

Health benefits of fruit and vegetables across the board



Dr Jean-Michel Lecerf

Nutrition & Physical Activity Department Preventive Health and Longevity Centre
Institut Pasteur de Lille, FRANCE

Dr. Jean-Michel Lecerf is a specialist in endocrinology and metabolic diseases. He has been a clinician at the Lille University Hospital, in lipidology, for more than 30 years. He has also been the head of the Nutrition Department at the Pasteur Institute of Lille since 1982, where he conducts applied research, public health and teaching in the field of nutrition. He is the author of numerous scientific publications and about 20 books on nutrition, cholesterol, obesity, diabetes and metabolism.

Countless studies are constantly being carried out, and no two are alike. Here is an overview of three studies exploring unusual targets of fruit and vegetable consumption.

- The first study dealt with inflammatory bowel disease (IBD), which encompasses Crohn's disease and ulcerative colitis (UC). The cause of these two conditions is unknown although the mechanism involved has been identified, with a strong inflammatory component. Data suggest that diet may trigger, aggravate or even favour them. Consumption of fibre was associated with a slight reduction in the risk of Crohn's disease, while fruit and vegetable consumption was linked to a decrease in Crohn's disease and UC. This may have been due to the anti-inflammatory effects of fruit and vegetables, their impact on the microbiota, or a favourable effect of the associated eating style (less fat and sugar, etc.). However, especially in the case-control studies, reverse causality could not be ruled out considering that the IBD patients reduced their consumption of produce during flare-ups.
- The second study focused on sulforaphane and foods high in it (i.e. cabbage and other cruciferous vegetables), and reviewed its effects on various diseases (inflammation, carcinogenesis, the microbiota, ageing processes, chronic kidney disease). Findings suggest that this compound, and therefore foods high in it, may be beneficial for patients with chronic kidney failure.
- The third publication reviewed various candidate nutrients for preventing female infertility, which is a genuine public health problem that seems to be worsening, either because of the increasing age of women wanting to have children or due to unfavourable changes in the eating or lifestyle (smoking, etc.) habits of these women. Oxidative stress seems to be involved in reducing female fertility (and also male fertility). And yet a large number of well-known nutrients with antioxidant effects are widely found in fruit and vegetables (vitamins C, E and A, carotenoids, polyphenols, etc.). The authors are in favour of undertaking clinical studies to provide evidence supporting this assumption and encourage the use of antioxidants in cases of infertility. As a precautionary measure, instead of advocating food supplements, it would be safer to propose fruit and vegetables.

Fruit and vegetables are therefore a safe bet for a growing number of health benefits.

Intake of dietary fiber, fruit, and vegetables and risk of inflammatory bowel disease

Inflammatory bowel disease (IBD) occurs in two forms, Crohn disease (CD) and ulcerative colitis (UC). Its prevalence is increasing worldwide, with more than 3 million people affected in Europe and 1.5 million in the U.S. (Park, 2014; Burisch, 2013). Factors such as an alteration in the gut microbiota, taking oral contraceptives, living in urban areas, and having a stressful lifestyle play an important role in IBD development. However, there is a lack of information regarding the contribution of dietary factors in IBD pathogenesis (Rampton, 2011). Several prospective studies have been conducted on the association between dietary fiber, fruit, and vegetable intake and IBD, but there is no meta-analysis that summarize these publications.

Therefore, the present meta-analysis aims to summarize the findings from these publications on the association between dietary fiber, fruit, and vegetable intake and the risk of IBD.

Dietary fiber intake is significantly associated with a reduced risk of Crohn disease and IBD, but not with ulcerative colitis

Combining 6 effect sizes from 5 studies revealed a significant inverse association between dietary fiber intake and Crohn disease.

When searching for nonlinear association, results also showed a significant association such that the highest risk reduction of Crohn disease was seen for fiber intake >22 g/d.

In the linear association, we found that an additional 10 g/d of fiber intake was associated with a 14% risk reduction of Crohn disease (cf. Table 1).

Table 1: Risk reduction of Crohn disease for additional intakes of dietary fiber, fruit, and vegetables.

	+10g/d of dietary fiber	+ 1 serving/d of fruit	+1 serving/d of vegetables
Risk reduction of Crohn disease	14%	19%	11%

However, regarding ulcerative colitis, no significant association was noted by combining data from 6 prospective cohort studies. Linear and nonlinear association were not significant neither.

On the other hand, when studies on Crohn disease and ulcerative colitis were combined, a significant inverse association was found between dietary fiber intake and risk of IBD.

KEY MESSAGES

- A significant association was found between dietary fiber and a reduced risk of Crohn disease and IBD, but not with ulcerative colitis.
- Dietary intake of fruit was significantly associated with a reduced risk of ulcerative colitis, Crohn disease and IBD.
- Vegetable consumption was significantly associated with a reduced risk of ulcerative colitis, Crohn disease, and IBD.
- Further prospective studies and clinical trials are needed to expand knowledge about the association in this regard.

Dietary intakes of fruit and vegetables are significantly associated with a reduced risk of ulcerative colitis, Crohn disease and IBD

Data combined from 4 studies showed a significant inverse association between fruit consumption and the risk of ulcerative colitis: individuals who were in the highest category of fruit intake had 31% lower risk of ulcerative colitis compared with those in the lowest category. For vegetables, the association was also significant, with 44% lower risk of ulcerative colitis in individuals in the top category of vegetable consumption compared with those in the bottom category.

Regarding Crohn disease, associations were also significant for fruit and vegetable consumption. Findings showed that individuals with the highest fruit consumption had a lower risk of Crohn disease development compared with those with the lowest intake. A significant association was also observed between a high intake of vegetables and a reduced risk of Crohn disease based on data for 3 studies. An additional 1 serving of fruit and 1 serving of vegetable per day was respectively associated with a 19% and 11% lower risk of Crohn disease according to nonlinear association (cf. Table 1).

When combining studies on Crohn disease and ulcerative colitis, fruit consumption was significantly associated with IBD risk. Vegetables consumption was also significantly associated with a reduced risk of IBD, so that those with the highest intake of vegetables had a 46% lower risk of IBD development compared with those with the lowest intake.



METHODOLOGY

- Relevant articles published up to 2019 were searched via PubMed, MEDLINE, Scopus, Embase, Cochrane Library, and Google Scholar.
- In final, 11 cohort studies (12 effect sizes) were included:
 - 6 prospective cohorts and 5 case-control studies
 - Mainly conducted in Sweden, United States, Australia, and Denmark
- A total of 478,604 participants were enrolled in the included studies, aged between 10 and 80 years old.

Based on: Milajerdi A, et al. Association of Dietary Fiber, Fruit, and Vegetable Consumption with Risk of Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. *Adv Nutr.* 2021 Jun 1;12(3):735-743.

References:

- Burisch J, Munkholm P. Inflammatory bowel disease epidemiology. *Curr Opin Gastroenterol.* 2013 Jul;29(4):357-62.
- Park SJ, et al. Clinical characteristics and treatment of inflammatory bowel disease: a comparison of Eastern and Western perspectives. *World J Gastroenterol.* 2014 Sep 7;20(33):11525-37.
- Rampton DS. The influence of stress on the development and severity of immune-mediated diseases. *J Rheumatol Suppl.* 2011 Nov;88:43-7.

The role of natural antioxidant compounds on female infertility prevention

Infertility, defined as the failure to conceive a pregnancy after a year or more of regular unprotected sexual intercourse, concerns almost 50 million of couples in the world (WHO, 2020).

With the prevalence of female infertility increasing yearly, it has become a global health issue. One of the main mediators of this condition is oxidative stress: it causes various reproductive pathologies in women such as endometriosis, preeclampsia, spontaneous abortion and unexplained infertility.

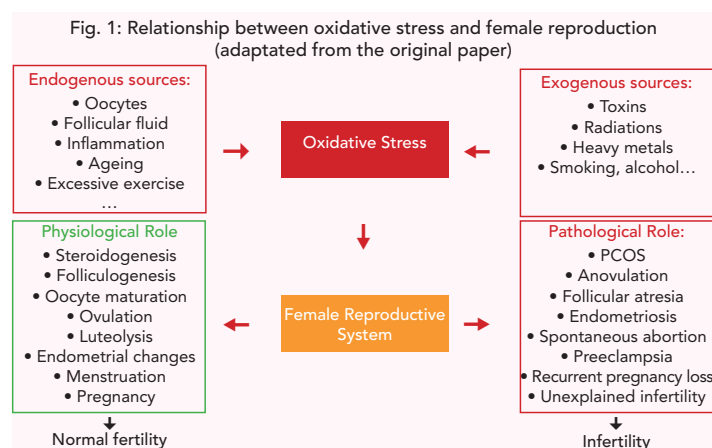
This article describes the main elements of a review conducted by an Indian team regarding the effectiveness of various natural antioxidant compounds found in fruits and vegetables - vitamins, carotenoids and polyphenols - in improving female fertility.

Association between infertility and oxidative stress

Numerous studies of literature related to the pathology of the couple's infertility involved oxidative stress in the pathophysiology of female infertility (Gupta *et al.*, 2014; Agarwal *et al.*, 2012).

Oxidative stress is considered as one of the major factors involved in the initiation of reproductive pathologies of females (Agarwal *et al.*, 2006), such as preeclampsia, recurrent pregnancy loss, embryonic resorption, intrauterine growth restriction, and fetal death (Gupta *et al.*, 2007). Oxidative stress is caused by mechanisms internal and external to the body:

- Endogenous sources : Oocytes, inflammation, ageing, excessive exercise...
- Exogenous sources : toxins, radiations, heavy metals, drugs, smoking... (figure 1)



Natural antioxidant compounds found in fruit and vegetables

An antioxidant may be defined as a molecule having the propensity to

neutralize or inhibit the free radical reactions and thus, delay or prevent cellular damage.

Natural antioxidant compounds found in fruit and vegetables can be broadly divided into three groups:

- **Vitamins**
 - Vitamin C is commonly found in fresh vegetables and fruits, particularly in citrus fruits. Ascorbic acid mainly has three natural functions of specific interest for reproduction, which depend on its reducing power: it is necessary for collagen synthesis, for peptide and steroid hormone synthesis, and for prevention of oxidation of biological molecules.
 - Vitamin E: Food like green vegetables, vegetable oil, kiwi fruits, and nuts such as almonds, walnuts, etc. are high in vitamin E. Apart from the various functions it performs in the body, vitamin E is primarily essential to maintain the normal fertility potential of both human and livestock species. In fact, it was first recognized as the critical dietary factor for the reproductive potential of both male and female rats (Evans *et al.*, 1922; Putman *et al.*, 1987).
 - Vitamin A plays an important role in the reproduction of females including steroidogenesis, follicular growth, and oocyte and embryo development (Gad *et al.*, 2018).

- **Carotenoids** are pigments naturally found in red or dark green and yellow fruits and vegetables. There are some carotenoids (α - and β -carotene, β -cryptoxanthin) which can be converted into vitamin A in humans and, thus, aid in providing this essential vitamin to the body. Women with spontaneous preterm birth defects have been found to have a lower concentration of carotenoids in the serum, while elevated serum concentrations of α - and β -carotene, α - and β -cryptoxanthin, and lycopene reduce premature birth risk (Kramer *et al.*, 2009). Consumption of a diet containing fruits and vegetables rich in carotenoids has also been documented in preventing premature birth (Englund-Ogge *et al.*, 2014).

- **Phenolic compounds** are found in various plant-based food such as vegetables, fruits, chocolate, nuts, wine, tea, and coffee. Studies related to the effects of dietary polyphenol consumption on reproductive health of humans are limited and show inconsistent results. However, based on the accumulated evidence from in vitro and in vivo animal studies, along with few human studies in various contexts, some researchers may believe that polyphenols have potential health benefit on human reproduction (Ly *et al.*, 2015).

Numerous studies in animals and humans have shown a decrease in the levels of oxidative stress markers after consumption of vegetables and fruits or antioxidant supplements.

Other studies show that low intake of antioxidant sources such as fruits and vegetables by females seems to increase their risk to endometriosis, one of the causative factors for female infertility (Parazzini *et al.*, 2004).

Larger well-designed, dose-response studies in humans are further warranted to incorporate natural antioxidant compounds into the clinical management of female infertility.

KEY MESSAGES

- Natural antioxidant compounds found in fruits, vegetables, and other dietary sources, alone or in combination with other antioxidants, were found to be effective in ameliorating the oxidative stress-mediated infertility problems in both natural and assisted reproductive settings.
- Although optimum levels of natural antioxidants have shown favorable results, however, their excessive intake may have adverse health impacts.

METHODOLOGY

- Review of 372 publications.

Based on: Bhardwaj JK, et al. Ameliorating Effects of Natural Antioxidant Compounds on Female Infertility: a Review. Reprod Sci. 2021 May;28(5):1227-1256.

References:

- Agarwal A, et al. The effects of oxidative stress on female reproduction: a review. Reprod Biol Endocrinol. 2012;10:49
- Agarwal A. Role of oxidative stress in female reproduction. ReprodBioMed Online. 2006;13:126–34.20.
- Englund-Ogge L, et al. Maternal dietary patterns during pregnancy and preterm delivery: a large prospective cohort study in China. BrMed J. 2014;348:1446
- Evans HM, Bishop KS. Inhibition of 5 alpha-reductase in genital skin fibroblasts and prostate tissue by dietary lignans and isoflavonoids. Science. 1922;56:650–1.123
- Gad A, et al. Retinoic acid improves maturation rate and upregulates the expression of antioxidant-related genes in in vitro matured buffalo (Bubalus bubalis) oocytes. Int J Vet Sci Med. 2018;6:279–85
- Gupta S, et al. The role of oxidative stress in spontaneous abortion and recurrent pregnancy loss: a systematic review. Obstet Gynecol Surv. 2007;62:335–47.
- Gupta S, et al. Power of proteomics in linking oxidative stress and female infertility. Biomed Res Int. 2014;9:162127
- Kramer MS, et al. Epidemiology. Antioxidant vitamins, long-chain fatty acids, and spontaneous preterm birth. 2009;20:707–13.
- Ly C, et al. The effects of dietary polyphenols on reproductive health and early development. Hum Reprod Update. 2015;21:228–48.
- Parazzini F, et al. Selected food intake and risk of endometriosis. Hum Reprod. 2004;19:1755–9
- Putnam ME, Comben N. Vitamin E. Vet Rec. 1987;121:541–5.

Cruciferous vegetables: potential benefits of sulforaphane-rich foods for patients with chronic kidney disease

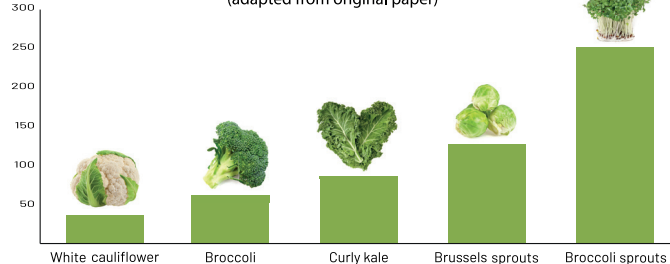
Numerous studies have shown health benefits of cruciferous vegetables. They contain vitamins, minerals, phenolic compounds, and more particularly sulforaphane. Sulforaphane is a sulfur-containing isothiocyanate which has numerous essential roles as an antimicrobial, antioxidant, anti-inflammatory, (Vanduchova, 2019; Houghton, 2019) and anti-oncogenic (Calcabrini et al, 2020) agent and as an epigenetic modulator (Hyun, 2019). Health benefits of sulforaphane have been more studied in the context of cancer and its potential preventive effects were examined on diabetes, cardiovascular and neurological diseases (Bai, 2015 ; Klomprens E, 2019). A recent review of the literature examined the potential benefits of sulforaphane against various diseases and some elements are described in this article.

Cruciferous vegetables: source of sulforaphane

Sulforaphane is a sulfur-containing isothiocyanate, formed when its precursor, glucoraphanin, an organic compound of the glucosinolate family, is transformed by an enzyme, myrosinase, as a result of damage to the plant (e.g. chewing), allowing the enzyme and its substrate to combine and react. Sulforaphane is one of the main activators of Nrf2 which neutralize oxidants.

Cruciferous vegetables such as broccoli, cauliflower, kale, and cabbage are rich in sulforaphane. Broccoli sprouts contain the highest concentration of sulforaphane with 1153 mg/100 dry weight (mature broccoli contains between 44 and 171 mg/100 g dry weight (see figure 1 relative to the glucosinolate content in cruciferous fresh vegetables)) (Nakagawa, 2006).

Figure 1 : Glucosinolate concentration in cruciferous fresh vegetables (adapted from original paper)



Literature on sulforaphane effects:

• Inflammation

Inflammation and oxidative stress are intrinsically involved in the

pathogenesis of chronic noncommunicable diseases such as cardiovascular disease, hypertension, obesity, chronic kidney disease, diabetes, and cancer. Accordingly, numerous nutritional strategies have been developed and applied to decrease inflammation and oxidative stress, and to improve the quality of life of affected individuals. According to studies summarized in this review, sulforaphane treatment seems to be an efficient anti-inflammatory and antioxidant strategy. Clinical studies in humans should be encouraged because only a limited number of published reports dealing with this topic currently exist in the literature. (Mazarakis, 2020; Tan SM, 2014).

• Microbiota

Dietary fibers and phytonutrients are known as essential modulators of the gut microbiota. Therefore, the intake of cruciferous vegetables can alter the composition of the gut microbiota and lead to the growth of specific bacteria that increase the production of sulforaphane, because gut microbiota metabolize glucosinolate to sulforaphane (Kaczmarek, 2009; Liu X, 2017).

• A modulator of ageing processes

Accumulating evidence suggests that isothiocyanates, including sulforaphane, can counteract aspects of the ageing process via a range of underlying mechanisms, from Nrf2-dependent or independent pathways to modification of the epigenetic landscape of ageing. Given the role of Nrf2 as a geroprotective agent and mediator of ageing processes, it is tempting to speculate on the capacity of sulforaphane to prevent or mitigate the progression of ageing-related diseases (Dai, 2020).

• Effect on chronic kidney disease

Sulforaphane acts as a geroprotectant, modulates the epigenetic landscape, protects against mitochondrial damage, and helps maintain a normative gut microbiota, thus suggesting a promising role for sulforaphane in the control of several diseases. In this context, patients with chronic kidney disease, a disease characterized by inflammation, oxidative stress, gut dysbiosis, mitochondrial dysfunction, and an altered epigenetic machinery, may be an ideal patient group for using food as a novel treatment strategy. Although there are no clinical studies demonstrating an effect of sulforaphane in chronic kidney disease, findings of studies in other patient groups suggest that sulforaphane could be a promising adjunctive therapy. Notably, sulforaphane therapy has already been shown to improve renal function in a range of preclinical models of renal damage. Clinical studies with patients with chronic kidney disease using sulforaphane should thus be encouraged to promote improvement in patients' quality of life.

KEY MESSAGES

- Sulforaphane is an important bioactive compound present in cruciferous vegetables
- An extensive literature has shown that the main route of action of sulforaphane is by its antioxidant potential and activation of the transcription factor Nrf2, which has a key role in the antioxidant response.
- Sulforaphane acts as a geroprotectant, modulates the epigenetic landscape, protects against mitochondrial damage, and helps maintain a normative gut microbiota, thus suggesting a promising role for sulforaphane in the control of several diseases, including chronic kidney disease

METHODOLOGY

- A total of 227 publications were included

Based on: Cardozo LFMF, et al. Cruciferous vegetables: rationale for exploring potential salutary effects of sulforaphane-rich foods in patients with chronic kidney disease. *Nutr Rev.* 2021 Oct 11;79(11):1204-1224.

References:

- Bai Y, et al. Sulforaphane protection against the development of doxorubicin-induced chronic heart failure is associated with Nrf2 Upregulation. *Cardiovasc Ther.* 2017;35:E12277.
- Calcabrini C, et al. Sulforaphane potentiates anticancer effects of doxorubicin and cisplatin and mitigates their toxic effects. *Front Pharmacol.* 2020;11:567.
- Dai L, et al. Early vascular ageing in chronic kidney disease: impact of inflammation, vitamin K, senescence and genomic damage. 2020;35:ii31-ii37.
- Houghton CA. Sulforaphane: its "coming of age" as a clinically relevant nutraceutical in the prevention and treatment of chronic disease. *Oxid Med Cell Longev.* 2019;2019:1-27.
- Hyun TK. A recent overview on sulforaphane as a dietary epigenetic modulator. *Excli J.* 2020;19:131-134.
- Klomprens E, Ding Y. The neuroprotective mechanisms and effects of sulforaphane. *Brain Circ.* 2019;5:74-83.
- Mazarakis N, et al. The potential use of L-sulforaphane for the treatment of chronic inflammatory diseases: a review of the clinical evidence. *Clin Nutr.* 2020;39:664-675.
- Nakagawa K et al. Evaporative light-scattering analysis of sulforaphane in broccoli samples: quality of broccoli products regarding sulforaphane contents. *J Agric Food Chem.* 2006;54:2479-2483.
- Tan SM, de Haan JB. Combating oxidative stress in diabetic complications with Nrf2 activators: how much is too much? *Redox Rep.* 2014;19:107-117.
- Vanduchova A. Isothiocyanate from broccoli, sulforaphane, and its properties. *J Med Food.* 2019;22:121-126.
- Kaczmarek JL et al. Broccoli consumption affects the human gastrointestinal microbiota. *J Nutr Biochem.* 2019;63:27-34. 163.
- Li F et al. Human gut bacterial communities are altered by addition of cruciferous vegetables to a controlled fruit- and vegetable-free diet. *J Nutr.* 2009;139:1685-1691.
- Liu X et al. Dietary broccoli alters rat cecal microbiota to improve glucoraphanin hydrolysis to bioactive isothiocyanates. *Nutrients.* 2017;9:262

The Mediterranean diet: current consumption patterns in Mediterranean countries are deviating from traditional habits and are no longer sustainable



Italian researchers analysed the greenhouse gas emissions associated with dietary patterns in seven Mediterranean countries – Cyprus, Croatia, Greece, Italy, Portugal, Spain and Malta – and 21 non-Mediterranean European countries. All of the dietary patterns analysed were associated with comparable GHG emissions: 4.46 kg CO₂eq/person/day for Mediterranean countries; 4.03 kg CO₂eq/person/day for non-Mediterranean countries. This was almost double that expected by a sustainable dietary pattern according to the EAT-Lancet Commission (2.49 kg CO₂eq/person/day). The main observed deviations from the traditional Mediterranean diet concerned the consumption of meat, cheese, fat and carbohydrate-rich food. The overconsumption of meat, in particular red meat, contributed to 60% of the greenhouse gas excess.

Castaldi S, et al. The positive climate impact of the Mediterranean diet and current divergence of Mediterranean countries towards less climate sustainable food consumption patterns. *Sci Rep.* 2022;12(1):8847.

Home-delivery produce prescription programmes: a first pilot study to assess their feasibility and potential impact



An American team conducted a pilot study on the feasibility and potential impact of a family-based, home-delivery produce prescription and nutrition education programme. Twenty-five families were included. This programme's results were encouraging but need to be confirmed and further explored. Indeed, following the intervention, fruit and vegetable consumption increased in a sub-group of children, but this intake remained below the recommended levels, particularly for vegetables. The findings also indicated improved access to food, although the food insecurity score was not significantly better after the intervention.

Fischer L, et al. Feasibility of a Home-Delivery Produce Prescription Program to Address Food Insecurity and Diet Quality in Adults and Children. *Nutrients.* 2022 May 10;14(10):2006.

Australia: the translational “Time for Healthy Habits” trial increased vegetable intakes



An Australian study assessed the effectiveness of two interventions focusing on nutrition and physical activity. This remote programme targeting parents aimed to increase their fruit and vegetable intake and that of their children. Four hundred and fifty-eight parents of children between the ages of two and six years were recruited and divided up into three groups: 1 (n=95) = telephone-based intervention; 2 (n=218) = online intervention; 3 (controls, n=145) = printed materials. Nine months after the programme's launch, the parents who received the telephone-based intervention had significantly higher vegetable intakes than those who received the printed materials (+0.41 servings/day). The authors therefore conclude that there may be some benefit to this programme but recommend confirming these results with a larger sample and exploring methods for increasing parent engagement.

Wyse RJ, et al. Parent Fruit and Vegetable Consumption Outcomes from the Translational ‘Time for Healthy Habits’ Trial: Secondary Outcomes from a Partially Randomized Preference Trial. *Int J Environ Res Public Health.* 2022 May 19;19(10):6165.

Mental health: consuming fruit more frequently may play a favourable role



A cross-sectional online study that included 428 healthy American adults measured the dietary habits and psychological health of the participants. The results showed that more frequent fruit consumption was associated with reduced symptoms of depression and greater psychological well-being. Conversely, consumption of savoury snacks was associated with anxiety. Further studies are needed to establish a potential causal relationship and determine whether these findings may represent modifiable dietary targets likely to directly (and indirectly) influence our psychological health.

Tuck NJ, et al. Frequency of fruit consumption and savoury snacking predict psychological health; selective mediation via cognitive failures. *Br J Nutr.* 2022 May 26:1-26.

Social media: a platform to facilitate nutrition and health behaviour change in young adults?



A study focusing on 234 young adults (aged 18 to 24) living in Australia explored the influence of social media on dietary behaviours. It was based on an analysis of data collected from online conversations. Some participants, more frequently women, expressed that exposure to online health-focused content made them feel guilty. Fast-food advertisements were perceived as a contributor to poor health behaviours and indicated as a major barrier to change. The participants therefore reported that social media is highly persuasive in terms of dietary behaviour. This suggests that social norms on the web are an important aspect of changing the health behaviours of young adults. Future social media-delivered dietary interventions should acknowledge the social and environmental factors that challenge the ability of young adults to make individual health behaviour improvements.

Friedman VJ, et al. The Use of Social Media as a Persuasive Platform to Facilitate Nutrition and Health Behavior Change in Young Adults: Web-Based Conversation Study. *J Med Internet Res.* 2022 May 18;24(5):e28063.