GEMs of the Week

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GEMs
GOOD EVIDENCE MATTERS

FPIN
Family Physicians Inquiries Network

What's in this week's issue?

Week of February 8 - 12, 2021

SPOTLIGHT: Is Coconut Oil Consumption Good for Your Heart?

Is Coconut Oil Consumption Good for Your Heart?

The Effect of Coconut Oil Consumption on Cardiovascular Risk Factors: A Systematic Review and Meta-Analysis of Clinical Trials

Neelakantan N, Seah JYH, van Dam RM. The Effect of Coconut Oil Consumption on Cardiovascular Risk Factors: A Systematic Review and Meta-Analysis of Clinical Trials. *Circulation*. 2020 Mar 10; 141(10):803–814.

KEY TAKEAWAY: Consumption of coconut oil raises cholesterol levels more than consumption of non-tropical vegetable oils.

STUDY DESIGN: Meta-analysis of 15 RCTs, 2 non-randomized trials

LEVEL OF EVIDENCE: STEP 2 (downgraded for significant heterogeneity and small study sizes)

BRIEF BACKGROUND INFORMATION: Coconut oil is high in saturated fat which is known to raise blood cholesterol levels. There is increasing popularity in the use of coconut oil as an additive to diet for potential benefits but investigation is needed to determine whether the benefits outweigh the risk.

PATIENTS: Adults 20-60 years old

INTERVENTION: Consumption of coconut oil for at least 2 weeks

CONTROL: Consumption of nontropical vegetable oils and palm oils

OUTCOME: LDL, HDL, total cholesterol and triglycerides

METHODS (BRIEF DESCRIPTION):

- Two reviewers independently screened, selected and extracted the trial data from four electronic databases (PedMed, SCOPUS, Cochrane Central, and Web of Science). Primary search terms included "coconut," "cardiovascular," "lipid," "cholesterol," "LDL," "HDL," and "triglycerides." The studies' quality was assessed, according to the PRISMA guidelines (Preferred Reporting Items for Systemic Reviews and Meta-Analyses).
- Studies were included if they were controlled clinical trials that examined effect of coconut oil/fat, compared with any other vegetable oil or animal fat, an intervention period of at least 2 weeks, and assessed cardiovascular outcomes including blood lipid levels.
- Studies excluded: infants, literature reviews, cross sectional or prospective studies, short term studies (<2 weeks), animal/cell studies or irrelevant interventions/outcomes
- There were a total of 418 male participants and 312 female participants in # of included trials:
  - 11 trials included participants who were normocholesterolemic and healthy (N=2, sequential feeding trial; N=7, randomized crossover; N=2, randomized parallel)
  - Two trials targeted obese adults (both randomized parallel)
  - Three trials enrolled hypercholesterolemic participants (all randomized crossover)
  - One trial was specific for those with stable coronary heart disease, on statins (randomized parallel)
  - Four trials used palm oil and 16 trials used non-tropical vegetable oil as controls
- Method of consumption varied by trial:
  - 10 trials provided meals or cooked foods
  - 5 trials only provided the cooking oils for home use
  - 2 trials provided coconut oil capsules to be taken orally
- All trials required at least 2 weeks of use of the coconut oil to allow blood lipid levels to stabilize.
- Lipid levels were measured pre and post intervention with comparison of changes in LDL, HDL, total cholesterol, and triglyceride levels.

INTERVENTION (# IN THE GROUP): Up to 730

COMPARISON (# IN THE GROUP): Up to 730

FOLLOW UP PERIOD: Ranged from 3–104 weeks

RESULTS:

Relative to controls, consuming coconut oil:

- Increased total cholesterol by a mean difference of 14.7 mg/dL (95% CI, 4.8 mg/dL–24.5 mg/dL; large degree of heterogeneity I2 = 91%)
- Increased LDL by 10.5 mg/dL (95% CI, 3 mg/dL–17.9 mg/dL; I2 = 84%) with percent change of 8.6%
- Increase HDL by 4 mg/dL (95% CI, 2.3 mg/dL–5.7 mg/dL; I2 = 72%) with percent change of 7.8%
- Did not change concentrations of triglycerides significantly compared to other vegetable oils

LIMITATIONS:

- Heterogeneity of trial design, conduct, and quality presented significant variations including the volume of oil, consumption method and compliance checks for participants (I2 ranged from 0–94%).
- Outcomes were surrogate markers instead of disease end points such as cardiovascular disease, stroke, morbidity or mortality.
- Studies were not designed or powered to demonstrate a dose-response with consumption of coconut oil and reported outcomes

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What Aren't Our Patients Telling Us? (Symptom Nondisclosure in UK General Practice)

Non-disclosure of symptoms in primary care: an observational study

Paskins Z, Sanders T, Croft PR, et al. Non-disclosure of symptoms in primary care: an observational study. *Family Practice*. 2018 Dec; 35(6):706–711.

KEY TAKEAWAY: 98.4% of patients disclosed their primary concern during consultation with a GP, however, additional symptoms were undisclosed in 22.6% of cases.

STUDY DESIGN: Observational study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Previous research has shown that symptoms may go undisclosed in up to ¼ of consultations with a general practitioner. Further characterization of patient agendas when seeking care, and the rates of nondisclosure of various symptoms are needed in order to more effectively deliver care and address patient concerns.

PATIENTS: Unselected sample of UK general practice patients aged 45+

INTERVENTION: Authors quantified the rate of reporting of various symptoms during consultation with their GP

CONTROL: Topics discussed during consultation compared to a patient self-report survey obtained previously

OUTCOME: Descriptive statistics regarding symptom disclosure across various symptoms

METHODS (BRIEF DESCRIPTION):

- Patient's in the UK aged 45 and older from 7 practices
- Preconsultation symptom questionnaire
- Recorded Consultations
- Consent obtained in a 3 tier manner allowing patients to opt out of the study at time of enrollment, immediately post consultation and 48 hours later
- Recorded consultation compared against the preconsultation questionnaire to determine the following:
    - Incidence of various symptoms
    - Rate of intention to disclose symptoms
    - Rate at which symptoms that patients intended to disclose were actually discussed during the consultation.

INTERVENTION (# IN THE GROUP): 190

COMPARISON (# IN THE GROUP): 190

FOLLOW UP PERIOD: Pre and post consultation with 48hr cool down period for patients to opt out of the study

RESULTS:

- In 98.4% of consultations the primary concern was disclosed.
- In 22.6% of consultations additional symptoms were undisclosed.
- In 25.2% of consultations symptoms which were not indicated on the preconsultation survey were disclosed by patients. Of those symptoms that patients intended to discuss tiredness and sleep disturbances were least likely to be disclosed at 34.8%.
- Rates of intention to disclose varied by symptom with skin rash being mist likely at 71% and stress/worry/sadness being least likely at 23.7%.

LIMITATIONS:

- Data may be difficult to generalize outside of single payer healthcare systems
- Completion of the symptom survey may have led to higher than baseline rates of patient reporting
- A single researcher reviewed the consultation, a potential source of observer bias
- Physicians were aware that they were being recorded. This may have impacted physician history taking behavior.
- Participants were recruited from a relatively small geographical region in the UK and were relatively ethnically and socioeconomically homogenous

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Clinical Predictors for the Accurate Diagnosis of Acute Rhinosinusitis and Acute Bacterial Rhinosinusitis

Accuracy of Signs and Symptoms for the Diagnosis of Acute Rhinosinusitis and Acute Bacterial Rhinosinusitis
Ebell MH, McKay B, Dale A, Guilbault R, Ermias Y. Accuracy of Signs and Symptoms for the Diagnosis of Acute Rhinosinusitis and Acute Bacterial Rhinosinusitis. *The Annals of Family Medicine* 2019; 17, 164–172.

KEY TAKEAWAY: Clinical suspicion is a poor predictor of accurate diagnosis of both acute rhinosinusitis (ARS) and Acute Bacterial Rhinosinusitis, (ABRS) but by using appropriate signs and symptoms we can slightly increase the likelihood of correct diagnosis.
STUDY DESIGN: Meta-analysis of 17 diagnostic comparison trials
LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Rhinosinusitis is an extremely common presenting complaint in the outpatient setting. Increasing a physician's ability to clinically determine the etiology of the disease reduces the amount of inappropriate antibiotic use.
PATIENTS: Outpatient adults and children suspected of acute respiratory tract infection (ARTI)
INTERVENTION: Clinical assessment for signs and symptoms consistent with ARS or ARTI
CONTROL: Signs and symptoms compared to reference standards for accuracy of diagnosis
OUTCOME: Likelihood ratios of present or absent signs or symptoms to rule in or rule out ARS or ABRS

METHODS (BRIEF DESCRIPTION):
- Database search performed identifying studies that compared interrater accuracy of rhinosinusitis diagnosis and studies that used diagnostic tests for confirmation
- 17 studies included patients presenting to outpatient setting with complaints of at least 1 sign or symptom of ARS
- Each patient included also had a confirmatory diagnostic test performed to categorize them as ARS vs. ABRS
- A bivariate meta-analysis for each sign/symptom was performed
- Likelihood ratios were generated to determine diagnostic accuracy

INTERVENTION (# IN THE GROUP): 2,546

COMPARISON (# IN THE GROUP): 2,546

FOLLOW UP PERIOD: N/A

RESULTS:
The signs and symptoms with highest positive LR to diagnosis ABRS vs ARS are overall impression, cacosmia, and pain in the teeth, although all had a positive LR less than 5:
- Overall impression: 3 trials
  - Sensitivity 0.74 (95% CI, 0.61–0.84)
  - Specificity 0.80 (95% CI, 0.72–0.87)
  - Positive LR 3.9 (95% CI, 2.4–5.9)
- Cacosmia: 3 trials
  - Sensitivity 0.23 (95% CI, 0.11–0.42)
  - Specificity 0.93 (95% CI, 0.59–0.99)
  - Positive LR 4.3 (95% CI, 0.94–14)
- Pain in the teeth: 3 trials
  - Sensitivity 0.38 (95% CI, 0.10–0.78)
  - Specificity 0.80 (95% CI, 0.37–0.97)
  - Positive LR 2.0 (95% CI, 1.1–3.7)

LIMITATIONS:
- Multiple different confirmatory diagnostic tests without appropriate comparisons
- Interrater differences in history taking
- Interpatient differences in signs/symptoms reporting
- Age variance in prevalence and ability to report signs/symptoms Potential for unmeasured confounders of risk factors for T2DM

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Long Term Methimazole, Is It Worth It?

Long-term Methimazole Therapy in Juvenile Graves' Disease: A Randomized Trial

Azizi F, Takyar M, Madreseh E, Amouzegar A. Long-term Methimazole Therapy in Juvenile Graves' Disease: A Randomized Trial. *Pediatrics.* 2019; 143(5):e20183034.

KEY TAKEAWAY: Long-term methimazole therapy (up to 120 months) reduces relapse and improves remission rates in hyperthyroid patients with juvenile Graves' disease compared to short-term methimazole therapy (less than 24 months).
STUDY DESIGN: Randomized trial
LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Treatment options for Graves' disease include radioiodine, ablation, and medication. Radioiodine treatment prevents the risk of vascular-related mortality, whereas ablative treatment commits a patient to long-term thyroid replacement. An attractive treatment alternative for Graves' disease is medication management with methimazole, although the optimal duration of methimazole treatment is yet to be determined.
PATIENTS: Patients with juvenile Graves' hyperthyroidism in iodine- sufficient Tehran
INTERVENTION: Long-term (LT) methimazole treatment (median 22 months plus an additional 96–120 months)
CONTROL: Short-term (ST) methimazole treatment (median 22 months)
OUTCOME: Relapse of hyperthyroidism

METHODS (BRIEF DESCRIPTION): Patients were less than 18 years old with TSH < 0.4 mU/L, T4 > 23 pmol/L and/or T3 > 200 ng/dL, and no history or evidence of any comorbidities. All patients received 0.25–0.5 mg/kg per day of methimazole in 2 divided doses in the first month. Methimazole was then tapered to maintain serum T4 concentrations between 10 and 22 pmol/L and serum TSH < 5.06 mU/L. All patients were treated for 18–24 months before random assignment at which time the ST patients stopped treatment, whereas the LT patients continued methimazole for at least 96 months. Both groups were followed for an additional 48 months after discontinuation of treatment.

INTERVENTION (# IN THE GROUP): 24 patients
COMPARISON (# IN THE GROUP): 24 patients

FOLLOW UP PERIOD: 48 months after discontinuation of methimazole treatment

RESULTS:
Primary outcome: hyperthyroidism relapse

- 3 patients in LT group (12.5%)
  - The 3 patients relapsed 6, 11, and 44 months respectively after discontinuing the methimazole treatment.
- 16 patients in ST Group (67%)
  - 10 patients relapsed within 6 months, 3 patients from 6 to 12 months, 2 patients in the 2nd year, and 1 patient in the 3rd year.
- Hazard ratio 0.104 (95% CI 0.021–0.529), p 0.006

LIMITATIONS:

- Since the patients were from a small area in Iran, it may not be applicable to other populations.
- Study was not double blinded, hence other biases may have influenced the results.
- Since it was a small patient number, subscale comparisons such as predictive factors of relapse could not be attained.

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The Two-Sided Coin: Migraines May Give You Protection from Developing Diabetes

Associations between Migraine and Type 2 Diabetes in Women Findings from the E3N Cohort Study
Fagherazzi G, El Fatouhi D, Fournier A, et al. (2019). Associations between Migraine and Type 2 Diabetes in Women: Findings from the E3N Cohort Study. *JAMA neurology*, 76(3), 257–263.

KEY TAKEAWAY: There appears to be a lower risk of development of Type 2 Diabetes Mellitus (T2DM) in women with active migraines.
STUDY DESIGN: Prospective cohort
LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Little is known regarding the association between migraines and T2DM.
PATIENTS: Women born between 1925 and 1950 without baseline diabetes
INTERVENTION: Women with migraines developing diabetes
CONTROL: Women with no migraine history developing diabetes
OUTCOME: Development of T2DM; migraine prevalence prior to diabetes diagnosis in active migraine patients.

METHODS (BRIEF DESCRIPTION):
A 1990 cohort of French women, mean age 61, with a particular health insurance was used to identify a subset of 74,247 women without a baseline diagnosis of T2DM as of 2002. Eight surveys completed between 1992 and 2011 were analyzed for presence of active migraines, a history of migraines, or no migraine history. Participants were followed prospectively from 2004–2014. Incident T2DM cases were identified through a drug reimbursement database. Hazard ratios for development of diabetes in the presence of migraines were adjusted for potential confounding diabetic risk factors such as body mass index, level of recreational physical activity, smoking status, history of hypertension, and family history of diabetes.

INTERVENTION (# IN THE GROUP): Prior Hx of migraine (17,209); Active Hx of migraine (7839)
COMPARISON (# IN THE GROUP): No history of migraine (49,199)

FOLLOW UP PERIOD: 10 years

RESULTS:
Of the 74,247 total patients, 2372 developed T2DM between 2004 and 2014.

Primary Outcome:

- A lower risk of incident T2DM was observed in women with active migraines (HR, 0.80 [95%CI, 0.60–0.96]).
- The magnitude of this association increased (HR,0.70 [95%CI,0.58–0.85]) when adjusted for level of education, level of recreational physical activity, body mass index, smoking status, history of hypertension, menopausal status, menopausal hormone therapy use, use of oral contraceptives, family history of diabetes, handedness, and use of antimigraine preparations frequently prescribed for migraines.

Secondary Outcome:

- Based on 4371 cases of diabetes that occurred between 1992 and 2014, 2-year prevalence of active migraines exhibited a linear decrease from 24 years before diabetes diagnosis (22% [95%CI, 16%–27%]) to the date of diagnosis (11% [95%CI,10%–12%]).
- Migraine prevalence stabilized (10–11%) T2DM diagnosis, persisting up to 22 years.

LIMITATIONS:

- Self-reporting migraine history
- No self-medication data available
- Only diabetes treated with prescription medication were identified
- Not generalizable for all patients since cohort consisted of insured, health-conscious, post-menopausal French women
- Potential for unmeasured confounders of risk factors for T2DM.

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