flexible inner lining of blood vessels] is critical for normal functioning of the body's tissues and organs and has been shown to be an important factor for heart health. Some evidence is also emerging for chronic improvements in inflammatory and oxidative stress markers, important risk factors for cardiovascular disease.

2.4.7 Diabetes Mellitus

2010 summary: A large observational study with 38,018 women and 8.8 years of follow-up, has shown that women consuming 1 apple per day had a significantly (28%) reduced risk of type 2 diabetes compared with those who consumed no apples. Two large epidemiological studies have both concluded that flavonols or flavones were not associated with diabetes-protection, suggesting that the effect of apples is not related to flavones such as quercetin.

2016 update: Three observation studies were identified [63-65]. Two found that apples and pear intake (combined category) was associated with a reduced risk of type 2 diabetes [63, 65] and the third [64] found apple consumption was inversely associated with gestational diabetes (diabetes developed during pregnancy).

Human intervention studies looked at whole apple [66], phlorizin-rich (type of flavonoid) apple powder from unripe apples [67] and apple extract [68]. Two studies [67, 68] found improvements in post-prandial glucose response in healthy adults and the other [66] reported improvements in fasting blood glucose levels in type 2 diabetics who were willing to consume 1 apply a day for 4 weeks compared to control (no apple). Dange et al also reported significant improvements in lipid profile [66].

In addition, seven studies using diabetic animal models [69-74] reported that a range of forms of apple (peel, juice extract and pomace) had beneficial effects on insulin [75] and glucose control [69, 70, 72-74], along with improvements in inflammatory markers [69], kidney and liver function [70] and lipids [69, 70, 74].

The observational evidence supports the previous findings that regular apple consumption may be associated with reduced risk of developing type 2 diabetes. In addition three new human intervention studies all showed some benefits of apple interventions on markers of diabetic control, however due to the heterogeneity of the apple components (whole apples, apple extracts) and populations investigated (healthy and diabetics) it is difficult to draw any firm conclusions. Animal studies support a range of mechanisms for apple components to modulate diabetic control. This area warrants further well-designed human intervention studies in populations at risk of, or with, type 2 diabetes.

2.4.8 DNA damage

2010 summary: The effects of apple consumption on some biomarkers of DNA damage, but not on others, in a single study needs to be confirmed in future studies as those data do not provide enough conclusive evidence of an effect of apple consumption on DNA damage.

2016 Update: Two animal studies [76, 77] were identified. Gomes et al [77] showed that DNA damage caused by cadmium exposure in rats was reduced following apple juice intake. Chan et al [76] showed that supplementation with apple juice concentrate can compensate for folate insufficiency in genetically compromised mice. The evidence remains limited and inconclusive in this area.

2.4.9 Gastrointestinal conditions

2010 summary: Combined apple pectin/camomile extracts may reduce the duration of diarrhea in children, although the effects need to be confirmed in larger study populations.

2016 update: *Three intervention studies [78-80] and 8 animal studies [81-88] were identified.*

One intervention study [79] compared the effect of administering diluted apple juice to children with gastroenteritis, with an apple flavoured electrolyte maintenance fluid. They found that the apple juice resulted in fewer treatment failures. Another intervention study [78] found that cloudy apple juice caused a significant decrease in enterococci (but not any other bacteria or total bacteria) compared with a control beverage in type 2 diabetics. The third intervention study [80] indicated that apple consumption is related to an improved intestinal environment, and apple pectin is one of the effective apple components improving the faecal environment.

The 8 animal studies [81-88] showed a range of mild benefits to the gut lining, gut microbiota and gut inflammation markers after consuming apple peel polyphenols and flavonoids, and apple pectin.

These results support the conclusions from 2010; apple and apple extracts appear to have a beneficial effect on diarrhoea/gastroenteritis and more broadly on gut health. This emerging area of research is worth monitoring for future studies to advance our understanding of this link.

2.4.10 Duodenal ulceration

2010 summary: There is no evidence of reduced duodenal ulceration from consumption of apples by humans.

2016 update: No further studies were identified looking at the effects of apple on duodenal ulceration.

2.4.11 Weight management, energy intake and satiety

2010 summary: Three studies [89-91] support the role of solid fruit consumption (including apples) increasing satiety compared with pureed fruit or juice, and this was associate with reduced energy intake at the subsequent meal [89]. A fourth study identified a possible effect on weight reduction which appeared to be related to the energy density of apples and not on their fibre content [92].

2016 update: Two observational studies [93, 94], 2 two human intervention studies [95, 96], and 5 animal studies [97-101] were identified.

Results from observational studies support an relationship between higher apple consumption and lower body mass index (BMI) in children [94] and adults [93]. The observational study in children indicated that the consumption of apples and apple products were associated with better nutrient profile, better diet quality and lower risk of obesity [94]. Data from three large prospective observational studies of adults in the United States showed that fruit consumption (incl. apples and pears) was associated with reduced weight gain over a period of four years [93].

An intervention study in children [96] showed that the consumption of an apple as mid-morning snack reduced their hunger compared with semi-skimmed milk, although they found no difference in the energy intake at the lunch and evening meals. In overweight and obese men, a significant reduction in body fat percentage was seen following daily consumption of 750 ml of polyphenol rich cloudy apple juice compared to a control beverage for 4 weeks. Interestingly, different genetic variants of obesity-related genes may influence this response to cloudy apple juice [95].

Studies in animal models suggest that the soluble fibre in apples (pectin) contributes to satiety and consequently body weight regulation [97, 98]. While other animal studies indicated that apple polyphenols might assist in preventing diet-induced obesity [99]. Dietary supplementation of apple pomace and apple juice concentrate may improve body weight and body fat loss in high-fat diet-induced obese rats [100].

The 2010 report suggested that the weight management potential of apples may be related to the low energy density of apples. However, more recent evidence suggests that the effects may also be mediated through the dietary fibre (pectin) and polyphenol components of apples. In total, five intervention studies have been identified across the two reviews, which relate to apples and satiety/appetite and weight control. It would be worth monitoring future research in this area. The addition of a further 1-2 well designed clinical trials may make it possible to perform a systematic review to determine if a general level health claim on satiety or appetite can be made.

2.4.12 Fruit juice/drug interactions

2010 summary: While consumption of food and juice may affect the bioavailability or delay the effect of certain drugs, the clinical importance of such effects has not been established.

2016 update: No further studies were identified on fruit juice/drug interactions.

2.4.13 Inflammation

2010 summary: There is no substantial evidence to support a role of apple consumption on chronic inflammation, as studies to date have provided contradictory results.

2016 update: Chronic low grade inflammation is thought to be a key biological mechanism in the development and progression of a wide range of chronic health conditions. Two observational studies were identified looking at apples and inflammation [102, 103]. Both found apple intake was associated with lower levels of inflammation. Four animal studies were identified. Two studies [104, 105] tested apple juice, one [106] looked at apple pectin and one [107] apple polyphenols. All four studies reported reduction in some measures/markers of inflammation.
Refer to section 2.4.6 (Cardiovascular disease risk) for evidence from human studies on inflammation.

2.4.14 Muscular injury

2010 summary: One animal study was identified which found apple polyphenols may have a protective effect against exercise-induced muscle strain.

2016 Update: Four animal studies [108-111] were identified which showed improvements to strength and weight of muscle, endurance of exercise and prevention of muscle injuries after consuming apple polyphenols and apple pomace extract, however there were no human studies on this effect.

New areas of research since 2010

2.4.15 Liver

No human studies were identified in this area, however ten animal studies were found [112-121]. Apple juice, peel and extracts were shown to be protective against liver damage in animal models. While these studies identified a number of possible mechanisms by which apple and apple products may modulate liver damage further research is needed to understand how this may translate to human health benefits.

2.4.16 Sexual health

One human observational study was identified which investigated the link between apple consumption and female sexual health [122]. They found daily apple consumers score significantly higher on the Female

Sexual Function Index (FSFI) in the total (p = 0.001; Cohen's d = 3.39) and lubrication domain (p = 0.001; Cohen's d = 3.02) compared to non-regular consumers (<1 apple/day). It is unclear what the hypothesized role of apples in sexual function may be and as this is the first study in this area no conclusion can be drawn.

2.4.17 Ageing

No human studies were identified in this area. Two animal studies [123, 124] looked at the effect of apples on ageing. Both studies found that apple extracts (polyphenols/phytochemicals) were able to increase lifespan in fruit fly [123] and nematode models [124].

2.4.18 Lung health

One animal study examined the effect of apple polyphenols on markers of chronic obstructive pulmonary disease (COPD) [125]. They found apple polyphenols administered over four days significantly and dose-dependently reduced the cigarette smoke-induced accumulation of inflammatory cells and significantly reversed oxidative stress in the lungs. The authors concluded that apple polyphenols may be a potential dietary nutrient supplement to improve quality of life of COPD patients by inhibiting cigarette smoke induced lung injury. As this was the only study identified, no conclusions can be drawn in this area.

2.4.19 General health

One observation study was identified which investigated whether "Eating an apple a day keeps the doctor away" [126]. In the adjusted analysis, apple eaters (≥1 apple a day) were not more likely to avoid doctors' visits compared to non-consumers (<1 apple/day), however apple eaters had 30% fewer prescription medications.

2.5 Summary conclusions

An updated literature review of the human health benefits of apples identified 122 new studies published since 2010. The greatest number of studies were in the areas of cardiovascular risk (34 studies), cancer (17 studies, various types) and diabetes (13 studies). Seventy-one studies were conducted in animals and 51 studies were in humans, of these 22 were intervention studies while the remainder (29 studies) were observational.

The largest body of evidence from human intervention studies was identified was in cardiovascular disease risk with a total of 21 human intervention studies across the 2010 and 2016 reviews. Human intervention studies are considered the most convincing level of evidence for demonstrating a causative link between a food or food property and a health outcome and hence are necessary to support a general or high level health claim. Five human intervention studies were also identified in the area of satiety and weight management.

Section 4 of this report makes recommendations on the next steps for translating these research findings into potential health messages for apples.

A range of emerging areas were identified as worth monitoring for future research. Regular reviewing of the literature in these areas may strengthen the evidence of health benefits and allow for health claims to be made in the future. These areas were:

- Arthritis- the use of apple peel extracts as a treatment to reduce symptoms
- Brain health and cognition- the role of polyphenol rich apple extracts on cognitive function
- Acute effects of apples on endothelial function (flexibility of blood vessels). Chronic effects of apple products on inflammation and oxidative stress, important risk factors for heart disease
- Blood lipids - specifically total cholesterol and LDL-C.
- Gut health
- Weight management

3 Nutrition content and health claims for apples and pears – Pre-approved claims.

3.1 Introduction

Food Standards Australia and New Zealand (FSANZ) are the body responsible for developing and administering the Australia New Zealand Food Standards Code (the Code). In January of 2016, Standard 1.2.7- Nutrition, Health and Related Claims [127] came into force, which sets the requirements for making a nutrition content or health claim on a food label or in an advertisement. The Code includes provisions for a number of pre-approved health claims, which can be made without requiring further substantiation through a systematic review process. For the purpose of this work we were interested in identifying the nutrition content and pre-approved health claims which could be used based on the current evidence on apples and pears.

3.2 Nutrition content claims

Nutrition content claims are claims about the presence or absence of certain nutritional properties of food. The nutrition content claims that are applicable to apples and pears are listed in table 2. While many of these claims may not seem directly relevant to the marketing of apples and pears, collectively they provide an overall picture of the nutrition benefits of apples or pears. Some examples of this are shown in table 5.

Table 2 Nutrition content claims applicable to apples and pears

Nutrient	Apples	Pears	Criteria to meet claim
Fibre	Contains dietary fibre	A **good source** of dietary fibre	Source= a serving of the food contains at least 2g of dietary fibre Good source= a serving of the food contains at least 4g of dietary fibre
Cholesterol	Low cholesterol	Low cholesterol	The food contains no more cholesterol than 20mg/100g for solid food
Fat	Low fat	Low fat	The food contains no more fat than 3g/100g for solid food
Saturated and trans fatty acids	Free	Free	The food contains no more saturated and trans fatty acids than 1.5g/100g for solid food
Saturated fatty acids	Free	Free	The food contains no detectable saturated fatty acids and no detectable trans fatty acids
Trans fatty acids	Free	Free	The food contains no detectable trans fatty acids and contains no more than 1.5g saturated fatty acids/100g solid food

Gluten	Gluten free	Gluten free	The food must not contain; a) detectable gluten; or b) oats or oat products; or c) cereals containing gluten that have been malted, or products of such cereals
Glycaemic index (GI)	Low GI (38[128])	Low GI (38[128])	The numerical value of the glycaemic index of the food is 55 or below
Lactose	Lactose free	Lactose free	The food contains no detectable lactose
Salt or sodium	Low sodium	Low sodium	The food contains no more sodium than 120mg/100g solid food
Sugar or sugars	No added	No added	The food contains no added sugars, honey, malt or malt extracts and the food contains no added concentrated fruit juice or deionised fruit juice, unless the food is any of the following; a) a brewed soft drink; b) an electrolyte drink; c) an electrolyte drink base; d) juice blend; e) a formulated beverage; f) fruit juice g) vegetable juice; h) mineral water or spring water i) a non-alcoholic beverage
Sugar or sugars	Unsweetened	Unsweetened	The food meets the condition for a nutrition content claim about no added sugar (above) and the food contains no intense sweeteners, sorbitol, mannitol, glycerol, xylitol, isomalt, malitol syrup or lactitol
Vitamin C	A source of vitamin C	A source of vitamin C	a) The vitamin or mineral is mentioned in column 1 of the table to section S1-2 or S1-3; and b) A serving of the food contains at least 10% RDI or ESADDI for that vitamin or mineral; and c) A claim is not for more than the particular vitamin or mineral than the amount permitted by section 1.3.2-4 or 1.3.2-5; and d) The food is not any of the following: a. A formulated caffeinated beverage; b. Food for infants;

			c. A formulated meal replacement; d. A formulated supplementary food; e. A formulated supplementary sports food
A nutrition content claim about properties of food not in schedule 4-3	E.g. antioxidants, polyphenols	E.g. antioxidants, polyphenols	May only state: a) that the food contains or does not contain b) that the food contains a specific amount of the property of food in a specific amount of that food; or c) a combination of paragraph (a) and (b)

ESADDI, Estimated safe and adequate daily dietary intake, RDI, recommended daily intake

N.B. Wording is not prescribed and wording may be modified so long as any modification to wording does not contradict or detract from the effect of the statement.

3.3 Health claims

Health claims are claims which state, suggest or imply that a food or a property of food has, or may have, a health effect. Health claims can either be pre-approved by FSANZ or a new food-health relationship can be self-substantiated by the process of a systematic literature review as set out in schedule 6 of The Code. Self-substantiated general level health claims are used exclusively by the business that has undertaken the literature review. A systematic literature review can be of the original scientific literature or by updating an existing systematic literature review where one is available.

In some instances health claims must include a context claim statement as part of the wording of the health claim e.g. Apples and pears contribute to heart health as part of a ***diet high in fruit and vegetables.*** The context claim statement must be included on a label, except in the instance that the food for sale is contained in a small package (surface area of less than 100 cm^2). There are two types of health claims, general level and high level health claims.

General level health claims

A general level health claim is any claim that states, suggests or implies that a food or property of food has or may have a health effect. General level health claims must not refer to a serious disease or to a biomarker of a serious disease. There are more than 200 pre-approved food-health relationships in the Code. Those identified as relevant to apples and pears are listed in table 3.

Table 3 Pre-approved general level health claims applicable to apples and pears

Food or property of food	Specific health effect*	Context claim statements	Conditions
Dietary fibre	Contributes to regular laxation	Nil	The food must meet the general conditions for making a nutrition content claim about dietary fibre (see table 2)

Carbohydrate	Contributes energy for normal metabolism	Nil	Carbohydrate must contribute at least 55% of the energy content of the food
Fruits and vegetables	Contributes to heart health	Diet containing an increased or high amount of fruit and vegetables	The food must contain no less than 90% fruit or vegetable by weight
Vitamin C	a) Contributes to iron absorption from food b) Necessary for normal connective tissue structure and function c) Necessary for normal blood vessel structure and function d) Contributes to cell protection from free radical damage e) Necessary for normal neurological function f) Contributes to normal growth and development (in children)		The food must meet the general claim conditions for making a nutrition content claim about vitamin C (see table 2).

*N.B. Wording is not prescribed and wording may be modified so long as any modification to wording does not contradict or detract from the effect of the statement.

High level health claims

A high level health claim means a health claim that refers to a serious disease or a biomarker of a serious disease. Only food-health relationships described in Schedule 2 of Standard 1.2.7 may be used for the making of high level health claims. There are currently 13 pre-approved food-health relationships for high level health claims listed in the Code. Those identified as relevant to apples and pears are listed in table 4.

Table 4 Pre-approved high level health claims applicable to apples and pears

Food or property of food	Specific health effect	Context claim statements	Conditions
A high intake [or an increased intake] of fruit and vegetables	Reduces risk of coronary heart disease	Diet containing a high amount of both fruit and vegetables	The food must contain no less than 90% fruit or vegetable by weight
Saturated fatty acids	Reduces total blood cholesterol or blood LDL cholesterol	Diet low in saturated fatty acids	The food must meet the conditions for making a nutrition claim about low saturated fatty acids (see table 2)

Saturated fatty acids and trans fatty acids	Reduces total blood cholesterol or blood LDL cholesterol	Diet low in saturated and trans fatty acids	The food must meet the conditions for making a nutrition claim about low saturated and trans fatty acids (see table 2)
Sodium or salt	Reduces blood pressure	Diet low in salt or sodium	The food must meet the conditions for making a nutrition claim about low sodium or salt (see table 2)

N.B. Wording is not prescribed and wording may be modified so long as any modification to wording does not contradict or detract from the effect of the statement.

3.4 Wording of health claims

While Schedule 4 of Standard 1.2.7 provides sample wording for nutrition content and health claims, The Code states that the wording are not prescribed and wording may be modified so long as any modification to wording does not contradict or detract from the effect of the statement (Standard 1.1.1-8). Table 5 gives an indication of how nutrition content and health claims could be combined, or wording altered to create marketing messages.

Table 5. Examples of potential marketing messages based on nutrition content and pre-approved health claims for apples and pears

Compare the pear…..compare pears with generic snack foods which are considered healthy e.g. muesli bar, snack pack of crackers, cheese & biscuits using nutrition content claims, e.g. glycaemic index, dietary fibre and added fat and sugar to highlight the pears superior nutritional properties as a snack choice
The pure pair (referring to apples and pears). Natures low GI, gluten free, fat free, unsweetened, fibre rich snacks
Comparing apples and…(similar concept to above but with apples and other snack foods)
Apples are a source of fibre, which promotes good digestive health
Pears are a good source of [high in/rich in] fibre, supporting good digestive health
Pears are a good source of [high in/rich in] fibre, to regulate digestive health
Pears are a good source of [high in/rich in] dietary fibre, promoting [supporting] good digestive health
Apples/Pears, as part of a diet high in fruits and vegetables, can contribute to [support] good heart health
Apples/Pears, as part of a diet high in fruits and vegetables, can help to reduce your risk of heart disease
Apples/Pears are a source of vitamin C, which supports muscle, cardiovascular and brain function

Apples/Pears contain antioxidants

Further suggestions for promoting the health benefits of apples and pears

- Nutrition section on the APAL website which promotes the findings of the CSIRO reports for health professionals
- A brochure for consumer and or health professionals which present the results from the CSIRO reports
- A website or brochure could combine the scientific results with fun facts, culinary tips and recipes to make it more appealing to a wide range of consumers- see Mushroom example (http://www.australianmushrooms.com.au/health-nutrition/)
- Tips could be linked to features of apples and pears identified in the evidence, e.g. did you know that most of the polyphenols [antioxidants] are in pears/apples peel? A recipe for a whole fruit smoothie containing apple
- Nutrition content or health claims presented on apple stickers, bags, tubes or fruit carriers

3.5 Nutrition Information Panel (NIP): requirements when nutrition content and health claims are made

Fresh fruit is unique to processed or packaged foods in that they are often sold without packaging and hence different rules apply about presentation of nutrition information. It is important to understand these when considering how you may present your nutrition content and health claims for apples and pears.

Standard 1.2.1-6 states that "If the food for sale is not in a package, it is not required to bear a label". However, when a nutrition content or health claim is made about foods exempt from the requirement to bear a label, this exemption no longer applies, and a NIP must be displayed on or in connection with the display of the food or provided to the purchaser on request. Standard 1.2.8-6 sets out what is required in a NIP, including the name and the average quantity of any nutrient or biologically active substance that a nutrition content or health claim refers to. The nutrition information provided can be from analysis performed in-house, or from a reference database such as NUTTAB [129], the FSANZ database.

3.6 Other resources and references

A guide to health claims for food industry is available from the FSANZ website. This document has been developed by the Implementation Subcommittee for Food Regulation to assist food business in building their nutrition content and health claims and demonstrate due diligence in attempting to comply with the Food Standards Code [130].
http://www.foodstandards.gov.au/publications/Pages/gettingyourclaimsright.aspx

If attempting to establish a new food-health relationship for a general level health claim by a process of systematic review, another document is available. This document outlines scientific best practice for undertaking a systematic review as described in schedule 6 [131].

http://www.foodstandards.gov.au/publications/Pages/Guidance-on-establishing-food-health-relationships-for-general-level-health-claims.aspx

3.7 Substantiation through systematic literature review

A systematic literature review is a significant undertaking, requiring an understanding of the explicit systematic process and specialist skills for appraising data arising from clinical trials and epidemiological studies. The person or group undertaking the systematic review would be expected to have a degree in a scientific- or health-related discipline (of at least three years duration) and one or more of the following: a) training in critical appraisal or biostatistics from a tertiary institution, b) a postgraduate degree (e.g. MSc, PhD) in a scientific or health related discipline, c) a specialist medical or health qualification. The amount of work required to complete a systematic literature review to support a health claim is significant and the time and effort involved is proportional to the number of studies in the area of interest [132].

4 Recommendations for new health claims that differentiate apples and pears – Next steps.

From the evidence that has been summarised on the health benefits of apples from both the 2010 Apple Review [1], the 2016 update and the 2015 Pear Review [2] there are a range of options to translate the scientific findings into marketing messages.

In order to make a general or high level health claim there are a number of steps in each process, these are broadly outlined in figure 2.

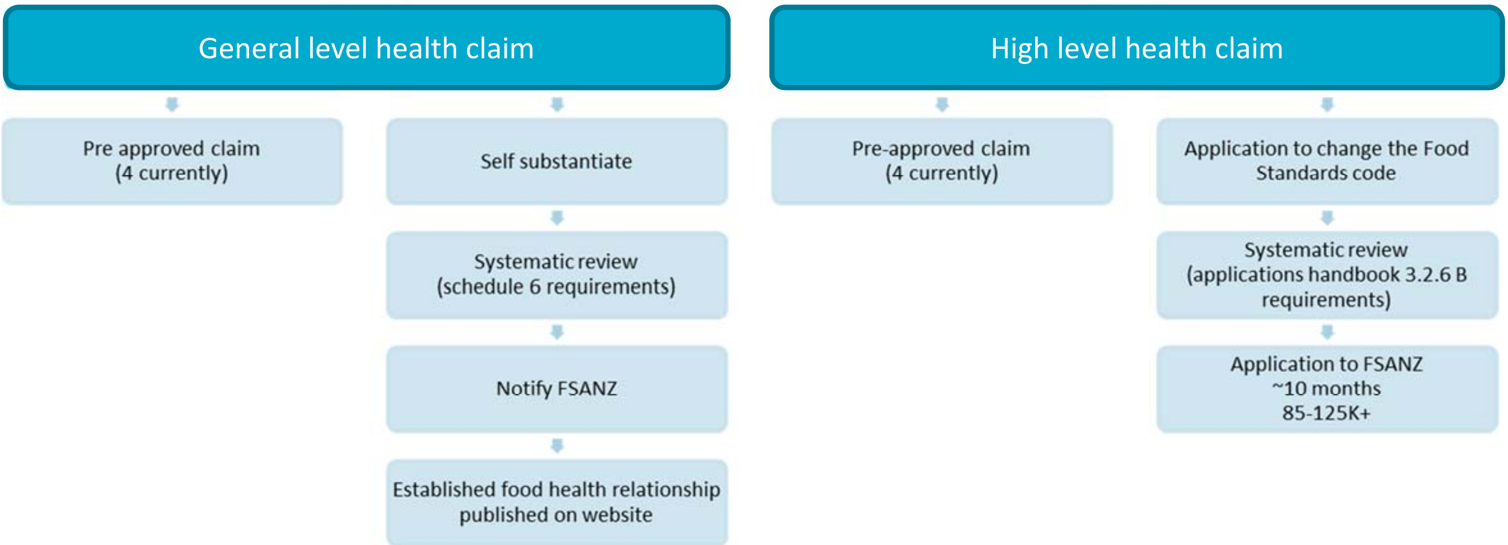

Figure 2. Pathways for making general and high level claims

For a general level health claim, a pre-approved claim can be used, otherwise self-substantiation of a new general level health claim requires a systematic literature review be undertaken. Once completed a company must notify FSANZ of the food-health relationship and certify that the relationship was established by a process of systematic review. The food-health relationships is then publicly listed on the FSANZ website. FSANZ does not evaluate or approve notified food-health relationships and listing the food-health relationship on the FSANZ website does not indicate acceptance or validation of the stated relationship. In the event that a health claim is questioned by an enforcement authority, the onus is on the business to show records demonstrating that a systematic review was conducted in accordance with Schedule 6 of the Standard and that the notified relationship is a reasonable conclusion of the systematic review.

In addition, food businesses are not able to use a relationship in the list that has been notified by another food business. A food business wishing to make a general level health claim based on a relationship that is already on the list must undertake its own systematic review and notify FSANZ of the relationship.

For a high level health claim, a pre-approved claim can be used, or, for a new high level health claim, an application must be made to change the Code. In this instance, along with substantiating the food-health relationship through a systematic literature review there are a number of additional steps in order to change the Code. If approved, the new high level health claim becomes part of the Code and can be used by other food businesses.

Tables 6 and 7 summarise the current number of human clinical studies in each health condition for apples and pears respectively as well as the next steps required for this area of research. For many areas, more research is required, however in some areas the preparation of an evidence dossier for a general level health claim or an application for a high level health claim are possible avenues.

Table 6. Summary of evidence from the 2010 and 2016 Apple Review and next steps for possible health claims in apples

	Number of human clinical trials 2010	Number of human clinical trials 2016	Further clinical trials needed	Evidence dossier (systematic review) for general level health claim	Application to change the code (High Level Health Claims Committee)
Allergy	2	0	✔		
Asthma	0	0	✔		
Arthritis	0	1	✔		
Brain health/cognition	0	2	✔		
Cancer	0	0	✔		
Cardiovascular disease risk	10	11		✔	✔
Diabetes		3	✔		
DNA damage	1	0	✔		
Duodenal ulceration	1	0	✔		

Energy intake, satiety and weight management	4	2	✔
Gastrointestinal health	1	3	✔
Inflammation	0	0	✔
Muscular injury	0	0	✔
Liver	0	0	✔
Sexual health	0	0	✔
Ageing	0	0	✔
Lung health	0	0	✔
General health	0	0	✔

Table 6 summarises the evidence from both the 2010 Apple Review and the 2016 apple update. It highlights that in the area of cardiovascular disease risk there is now a substantial number of human clinical trials which have been undertaken (21 studies in total). The number of studies in this area make it possible to perform a systematic literature review of the evidence, in particular focusing on a claim related to the cholesterol lowering effects of apples and apple components. However, as a claim about cholesterol reduction would be considered a high level claim (refers to a biomarker of a serious disease) in order to be successful in this sort of claim, an application would need to be made to change the Food Standards Code. This is a lengthy and expensive process as described in figure 2. An alternative to this may be to apply for a general level health claim about apples and heart health based on the current observational and human intervention studies which look at a range of cardiovascular risk factors which contribute to overall heart health. As described in figure 2, this would require a systematic review to be undertaken in line with the requirements of schedule 6, as the current reviews performed would be sufficient to satisfy the FSANZ requirements.

Table 7. Summary of next steps for health claims in pears

	Number of human clinical trials	Further clinical trials needed	Evidence dossier (systematic review)	Application to change the code (High Level Health Claims Committee)
Alcohol hangover	1	✔		
Cardiovascular disease	0	✔		
Digestive effects	0	✔		

Type 2 diabetes	0	✔
Metabolic health markers (chol, BP)	1	✔
Cancer	0	✔
Allergy and respiratory disease	0	✔
Weight control	1	✔
Antioxidant effects	0	✔

Table 7 shows that in comparison to apples, there is significantly less evidence from human intervention studies (clinical trials) regarding pears and health. For pears it would be necessary for more clinical trials to be undertaken in any one area in order to progress towards making health claims.

In our review of the evidence for pears the area there most potential for future research in the digestive health effects of pears. The unique composition of fibre, sorbitol and fructose in pears means they have the potential to stand out in comparison to other fruits in their digestive regulating function. Since no human evidence is avaiable on this effect to date, this requires substantation through clinical trials and the preparation of an evidence dossier (systematic literature review) in line with the FSANZ guidelines set out in schedule 6 of the Code.

Recommendations

In summary, a number of next steps were identified for the marketing messages for apples and pears. These include:

- Consideration of a general level claim on apples and heart health
- Consideration of a clinical trial on the digestive health effects of pears.
- Use of the identified pre-approved nutrition content and health claims which do not require further investment in research or substantiation.
- Continue to update the apple and pear reviews to monitor for future research which strengthens the evidence for particular health conditions.

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