# **BMJ Open** Effects of inulin-type fructans supplementation on cardiovascular disease risk factors: a protocol for a systematic review and meta-analysis of randomised controlled trials

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#### **ABSTRACT**

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Correspondence to Dr Russell J de Souza; desouzrj@mcmaster.ca **Introduction** This review aims to assess the effects of dietary supplementation with inulin-type fructans (ITF) compared with no supplementation on cardiovascular disease risk factors in adults and assess the quality of trial reporting using the Consolidated Standards of Reporting Trials (CONSORT) and CONSORT for abstract (CONSORT-A) checklists.

Methods and analysis We will search randomised controlled trials (RCTs) in MEDLINE, EMBASE, CINAHL, Emcare, AMED and the Cochrane Database of Systematic Reviews from inception to 31 March 2022, without any language restrictions. The RCTs need to administer ITF in adults for at least 2 weeks and assess effects on at least one cardiovascular risk factor. We will exclude RCTs that (1) assessed the postprandial effects of ITF; (2) included pregnant or lactating participants; (3) enrolled participants undergoing treatment that might affect the response to ITF. We will assess the study risk of bias (RoB) using V.2 of the Cochrane RoB tool for RCTs (RoB 2) and the certainty of the evidence using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach. We will pool data using a random-effects model. We will use the  $\chi^2$  test to compare compliance of CONSORT and CONSORT-A checklists and Poisson regression to identify factors associated with better reporting.

**Ethics and dissemination** Ethics approval is not required for secondary analysis of already published data. We will publish the reviews in a peer-review journal. **PROSPERO registration number** CRD42019136745.

#### **INTRODUCTION**

Cardiovascular disease (CVD) is a major cause of death worldwide.<sup>1</sup> In 2019, CVD caused an estimated 17.9 million deaths globally<sup>1</sup> and by 2030, 23.6 million people are expected to die from CVD.<sup>2</sup> In 2019, it was responsible for 359 million years of life lost (age-standardised rate approximately 4439 per 100 000 population)

#### STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ We will follow Cochrane guidance to conduct this systematic review including screening titles and abstracts, selecting studies and extracting data independently and in duplicate.
- ⇒ We will use the Grading of Recommendations, Assessment, Development and Evaluations approach to assess certainty of evidence.
- ⇒ We will follow the Instrument to assess the Credibility of Effect Modification Analyses (ICEMAN) guidance to conduct subgroup analyses for our systematic review.
- ⇒ Pooled effect estimates are likely to be heterogeneous because of the different types of inulin-type fructans used, and duration of interventions.

and 393 million disability-adjusted life years (age-standardised rate approximately 4864 per 100 000 population).<sup>3</sup>

CVD can lead to an acute coronary syndrome, heart failure and stroke, mainly through the development of atherosclerotic plaque.<sup>1 2 4</sup> Plaques are composed of fat, calcium and cholesterol, and they block and/ or narrow arteries, which limits the flow of oxygen-rich blood to the heart and brain.<sup>56</sup> Furthermore, plaques are recognised by the immune system as a foreign body, which stimulates an inflammatory response.<sup>7 8</sup> If these plaques rupture, their contents cause clot formation, which is a precursor to heart attack or ischaemic stroke.<sup>78</sup> Some of the wellestablished risk factors for CVD include high blood pressure, high cholesterol, diabetes, and excess body fat.

Dietary fibres are the edible parts of plants that are resistant to digestion and absorption in the human small intestine. Dietary patterns high in fibre has been shown to improve several cardiovascular risk factors, and reduce the risk of cardiovascular events.<sup>10–12</sup> Low dietary fibre intake is considered a major contributor to the epidemic of CVD.<sup>13</sup> The beneficial effects of dietary fibres are partially due to their ability to reduce serum cholesterol through a variety of mechanisms. First, soluble fibre binds cholesterol in the lumen of the small intestine to reduce cholesterol absorption. Second, soluble fibre increases the faecal excretion of bile acids, diverting hepatic cholesterol for bile acid production and lowering circulating plasma LDL cholesterol as it is taken up by the liver from the plasma. Third, fibres that are freely fermentable by the colonic bacteria are converted into short-chain fatty acids such as acetic, propionic and butyric acids. Propionic acid can be absorbed and inhibit the liver's rate-limiting cholesterol synthesis enzyme 3-hydroxy-3-methylglutaryl coenzyme A reductase.<sup>1415</sup> The Canadian Cardiovascular Harmonized National Guidelines Endeavour recommends a dietary pattern that includes  $\geq 30$  g of fibre per day to lower the risk of CVD.<sup>16</sup> People with the highest dietary fibre intakes show a 16%–23% lower risk of all-cause mortality than those with the lowest.<sup>17–19</sup>

Inulin-type fructans (ITF) are carbohydrates<sup>20</sup> that occur naturally in vegetables and plants including leeks, onions, artichokes, bananas, garlic, wheat and chicory.<sup>20–22</sup> ITF include fructo-oligosaccharides, oligofructose and inulin, which are soluble dietary fibres known as prebiotics.<sup>23</sup> Prebiotics promote the growth and activity of beneficial gut bacteria<sup>24</sup> and confer various health benefits, including improvements in CVD risk factors.<sup>25</sup> Several systematic reviews have demonstrated the beneficial effects of ITF on some CVD risk factors in certain subgroups.<sup>24 26–28</sup>

Our systematic review will advance previous reviews of this topic in the following ways: (1) through an updated literature search; (2) assessing the effect of dietary supplementation with ITF on low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), fasting blood glucose (FBG), body mass index (BMI), diastolic blood pressure (DBP), systolic blood pressure (SBP), waist circumference (WC), waist-to-hip ratio, body weight, apolipoprotein A1 (ApoA1), apolipoprotein B (ApoB), glucose haemoglobin A1c (HbA1c), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), very low-density lipoprotein cholesterol (VLDL-C) in adults with or without pre-existing cardiometabolic conditions; (3) assessing the quality of evidence using Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach; (4) an assessment of clinically relevant subgroups which may derive particular benefits, such as those with dyslipidaemia, type 2 diabetes and obesity and (5) assessing compliance with the Consolidated Standards of Reporting Trials (CONSORT) statement and the CONSORT extension for abstract (CONSORT-A) in included randomised controlled trials (RCTs).

#### **METHODS**

This protocol is reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols.<sup>29</sup> We established our methods for this systematic review a priori. We will conduct our systematic review using Cochrane methods.<sup>30</sup>

#### Criteria for considering studies for this review Types of studies

We will include only RCTs in our review.

#### Types of participants

We will include studies of adults (aged 18 years or older) with or without pre-existing CVD, diabetes, hypertension or dyslipidaemia. Studies will be ineligible if they only look at the postprandial effects of ITF or involved participants with conditions or undergoing treatment that seriously alters normal digestion or absorption of nutrients. These include chemotherapy, dialysis, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, chronic obstructive pulmonary disease, inflammatory bowel disease, irritable bowel syndrome, chronic pancreatitis, chronic kidney disease and previous gastric bypass surgery. Additionally, we will exclude studies that included pregnant or lactating participants because of the transient effects on cardiometabolic risk factors during these life stages.

#### Types of interventions

Eligible interventions include the administration of a clearly specified type of ITF for a minimum of 2 weeks. Studies that administered ITF with a co-intervention are eligible if the co-intervention was present in both the treatment and control arms and likely operates through a mechanism independent of the ITF (eg, Roshanravan *et al*<sup>31</sup> compared butyrate versus butyrate+inulin to assess the effect of butyrate and inulin supplementation in patients with diabetes).

#### Comparator(s)

The comparator(s) will include administration of placebo or control foods for a minimum of 2 weeks.

#### Types of outcome measures

The main outcomes of our review are LDL-C, TG and FBG. The secondary outcomes of our review are body mass index (BMI), body weight, WC, waist-to-hip ratio, SBP, DBP, HDL-C, VLDL-C, TC, ApoA1, Lipoprotein B (ApoB) and HbA1c.

#### Search methods for identification of studies Electronic searches

We developed the search strategies in consultation with a librarian at the McMaster Health Sciences Library (online supplemental file 1). We will search MEDLINE, EMBASE, CINAHL, Emcare, AMED and Cochrane Database of Systematic Reviews databases from inception through 31 March 2022, without any language restrictions.

#### Searching other resources

We will examine the reference lists of eligible RCTs and relevant reviews to augment our database search.

#### **Data collection and analysis**

#### Selection of studies

A pair of reviewers will screen the titles, abstracts and full-text articles independently and in duplicate. The reviewers will select the full-text articles based on inclusion criteria. They will resolve any disagreement through discussion or consultation with a third reviewer if needed. If there are multiple publications from the same study, then we will consider each study as a unit of interest instead of each report for our review. We will combine information from multiple publications to avoid overlap in participants, prioritising the study with the largest sample size and longest follow-up for each outcome of interest. The reviewers will document the reasons for the exclusion of the studies. We will present the study selection process in a flow diagram.

#### Data extraction and management

A pair of reviewers will extract information about the study characteristics and results independently and in duplicate. They will resolve any disagreement through discussion or consulting a third reviewer. They will extract information about the study (basic bibliometric information, design, conflicts of interest, funding source, country or countries of conduct), characteristics of participants (baseline information for all relevant outcome measures, baseline comorbidities of the study population, age, BMI, percentage of the population that has comorbidities), intervention (length of intervention, dosage, regimen and any co-interventions) and outcomes reported. The reviewers will extract data presented only in graphs using a Plot Digitizer (http://plotdigitizer.sourceforge.net/).

We will enter data in duplicate into a spreadsheet template (Microsoft Excel, Microsoft) and collect reported outcome measures based on the following hierarchy for parallel RCTs: (1) change in measure from baseline or between-group difference in change from baseline or per cent change in measure from baseline (if baseline score is reported); (2) measure at follow-up or between-group difference in measure at follow-up; (3) regression coefficients. We will extract data based on the following hierarchy for crossover RCTs: (1) between-group difference in change from baseline; (2) between-group difference in measure at follow-up; (3) change in measure from baseline; (4) per cent change in measure from baseline when baseline score is reported; (5) regression coefficients for change score; (6) measure at follow-up. We will apply paired analyses to all crossover trials according to the methods of Cochrane Handbook, Elbourne et al or Curtin et al.<sup>30 32 33</sup> To investigate the effect of imputed correlation coefficients on paired analyses, we will perform sensitivity analyses across a range of possible

A pair of reviewers will assess the RoB using the Cochrane RoB 2.0 tool<sup>34</sup> independently and in duplicate. The reviewers will assess the RoB based on bias arising from the randomisation process, bias due to deviations from the intended interventions, bias due to missing outcome data, bias in measurement of the outcome and bias in selection of the reported results. The reviewers will resolve any disagreement in the RoB assessment through discussion or consulting a third reviewer, if necessary.

correlation coefficients (0, 0.33, 0.66 and 0.99). To

mitigate the unit-of-analysis error from including trials

with multiple intervention groups, we will combine

groups to create single pairwise comparisons.<sup>30</sup>

#### Measures of treatment effect

The data for our meta-analysis will be continuous measures, reported in SI units (eg, mmol/L). We outlined the rules for converting outcome data in online supplemental file 2. We will compute the pooled mean difference if the reported measurement scales are the same (or interconvertible, such as mg/dL to mmol/L), otherwise, the standardised mean difference will be used if the reported measurement scales are different and not interconvertible. Pooled effects along with associated 95% confidence intervals (CIs will be presented. If a study reports multiple arms, then we will only include the relevant arms for our systematic review.

#### Unit of analysis

We will consider the unit of randomisation of included studies as the unit of analysis. In the case of multi-arm trials, if there is one control arm but more than one relevant intervention arms, we will either combine the two intervention arms to make a single pairwise arm or exclude the intervention arm which is less appropriate for this review as described in Cochrane Handbook.<sup>30</sup>

#### Dealing with missing data

We will contact the study authors to obtain any missing outcome data. If study authors are unresponsive, we will conduct a sensitivity analysis to determine the potential impact of missing data relevant to the outcomes of interest. We will use published methods of sensitivity analyses for missing outcome data using extreme but plausible assumptions.<sup>35 36</sup>

#### Assessment of heterogeneity

Initially, we will visually inspect the forest plot to assess heterogeneity. Then we will assess the heterogeneity among studies using I<sup>2</sup> statistics and a  $\chi^2$  test. We will use the criteria suggested in the Cochrane Handbook to interpret I<sup>2</sup> statistics for heterogeneity. Specifically, 0%–40%: might not be important; 30%–60%: may represent moderate heterogeneity; 50%–90%: may represent substantial heterogeneity; 75%–100%: considerable heterogeneity.<sup>30</sup> If there is substantial heterogeneity among the studies, we will attempt to explain this through subgroup analysis or meta-regression.<sup>30</sup>

#### Assessment of publication bias

We will visually inspect and conduct statistical tests (eg, Egger's regression), if there are >10 studies to assess the potential for publication bias as per published guidelines.<sup>37</sup>

#### Data synthesis

Where two or more studies for a given outcome are eligible, we will conduct a meta-analysis using the 'metafor' package in R. We will use the random-effects model for meta-analysis using the Restricted Maximum Likelihood estimator considering there will be some heterogeneity between studies based on participants and interventions. We will also use a fixed-effects model for meta-analysis if there are fewer than five studies. If we do not have enough data for statistical pooling, then we will conduct a narrative synthesis of the findings.

#### Subgroup analysis and investigation of heterogeneity

We will follow the Instrument to assess the Credibility of Effect Modification Analyses (ICEMAN) guidance (ie, hypothesising direction of subgroup effects a priori, prior evidence of subgroup effect, using a test for interaction, testing only a small number of subgroups and avoiding arbitrary cut-off points) to conduct subgroup analyses for our systematic review.<sup>38</sup>

We will conduct the following six subgroup analyses to understand the effects of sex, baseline disease condition, ITF type, ITF dose, RoB and duration of intervention on health outcomes:

- Sex: a recent meta-analysis suggests that ITF intake leads to better outcomes (eg, reduces fasting blood glucose and HbA1c) for females compared with males.<sup>27</sup> We hypothesise the same. We will conduct a subgroup analysis to understand the effects of ITF on females compared with males.
- 2. Baseline disease condition: we hypothesise that participants without pre-existing CVD, diabetes, hypertension or dyslipidaemia in the baseline will exhibit better outcomes. We will conduct a subgroup analysis comparing the studies that include people with these conditions versus without.
- 3. Types of ITF: evidence suggests that inulin may be more efficacious than other ITF.<sup>27</sup> We hypothesise the same. We will conduct a subgroup analysis to compare the effects of inulin with other types of ITF.
- 4. Dose of ITF: evidence suggests that 10 g ITF intake per day is an optimal dose.<sup>27</sup> We will test this hypothesis by comparing the effects of 10 g ITF intake with other doses of ITF intake. We will also use dose as a continuous variable to explore the effects of lower versus higher intake of ITF. We will also look at the interaction between dose and duration of intervention.
- 5. Risk of bias: studies with high or unclear RoB usually exaggerate effect estimates.<sup>39</sup> We hypothesise that

studies with higher or unclear RoB will report larger effect estimates. We will conduct a subgroup analysis to compare the studies with higher or unclear RoB with lower RoB.

6. Duration of intervention: it is recommended to supplement ITF for 6 weeks or longer.<sup>27</sup> We will conduct a subgroup analysis to compare the effects of ITF supplemented for  $\geq$ 6 weeks vs <6 weeks. We will also use weeks as a continuous outcome to explore the effects of the duration of ITF intake on health outcomes.

#### Sensitivity analysis

We will repeat the analysis by excluding the high RoB studies to understand their influence on the results. We will perform a sensitivity analysis based on parallel versus crossover study designs. We will also conduct a sensitivity analysis only including food-controlled trials to understand whether the results changed based on control arms. Additionally, if any unanticipated study design or conduct issues are identified during the conduct of the review that we believe would have a potential impact on the results, additional sensitivity analyses will be conducted to quantify their impact on findings. Such ad hoc decisions will be documented appropriately.

#### Certainty of the evidence

We will use the GRADE approach to assess the certainty of the evidence of each outcome.<sup>40</sup> The GRADE approach considers five domains, including the RoB, imprecision, inconsistency, indirectness and likelihood of publication bias for each outcome of interest. We will rate each outcome as either high, moderate, low or very low certainty evidence based on these domains.

#### Summary of findings table

A summary of findings table provides a succinct summary of the key information from systematic reviews needed by decision-makers.<sup>41</sup> We will prepare the GRADE summary of findings tables to report the main comparisons of this review.<sup>41</sup>

### Substudy

#### Background

The RCT is considered the gold standard to assessing the effectiveness of health interventions.<sup>42–44</sup> A wellconducted RCT can transform patient care. However, reporting of the study design, conduct, analysis and interpretation of an RCT must be transparent and sufficiently detailed such that readers and practitioners can appropriately judge the validity and applicability of the trial to particular practice settings.<sup>45</sup> This is difficult to do when trial reporting is inadequate.<sup>46</sup> At worst, inadequate reporting can lead to a biased estimate of the treatment effect, leading physicians to avoid truly effective treatments or promote truly ineffective treatments.<sup>47</sup> The CONSORT statement intends to facilitate improved and transparent reporting of trials by authors.<sup>48</sup>

Just as importantly, abstracts of RCT reports must also adhere to reporting guidelines because clinicians often make treatment decisions based on the abstracts of research articles<sup>46 49 50</sup> owing to time limitations, language barriers or paywalls.<sup>51</sup> Ideally, authors should provide sufficient information in an abstract to allow readers to assess the validity of an RCT. The CONSORT-A is intended to guide the authors to provide a minimum list of key details about an RCT.<sup>46 50</sup>

#### Objective

The objective of this study is to compare reporting quality of RCTs and abstracts of RCTs that assessed the effects of ITF supplementation on CVD risk factors in adults, published before and after publication of CONSORT and CONSORT-A respectively.

#### Data extraction and management

The CONSORT statement was developed in 199645 and revised and updated in 2001 and 2010.42 52 The CONSORT-A statement was developed in 2008.<sup>46</sup> The reviewers will collect data following 25- item CONSORT 2010 checklists and 17-item CONSORT-A checklists for RCT publications selected for our systematic review.<sup>42454652</sup> We will simply count (yes/no) to understand whether the RCTs adhered to each item.

#### Data analysis

We will compare the studies published before and after the publication of CONSORT 2010 and CONSORT-A 2008 statements to assess conformity with CONSORT and CONSORT-A statements. We will use the  $\chi^2$  test to assess compliance. We will use Poisson regression to adjust confounders including study publication year (before or after the publication of CONSORT and CONSORT-A guidance), journal endorsement (endorsed CONSORT vs non-endorsed), journal impact (high impact vs others), the statistical significance of primary outcome (significant vs non-significant), funding status (industry-funded vs others), sample size (≤100 vs >100), study design (parallel vs crossover), authors' expertise (expertise in research methodology, biostatistics and subject matter vs no such expertise) and interventions (pharmacological vs non-pharmacological).

#### ETHICS AND DISSEMINATION

Consistent with our institution's policy, ethics approval is not required for secondary analysis of already published data. We will publish the reviews in a peer-review journal. We will also present the results of these reviews in conferences and meetings with other researchers and clinicians.

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Contributors RJdS conceived the work. JRT drafted the manuscript. RJdS, LM, JRT, DZ, MAC, LL, RA, RB, SJ, VH, PBD, JLS and DJAJ contributed to the data analysis plan. LB contributed to the search strategy development. RJdS, LM, JRT, DZ, MAC, LL, RA, RB, SJ, VH, PBD, JLS, DJAJ and LB will collaborate on data interpretation. RJdS is the guarantor of this study. RJdS, LM, DZ, MC, LL, RA, RB, SJ, VH, PBD, JLS and DJAJ revised the manuscript critically for important intellectual content.

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Competing interests RJ de Souza has served as an external resource person to the World Health Organization's Nutrition Guidelines Advisory Group on trans fats, saturated fats, and polyunsaturated fats. The WHO paid for his travel and accommodation to attend meetings from 2012-2017 to present and discuss this work. He has presented updates of this work to the WHO in 2022. He has also done contract research for the Canadian Institutes of Health Research's Institute of Nutrition, Metabolism, and Diabetes, Health Canada, and the World Health Organization for which he received remuneration. He has received speaker's fees from the University of Toronto, and McMaster Children's Hospital. He has held grants from the Canadian Institutes of Health Research, Canadian Foundation for Dietetic Research, Population Health Research Institute, and Hamilton Health Sciences Corporation as a principal investigator, and is a co-investigator on several funded team grants from the Canadian Institutes of Health Research. He has served as an independent director of the Helderleigh Foundation (Canada). He serves as a member of the Nutrition Science Advisory Committee to Health Canada (Government of Canada), and a co-opted member of the Scientific Advisory Committee on Nutrition (SACN) Subgroup on the Framework for the Evaluation of Evidence (Public Health England). JLS has received research support from the Canadian Foundation for Innovation, Ontario Research Fund, Province of Ontario Ministry of Research and Innovation and Science, Canadian Institutes of health Research (CIHR), Diabetes Canada, PSI Foundation, Banting and Best Diabetes Centre (BBDC), American Society for Nutrition (ASN), INC International Nut and Dried Fruit Council Foundation, National Dried Fruit Trade Association, National Honey Board (the US Department of Agriculture (USDA) honey 'Checkoff' programme), International Life Sciences Institute (ILSI), Pulse Canada, Quaker Oats Center of Excellence, The United Soybean Board (the USDA soy 'Checkoff' programme), The Tate and Lyle Nutritional Research Fund at the University of Toronto, The Glycemic Control and Cardiovascular Disease in Type 2 Diabetes Fund at the University of Toronto (a fund established by the Alberta Pulse Growers) and The Nutrition Trialists Fund at the University of Toronto (a fund established by an inaugural donation from the Calorie Control Council). He has received in-kind food donations to support a randomised controlled trial from the Almond Board of California, California Walnut Commission, Peanut Institute, Barilla, Unilever/Upfield, Unico/Primo, Loblaw Companies, Quaker, Kellogg Canada, WhiteWave Foods/Danone and Nutrartis. He has received travel support, speaker fees and/or honoraria from Diabetes Canada,

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#### **Open access**

Dairy Farmers of Canada, FoodMinds, International Sweeteners Association, Nestlé, Pulse Canada, Canadian Society for Endocrinology and Metabolism (CSEM), Gl Foundation, Abbott, General Mills, Biofortis, ASN, Northern Ontario School of Medicine, INC Nutrition Research & Education Foundation, European Food Safety Authority (EFSA), Comité Européen des Fabricants de Sucre (CEFS), Nutrition Communications, International Food Information Council (IFIC), Calorie Control Council, and Physicians Committee for Responsible Medicine. He has or has had ad hoc consulting arrangements with Perkins Coie, Tate & Lyle, Wirtschaftliche Vereinigung Zucker, Danone and INQUIS Clinical Research. He is a member of the European Fruit Juice Association Scientific Expert Panel and former member of the Soy Nutrition Institute (SNI) Scientific Advisory Committee. He is on the Clinical Practice Guidelines Expert Committees of Diabetes Canada, European Association for the study of Diabetes (EASD), Canadian Cardiovascular Society (CCS) and Obesity Canada/Canadian Association of Bariatric Physicians and Surgeons. He serves or has served as an unpaid scientific advisor for the Food. Nutrition and Safety Program (FNSP) and the Technical Committee on Carbohydrates of ILSI North America. He is a member of the International Carbohydrate Quality Consortium (ICQC), Executive Board Member of the Diabetes and Nutrition Study Group (DNSG) of the EASD and Director of the Toronto 3D Knowledge Synthesis and Clinical Trials foundation. His wife is an employee of AB InBev.DJAJ received salary support and discretionary funding from the Canada Research Chair (CRC) endowment of the federal government of Canada. He has received research grants from Saskatchewan & Alberta Pulse Growers Associations, the Agricultural Bioproducts Innovation Program through the Pulse Research Network, the Advanced Foods and Material Network, Loblaw Companies, Unilever Canada and Netherlands, Barilla, the Almond Board of California. Agriculture and Agri-food Canada. Pulse Canada. Kellogg's Company, Canada, Quaker Oats, Canada, Procter & Gamble Technical Centre, Bayer Consumer Care, Springfield, New Jersey, Pepsi/Quaker, International Nut & Dried Fruit Council (INC), Soy Foods Association of North America, the Coca-Cola Company (investigator initiated, unrestricted grant), Solae, Haine Celestial, the Sanitarium Company, Orafti, the International Tree Nut Council Nutrition Research and Education Foundation, the Peanut Institute, Soy Nutrition Institute (SNI), the Canola and Flax Councils of Canada, the Calorie Control Council, the Canadian Institutes of Health Research (CIHR), the Canada Foundation for Innovation (CFI) and the Ontario Research Fund (ORF). He has received in-kind supplies for trials as a research support from the Almond Board of California, Walnut Council of California, the Peanut Institute, Barilla, Unilever, Unico, Primo, Loblaw Companies, Quaker (Pepsico), Pristine Gourmet, Bunge Limited, Kellogg Canada, WhiteWave Foods. He has been on the speaker's panel, served on the scientific advisory board and/or received travel support and/or honoraria from Nutritional Fundamentals for Health (NFH)-Nutramedica, Saint Barnabas Medical Center, The University of Chicago, 2020, China Glycemic Index (GI) International Conference, Atlantic Pain Conference, Academy of Life Long Learning, the Almond Board of California, Canadian Agriculture Policy Institute, Loblaw Companies, the Griffin Hospital (for the development of the NuVal scoring system), the Coca-Cola Company, Epicure, Danone, Diet Quality Photo Navigation (DQPN), Better Therapeutics (FareWell), Verywell, True Health Initiative (THI), Heali Al Corp, Institute of Food Technologists (IFT), Soy Nutrition Institute (SNI), Herbalife Nutrition Institute (HNI), Saskatchewan & Alberta Pulse Growers Associations, Sanitarium Company, Orafti, the International Tree Nut Council Nutrition Research and Education Foundation, the Peanut Institute, Herbalife International, Pacific Health Laboratories, Barilla, Metagenics, Bayer Consumer Care, Unilever Canada and Netherlands, Solae, Kellogg, Quaker Oats, Procter & Gamble, Abbott Laboratories, Dean Foods, the California Strawberry Commission, Haine Celestial, PepsiCo, the Alpro Foundation, Pioneer Hi-Bred International, DuPont Nutrition and Health, Spherix Consulting and WhiteWave Foods, the Advanced Foods and Material Network, the Canola and Flax Councils of Canada, Agri-Culture and Agri-Food Canada, the Canadian Agri-Food Policy Institute, Pulse Canada, the Soy Foods Association of North America, the Nutrition Foundation of Italy (NFI), Nutra-Source Diagnostics, the McDougall Program, the Toronto Knowledge Translation Group (St. Michael's Hospital), the Canadian College of Naturopathic Medicine. The Hospital for Sick Children, the Canadian Nutrition Society (CNS), the American Society of Nutrition (ASN), Arizona State University, Paolo Sorbini Foundation and the Institute of Nutrition, Metabolism and Diabetes. He received an honorarium from the US Department of Agriculture to present the 2013 W.O. Atwater Memorial Lecture. He received the 2013 Award for Excellence in Research from the International Nut and Dried Fruit Council. He received funding and travel support from the Canadian Society of Endocrinology and Metabolism to produce mini cases for the Canadian Diabetes Association (CDA). He is a member of the International Carbohydrate Quality Consortium (ICQC). His wife, Alexandra L Jenkins, is a director and partner of INQUIS Clinical Research for the Food Industry, his two daughters, Wendy Jenkins and Amy Jenkins, have published a vegetarian book, The Portfolio Diet for Cardiovascular Risk Reduction

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(Academic Press/Elsevier 2020 ISBN:978-0-12-810510-8) and his sister, Caroline Brydson, received funding through a grant from the St. Michael's Hospital Foundation to develop a cookbook for one of his studies. He is also a vegan.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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