GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of February 26 - March 1, 2024

SPOTLIGHT: Should Vegetarian Diets Be Prescribed for Patients at Risk for Cardiomatabolic Disease?

Should Vegetarian Diets Be Prescribed for Patients at Risk for Cardiometabolic Disease?

Vegetarian Dietary Patterns and Cardiometabolic Risk in People with or at High Risk of Cardiovascular Disease: A Systematic Review and Meta-Analysis

Wang T, Kroeger CM, Cassidy S, et al. Vegetarian Dietary Patterns and Cardiometabolic Risk in People With or at High Risk of Cardiovascular Disease: A Systematic Review and Meta-analysis. *JAMA Netw Open.* 2023;6(7):e2325658. Published 2023 Jul 3. doi:10.1001/jamanetworkopen.2023.25658

KEY TAKEAWAY: Vegetarian diets improve LDL-C, HbA1c, and body weight, but not systolic blood pressure (SBP) in individuals with or at high risk for cardiovascular disease (CVD).

STUDY DESIGN: Systematic review and meta-analysis of 20 randomized clinical trials, seven ongoing trials, and two crossover trials (N=3,756)

LEVEL OF EVIDENCE: STEP 2 (downgraded due to only disease-oriented evidence)

BRIEF BACKGROUND INFORMATION: Poor diet is linked to an increased risk of developing CVD and type 2 diabetes (T2DM). Cardiac and diabetes organizations recommend incorporating plant-based diets and decreasing meats. No meta-analysis studies have demonstrated the benefits of a vegetarian diet to a population at risk of CVD.

PATIENTS: Adults with or at high risk of CVD

INTERVENTION: Vegetarian diet

CONTROL: Standard non-vegetarian diet

PRIMARY OUTCOME: LDL-C, HbA1c, and SBP

Secondary Outcome: Body weight, overall dietary intake

METHODS (BRIEF DESCRIPTION):

- Adults ≥18 years old (mean 28–64 years) with or at risk of CVD and patients with T2DM were included.
- At risk for CVD included at least two of the following risk factors:
  - Body mass index (BMI) ≥25 kg/m2
  - SBP ≥130 mmHg; diastolic blood pressure (DBP) ≥80 mmHg
  - Blood lipid total cholesterol (TC) ≥200 mg/dL; or 100 mg/dL; or triglycerides (TG) ≥150 mg/dL
  - HbA1c ≥5.7%
  - Metabolic syndrome (if ≥3 met)
    - Waist circumference >40 inches (men) or >35 inches (women)
    - Fasting high-density lipoprotein (HDL) <40 mg/dL (men) or <50 mg/dL (women)
    - Fasting blood sugar ≥100 mg/dL
- Vegetarian diets included very low-fat lacto-ovo-vegetarian, lacto-vegetarian, and low-fat vegan.
- The control groups received a non-vegetarian diet.
  - Frequency and amount of food were not stated in these studies

INTERVENTION (# IN THE GROUP): 1,878

COMPARISON (# IN THE GROUP): 1,878

FOLLOW-UP PERIOD: 2–24 months

RESULTS:

Primary Outcome –

- Participants who received the lacto-ovo vegetarian diets had a significant decrease in LDL-C compared to those on the standard diet (14 trials, n=955; mean difference [MD] –14 mg/dL; 95% CI, –25 to –3.6 mg/dL).
- Vegetarian diets decreased HbA1c compared to baseline pre-intervention (10 trials, n=778; MD –0.24%; 95% CI, –0.40 to –0.07).
- HbA1c decreased in vegetarian diets compared to with and without energy-restricted conventional diabetic diets (10 trials, n=778; MD –0.26%; 95% CI, –0.48 to –0.05).
- Vegan diets showed decreased HbA1c compared to baseline (10 trials, n=778; MD –0.21%; 95% CI, –0.38 to –0.05).
- Vegetarian diets showed no difference in SBP compared to baseline (14 trials, n=955; MD –0.1%; 95% CI, –2.8 to 2.6).

Secondary Outcome –

- Overall weight decreased in individuals on vegetarian diets compared to baseline (16 trials, n=1,395; MD –3.4 kg; 95% CI, –4.9 to –2.0).
- Greatest weight reduction in high risk of CVD compared to baseline (16 trials, n=1,395; MD –3.6 kg; 95% CI, –5.8 to –1.4).

LIMITATIONS:

- Low sample size (4 trials, each ≤100 participants) for patients with CVD on vegetarian diets.

- Inability to explain adherence to diet; the length of studies did not go beyond six months.
- Inability to explain diet quality; macronutrients were not specified including saturated or trans-fat, total cholesterol, and fiber.
- The quality of vegetarian diets was unable to be assessed.
- 17 studies were conducted in Western countries with 14 from the United States.
- Studies published only in English and Chinese were included.
- Only disease-oriented evidence was provided.
- High heterogeneity with HbA1c, SBP, and weight reduction in CVD.

Mary Anne P. Mendes, MD, MS
Capitol Health Medical Center FMRP
Hopewell, NJ

Fatty Acids for Fast Recovery from Sport-Related Concussion? Safe, but More Studies Needed

A Pilot Randomized Controlled Trial of Docosahexaenoic Acid for the Treatment of Sport-Related Concussion in Adolescents

Miller SM, Zynda AJ, Sabatino MJ, Jo C, Ellis HB, Dimeff RJ. A Pilot Randomized Controlled Trial of Docosahexaenoic Acid for the Treatment of Sport-Related Concussion in Adolescents. *Clin Pediatr (Phila).* 2022;61(11):785-794. doi:10.1177/00099228221101726

KEY TAKEAWAY: 2 g/day of docosahexaenoic acid (DHA) is safe and generally well-tolerated in the adolescent population, however, more studies are needed to assess its efficacy in the treatment of sport-related concussion (SRC).

STUDY DESIGN: Double-blind parallel-group randomized placebo-controlled pilot trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: While the management of SRC has improved over time, there is still no research supporting the pharmacological treatment of SRC in pediatric and adolescent populations. DHA has been suggested to have neuroprotective and therapeutic effects in the recovery and prevention of concussion, but there are no published randomized controlled trials assessing the effects of DHA in adolescent athletes.

PATIENTS: Adolescents with SRC

INTERVENTION: DHA

CONTROL: Placebo

PRIMARY OUTCOME: Compliance and adverse events

Secondary Outcome: Time to symptom-free

METHODS (BRIEF DESCRIPTION):

- Participants were adolescents 14–18 years old seen within four days of injury at the Sports Medicine Center at Children's Medical Center in Plano, TX.
- A total of 40 participants were enrolled with 20 in each group and no significant differences in demographics between the groups.
- 68% of participants were male, 72% of participants were white, 70% had no prior concussion history, and 90% did not have a concussion in the last 12 months.
- The most common sport played at the time of concussion in both groups was American football (43%), with the most common location of impact at the front of the head (28%).
- Participants were excluded if they had previously taken DHA or fish oil, had radiographic evidence of traumatic brain injury, were injured during motorized sport, diagnosed with a previous concussion within the last six months, pregnant, sensitive to aspirin, diagnosed and treated with medication for hypertension, allergic to soybean or corn oil, or were unable to fully swallow the pills.
- Patients were randomly assigned to DHA or placebo in a 1:1 manner.
- All participants received capsules, either DHA (2000 mg/day) or placebo (corn and soy oil), and were instructed to take two 500 mg capsules in the morning and two 500 mg capsules in the evening with meals for 12 weeks.
- Both capsules were flavored with masking agents to prevent recognition by smell or taste.
- The principle investigator, treating physician, nurse, athletic trainer, research coordinators, and participants were blinded to group allocation.
- Participants were evaluated at one, two, four, and 12 weeks.
    - If participants had complete symptom resolution before the four-week follow-up, they were exempt from additional study visits, but still required to take the study drug and return for the 12-week visit.
- Standardized concussion measures including SCAT3 and the modified Balance Error Scoring System (mBESS), adverse effects, and drug compliance were collected at all follow-up visits.
    - The mBESS assesses balance with three 20-second tests and is scored 0–30, higher scores/more errors indicate a worse outcome.
    - The SCAT3 was the most current version validated at the time of IRB approval. It includes a symptom assessment of 22 post-concussion symptoms, with higher scores indicating greater symptoms. The symptom checklist suggests a strong sensitivity to concussion diagnosis.

INTERVENTION (# IN THE GROUP): 20

COMPARISON (# IN THE GROUP): 20

FOLLOW-UP PERIOD: 12 weeks

RESULTS:

Primary Outcome –

- The overall drug compliance was 75% in the DHA group and 84% in the placebo group.
- One minor drug-related adverse effect was reported in the DHA group and no adverse effects were reported in the placebo group.
- Statistical analysis was not completed on this outcome.

Secondary Outcome –

- The time to symptom-free was not statistically significant between DHA vs placebo, though the DHA group was symptom-free approximately five days earlier than the placebo.

LIMITATIONS:

- The sample size was small and not powered to detect differences in outcomes between groups or to adjust for confounding variables.
- Compliance declined markedly after the four-week visit with only 25 (62.5%) participants completing the 12-week visit.

Sara McCall, DO
David Grant USAF Medical Center- Travis AFB
Fairfield, CA

The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Air Force Medical Department, the Air Force at large, or the Department of Defense.

To PRP or Not to PRP?

Double-Blind Randomized Controlled Trial Comparing Platelet-Rich Plasma with Intra-Articular Corticosteroid Injections in Patients with Bilateral Knee Osteoarthritis

Pretorius J, Nemat N, Alsayed A, et al. Double-Blind Randomized Controlled Trial Comparing Platelet-Rich Plasma With Intra-Articular Corticosteroid Injections in Patients With Bilateral Knee Osteoarthritis. *Cureus*. 2022;14(9):e29744. Published 2022 Sep 29. doi:10.7759/cureus.29744

KEY TAKEAWAY: Both platelet-rich plasma (PRP) and steroid injections improved pain, stiffness, and function in patients with mild to moderate bilateral knee osteoarthritis (OA) however, there was no significant difference between the two.

STUDY DESIGN: Double-blinded randomized controlled trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to small sample size and lack of a different control group)

BRIEF BACKGROUND INFORMATION: Knee OA is a common debilitating condition for which patients visit primary care physicians. Intra-articular injections are one way of treating pain and stiffness while restoring function for some patients. It is unknown if PRP injections are more effective than steroid injections in patients with mild-moderate knee OA as they have not been studied in the same patient. This study compares the two treatments in the same patient.

PATIENTS: Adults with knee OA

INTERVENTION: PRP injection

CONTROL: Steroid injection

PRIMARY OUTCOME: Pain, stiffness, and function

METHODS (BRIEF DESCRIPTION):

- Patient demographic characteristics: Mean age of 64 years old, 58% female, average BMI of 33 kg/m2.
- Radiographically identified mild to moderate bilateral knee OA as Grade II/III via the Kellgren-Lawrence scale.
- Intervention and control knees were randomized.
  - Intervention: 5 mL of autologous PRP preparation injected into the knee
  - Control: 80 mg methylprednisolone with 40 mg levobupivicaine was injected into the contralateral knee via the inferolateral approach.
  - Each knee was flexed at 70 degrees.
- Two blinded experienced physicians recorded the initial, six-week, three-month, and six-month follow-up scores using:
  - Western Ontario and McMaster University Arthritis Index (WOMAC) measures pain (0–20), stiffness (0–8), and function (0–68) with higher scores indicating worse outcomes on all scales.
  - The visual numerical pain rating scale (VNS) scored zero for no pain and 10 for maximum pain.

INTERVENTION (# IN THE GROUP): 29

COMPARISON (# IN THE GROUP): 29

FOLLOW-UP PERIOD: Six months

RESULTS:

Primary Outcome –

- PRP injection did not improve the composite of pain, stiffness, and function compared to steroid injection at 26 weeks (mean difference [MD] 0.87; 95% CI, –66 to 8.8).
- PRP injection did not improve pain compared to steroid injection at 26 weeks (MD 0.2; 95% CI, –1.3 to 0.76).
- PRP and the steroid injection were both effective in decreasing pain, stiffness, and function over 26 weeks (F2,139=5.6; *P*=.005).

LIMITATIONS:

- Short to midterm follow-up time.
- Small sample size.
- Use of patients as own control.
- Lack of ultrasound guidance.

Katina Rue, DO
Trios Health FMR
Kennewick, WA

Can Vigorous Intermittent Physical Activity Reduce Cancer Risk?

Vigorous Intermittent Lifestyle Physical Activity and Cancer Incidence Among Nonexercising Adults: The UK Biobank Accelerometry Study

Stamatakis E, Ahmadi MN, Friedenreich CM, et al. Vigorous Intermittent Lifestyle Physical Activity and Cancer Incidence Among Nonexercising Adults: The UK Biobank Accelerometry Study. *JAMA Oncol.* 2023;9(9):1255-1259. doi:10.1001/jamaoncol.2023.1830

KEY TAKEAWAY: Vigorous intermittent lifestyle physical activity (VILPA) is associated with a reduction in total incident cancer and the incidence of physical activity-related cancer.

STUDY DESIGN: Prospective observational cohort study (N=22,398)

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Vigorous physical activity, compared to lower intensity, has been associated with a reduction in the risk of developing certain cancers. However, many adults are unable or not motivated to set aside time for structured sessions of vigorous physical activity.VILPA refers to brief and sporadic, 1–2 minute long episodes of vigorous-intensity physical activity that occur as part of daily living, such as walking fast to a destination or climbing stairs. This study examined the association of daily VILPA with cancer incidence and the estimated minimum amount of VILPA for cancer risk reduction.

PATIENTS: Non-exercising adults

INTERVENTION: VILPA

CONTROL: No VILPA

PRIMARY OUTCOME: Dose-response associations of daily VILPA

METHODS (BRIEF DESCRIPTION):

- Data from the UK Biobank wrist accelerometry sub-study activity was analyzed.
- Mean age of participants was 62 years old ± 7.6 years and 45% were men.
- Inclusion criteria: Participants with no leisure time exercise and ≤1 recreational walk per week.
- Exclusion criteria: Participants with missing covariate data, history of cancer or cancer in the first year of study, or insufficient use of accelerometer.
- Cancer incidence data was obtained from cancer registrations, hospitalizations, or deaths (in situ, nonmelanoma skin cancer, and cancers that were not well-defined were excluded).
- Physical activity (PA) related cancer incidence was derived from a composite outcome of 13 cancer sites associated with low physical activity. These sites include esophageal adenocarcinoma, liver, lung, kidney, gastric cardia, endometrial, myeloid leukemia, myeloma, colon, head and neck, rectal, bladder, and breast.
- Primary outcome measured the minimum and median dose for daily VILPA.
    - 97% of VILPA episodes lasted a minimum of two minutes.
    - Median daily VILPA was 4.5 minutes.

INTERVENTION (# IN THE GROUP): 21,009

COMPARISON (# IN THE GROUP): 1,389

FOLLOW-UP PERIOD: Mean 6.7 ± 1.2 years

RESULTS:

Primary Outcome –

- Minimum dose for daily VILPA of 3–4 minutes was associated with reduced incidence of:
    - Total cancer (hazard ratio [HR] 0.83; 95% CI, 0.73–0.93)
    - PA-related cancer (HR 0.72; 95% CI, 0.59–0.88)
- Median dose for daily VILPA of 4.5 minutes was associated with a reduced risk of:
    - Total cancer (HR 0.80; 95% CI, 0.69–0.92)
    - PA-related cancer (HR 0.69; 95% CI, 0.55–0.86)

LIMITATIONS:

- Lifestyle changes between responses to the leisure-time exercise questions and the recording of the accelerometry can affect results.
- The generalizability of results was limited by participant age and ethnicity (96% White).

Lena Nowacki, DO
Womack Army Medical Center FMRP
Fort Liberty, NC

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