GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

Volume 5 - Issue 7

FPIN
Family Physicians Inquiries Network

What's in this week's issue?

Week of February 17-21, 2025

SPOTLIGHT:

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- Cut or Condition? A Randomized Trial on Surgery vs Therapy for Meniscus Tears in Young Adults
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- Smart Prescribing in Pregnancy: Is Antibiotic Use in Pregnancy Associated with Neurocognitive Disorders?
- Adding Technology Does Not Equate to Additional Weight Loss

Bone Health and Weight Loss: Does GLP-1RA + Exercise Reduce Bone Density?

Bone Health After Exercise Alone, GLP-1 Receptor Agonist Treatment, or Combination Treatment: A Secondary Analysis of a Randomized Clinical Trial

Jensen SBK, Sørensen V, Sandsdal RM, et al. Bone Health After Exercise Alone, GLP-1 Receptor Agonist Treatment, or Combination Treatment: A Secondary Analysis of a Randomized Clinical Trial. *JAMA Netw Open*. 2024;7(6):e2416775. Published 2024 Jun 3. doi:10.1001/jamanetworkopen.2024.16775

KEY TAKEAWAY: Combining GLP-1 therapy with exercise does not reduce bone mineral density during weight loss compared to placebo.

STUDY DESIGN: Secondary analysis of a randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Bone health and preservation are critical considerations in the medical management of obesity, as weight loss is often associated with a decline in bone mineral density. With the growing use of GLP-1 receptor agonists in obesity treatment within the scope of the family medicine practice, further research is necessary to understand their effects on bone health. This study investigated the effects of GLP-1 receptor agonist therapy in combination with exercise on weight loss outcomes and bone mineral changes, aiming to provide insights into optimizing obesity management strategies while mitigating risks to skeletal health.

PATIENTS: Obese adults without diabetes

INTERVENTION: GLP-1 daily therapy + exercise

CONTROL: Placebo

PRIMARY OUTCOME: Bone mineral density

Secondary Outcome: Weight loss

METHODS (BRIEF DESCRIPTION):

- Non-diabetic adults 18–65 years old with a BMI of 32–43 kg/m^2 without a history of bone deficiency or fragility fractures were included in the study.
  - 124 females and 77 males
  - Mean BMI of 37 kg/m^2
  - Mean age of 43 years old
- Each participant underwent an eight-week, 800 kcal a day diet comprised of four meal replacement products provided by Cambridge Weight Plan before starting group-specific treatment.
- Changes in body composition, including weight changes, were evaluated throughout the study.
- All participants required to exercise were enrolled in supervised exercise and wore heart rate monitors to ensure accurate compliance with moderate to vigorous exercise.
- GLP-1 included 3.0 mg per day of liraglutide (or the highest tolerable dose) injected subcutaneously into the abdomen.
- The placebo group received exact volume-based placebo injections and did not participate in structured exercise.
- Participants and providers were blinded to the medication study arm.
- DEXA scans were performed to measure bone mineral density on separate occasions of the lumbar spine and left hip.
- The trial lasted 52 weeks following the eight-week diet.
- A constrained linear mixed model with an inherent baseline was used to analyze the randomized participant population.

INTERVENTION (# IN THE GROUP): 49

COMPARISON (# IN THE GROUP): 49

FOLLOW-UP PERIOD: One year

RESULTS:

Primary Outcome –

- GLP-1 + exercise did not affect hip bone mineral density compared to placebo alone (mean change –0.006; 95% CI, –0.017 to 0.004).
- GLP-1 + exercise did not affect spine bone mineral density compared to placebo alone (mean change –0.010; 95% CI, –0.025 to 0.005).
- GLP-1 + exercise did not affect forearm bone mineral density compared to placebo alone (mean change 0.04; 95% CI, –0.006 to 0.014).

Secondary Outcome –

- The placebo group achieved 7.0 kg of weight loss during the study (mean change 7.0 kg; 95% CI, 4.3–9.8).

- The combination group achieved 17 kg of weight loss during the study (mean change 17 kg; 95% CI, 14–20).

LIMITATIONS:

- As this is a secondary review, the initial sample size was not stratified for bone mineral density.
- The study did not include older patients who may be more prone to bone density issues which would potentially alter the data results.

Madeleine Gwinn, DO
United Hospital Center FMRP
Bridgeport, WV

Cut or Condition? A Randomized Trial on Surgery vs Therapy for Meniscus Tears in Young Adults

Arthroscopic Partial Meniscectomy vs Physical Therapy for Traumatic Meniscal Tears in a Young Study Population: A Randomized Controlled Trial

van der Graaff SJA, Eijgenraam SM, Meuffels DE, et al. Arthroscopic partial meniscectomy versus physical therapy for traumatic meniscal tears in a young study population: a randomized controlled trial. *Br J Sports Med*. Published online June 8, 2022. doi:10.1136/bjsports-2021-105059

KEY TAKEAWAY: In young patients with isolated traumatic meniscal tears, early arthroscopic partial meniscectomy does not improve knee symptoms, function, or ability to participate in sports compared to physical therapy (PT) at 24 months.

STUDY DESIGN: Open-labeled, multicenter, parallel, randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Multiple high-level studies have shown that partial meniscectomy has no benefit compared to non-operative treatment in middle-aged and older patients with chronic degenerative tears. Young patients with acute meniscal tears are usually offered meniscectomy because of the belief that surgery is needed to decrease mechanical complaints. However, there have not been any randomized controlled trials in young patients with meniscal tears in otherwise healthy knees. This study aimed to provide additional insight into the statistical benefit of surgical vs non-surgical management.

PATIENTS: Patients 18–45 years old with knee trauma

INTERVENTION: Arthroscopic partial meniscectomy

CONTROL: PT

PRIMARY OUTCOME: Symptoms, knee function, and ability to participate in sports

Secondary Outcome: Overall knee pain, knee function, knee pain at rest and during activity, satisfaction with knee function, health-related quality of life, sporting activity level

METHODS (BRIEF DESCRIPTION):

- Patients from the emergency department or general practitioner with a meniscal injury were referred to the participating outpatient clinics in the Netherlands.
- Those who met inclusion criteria (18–45 years old, knee trauma in the past 6 months, grade 3 meniscal tear on MRI) were eligible and given information about the trial information.
- Participants were randomized 1:1 ratio into either the partial meniscectomy group or PT.
  - Partial meniscectomy: Completed within six weeks of randomization by an orthopedic surgeon who was well-versed in the procedure (at least 50 knee arthroscopies per year).
  - The PT program lasted three months and consisted of three phases, which included reducing knee effusion and optimizing range of motion, stimulating activities of daily living, and returning to sport.
- The primary outcome measured the patient's perception of symptoms, knee function, and ability to participate in sports and was assessed via the International Knee Documentation Committee (IKDC) score at the 24-month follow-up. Scores range from 0–100, with a score of 100 being the optimal score.
- The secondary outcome measured the following:
  - Overall knee pain was assessed using the Knee Injury and Osteoarthritis Outcome Score (KOOS). Scores range from 0–100 with a score of 100 being the optimal score.
  - Knee function was assessed using the Lysholm. Scores range from 0–100, with a score of 100 being the optimal score.
  - Knee pain at rest and during activity was assessed using the Numeric Rating Scale (NRS). Scores range from 0–10, with lower scores indicating a lower level of pain.
  - Health-related quality of life was assessed using the Western Ontario Meniscal Evaluation Tool (WOMET). Scores range from 0–100 with a score of 100 being the optimal score.
  - Sporting activity level was assessed using the Tegner score. Scores range from 0–10 with higher scores indicating a higher level of activity.
  - Satisfaction with knee function was assessed with a Visual Analog Scale (VAS). Scores range

from 0–100 with higher scores indicative of increased satisfaction.

- Participants completed all questionnaires digitally at zero, three, six, nine, 12, and 24 months, except for the KOOS and Lysholm.
  - The KOOS questionnaire was completed at zero and 24 months and the Lysholm questionnaire was completed at zero, 12, and 24 months.
- For statistical analysis, a linear regression model with IKDC score was used.

INTERVENTION (# IN THE GROUP): 49

COMPARISON (# IN THE GROUP): 51

FOLLOW-UP PERIOD: 24 months

RESULTS:

Primary Outcome –

- Arthroscopic partial meniscectomy did not significantly improve symptoms, knee function, and ability to participate in sports compared to PT (between-group difference 0.1; 95% CI, –7.6 to 7.7).

Secondary Outcome –

- Arthroscopic partial meniscectomy did not show superiority compared to PT for the following:
  - Overall knee pain (between-group difference 1.9; 95% CI, –5.7 to 9.6)
  - Knee pain at rest (between-group difference –0.1; 95% CI, –0.8 to 0.7)
  - Knee pain during activity (between-group difference 0.4; 95% CI, –0.8 to 1.5)
  - Knee function (between-group difference –1.0; 95% CI, –6.2 to 4.1)
  - Health-related quality of life (between-group difference –3.8; 95% CI, –14 to 6.2)
  - Sporting activity level (between-group difference 0.3; 95% CI, –0.6 to 1.3)
  - Satisfaction with knee function (between-group difference 1.5; 95% CI, –9.3 to 12)

LIMITATIONS:

- Patient preference for a treatment may induce recruitment bias.
- An absence of blinding was present for patients assigned to the intervention group.
- The study included patients with a wide range of time from trauma to inclusion (0–6 months), so patients may have already followed a non-operative treatment before inclusion.

Melinda W Ng, MD
David Grant USAF Medical Center- Travis AFB
Fairfield, CA

Glucose Alert: Tracing Diabetes' Link to Parkinson's Risk

Diabetes Mellitus, Prediabetes and the Risk of Parkinson's Disease: A Systematic Review and Meta-Analysis of 15 Cohort Studies with 29.9 Million Participants and 86,345 Cases

Aune D, Schlesinger S, Mahamat-Saleh Y, Zheng B, Udeh-Momoh CT, Middleton LT. Diabetes mellitus, prediabetes and the risk of Parkinson's disease: a systematic review and meta-analysis of 15 cohort studies with 29.9 million participants and 86,345 cases. *Eur J Epidemiol*. 2023;38(6):591-604. doi:10.1007/s10654-023-00970-0

KEY TAKEAWAY: Diabetes mellitus (DM) increases an individual's risk of developing Parkinson's disease compared to those without diabetes. The same but smaller risk is present for prediabetic individuals.

STUDY DESIGN: Systematic review and meta-analysis of 15 cohort studies (N=29,900,000)

LEVEL OF EVIDENCE: STEP 2 (downgraded due to significant heterogeneity)

BRIEF BACKGROUND INFORMATION: Research has shown a link between diabetes and an increased risk of Parkinson's disease, but the findings have been mixed. Some studies show a strong connection, while others show no link or even suggest that certain aspects of diabetes might protect against Parkinson's. This study aimed to clear up these conflicting results by closely examining the relationship between diabetes, prediabetes, and the risk of developing Parkinson's disease.

PATIENTS: Individuals diagnosed with DM or prediabetes

INTERVENTION: Presence of DM

CONTROL: Individuals without DM

PRIMARY OUTCOME: Risk of developing Parkinson's disease

METHODS (BRIEF DESCRIPTION):

- Included adults from various cohort studies, focusing on those diagnosed with DM or prediabetes.
- Individuals without a clear diagnosis were excluded from the study.
- Diabetes and prediabetes status was confirmed through medical records, confirmed diagnoses, self-reports, or blood sugar measurements.
- Individuals without diabetes or prediabetes were used as the comparator to establish a baseline risk for Parkinson's disease.
- The main outcome was the risk of developing Parkinson's disease measured using a self-reported diagnosis of diabetes, linked medical records, or fasting blood glucose levels.
- This was quantified using relative risk estimates with 95% confidence intervals from the data pooled across studies.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: Varied

RESULTS:

Primary Outcome –

- Individuals with DM are at an increased risk for Parkinson's disease compared to individuals without DM (15 studies, N=29,900,000; relative risk [RR] 1.3; 95% CI, 1.2–1.4; I^2=82%).
- Individuals with prediabetes are at a minimally increased risk for Parkinson's disease compared to individuals without DM (2 studies, n=11,547,811; RR 1.04; 95% CI, 1.02–1.1; I^2=0%).

LIMITATIONS:

- Significant heterogeneity was present among the included studies.
- Potential biases related to publication and measurement may have influenced the results.
- There was variation in the assessment of diabetes across studies.

Ahmed Abuzoor, MD
Northeast Georgia Medical Center FMRP
Gainesville, GA

Smart Prescribing in Pregnancy: Is Antibiotic Use in Pregnancy Associated with Neurocognitive Disorders?

Association Between Exposure to Antibiotics During Pregnancy or Early Infancy and Risk of Autism Spectrum Disorder, Intellectual Disorder, Language Disorder, and Epilepsy in Children: Population-Based Cohort Study

Choi A, Lee H, Jeong HE, et al. Association between exposure to antibiotics during pregnancy or early infancy and risk of autism spectrum disorder, intellectual disorder, language disorder, and epilepsy in children: population-based cohort study. *BMJ*. 2024;385:e076885. Published 2024 May 22. doi:10.1136/bmj-2023-076885

KEY TAKEAWAY: Antibiotic use in pregnancy or early infancy may be associated with a small increased risk of autism spectrum disorder (ASD), intellectual disorder (ID), language disorder (LD), and epilepsy.

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Antibiotic use in pregnancy and early infancy is a common intervention known to alter the gut microbiome. Fetal and infant life is a critical period for both neurodevelopment and the development of the gut microbiome.

Neurodevelopmental disorders have become a rising public health issue with lifelong impacts on individuals, families, and institutions. Few studies have investigated an association between antibiotic use and neurodevelopmental disorders.

PATIENTS: Children in South Korea

INTERVENTION: Antibiotic exposure in the perinatal period or early infancy

CONTROL: No antibiotic exposure

PRIMARY OUTCOME: Diagnosis of ASD, ID, LD, and epilepsy

METHODS (BRIEF DESCRIPTION):

- The patients were all children born between 2009 and 2020 in Korea using the National Health Insurance Service database.
  - The patients were followed until 2021.
- Mothers who received antibiotics during pregnancy (pregnancy cohort) or the children who received antibiotics within the first six months of life (infancy cohort) were assigned to the intervention group.
- The comparison groups did not receive antibiotics during the above time frames.
- To control for potential confounding, trialists performed 1:1 propensity score matching.
- To assess for unmeasured confounding from familial factors, sibling-controlled analyses were undertaken. Subgroup and sensitivity analyses were performed as well.
- The primary outcome measured the diagnosis of ASD, ID, LD, or epilepsy based on the International Classification of Diseases (ICD) codes and diagnosed by pediatricians and psychiatrists in South Korea.
- The results were adjusted for demographics, indications for antibiotic use, infection-related healthcare utilization, maternal conditions, medication use, measures of healthcare utilization, sex of child, preterm birth, cesarean section, birthweight, type of feeding, and siblings.

INTERVENTION (# IN THE GROUP):

- Antibiotics during pregnancy: 980,872
- Antibiotics during early infancy: 804,887

COMPARISON (# IN THE GROUP):

- Not exposed to antibiotics in pregnancy: 980,872
- Not exposed to antibiotics in early infancy: 804,887

FOLLOW-UP PERIOD: Seven years

RESULTS:

Primary Outcome –

- In the propensity score-matched analysis, antibiotic use in pregnancy and early infancy was associated with increased rates of all outcomes compared to the unexposed cohort.
  - Antibiotic exposure in pregnancy:
    - ASD (hazard ratio [HR] 1.1; 95% CI, 1.1–1.2)
    - ID (HR 1.2; 95% CI, 1.1–1.2)
    - LD (HR 1.1; 95% CI, 1.1–1.1)
    - Epilepsy (HR 1.1; 95% CI, 1.1–1.1)
  - Antibiotic exposure in early infancy:
    - ASD (HR 1.04; 95% CI, 1.01–1.1)
    - ID (HR 1.2; 95% CI, 1.2–1.3)
    - LD (HR 1.1; 95% CI, 1.04–1.1)
    - Epilepsy (HR 1.2; 95% CI, 1.2–1.3)
- In the sibling analysis, antibiotic exposure compared to the unexposed cohort yielded mixed results.
  - Antibiotic exposure in pregnancy was associated with an increased risk of:

        - ASD (HR 1.1; 95% CI, 1.01–1.1)
        - LD (HR 1.1; 95% CI, 1.02–1.1)
    - Antibiotic exposure in pregnancy was not associated with an increased risk of:
        - Epilepsy (HR 1.0; 95% CI, 0.98–1.1)
        - ID (HR 1.0; 95% CI, 0.93–1.1)
    - Antibiotic exposure in early infancy was associated with an increased risk of epilepsy (HR 1.1; 95% CI, 1.1–1.2).
    - Antibiotic exposure in early infancy was not associated with an increased risk of:
        - ASD (HR 1.0; 95% CI, 0.96–1.0)
        - ID (HR 1.1; 95% CI, 0.98–1.2)
        - LD (HR 1.0; 95% CI, 1.0–1.1)

LIMITATIONS:

- Body mass index (BMI) or smoking was not controlled for.
- Exposure misclassification is possible due to the use of a prescription database, but actual administration is unknown.
- There was possible outcome misclassification for ASD, ID, and LD.
- Paternal characteristics were not available in the database.
- No direct measurement of infection severity
- Sibling comparison design susceptible to carryover effects
- Possible effects of information bias related to the COVID-19 pandemic
- Inability to establish causation

Prasun Mandal, DO
Rebecca Steineck, DO
University of Iowa Hospitals and Clinics FMRP
Sioux City, IA

Adding Technology Does Not Equate to Additional Weight Loss

A Cluster-Randomized Study of Technology-Assisted Health Coaching for Weight Management in Primary Care

Jay MR, Wittleder S, Vandyousefi S, et al. A Cluster-Randomized Study of Technology-Assisted Health Coaching for Weight Management in Primary Care. *Ann Fam Med*. 2024;22(5):392-399. doi:10.1370/afm.3150

KEY TAKEAWAY: The use of technology-associated weight loss tools does not result in greater weight loss compared to standard educational handouts and routine primary care counseling.

STUDY DESIGN: Multicenter, unblinded cluster randomized controlled trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to lack of blinding)

BRIEF BACKGROUND INFORMATION: Technology-assisted health coaching has emerged as a promising strategy to support patients in achieving sustainable weight loss by complementing traditional care with personalized guidance. Despite its potential, evidence of its effectiveness in routine clinical practice remains limited, necessitating further research to guide implementation.

PATIENTS: Overweight and obese adults

INTERVENTION: Technology-assisted coaching

CONTROL: Education handouts

PRIMARY OUTCOME: Weight loss

Secondary Outcome: Change in body mass index (BMI), blood pressure, >5% loss of baseline body weight, waist circumference, health behaviors

METHODS (BRIEF DESCRIPTION):

- This unblinded, cluster-randomized study was conducted at multiple Veterans Affairs (VA) clinics in New York City, expanding from the Goals for Eating and Moving (GEM) pilot study.
- Adults 18–69 years old, with a BMI ≥30 kg/m² or BMI 25–29 kg/m² with at least one obesity-related comorbidity (hypertension, hyperlipidemia, etc.) were included in the study.
- Patients with diabetes, prior bariatric surgery, concomitant use of an antipsychotic or anti-obesity drug(s), and medical conditions that precluded exercise (severe arthritis, active cancer, psychosis) were excluded from the study.
- Participants had an average age of 50 years, 44% identified as male, 41% identified as Hispanic, and 44% identified as non-Hispanic Black.
- The intervention group received the GEM protocol for 12 months, which included a tablet with an individualized goal-setting tool for weight, diet, and exercise, one in-person health coach visit, up to 12 telephone coaching calls, and brief primary care provider (PCP) counseling.
- The control group received standard weight management and general health education handouts based on the Veteran's Association-developed "Healthy Living Messages" and Weight Management Program for Veterans (MOVE! Program) via their primary care provider or the research assistants without additional coaching or technological tools.
- The primary outcome was kilograms of weight loss at 12 months.
- The secondary outcomes included the number of patients that achieved weight loss of ≥5% and a reduction in BMI, waist circumference, and blood pressure at six, 12, and 24 months.
- The authors also examined behavioral changes (change in healthy diet consumption, improved physical activity) at baseline and 12 months.

INTERVENTION (# IN THE GROUP): 220

COMPARISON (# IN THE GROUP): 269

FOLLOW-UP PERIOD: 24 months

RESULTS:

Primary Outcome –

- At 12 months, there was no significant difference in mean adjusted weight loss between the intervention group and the control group (–1.4 kg vs –0.8 kg, respectively; difference –0.7 kg; 95% CI, –2.4 to –1.1).

Secondary Outcome –

- A similar percentage of participants in each group achieved ≥5% weight loss.
- There was no significant difference between the two groups for the outcomes of change in BMI,

waist circumference, or reduction of systolic or diastolic blood pressure.
- There was no significant difference between the groups when evaluating behavioral changes, such as improved healthy diet consumption and increased physical activity.

LIMITATIONS:

- The study's generalizability is limited as all study participants were veterans, and clinical sites utilized a patient-centered medical home (PCMH) model, which is not universally implemented across the US.
- The study was conducted before, during, and after the COVID-19 pandemic, which may have impacted recruitment and resulted in a 27% dropout rate.
- In-person aspects of the study were paused due to the pandemic, potentially affecting the intervention's delivery and participant engagement.
- The study included PCPs who had previously been trained on and participated in the initial pilot study, potentially introducing PCP bias towards the intervention.

Corey McKenzie, MD
Naval Medical Center Camp Lejeune FMRP
Camp Lejeune, NC

The views expressed herein are those of the author and do not necessarily reflect the official policy of the Department of the Navy, Defense Health Agency, Department of Defense, or the US Government.