Latest Publications You Should Not Miss

Selected by Karin Kraft, Rostock

Reynolds A, Mann J, Cummings J, Winter N, Mete E, Te Morenga L: Carbohydrate quality and human health: a series of systematic reviews and meta-analyses. Lancet. 2019 Jan 10. pii: S0140-6736(18)31809-9. doi: 10.1016/S0140-6736(18)31809-9.

Background: Previous systematic reviews and meta-analyses explaining the relationship between carbohydrate quality and health have usually examined a single marker and a limited number of clinical outcomes. We aimed to more precisely quantify the predictive potential of several markers, to determine which markers are most useful, and to establish an evidence base for quantitative recommendations for intakes of dietary fibre.

Methods: We did a series of systematic reviews and meta-analyses of prospective studies published from database inception to April 30, 2017, and randomised controlled trials published from database inception to Feb 28, 2018, which reported on indicators of carbohydrate quality and non-communicable disease incidence, mortality, and risk factors. Studies were identified by searches in PubMed, Ovid MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials, and by hand searching of previous publications. We excluded prospective studies and trials reporting on participants with a chronic disease, and weight loss trials or trials involving supplements. Searches, data extraction, and bias assessment were duplicated independently. Robustness of pooled estimates from random-effects models was considered with sensitivity analyses, meta-regression, dose-response testing, and subgroup analyses. The GRADE approach was used to assess quality of evidence.

Findings: Just under 135 million person-years of data from 185 prospective studies and 58 clinical trials with 4635 adult participants were included in the analyses. Observational data sug-

gest a 15–30% decrease in all-cause and cardiovascular related mortality, and incidence of coronary heart disease, stroke incidence and mortality, type 2 diabetes, and colorectal cancer when comparing the highest dietary fibre consumers with the lowest consumers. Clinical trials show significantly lower bodyweight, systolic blood pressure, and total cholesterol when comparing higher with lower intakes of dietary fibre. Risk reduction associated with a range of critical outcomes was greatest when daily intake of dietary fibre was between 25 g and 29 g. Dose-response curves suggested that higher intakes of dietary fibre could confer even greater benefit to protect against cardiovascular diseases, type 2 diabetes, and colorectal and breast cancer. Similar findings for whole grain intake were observed. Smaller or no risk reductions were found with the observational data when comparing the effects of diets characterised by low rather than higher glycaemic index or load. The certainty of evidence for relationships between carbohydrate quality and critical outcomes was graded as moderate for dietary fibre, low to moderate for whole grains, and low to very low for dietary glycaemic index and glycaemic load. Data relating to other dietary exposures are scarce.

Interpretation: Findings from prospective studies and clinical trials associated with relatively high intakes of dietary fibre and whole grains were complementary, and striking dose-response evidence indicates that the relationships to several non-communicable diseases could be causal. Implementation of recommendations to increase dietary fibre intake and to replace refined grains with whole grains is expected to benefit human health. A major strength of the study was the ability to examine key indicators of carbohydrate quality in relation to a range of non-communicable disease outcomes from cohort studies and randomised trials in a single study. Our findings are limited to risk reduction in the population at large rather than those with chronic disease.

O'Connor S, Turcotte AF, Gagnon C, Rudkowska I. Increased Dairy Product Intake Modifies Plasma Glucose Concentrations and Glycated Hemoglobin: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Adv Nutr. 2019;0:1–18.

Introduction: Dairy product intake is inversely associated with the risk of type 2 diabetes (T2D) in numerous cohort studies; yet, the beneficial effects of increased dairy product intake on T2D risk factors such as fasting plasma glucose, fasting insulin, insulin resistance with the homeostasis model assessment, and glycated hemoglobin (HbA1c) remain inconclusive in clinical trials. The objective of this study was to systematically review clinical trials observing the effects of elevated compared with minimal intake of dairy products on T2D risk factors in subjects without diabetes.

Methods: Five databases [Medline, EMBASE, Central, CINAHL, AMED (Allied and Complementary Medicine)] were searched to identify randomized controlled trials that used elevated quantities of dairy products from ruminant sources in comparison with a lower intake in control groups. The review outcomes were fasting blood glucose, fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR), and HbA1c. Risk of bias and quality of evidence according to Grading of Recommendations Assessment, Development, and Evaluation were addressed. From the 10,627 citations screened, 44 studies (3016 participants) were included, 38 of which were used in the meta-analyses.

Results: Fasting glucose was positively associated with elevated dairy intake [34 studies, $n = 2678$; mean difference (MD): 0.07 mmol/L; 95% CI: 0.01, 0.12 mmol/L; $P = 0.01$, $I^2 = 23\%$]. Fasting insulin (29 studies, $n = 1902$; MD: -2.97 pmol/L; 95% CI: -7.05 , 1.10 pmol/L; $P = 0.15$, $I^2 = 21\%$) and HOMA-IR (13 studies, $n = 840$; standardized MD: -0.07 ; 95% CI: -0.26 , 0.12 ; $P = 0.49$, $I^2 = 38\%$) were not associated with elevated dairy consumption. HbA1c was negatively associated with elevated dairy product intake in 4 studies ($n = 512$; MD: -0.09% ; 95% CI: -0.09% , -0.03% ; $P = 0.005$, $I^2 = 0\%$). Most studies had high risk of bias and the quality of evidence was very low or low.

Conclusion: In conclusion, evidence suggests that elevated dairy product intake is associated with increased fasting plasma glucose concentrations together with reduced HbA1c in nondiabetic subjects. Hence, the clinical significance of these results remains uncertain. Additional well-designed, long-term studies are required.

Serebrovskaya TV, Portnychenko AG, Portnichenko VI, Xi L, Egorov E, Antoniuk-Shcheglova I, Naskalova S, Shatylo VB. Effects of intermittent hypoxia training on leukocyte pyruvate dehydrogenase kinase 1 (PDK-1) mRNA expression and blood insulin level in prediabetes patients. Eur J Appl Physiol. 2019 Jan 30. doi: 10.1007/s00421-019-04072-2.

Purpose: Intermittent hypoxia training/treatment (IHT) is an emerging therapeutic approach to alleviate chronic diseases, such as diabetes. The present study investigated the effects of IHT on blood leukocyte pyruvate dehydrogenase kinase 1 (PDK-1) mRNA expression and its relationship with the changes in blood insulin level.

Methods: Seven adult healthy volunteers and 11 prediabetic patients participated in this study. A 3-week course of IHT consisted of a 40-min session of 4 cycles of 5-min 12% O₂ and 5-min room air breathing per day, 3 sessions per week for 3 weeks (i.e., total 9 sessions of IHT). Plasma insulin levels and leukocyte PDK-1 mRNA expres-

sion were determined at various time points either under fasting condition or following oral glucose tolerance test (OGTT). Correlation between the IHT-induced changes in PDK-1 mRNA and insulin or glucose levels in the same serological samples was analyzed.

Results: At pre-IHT baseline, PDK-1 mRNA expression was two times higher in prediabetes than control subjects. IHT resulted in significant augmentation in PDK-1 mRNA expression (> 2 -fold) in prediabetes at the end of 3-week IHT and remained elevated 1 month after IHT, which was correlated with a significantly reduced insulin release and lower blood glucose after glucose loading with OGTT.

Conclusion: IHT can trigger beneficial effects in normalizing blood insulin levels in prediabetic patients under oral glucose load, which were closely correlated with an enhanced mRNA expression of PDK-1 in leukocytes. Further clinical trials are warranted to validate the utility of IHT as a non-invasive complementary therapy against diabetes-associated pathologies.

Ryan JJ, Hanes DA, Corroon J, Taylor J, Bradley R: Prospective safety evaluation of a cardiovascular health dietary supplement in adults with prehypertension and stage I hypertension. The Journal of Alternative and Complementary Medicine 2019; 25:249–256.

Objective: To prospectively examine the long-term safety of a cardiovascular health dietary supplement by assessing a comprehensive set of safety measures.

Methods: Design: Single-arm, open-label study. Location: National University of Natural Medicine, Portland, OR. Subjects: Thirty adults with screening blood pressure readings consistent with prehypertension or stage I hypertension. Intervention: One caplet per day of a dietary supplement for 6 months. The investigated herbal-mineral supplement contains several ingredients, most notably *Rauwolfia serpentina*. Outcome measures: Primary measures included b-type natriuretic peptide (NT-proBNP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), estimated glomerular filtration rate (eGFR), electrolytes, and the Patient Health Questionnaire (PHQ-9). Exploratory measures included physical vital signs, cholesterol levels, high-sensitivity cardiac troponin-I, cystatin C, endothelin, interleukin (IL)-6, IL-17a, tumor necrosis factor- α , high-sensitivity C-reactive protein, blood counts, and the Patient Reported Outcome Measure Information System (PROMIS) Sleep Disturbance Short Form 8b.

Results: NT-proBNP, AST, ALT, eGFR, sodium, calcium, magnesium, PHQ-9 score, and the majority of exploratory measures did not change. However, serum potassium increased ($p < 0.05$), systolic blood pressure decreased ($p < 0.0001$), and diastolic blood pressure decreased ($p < 0.0001$). There were no serious adverse events, but 30% of participants withdrew citing potential side effects, most commonly nasal congestion or fatigue; most participants who reported nasal congestion also reported concomitant seasonal allergies. Adherence to the supplement was 90.9%.

Conclusions: The findings of this study suggest that the investigated dietary supplement is safe for long-term use in adults with prehypertension and stage I hypertension. Additional results of this study, particularly the increase in serum potassium and decreases in systolic and diastolic blood pressure, are promising and suggest that future research on this dietary supplement, or its ingredients, should further explore effects on blood pressure and biologic mechanisms of action, which may involve potassium-sparing and diuretic effects.

Mattias Carlström M, Larsson SC: Coffee consumption and reduced risk of developing type 2 diabetes: a systematic review with meta-analysis. Nutrition Reviews 2018 76(6):395–417.

Context: Type 2 diabetes (T2D) is a major health problem worldwide that is associated with increased morbidity and mortality. There is increased interest in the value of different nutrition-based strategies for preventing the development of T2D.

Objective: This review aims to cover current knowledge regarding the effects of coffee consumption on development of T2D or modulation of adverse complications. A meta-analysis on coffee consumption and the risk of T2D was conducted. Moreover, bioactive components in coffee, polymorphisms, and potential underlying mechanism(s) in relation to T2D and adverse complications are discussed.

Data sources: PubMed was searched up to December 1, 2017, and prospective cohort and nested case-control studies of the association between coffee consumption and T2D risk were selected.

Data extraction: Two investigators independently extracted data from included studies.

Results: A total of 30 prospective studies with 1 185 210 participants and 53 018 incident T2D cases were included in the meta-analysis. The pooled relative risk (RR) was 0.71 (95% confidence interval [CI], 0.67–0.76) for the highest category of coffee consumption (median consumption, 5 cups/d) vs the lowest category (median consumption, 0 cups/d). The risk of T2D decreased by 6% (RR ¼ 0.94; 95%CI, 0.93–0.95) for each cup-per-day increase in coffee consumption. Results were similar for caffeinated coffee consumption (per additional cup of coffee per day: RR ¼ 0.93; 95%CI, 0.90–0.96) and decaffeinated coffee consumption (corresponding RR ¼ 0.94; 95%CI, 0.90–0.98).

Conclusions: Available evidence indicates that coffee consumption is inversely associated with risk of T2D. Possible mechanisms behind this association include thermogenic, antioxidative, and anti-inflammatory effects; modulation of adenosine receptor signaling; and microbiome content and diversity.

Seidemann SB, Claggett B, Cheng S, Henglin M, Shah A, Steffen LM, Folsom AR, Rimm EB, Willett WC, Solomon SD: Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis. Lancet Public Health 2018;3: e419–28. [http://dx.doi.org/10.1016/S2468-2667\(18\)30135-X](http://dx.doi.org/10.1016/S2468-2667(18)30135-X).

Background: Low carbohydrate diets, which restrict carbohydrate in favour of increased protein or fat intake, or both, are a popular weight-loss strategy. However, the long-term effect of carbohydrate restriction on mortality is controversial and could depend on whether dietary carbohydrate is replaced by plant-based or animal-based fat and protein. We aimed to investigate the association between carbohydrate intake and mortality.

Methods: We studied 15 428 adults aged 45–64 years, in four US communities, who completed a dietary questionnaire at enrolment in the Atherosclerosis Risk in Communities (ARIC) study (between 1987 and 1989), and who did not report extreme caloric intake (<600 kcal or >4200 kcal per day for men and <500 kcal or >3600 kcal per day for women). The primary outcome was all-cause mortality. We investigated the association between the percentage of energy from carbohydrate intake and all-cause mortality, accounting for possible non-linear relationships in this cohort.

We further examined this association, combining ARIC data with data for carbohydrate intake reported from seven multinational prospective studies in a meta-analysis. Finally, we assessed whether the substitution of animal or plant sources of fat and protein for carbohydrate affected mortality.

Findings: During a median follow-up of 25 years there were 6283 deaths in the ARIC cohort, and there were 40 181 deaths across all cohort studies. In the ARIC cohort, after multivariable adjustment, there was a U-shaped association between the percentage of energy consumed from carbohydrate (mean 48.9%, SD 9.4) and mortality: a percentage of 50–55% energy from carbohydrate was associated with the lowest risk of mortality. In the meta-analysis of all cohorts (432 179 participants), both low carbohydrate consumption (<40%) and high carbohydrate consumption (>70%) conferred greater mortality risk than did moderate intake, which was consistent with a U-shaped association (pooled hazard ratio 1.20, 95% CI 1.09–1.32 for low carbohydrate consumption; 1.23, 1.11–1.36 for high carbohydrate consumption). However, results varied by the source of macronutrients: mortality increased when carbohydrates were exchanged for animal-derived fat or protein (1.18, 1.08–1.29) and mortality decreased when the substitutions were plant-based (0.82, 0.78–0.87).

Interpretation: Both high and low percentages of carbohydrate diets were associated with increased mortality, with minimal risk observed at 50–55% carbohydrate intake. Low carbohydrate dietary patterns favouring animal-derived protein and fat sources, from sources such as lamb, beef, pork, and chicken, were associated with higher mortality, whereas those that favoured plant-derived protein and fat intake, from sources such as vegetables, nuts, peanut butter, and whole-grain breads, were associated with lower mortality, suggesting that the source of food notably modifies the association between carbohydrate intake and mortality.

Neuendorf R, Corn J, Hanes D, Bradley R: Impact of Food Immunoglobulin G-Based Elimination Diet on Subsequent Food Immunoglobulin G and Quality of Life in Overweight/Obese Adults. The Journal of Alternative and Complementary Medicine 2019; 25: 241–248.

Objectives: The goal of this study was to assess changes in serum immunoglobulin G (IgG) food antibody titers and quality-of-life measurements following a targeted elimination diet in overweight/obese adults.

Methods: We performed a randomized control trial. Participants were randomized in a 2:1 ratio to either an intervention group or waitlist group for 3 months. Food IgG testing was performed on all participants. The intervention group was instructed to eliminate up to 10 foods, for which they had high titers of IgG and communicated with health coaches for nutritional counseling for meal planning and adherence. The waitlist group did not receive their IgG testing results or health coaching. Primary outcome was serum IgG titers for foods eliminated during the trial, compared with baseline concentrations. Secondary outcomes were health related quality of life measured by Patient-Reported Outcomes Measurement Information System (PROMIS-29) and change in participant-identified symptom severity measured by Measure Yourself Medical Outcome Profile. Exploratory outcomes were changes in body weight and waist circumference.

Results: IgG antibody concentrations decreased in 83% of the targeted foods in the treatment group and in 60% of the foods in the waitlist group, but this was not found to be a statistically sig-

nificant difference. The intervention group reported improvement in sleep during the trial compared with waitlist, which was the only statistically significant finding in the study.

Conclusions: The findings are consistent with changes in IgG titer measurements following an elimination diet based on IgG testing. Future larger clinical trials are necessary to determine the degree to which these findings are generalizable.

Jeong SM, Seo BK, Park YC, Baek YH: A review of complementary and alternative medicine therapies on muscular atrophy: A literature review of in vivo/ in vitro studies. Evidence-Based Complementary and Alternative Medicine 2018; Article ID 8654719. <https://doi.org/10.1155/2018/8654719>.

Objective: The objective of this review is to evaluate the recent treatment and study trends of complementary and alternative medicine (CAM) treatments on muscular atrophy by reviewing in vivo/in vitro studies.

Materials and Methods: The searches were conducted via electronic databases including PubMed, the Cochrane Library, China National Knowledge Infrastructure (CNKI), WanfangMED, and five Korean databases. Only in vivo and in vitro studies were included in this study.

Results: A total of 44 studies (27 in vivo studies, 8 in vitro studies, and 9 in vivo with in vitro) were included. No serious maternal or fetal complications occurred. There were various animal models induced with muscular atrophy through “hindlimb suspension”, “nerve damage”, “alcohol or dexamethasone treatment”, “diabetes”, “CKD”, “stroke”, “cancer”, “genetic modification”, etc. In 28 of 36 articles measuring muscle mass, CAM significantly increased the mass. Additionally, 10 of them showed significant improvement in muscle function. In most in vitro studies, significant increases in both the diameter of myotubes and muscle cell numbers were reported. The mechanisms of action of protein synthesis, degradation, autophagy, and apoptotic markers were also investigated.

Conclusions: These results demonstrate that CAM could prevent muscular atrophy. Further studies about CAM on muscular atrophy are needed.

Steel A, Peng W, Gray A, Adams J: The role and influence of traditional and scientific knowledge in naturopathic education: A Qualitative Study. The Journal of Alternative and Complementary Medicine 2019;25:196–201.

Objectives: To explore the perceptions, experiences, and attitudes toward scientific and traditional knowledge within contemporary naturopathic education.

Methods: Design: A qualitative focus group and semistructured individual interview study.

Settings/Location: Naturopathic educational organizations and institutions in North America (United States/Canada) and Australia. Subjects: Seven focus groups (three in Australia and four in the United States/Canada) involving a total of 29 students, and one-on-one interviews with 28 faculty and professional leaders of the naturopathic profession from Australia, Canada, and the United States.

Results: Four themes have been identified in this study, including finding the balance between traditional and scientific knowledge; supporting the balance through critical appraisal in the cur-

riculum; the exception of traditional knowledge in the critical gaze; and focusing on critical thinking in the naturopathic curriculum. Both naturopathic students and leaders highlight the significance of balancing tradition and science in the naturopathic educational context, although they hold diverse differing viewpoints. The importance of critical appraisal skills as well as the differentiation between critical thinking and critical appraisal have also been emphasized by participants with regard to the future development of naturopathic curriculum.

Conclusions: This is the first study focusing on the interface between traditional and scientific knowledge within the naturopathic education setting. The development of a framework for the critical appraisal of traditional naturopathic knowledge is required to help navigate the variety of knowledge sources available to naturopathic students and to help deliver the best outcomes for their future clinical practice.

Aucoin M, Cooley K, Knee C, Tsui T, Grondin D: Naturopathy special interest group research capacity and needs assessment survey. The Journal of Alternative and Complementary Medicine 2019;25:189–195.

Objectives: Despite recent shifts in regulation and recognition of the role that naturopathy plays in health care delivery in Canada, comparatively little research has been conducted regarding individuals who conduct naturopathy-related research. A survey was undertaken to better understand the needs and capacity of these individuals to conduct more research.

Design, Setting, and Subjects: The Naturopathy Special Interest Group (N-SIG) of the Interdisciplinary Network of Complementary and Alternative Medicine (INCAM) Researchers created and distributed a survey of individuals interested in naturopathy-related research to assess gaps between current and desired research activity and needs for further participation.

Outcome measures: Results from a previous pilot study (2014; n = 58) were used to inform the design and distribution. This study received approval and oversight from the Research Ethics Board of the Canadian College of Naturopathic Medicine.

Results: The survey was completed by 201 individuals (*5%–10% of all naturopathic doctors and naturopathy researchers in Canada). The majority (70%) had no peer-reviewed publication experience; however, 63% reported having published in a nonpeer-reviewed medium. Respondents reported differing levels of confidence in completing various components of a research project. Frequently selected obstacles included lack of time due to professional and personal obligations, as well as insufficient training, funding, and mentorship. The greatest identified needs for participation in research were mentorship/support, access to a wider degree of scientific journals, and targeted funding opportunities for CAM research. Overall, the results of this survey suggest that there is interest in further conducting naturopathy-related research in Canada. There are individuals who are already involved and have expressed skills in the area of evidence-based medicine.

Mentorship, research training, resources, and critical appraisal and writing skills may be important leverage points.

Conclusion: Findings from this investigation will be used to inform an agenda for naturopathy-related research and activities of the N-SIG with respect to enhancing research capacity. Other CAM groups or geographic regions could consider using similar methodology to assess capacity and needs for research participation.