GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of April 8 - 12, 2024

SPOTLIGHT:
Ultra-Processed Foods and Mental Health: You Are What You Eat

- Nirsevimab Reduces RSV Risk in Term and Preterm Infants
- Do Local Steroid Injections for Idiopathic Carpal Tunnel Syndrome Confer Long-Term Benefits?
- Practice and Policy Changes (and Mouthguards) Reduce Sport-Related Concussions
- Voter Turnout Among Those with Chronic Conditions

Ultra-Processed Foods and Mental Health: You Are What You Eat

Ultra-Processed Food Consumption and Mental Health: A Systematic Review and Meta-Analysis of Observational Studies

Lane MM, Gamage E, Travica N, et al. Ultra-Processed Food Consumption and Mental Health: A Systematic Review and Meta-Analysis of Observational Studies. *Nutrients*. 2022;14(13):2568. Published 2022 Jun 21. doi:10.3390/nu14132568

KEY TAKEAWAY: Greater ultra-processed food consumption is associated with an increased prevalence of depressive and/or anxiety symptoms, as well as an increased risk of diagnosed depression.

STUDY DESIGN: Systematic review and meta-analysis of 17 observational, 15 cross-sectional, and two prospective studies (N=385,541)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Mental health disorders present a major global burden and have not declined since 1990. Ultra-processed foods are nutrient-poor and have been implicated in the prevalence, incidence, and severity of depression through several interacting pathways, including inflammation, oxidative stress, and the gut microbiome. Poor diet is a modifiable risk factor. This systematic review and meta-analysis of up-to-date observational studies assessed the association of anxiety and depression symptoms with high consumption of ultra-processed foods.

PATIENTS: Adults, adolescents, and children in the USA, Europe, and Brazil

INTERVENTION: Higher consumption of ultra-processed foods

CONTROL: Lowest consumption of ultra-processed foods

PRIMARY OUTCOME: Anxiety and depression symptoms

Secondary Outcome: Depression diagnosis or symptoms

METHODS (BRIEF DESCRIPTION):

- Study subjects were comprised of adults (mean age 45 years old), adolescents (mean age 15 years old), and children (mean age 10 years old), recruited from general and clinical populations. 45% of the study population were males.
- All studies used the NOVA classification system to categorize the level of food processing (1-unprocessed or minimal, 2-processed culinary ingredients, 3-processed food, 4-ultra-processed food).
- Researchers assessed dietary data through self-reports (10 studies), interviews (7), food frequency questionnaires (10), 24-hour dietary recalls (6), and two-week dietary history (1).
- Comparison of higher vs lower consumption of ultra-processed foods was performed in several ways: As an exposure variable (11 studies), categorically comparing the highest vs the lowest half, tertile, or quartile (8), or continuously (3).
- Depression and anxiety diagnosis and symptoms were defined using the Diagnostic and Statistical Manual of Mental Disorders 5th edition.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: Mean 7.9 years

RESULTS:

Primary Outcome –

- Higher consumption of ultra-processed foods, when compared with lower consumption, was associated with:
  - Greater prevalence of anxiety and depression symptoms combined (odds ratio [OR]1.5; 95% CI, 1.4–1.6)
  - Higher prevalence of depression symptoms separately (OR 1.4; 95% CI, 1.1–1.8)
  - Increased prevalence of anxiety symptoms (OR 1.5; 95% CI, 1.4–1.6)

Secondary Outcome –

- Higher consumption of ultra-processed foods, compared with lower consumption, was associated with the increased diagnosis of depression or onset of depression symptoms over time (hazard ratio [HR] 1.2; 95% CI, 1.2–1.3).

LIMITATIONS:

- The observational studies relied largely on self-report and recall for dietary data, with potential for error.
- Cross-sectional observational studies can only report the association of symptoms with diet composition at one point in time.
- Between-study differences in analytical approach and food intake modeling make it difficult to

compare studies and quantify the proportion of ultra-processed food associated with increased anxiety/depression symptoms.

- Because more than half of the studies were done in Brazil, it is unclear if the results are generalizable to other populations.
- The quality of several studies demonstrated an unclear risk of bias.

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Nirsevimab Reduces RSV Risk in Term and Preterm Infants

Efficacy of Nirsevimab Against Respiratory Syncytial Virus Lower Respiratory Tract Infections in Preterm and Term Infants, and Pharmacokinetic Extrapolation to Infants with Congenital Heart Disease and Chronic Lung Disease: A Pooled Analysis of Randomized Controlled Trials

Simões EAF, Madhi SA, Muller WJ, et al. Efficacy of nirsevimab against respiratory syncytial virus lower respiratory tract infections in preterm and term infants, and pharmacokinetic extrapolation to infants with congenital heart disease and chronic lung disease: a pooled analysis of randomized controlled trials. *Lancet Child Adolesc Health.* 2023;7(3):180-189. doi:10.1016/S2352-4642(22)00321-2

KEY TAKEAWAY: A single dose of nirsevimab reduced medically attended respiratory syncytial virus (RSV), lower respiratory tract infections (LRTI), and hospitalizations for RSV LRTI, and very severe RSV LRTI in healthy preterm and term infants.

STUDY DESIGN: Randomized placebo-controlled trial (RCT)

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: RSV LRTI is the most common reason for hospital admission during infancy. Preterm infants and infants with underlying cardiac and pulmonary disease may receive palivizumab to reduce the risk of an RSV-mediated LRTI; however, there are no FDA-approved therapies to reduce the risk of RSV LRTI in healthy infants.

PATIENTS: Preterm or term infants

INTERVENTION: Nirsevimab

CONTROL: Placebo

PRIMARY OUTCOME: Medically-attended RSV LRTI

Secondary Outcome: Hospital admissions for RSV LRTI, very severe RSV LRTI, medically attended LRTI of any cause, hospital admission for respiratory illness of any cause, nirsevimab drug levels in high-risk infants

METHODS (BRIEF DESCRIPTION):

- Subjects in the main RCT were healthy term (>37 weeks gestation), preterm (27 up to 35 weeks gestation), and late preterm (35–37 weeks) infants (55% term, 27% preterm, 10% late preterm) under three months old from North America, South America, Europe, and Australasia.
- Subject demographics comprised 60% Caucasian, 25% African, 4% American Indian/Alaskan Native, 3% Asian, and 1% Native Hawaiian or Pacific Islander.
- Exclusion criteria included acute illness warranting palivizumab treatment and RSV infection at or before enrollment.
- A second trial measured nirsevimab serum levels in high-risk infants with congenital heart disease, chronic lung disease, and gestational age <29 weeks.
- Subjects received a single nirsevimab IM injection of 50 mg if the infant weighed <5 kg or 100 mg if the infant weighed ≥5 kg.
- The primary outcome, in the main RCT was the diagnosis of RSV LRTI at a medical encounter within 150 days post-dose. Diagnosis required all of the presence of RSV on a central test (RT-PCR assay), at least one clinical sign of severe respiratory disease, and clinical signs of LRTI on chest auscultation.
- Secondary outcomes for the main RCT included hospital admission for primary outcome, very severe RSV LRTV (hospitalization for above requiring supplemental oxygen or intravenous fluids), and hospitalization for respiratory illness of any cause.
- The outcome for the second trial was the nirsevimab blood level, with samples collected at selected intervals during the first 150 days post-dose.

INTERVENTION (# IN THE GROUP):

- Main RCT: 1,564 nirsevimab
- Second trial: Not available

COMPARISON (# IN THE GROUP):

- Main RCT: 786 placebo
- Second trial: Not available

FOLLOW-UP PERIOD: 150 days

RESULTS:

Primary Outcome –

- Nirsevimab reduced medically attended RSV LRTI when compared to placebo (relative risk reduction [RRR] 80%; 95% CI, 66–88).

Secondary Outcome –

- Nirsevimab reduced hospitalization for RSV LRTI compared to placebo (RRR 77%; 95% CI, 50–90).
- Nirsevimab reduced hospitalization with very severe RSV LRTI compared to placebo (RRR 86%; 95% CI, 63–95).
- Nirsevimab reduced hospitalization for respiratory illness of any cause compared to placebo (RRR 43.8%; 95% CI, 19–61).
- Nirsevimab produced serum levels above target in 94% of high-risk infants overall.

LIMITATIONS:

- The subjects' median ages (1.6–2.6 months) limit applicability to older infants.
- Two infants with RSV resistant to nirsevimab were not included because they did not receive weight-based dosing.
- The efficacy of nirsevimab was extrapolated to high-risk infants based on drug levels.

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Do Local Steroid Injections for Idiopathic Carpal Tunnel Syndrome Confer Long-Term Benefits?

Extended Follow-up of Local Steroid Injection for Carpal Tunnel Syndrome: A Randomized Clinical Trial

Hofer M, Ranstam J, Atroshi I. Extended Follow-up of Local Steroid Injection for Carpal Tunnel Syndrome: A Randomized Clinical Trial. *JAMA Netw Open.* 2021;4(10):e2130753. Published 2021 Oct 1. doi:10.1001/jamanetworkopen.2021.30753

KEY TAKEAWAY: Local steroid injections for carpal tunnel syndrome (CTS) reduce and delay the need for surgical intervention. There was no difference between placebo vs steroid groups at the five-year follow-up regarding symptom severity.

STUDY DESIGN: Randomized, double-blind, placebo-controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Though steroid injections for CTS are known to help reduce symptoms in the short term, their effectiveness in the long term is unknown. The current study sought to answer this question with a five-year follow-up of patients who received steroid injections for CTS.

PATIENTS: Adults with idiopathic CTS

INTERVENTION: Methylprednisolone injection

CONTROL: Saline injection

PRIMARY OUTCOME: Symptom severity and surgical intervention

Secondary Outcome: Pain, disability

METHODS (BRIEF DESCRIPTION):

- Patients: 22–69 years old, with a mean age of 47 years old, 73% were women, and 27% were men.
- Inclusion criteria: Patients with symptoms suspicious for CTS according to the Katz diagnostic criteria and those who failed a two-month trial of wrist splinting.
- Those with diabetes mellitus, thyroid disease, inflammatory diseases, or otherwise serious illnesses were excluded from the trial as well as pregnant individuals.
- Patients were randomized in a 1:1:1 ratio to receive one injection of:
  - Methylprednisolone 40 mg injection (1 mL of 40 mg/mL solution + 1 mL saline)
  - Methylprednisolone 80 mg injection (2 mL of solution)
  - Saline 2 mL injection for placebo
- Injections were given by a single surgeon who was blinded to the treatment arms.
- Primary outcomes were rates of surgical intervention on the study hand and symptom severity score at five years.
  - Symptom severity was measured via the 11-item symptom severity scale based on pain and numbness/tingling. A score of one indicates no symptoms and a score of five indicates severe symptoms.
  - The minimal clinically important difference (MCID) was 0.79 points.
- Secondary outcomes were time between steroid injection and surgery, short-form 36 (SF-36) pain score, and score on the 11-item disabilities of the arm, shoulder, and hand (QuickDASH) scale.
  - SF-36 pain score ranges from 0 (severe pain) to 100 (pain absent). No MCID is available for patients with CTS.
  - QuickDASH measures how CTS affects participants' abilities to perform daily tasks. It is scored from 0 (absence of disability) to 100 (severe disability). MCID was determined to be 6.8 points.
- The level of significance was *P*=.05

INTERVENTION (# IN THE GROUP):

- 40 mg methylprednisolone: 37
- 80 mg methylprednisolone: 37

COMPARISON (# IN THE GROUP): 37

FOLLOW-UP PERIOD: Five years

RESULTS:

Primary Outcome –

- Local methylprednisolone injection, 40 mg or 80 mg, did not result in statistically significant improvement in symptom severity scores compared to placebo.
  - 40 mg methylprednisolone (mean change 0.12; 95% CI, –0.19 to 0.43)
  - 80 mg methylprednisolone (mean change 0.14; 95% CI, –0.17 to 0.45)
- Compared to placebo, 80 mg methylprednisolone injection reduced the rate of surgical intervention

(84% vs 97%) and delayed the time to surgery (180 days vs 121 days). These results were statistically significant compared to placebo (log-rank test, *P*=.002).

- Compared to placebo, 40 mg methylprednisolone injection reduced the rate of surgical intervention (92% vs 97%) and delayed the time to surgery (185 days vs 121 days). These results were statistically significant compared to placebo (log-rank test, *P*=.02).
- There was no statistically significant difference between 40 mg vs 80 mg methylprednisolone injection with a reduction in surgery rate (92% vs 84%) and time to surgery (185 days vs 180 days) (log-rank test, *P*=.37).

Secondary Outcome –

- At the 5-year follow-up, neither 40 mg nor 80 mg methylprednisolone injections improved pain or disability compared to placebo.

LIMITATIONS:

- Small sample size
- Single-center study design
- At the one-year follow-up period, the participants were unblinded to injection. They completed their pain score questionnaires after unblinding, which might have affected scoring.
- Exclusion criteria excluded participants with common conditions that cause secondary CTS (i.e., pregnancy, diabetes mellitus, thyroid disease).

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Practice and Policy Changes (and Mouthguards) Reduce Sport-Related Concussions

Prevention Strategies and Modifiable Risk Factors for Sport-Related Concussions and Head Impacts: A Systematic Review and Meta-Analysis

Eliason PH, Galarneau JM, Kolstad AT, et al. Prevention strategies and modifiable risk factors for sport-related concussions and head impacts: a systematic review and meta-analysis. *Br J Sports Med*. 2023;57(12):749-761. doi:10.1136/bjsports-2022-106656

KEY TAKEAWAY: Changes in policy in the sport of ice hockey and practice strategies in American football reduce sport-related concussions (SRC), as do mouthguards in ice hockey and neuromuscular training in rugby athletes.

STUDY DESIGN: Systematic review and meta-analysis of 13 trials (randomized controlled, quasi-experimental, cohort, case-control, or cross-sectional)

LEVEL OF EVIDENCE: STEP 3 (downgraded due to inconsistently applied reference standards, different sports/leagues with non-overlapping uses of equipment and rules)

BRIEF BACKGROUND INFORMATION: Sport-related concussions have been a growing concern amongst amateur and professional sports for well over a decade. Reducing concussions is vital to the long-term safety of the athlete and requires research that requires a multi-faceted approach including equipment review, policy changes, rule changes, and practice strategies.

PATIENTS: Competitive athletes

INTERVENTION: Personal protective gear, rule changes, practice changes, and preventative training

CONTROL: No intervention

PRIMARY OUTCOME: Sports-related concussion

METHODS (BRIEF DESCRIPTION):

- Study participants (male and female) included children (5–12 years old), adolescents (13–18 years old), and adults competing in sports in North America, Europe, and Australia.
- Interventions:
  - Mandatory mouthguards in ice hockey (child/adolescent/adult)
  - Policies outlawing bodychecking in ice hockey (child/adolescent)
  - Rules limiting contact during practice in American football (adolescent/adult)
  - Neuromuscular training during warm-ups in rugby (adolescent)
- Investigators compared SRC rates in intervention groups relative to groups without the intervention.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: Not available

RESULTS:

Primary Outcome –

- Mouthguards reduced SRC in children and adolescents playing ice hockey (incidence rate ratio [IRR] 0.74; 95% CI, 0.65–0.85).
- Bodychecking bans reduced SRC in children and adolescents playing ice hockey (IRR 0.42; 95% CI, 0.33–0.53).
- Reduced contact during practice in American football reduced SRC (IRR 0.36; 95% CI, 0.14–0.93).
- Neuromuscular training warm-ups in rugby reduce SRC (IRR 0.41; 95% CI, 0.17–0.99).

LIMITATIONS:

- The quality of most studies was rated “sufficient”.
- There was limited ability to evaluate interventions by gender or for parasports.
- It is unclear if concussion symptoms were reported consistently across all sports because of measurement bias.
- Increased media attention may have influenced concussion reporting rates.
- This study evaluated SRC but excluded traumatic brain injury or other head injuries.

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Voter Turnout Among Those with Chronic Conditions

Chronic Health Conditions and Voter Turnout: Results from the 2012 United States Presidential Election

McGuire CM, Rahn W, Gollust SE. Chronic health conditions and voter turnout: Results from the 2012 United States presidential election. *World Med Health Policy.* 2021;13(2):313-327. doi:10.1002/wmh3.454

KEY TAKEAWAY: Individuals diagnosed with diabetes were 6% more likely to vote than those without diabetes in the 2012 presidential election.

STUDY DESIGN: Cross-sectional study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Many research studies have identified a link between civic engagement and health outcomes, prompting voting to be recognized as an important social determinant of health. The relationship between chronic conditions and the likelihood of voter turnout is an area that needs more exploration and may provide insight into systemic causes of health inequities. The objective of this study was to examine the associations between diagnoses of five chronic health conditions including diabetes, cancer, heart disease, asthma, and arthritis on voter turnout in the 2012 US presidential election.

PATIENTS: American adults with a chronic health condition

INTERVENTION: Voted

CONTROL: Did not vote

PRIMARY OUTCOME: Voter turnout in the 2012 presidential election

Secondary Outcome: Voter turnout by race/ethnicity

METHODS (BRIEF DESCRIPTION):

- Adults ≥18 years old from 16 states who participated in the 2013 or 2014 Behavioral Risk Factor Surveillance System telephone survey (N=111,155) who had the following health conditions:
  - Diabetes (10%), arthritis (25%), heart disease (3.9%), asthma (14%), cancer (11%), and at least one chronic condition (41%).
- As part of a telephone survey, adults were asked to self-report if they had a chronic health condition which included: Diabetes, arthritis, asthma, cancer, and heart disease.
  - They were also asked if they voted in the last presidential election.
- The group for voter turnout was compared to the group with no voter turnout.
- The chronic conditions were used in a logistic regression model to estimate voter turnout and to predict the probability of voter turnout by condition.
- Marginal effects were reported by using stratified analyses by race/ethnicity to assess whether the relationship between chronic health conditions and turnout varies within each racial/ethnic group.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: Not applicable

RESULTS:

Primary Outcome –

- People with diabetes were more likely to vote than those with other chronic health conditions (75% vs 69%, respectively; odds ratio [OR] 1.6; 95% CI, 1.0–2.4).
- No other chronic health condition had a significant impact on voter turnout.

Secondary Outcome –

- The relationship between those with diabetes and voter likelihood was more pronounced in those who identified as being Hispanic or multiracial vs other ethnic/racial groups.
- Per self-identified race the following results were present:
  - White: Higher turnout for those with arthritis (marginal effect=3.0; p=.026) and diabetes (marginal effect=2.8; p=.034)
  - Black: Higher turnout for those with arthritis (marginal effect=4.0; p=.045) and heart disease (marginal effect=5.9; p=.019)
  - Hispanic: Higher turnout for those with asthma (marginal effect=4.2; p<.001), diabetes (marginal effect=11; p<.001), or cancer (marginal effect=7.1; p<.001)
  - Multiracial: Higher turnout for those with asthma (marginal effect=5.6; p<.001), diabetes (marginal effect=14; p<.001), or cancer (marginal effect=7.1; p<.001)

- Those diagnosed with arthritis (marginal effect= –11; p=.039) or cancer (marginal effect= –11; p<.001) were significantly less likely to vote.

LIMITATIONS:

- Only 16 states were represented in the study so cannot generalize to the entire United States population.
- The survey was done 1–2 years after the election and may have caused recall errors for voter turnout and/or errors with chronic disease reporting which could have started after the election.
- The survey was done via telephone which may have caused selection bias.
- Cross-sectional studies do not estimate causal relationships.
- There are differing degrees of functioning and debility within chronic disease groups.

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