GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

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SPOTLIGHT: Team Sports Reduce Depression and Anxiety in Adolescents with ACEs

Team Sports Reduce Depression and Anxiety in Adolescents with ACEs

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Association of Team Sports Participation with Long-term Mental Health Outcomes Among Individuals Exposed to Adverse Childhood Experiences.

Easterlin MC, Chung PJ, Leng M, Dudovitz R. Association of Team Sports Participation With Long-term Mental Health Outcomes Among Individuals Exposed to Adverse Childhood Experiences. *JAMA Pediatr.* 2019; 173(7):681–688. doi:10.1001/jamapediatrics.2019.1212

KEY TAKEAWAY: Participation in team sports during adolescence may be associated with better mental health outcomes in adulthood for individuals with adverse childhood experiences (ACEs).

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Long-term poor mental health in adulthood is linked to ACEs. It is unclear whether adolescent participation in team sports for individuals with ACEs is associated with improved mental health outcomes.

PATIENTS: 7th to 12th graders with ACEs

INTERVENTION: Team sport participation during adolescence

CONTROL: No team sport participation in adolescence

OUTCOME: Diagnosis of anxiety and/or depression; depressive symptoms

METHODS (BRIEF DESCRIPTION):

- Data was collected from 9,668 individuals who were in wave 1 (1994-1995) and wave 4 (2008) of the National Longitudinal Study of Adolescent to Adult Health (Add Health).
- Add Health was used to compare the evolution and occurrence of anxiety, depression, and depressive symptoms of 24-32 years old.
- ACEs included physical abuse, emotional neglect, sexual abuse, parental alcohol misuse, parental incarceration, and living with a single parent.
- Out of the 9,668 individuals, 4,888 (49%) reported one or more ACEs and 2,084 (21%) reported two or more ACEs.
- Depressive symptoms were based on a 10-item subscale of the Center for Epidemiologic Studies Depression scale (CES-D–10).
- The same individuals from wave 1 were assessed as an adult in wave 4.

INTERVENTION (# IN THE GROUP): 4,888

COMPARISON (# IN THE GROUP): 4,780

FOLLOW UP PERIOD: 13 years

RESULTS:

- Team sport participation during adolescence was associated with better adult mental health outcomes.
  - Depression diagnosis (17% vs 22%; propensity score–weighted (PWS) adjusted odds ratio (aOR) 0.76; 95% CI, 0.59–0.97)
    - However, team sport participation did not affect depressive symptoms (22% vs 28%; PSW aOR 0.85; 95% CI, 0.71–1.0).
  - Anxiety diagnosis (12% vs 17%; PSW aOR 0.70; 95% CI, 0.56–0.89)

LIMITATIONS:

- Adverse childhood experiences can be based off subjective experiences like “emotional neglect”.
- Observational study, therefore true causality cannot be determined.
- Some loss to follow-up and incomplete data.

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Metformin Prolongs Gestation in Preterm Pre-eclampsia

Use of metformin to prolong gestation in preterm pre-eclampsia

Cluver CA, Hiscock R, Decloedt EH, et al. Use of metformin to prolong gestation in preterm pre-eclampsia: randomised, double blind, placebo controlled trial. *BMJ.* 2021; 374:n2103. Published 2021 Sep 22. doi:10.1136/bmj.n2103

KEY TAKEAWAY: Metformin may safely prolong gestation in women being expectantly managed for preterm pre-eclampsia.

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

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Pre-eclampsia is a leading cause of maternal and neonatal morbidity and mortality. Risks are substantially increased when preterm. Currently, no treatment exists except for delivery. A safe treatment could delay the progression of preterm pre-eclampsia and prevent preterm delivery.

PATIENTS: Women being expectantly managed for preterm pre-eclampsia between 26 to 31 weeks of gestation

INTERVENTION: Extended-release metformin

CONTROL: Matching placebo

OUTCOME: Prolongation of gestation

Secondary Outcomes: Composites of maternal, fetal, and neonatal mortality and morbidity

METHODS (BRIEF DESCRIPTION):

- Subjects were diagnosed with pre-eclampsia based on proteinuria >300 mg/24 hours plus new onset hypertension (HTN) after 20 weeks' gestation or loss of control if receiving treatment for chronic HTN.
- Subjects were treated with either 3 g of extended-release metformin (1,000 mg three times daily) or matching placebo.
  - If side effects developed, dose could be decreased to 500 mg BID and then increased if symptoms improved.
- Expectant management involved hospital admission, blood pressure checks every four hours, clinical assessments, and lab monitoring.
- Fetal surveillance included ultrasonography for size and Doppler velocimetry soon after admission, followed by reviews at least twice a week, and cardiotocography every six hours.
- When patients were first admitted, two doses of betamethasone were given 24 hours apart, followed by a single repeat dose one week later if no delivery had occurred.
- Expectant management was stopped at 34 weeks' gestation when delivery took place.

INTERVENTION (# IN THE GROUP): 89

COMPARISON (# IN THE GROUP): 90

FOLLOW UP PERIOD: Six weeks after expected due date

RESULTS:

- Metformin increased time to delivery compared to placebo (randomization to delivery time 17.7 days vs 10.1 days, *P*=.057).
- Composite maternal, fetal, and neonatal morbidity and mortality outcomes were not different between the two groups.
- Women in the metformin arm experienced clinically significant more diarrhea than control (33% vs 6%).
- No adverse events occurred.

LIMITATIONS:

- Small sample size (179 participants) limited power, especially since many participants discontinued or reduced their drugs.
- Single-center study limited generalizability.
- 11% of patients in the metformin arm were taking aspirin, versus 4% in the placebo arm, however sensitivity analysis suggested that this would not have changed the outcomes.

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Osteopathic Treatments Can Be Effective in Treating Chronic Low Back Pain

Effectiveness of osteopathic interventions in chronic non-specific low back pain: A systematic review and meta-analysis.

Dal Farra F, Risio RG, Vismara L, Bergna A. Effectiveness of osteopathic interventions in chronic non-specific low back pain: A systematic review and meta-analysis. *Complement Ther Med*. 2021; 56:102616. doi:10.1016/j.ctim.2020.102616

KEY TAKEAWAY: Osteopathic treatment is more effective in improving pain levels and functional status in Nonspecific-Chronic Low Back Pain (NS-CLBP) than non-osteopathic treatments.

STUDY DESIGN: Meta-analysis of 10 RCTs (N=1,150)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: NS-CLBP is lumbar pain persisting for longer than three months in the absence of suspected pathology, resulting in significant physical disabilities and psychological distress. Central sensitization plays a key role that could explain why pharmacological treatments are not particularly recommended. Osteopathic interventions, with a therapeutic aim towards improving physiological function and supporting homeostasis, may prove to be beneficial.

PATIENTS: Adults 18-70 years old with NS-CLBP

INTERVENTION: Osteopathic treatment

CONTROL: Non-osteopathic treatments

OUTCOME: Pain, disability

METHODS (BRIEF DESCRIPTION):

- Study used adult subjects from 18-70 years old.
- NS-CLBP is defined as pain lasting for at least three months with no specific cause of pain.
- The intervention group included subjects receiving osteopathic treatment, but excluded other forms of manual and manipulative therapies including chiropractic and physiotherapy.
- The control group included usual care, sham therapy (both manual and through devices) and other treatments such as pharmacological or non-pharmacological.
- Pain levels and functional status (or disability) were measured at post-intervention and at follow-up.
- Subgroup analysis was also performed to compare effectiveness of single osteopathic modalities (ex. MFR) to a more general semi-standardized approach.

INTERVENTION (# IN THE GROUP): 538

COMPARISON (# IN THE GROUP): 612

FOLLOW UP PERIOD: 4 - 24 weeks

RESULTS:

- Osteopathic treatments significantly improved pain in NS-CLBP compared to non-osteopathic treatments (10 trials, N=1049; ES = -0.59; 95% CI, -0.81 to -0.36).
- In subgroup analysis, the following modalities significantly reduced pain:
  - Myofascial Release (MFR): 2 trials, N=128; ES = -0.69; 95% CI, -1.1 to -0.33
  - Osteopathic Manipulative Treatment (OMT): 8 trials, N=837; ES = -0.57; 95% CI, -0.90 to -0.25
- Osteopathic treatments significantly improved functional status in patients with NS-CLBP compared to non-osteopathic treatments (10 trials, N=1055; ES = -0.42; 95% CI, -0.68 to -0.15).
- In subgroup analysis, the following modalities significantly improved functional status:
  - MFR: 2 trials, N=128; ES = -0.73; 95% CI, -1.3 to -0.21)
  - OMT: 8 trials, N=843; ES = -0.33; 95% CI, -0.65 to -0.01

LIMITATIONS:

- Data was not always retrievable in the article or was presented in a modality that was not useful to perform meta-analysis.
- Osteopathic manipulative techniques varied.
- There were reports of high risk of bias in methodological steps.

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Manipulating Babies: Exploring the Effects of OMT on NICU Patients

Osteopathic Manipulative Treatment in Neonatal Intensive Care Units

Cicchitti L, Di Lelio A, Barlafante G, et al. Osteopathic Manipulative Treatment in Neonatal Intensive Care Units. *Med Sci (Basel).* 2020; 8(2):24. Published 2020 Jun 24. doi:10.3390/medsci8020024

KEY TAKEAWAY: OMT may benefit both weight gain and length of stay in certain groups of premature infants admitted to the NICU.

STUDY DESIGN: Observational, longitudinal, retrospective study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Premature babies have higher rates of severe disease in the first five years and have considerably longer stays in the NICU. Low birth weight contributes to 60-80% of all neonatal deaths. OMT is currently being used in some Italian NICU's to improve outcomes in neonates. However, data supporting this approach is so-far limited.

PATIENTS: Babies admitted to the NICU

INTERVENTION: OMT

CONTROL: Standard care

OUTCOME: Weight gain

Secondary Outcomes: Decrease in length of stay, spontaneous stools, blood stasis, bilious stasis, regurgitation, gastric vomiting

METHODS (BRIEF DESCRIPTION):

- A chart review was performed for all babies admitted to the Santo Spirito Hospital NICU in Pescara, Italy from September 2008 to November 2016.
- Babies were divided into OMT and routine practice groups.
- Both groups were then divided into full-term and preterm groups.
- The preterm group was then divided based on gestational age: 27-31 weeks, 32-33 weeks, and 34-36 weeks.
- OMT techniques: myofascial release, balanced ligamentous/membranous tension, indirect fluidic and v-spread
  - The intervention group also received standard care.
- Standard care: Reducing environmental stressors, managing pain and stress, protecting sleep, feeding and positioning the neonate, minimizing separation from caregivers, ensuring caregiver interactions and skin to skin contact
- Outcomes were recorded twice a week on an electronic clinical database routinely used in the NICU.
- Weight change from admission was analyzed through mixed models, length of stay was analyzed using adjusted linear regression, and all other outcomes were analyzed using Poisson regression models

INTERVENTION (# IN THE GROUP): 597 (297 premature)

COMPARISON (# IN THE GROUP): 652 (315 premature)

FOLLOW UP PERIOD: Length of their hospital stay

RESULTS:

Primary Outcome –

- OMT resulted in more weight gain than routine care (83 g vs 35 g, respectively; difference 48 g; 95% CI, 32–64).
  - Premature infants benefitted the most (86 g vs 37 g; difference 49; 95% CI, 37–64).

Secondary Outcome –

- OMT resulted in a shorter length of stay for premature infants (mean difference of 12 days; 95% CI -24 to -0.5).
- OMT increased the likelihood of spontaneous stools by 14% (95% CI, 3% to 27%).
  - There was no statistically significant difference in the premature group.
- OMT decreased the likelihood of change in blood stasis by 43% (95% CI, 15% to 61%).
  - An 86% decrease was observed in premature infants (95% CI, 70% to 93%).
- OMT increased the likelihood of bilious stasis by 91% (95% CI, 34% to 173%).
  - A 231% increase was observed in premature infants (95% CI, 47% to 264%).
- There was no difference in regurgitation or gastric vomiting.

LIMITATIONS:

- The study used a retrospective design reliant on data from the past that may be inaccurate or no-longer up to date.
- There was a lack of information about other potential confounders.

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Incentives Don't Increase Uptake of Colorectal Cancer Screening

Financial Incentives to Increase Colorectal Cancer Screening Uptake and Decrease Disparities

Green BB, Anderson ML, Cook AJ, et al. Financial Incentives to Increase Colorectal Cancer Screening Uptake and Decrease Disparities: A Randomized Clinical Trial. *JAMA Netw Open.* 2019; 2(7):e196570. Published 2019 Jul 3. doi:10.1001/jamanetworkopen.2019.6570

KEY TAKEAWAY: Mailed incentives do not increase colorectal screenings. Providing information and a $10 incentive increased FIT screenings compared to information alone.

STUDY DESIGN: Multicenter, parallel, three-arm randomized clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Colorectal cancer (CRC) is a leading cause of cancer-related death in the United States. In the US only 62% of eligible adults are up to date on their screening. Rates of screening are lower than desired, especially in socioeconomically disadvantaged groups.

PATIENTS: Adults 50–75 years old due for CRC screening

INTERVENTION: Information included with either money or lottery

CONTROL: No antihypertensive treatment

OUTCOME: CRC screening

Secondary Outcomes: FIT screening

METHODS (BRIEF DESCRIPTION):

- 10,000 Kaiser Permanente patients enrolled across multiple centers in Washington. They were randomly selected from 34,000 who met inclusion criteria (had no history of CRC, colectomy, or inflammatory bowel disease and no screening in last 9 years).
- Patients were enrolled after returning an initial questionnaire including consent to participate and confirmed eligibility criteria.
- 898 eligible adults returned their surveys and were randomized into three arms.
- All participants received three mailings:
  - First, information on screening and benefits
  - Second, received FIT kit with instructions
  - Third, if not returned within 3 weeks received a reminder
- Additionally, one group was told they would receive a guaranteed incentive of $10 cash if they completed FIT or other screening.
- Additionally, another group was given a probabilistic incentive of being entered into a lottery for $50 with a 1 in 10 chance of winning.
- Completion of screening was then tracked for six months.
- Data was sufficient to provide 80% power to detect 11% difference between the three arms.
- Models to analyze data included generalized linear and logistic regression. Secondary post hoc analysis also looked for modifiers related to patient characteristics such as race or financial status to evaluate possible modifiers.

INTERVENTION (# IN THE GROUP):

- Information and money: 248
- Information and lottery: 239

COMPARISON (# IN THE GROUP):

- Information alone: 259

FOLLOW UP PERIOD: Six months

RESULTS:

Primary Outcome –

- There was no difference in CRC screening completion between the groups (*P*=.11).
  - Information and money 72%
  - Information and lottery 77%
  - Information alone 75%

Secondary Outcome –

- The information and money group was more likely to complete FIT screening than the information only group (difference 7.7%; 95% CI, 0.3–15).

LIMITATIONS:

- Limited Generalizability:
  - Population was limited to those in Washington and specifically at Kaiser, limiting ability to generalize cultural factors in response to incentives.
  - Only patients who responded to initial survey were included in the study, leaving out people who may be less motivated to complete tasks.
- Patients may have chosen FIT to return over colonoscopy due to ease of completion to receive incentive.
- Questionnaire also included $2 thus possibly attracting those who are already responsive to an incentive.

- Study may be underpowered, sample size of less than 900.

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Consult or Not for OMT in Hospitalized Patients?

Osteopathic Manipulative Medicine Consultations for Hospitalized Patients

Levy VJ, Holt CT, Haskins AE. Osteopathic Manipulative Medicine Consultations for Hospitalized Patients. *J Am Osteopath Assoc.* 2019; 119(5):299–306. doi:10.7556/jaoa.2019.051

KEY TAKEAWAY: For inpatient OMT consultations, musculoskeletal complaints are the most common reasons.
STUDY DESIGN: Retrospective chart review
LEVEL OF EVIDENCE: STEP 4 (downgraded due to lack of statistical analysis)

BRIEF BACKGROUND INFORMATION: Osteopathic manipulative treatment benefits individuals with various conditions, including both musculoskeletal and visceral disease states. Consultations for specific disease processes are more likely to be consulted than others. Through examination of one academic center with a designated osteopathic consultation department, consultations were documented and categorized.

PATIENTS: Hospitalized Patients
INTERVENTION: Reasons for OMT consultation
CONTROL: Not applicable
OUTCOME: Most common reasons for OMT consultation

METHODS (BRIEF DESCRIPTION):

- Retrospective review at an academic medical center
- Review of OMT consultations for hospitalized patients within a six-month period and the reason for the consultation.
- Categories of consultation
  - Musculoskeletal: Pain and related issues to the musculoskeletal system
  - Newborn consultations: Patients less than 1 year old
  - Other non-musculoskeletal: Complaints not directly related to musculoskeletal concern

INTERVENTION (# IN THE GROUP): 1,310
COMPARISON (# IN THE GROUP): Not Applicable

FOLLOW UP PERIOD: Not applicable

RESULTS:

- Most consultations were given for musculoskeletal complaints, with newborn feed problems being the second most common reason.
  - Musculoskeletal complaints (47%)
    - Back pain (18%)
    - Neck pain (5%)
    - Headache (4%)
  - Newborn consultations (32%)
    - Newborn feeding difficulty (27%)
    - Other consultation of newborn (5%)
  - Other non-musculoskeletal complaints (21%)
    - Generalized nonspecific (7%)
    - Respiratory (4%)
    - Post operative (16%)
    - Postpartum (9.5%)
    - Cystic fibrosis (4.4%)
    - Constipation (1.6%)

LIMITATIONS:

- This was a descriptive study only.
- Newborn consultations were calculated as less than one year old instead of less than 1 month old.
- No review of treatment outcomes.
- No statistical analysis performed on outcomes.

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