GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of December 23- 27, 2024

SPOTLIGHT:

Can Exercise Reduce the Severity of Postpartum Depression?

- Medical Marijuana Use for Parkinson's, Epilepsy, and Other Common Illness
- Optimizing Hormonal Therapy for Insomnia in Menopausal Women
- Bariatric Surgery Leads to Superior Diabetes Control
- To "Z" or Not to "Z": Ezetimibe as a Workaround to High-Intensity Statin Therapy
- Pelvic Floor Therapy in Men with Benign Prostate Hyperplasia
- A Sharp New Point: Acupuncture is a Successful Therapy for TMD
- Does Phentermine/Topiramate Help Adolescent Patients with Weight Loss?
- Untold Struggles: Exploring the Trauma of Parents with Cancer-Diagnosed Children

Can Exercise Reduce the Severity of Postpartum Depression?

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

The Impact of Physical Activity Intervention on Perinatal Depression: A Systematic Review and Meta-Analysis

He L, Soh KL, Huang F, et al. The impact of physical activity intervention on perinatal depression: A systematic review and meta-analysis. *J Affect Disord*. 2023;321:304-319. doi:10.1016/j.jad.2022.10.026

KEY TAKEAWAY: Physical exercise in pregnant women may reduce the severity of postpartum depression (PPD).

STUDY DESIGN: Meta-analysis of 35 randomized controlled trials (RCTs) (N=5,084)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: PPD affects anywhere from 5–25% of mothers. PPD has been associated with poor mother-baby bonding and decreased breastfeeding. Finding additional methods of treatment could potentially improve these outcomes.

PATIENTS: Perinatal women

INTERVENTION: Perinatal physical activity regimen

CONTROL: Standard perinatal care

PRIMARY OUTCOME: Depression severity

METHODS (BRIEF DESCRIPTION):

- A literature search using PubMed, Embase, Cochrane Library, and Web of Science was conducted.
- The search ranged from database inception to September 28, 2021, which included a comprehensive literature review of RCTs.
- Studies with perinatal women of any age, race, or nationality published in English were included in the review.
  - Age: 18–39 years old
  - Race: Not reported
  - Nationality: United States 22%, Spain and China 17%, Australia 11%, UK 5%
- Studies excluded were those involving animals or in vitro subjects, as well as any non-RCT studies.
- Treatment interventions were defined by low, moderate, and high-intensity exercise as defined by 1.6–2.9 metabolic equivalents (METS), 3.0–5.9 METS, and ≥6 METS, respectively.
  - Low-intensity exercises include yoga, tai chi, and group walking.
  - Moderate-intensity exercises include aerobic, strength, and walking activities.
  - High-intensity exercises include aerobic exercise classes, endurance, and strength training.
- Depression severity was measured using the Edinburgh Postnatal Depression Scale (EPDS). Scores range from 0–40 with higher scores indicating a higher level of depression.

INTERVENTION (# IN THE GROUP): 2,517

COMPARISON (# IN THE GROUP): 2,567

FOLLOW-UP PERIOD: 6–12 weeks (33 RCTs), six months (2 RCTs)

RESULTS:

Primary Outcome –

- Physical activity significantly reduced postpartum depression compared to no physical activity (8 trials; weighted mean difference [WMD] –3.4; 95% CI, –5.2 to –1.6).
- Subgroup analysis of these trials showed that both low and moderate activity reduced postpartum depression compared to no physical activity.
  - Low intensity (WMD –2.5; 95% CI, –4.4 to –0.64)
  - Moderate intensity (WMD –4.6; 95% CI, –8.3 to –0.90)
- Postpartum depression decreased regardless of the duration of physical activity compared to no physical activity.
  - <12 weeks (WMD –5.3; 95% CI, –6.3 to –4.2)
  - ≥12 weeks (WMD –2.8; 95% CI, –4.5 to –1.1)

LIMITATIONS:

- The heterogeneity of physical activity types used in the intervention group may introduce variability in outcomes and reduce the ability to draw specific conclusions about the intervention's effectiveness.

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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.

Medical Marijuana Use for Parkinson's, Epilepsy, and Other Common Illness

Medical Cannabinoids: A Pharmacology-Based Systematic Review and Meta-Analysis for all Relevant Medical Indications

Bilbao A, Spanagel R. Medical cannabinoids: a pharmacology-based systematic review and meta-analysis for all relevant medical indications. *BMC Med*. 2022;20(1):259. Published 2022 Aug 19. doi:10.1186/s12916-022-02459-1

KEY TAKEAWAY: Medical cannabinoids appear to be helpful in the treatment of epilepsy and Parkinson's. They may be useful in treating chronic pain, spasticity, Tourette's, sleep, and substance use disorders (SUDs).

STUDY DESIGN: Meta-analysis of 152 randomized controlled trials (RCTs) (N=12,123)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Medial cannabinoids differ in their pharmacologic action. Previous similar meta-analyses have not differentiated treatment efficacy among specific cannabinoid agents. This meta-analysis aimed to examine the efficacy of individual cannabinoids in treating specific medical conditions.

PATIENTS: Patients with a medical condition

INTERVENTION: Medical cannabinoids

CONTROL: Placebo

PRIMARY OUTCOME: Chronic pain, spasticity, nausea and vomiting, appetite, amyotrophic lateral sclerosis (ALS), irritable bowel syndrome (IBS), multiple sclerosis (MS), Huntington's chorea, epilepsy, dystonia, Parkinsonism, glaucoma, attention deficit hyperactivity disorder (ADHD), anorexia nervosa, anxiety, dementia, depression, schizophrenia, post-traumatic stress disorder (PTSD), sleeping disorders, SUD, Tourette's

Secondary Outcome: Retention, adverse events

METHODS (BRIEF DESCRIPTION):

- Studies included randomized controlled parallel and cross-over trials with allocation concealment that was single or double-blinded.
- Participants included people of any age or sex with chronic pain, spasticity, nausea and vomiting, appetite loss, ALS, IBS, MS, Huntington's chorea, epilepsy, dystonia, Parkinsonism, glaucoma, ADHD, anorexia nervosa, anxiety, dementia, depression, schizophrenia, PTSD, sleeping disorders, SUD and Tourette.
- All patients were treated with a medical cannabinoid either dronabinol, nabilone, cannabidiol, nabiximol, or placebo.
- Outcomes measured were "patient-important and disease-specific " however, detail regarding these was not provided.
    - Evidence quality was assessed using Cochrane Risk of Bias and GRADE tools.
    - Analyses were conducted with the Review Manager (RevMan).
    - Retention and adverse events were calculated as odds ratios.
    - Effects were calculated using standardized mean difference.
- Analyses were stratified by outcome and subgrouped by cannabinoid type and comparator.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: 2–14 weeks

RESULTS:

Primary Outcome –

- Medical cannabinoids reduced the frequency of seizures in patients with epilepsy compared to placebo or active comparators (6 trials, n=956; standardized mean difference [SMD] –0.5; 95% CI, –0.62 to –0.38; I^2=0%).
- Cannabinoid use resulted in a significant reduction in Parkinson's symptoms compared to placebo (3 trials, n=101; SMD –0.41; 95% CI, –0.75 to –0.08).
- Dronabinol use was associated with a significant improvement in conditions causing chronic pain compared to placebo (15 trials, n=1,528; SMD –0.13; 95% CI, –0.46 to –0.15).
- Dronabinol use was associated with a stimulating effect on appetite compared to placebo (10 trials, n=599; SMD –0.50; 95% CI, –0.87 to –0.15).
- Dronabinol was associated with improvement in Tourette's symptoms compared to placebo (2 trials, n=41; SMD –1.01; 95% CI, –1.6 to –0.44).
- Nabiximol use was associated with a significant improvement in conditions causing chronic pain

compared to placebo (32 trials, n=3,238; SMD –0.25; 95% CI, –0.37 to –0.14).

- Nabiximol use was associated with improvements when treating spasticity compared to placebo (14 trials, n=1,658; SMD –0.36; 95% CI, –0.54 to –0.19).
- Nabiximol use was associated with improved sleep scores compared to placebo (23 trials, n=3,659; SMD –0.24; 95% CI, –0.35 to –0.14).
- Nabiximol was beneficial in the treatment of SUD (4 trials, n=237; SMD –0.48; 95% CI, –0.92 to –0.04).

Secondary Outcome –

- Cannabidiol, dronabinol, and nabilone did not result in different retention rates compared to placebo.
- Cannabidiol had more adverse events than placebo (22 trials, n=1,736; odds ratio [OR] 1.8; 95% CI, 1.1–3.1; I^2=58%).
- Dronabinol had more adverse events compared to placebo (37 trials, n=707; OR 2.2; 95% CI, 1.6–2.9; I^2=56%).
- Nabilone had more adverse events compared to placebo (16 studies, n=996; OR 3.1; 95% CI, 1.5–6.4; I^2=76%).
- There was no significant evidence for the treatment of nausea, vomiting, appetite, ALS, IBS, MS, Huntington's chorea, dystonia, glaucoma, ADHD, anorexia nervosa, anxiety, dementia, depression, schizophrenia, and PTSD with medical cannabinoids.

LIMITATIONS:

- 23 of the 153 studies had a small patient population of <20 patients.
- Many study types were excluded that could be of value.
- Sex, age, and nationality data were not available for individual studies
- Lack of clarity on how the "patient-important and disease-specific " outcomes were measured in each study.

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Optimizing Hormonal Therapy for Insomnia in Menopausal Women

Different Regimens of Menopausal Hormone Therapy for Improving Sleep Quality: A Systematic Review and Meta-Analysis

Pan Z, Wen S, Qiao X, Yang M, Shen X, Xu L. Different regimens of menopausal hormone therapy for improving sleep quality: a systematic review and meta-analysis. *Menopause*. 2022;29(5):627-635. Published 2022 May 1. doi:10.1097/GME.0000000000001945

KEY TAKEAWAY: Top-dose and mid-dose phentermine/topiramate (PHEN/TPM) are effective in reducing body mass index (BMI) in adolescent patients with obesity.

STUDY DESIGN: Meta-analysis and systematic review of 15 randomized controlled trials (N=27,715)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: During menopause, women experience significant hormonal changes, including a decline in estrogen and progesterone levels. Along with vasomotor symptoms, such as hot flashes, insomnia is frequently reported and can greatly affect quality of life. While hormone replacement therapy is a standard treatment for menopausal symptoms, the optimal hormonal formulations for improving sleep quality remain unclear. This review analyzed the current literature to understand the association between HT and sleep disturbance.

PATIENTS: Menopausal and postmenopausal adult women with insomnia

INTERVENTION: Oral and transdermal estrogen and progesterone

CONTROL: Placebo treatment

PRIMARY OUTCOME: Sleep quality and sleep parameters Secondary Outcome: Sleep quality comparing different formulations of estrogen, sleep quality with estrogen alone compared to estrogen and progesterone, sleep quality with estrogen comparing different formulations of progesterone

METHODS (BRIEF DESCRIPTION):

- Meta-analysis and systematic review of randomized controlled trials comparing hormone therapy (estrogen and/or progesterone) to placebo.
- Women ≥18 years old with menopause were included in the review.
- The included studies used a variety of hormone formulations and preparations.
- Estrogen formulations:
  - Oral conjugated equine estrogen 0.625 mg
  - Oral estrogen valerate 1–2 mg
  - Oral estradiol 2 mg
  - Transdermal estradiol 1 mg
  - Estrogel 2.5 mg
  - Transdermal estrogen 50 μg
  - Oral 17β-estradiol 0.5 mg
  - Transdermal 17β-estradiol 0.045–0.05 mg
- Progesterone formulations:
  - Oral micronized progesterone 10–200 mg
  - Oral medroxyprogesterone acetate 2.5–5 mg
  - Oral dydrogesterone 100 mg
  - Oral dienogest 3 mg
  - Transdermal levonorgestrel 0.015–0.040 mg
  - Oral trimegestone 0.13 mg
- Combined formulations:
  - Oral norethisterone 0.7 mg
  - Oral norethindrone acetate 0.5 mg
  - Oral tibolone 2.5 mg
- The primary outcome was a change in self-reported sleep quality questionnaire scores and objective improvement of sleep parameters using polysomnography to assess changes in sleep time, sleep latency, sleep efficiency, and arousal number.
  - Five trials used polysomnography.
  - 12 trials used a variety of subjective sleep questionnaires.

INTERVENTION (# IN THE GROUP): 14,058

COMPARISON (# IN THE GROUP): 13,657

FOLLOW-UP PERIOD: Four weeks to 48 months

RESULTS:

Primary Outcome –

- HT did not improve sleep time measured by polysomnography compared to placebo (3 trials, N=142; standardized mean difference [SMD] –0.14; 95% CI, –0.48 to 0.20; I^2=10%).
- HT did not improve sleep latency measured by polysomnography compared to placebo (3 trials, N=126; SMD –0.22; 95% CI, –0.57 to 0.13; I^2=0%).

- HT did not improve sleep efficiency measured by polysomnography compared to placebo (5 trials, N=187; SMD –0.09; 95% CI, –0.39 to 0.2; I^2=0%).
- HT did not improve sleep arousal measured by polysomnography compared to placebo (3 trials, N=126; SMD –0.07; 95% CI, –0.42 to 0.28; I^2=0%).
- HT improved self-reported sleep quality compared to placebo (12 trials, N=27,608; SMD –0.13; 95% CI, –0.18 to –0.08; I^2=41%).

Secondary Outcome –

- 17β-estradiol improved self-reported sleep quality compared to placebo (3 trials, N=577; SMD –0.24; 95% CI, –0.51 to –0.17; I^2=0%).
- Conjugated equine estrogen improved self-reported sleep quality compared to placebo (4 trials, N=26,653; SMD –0.10; 95% CI, –0.12 to –0.07; I^2=0%).
- Estrogen with progesterone improved self-reported sleep quality compared to placebo (6 trials, N=17,804; SMD –0.10; 95% CI, –0.13 to –0.07; I^2=0%).
- Estrogen with micronized progesterone improved self-reported sleep quality compared to placebo (2 trials, N=670; SMD –0.22; 95% CI, –0.37 to –0.06; I^2=0%).
- Estrogen and medroxyprogesterone acetate improved self-reported sleep quality compared to placebo (2 trials, N=17,079; SMD –0.10; 95% CI, –0.13 to –0.07; I^2=0%).
- Estrogen therapy alone, estradiol valerate, and estrogen with dienogest or norethisterone did not improve self-reported sleep quality compared to placebo.

LIMITATIONS:

- Moderate heterogeneity was present between the included studies.
- Significant variability of utilized sleep questionnaires between included studies.
- Included studies carry the risk of attrition and publication bias with some studies being funded by the pharmaceutical industry.
- No dose-response data for the use of 17β-estradiol or micronized progesterone was calculated.
- The included studies cannot differentiate between improved sleep quality due to indirect reduction of vasomotor symptoms and therefore improved insomnia.
- Unknown optimal duration of therapy for improvement of insomnia.

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Bariatric Surgery Leads to Superior Diabetes Control

Long-Term Outcomes of Medical Management vs Bariatric Surgery in Type 2 Diabetes

Courcoulas AP, Patti ME, Hu B, et al. Long-Term Outcomes of Medical Management vs Bariatric Surgery in Type 2 Diabetes. *JAMA*. 2024;331(8):654-664. doi:10.1001/jama.2024.0318

KEY TAKEAWAY: Patients who undergo bariatric surgery have a more effective and longer-term improvement in their glycemic control compared to medical/lifestyle management of type 2 diabetes mellitus (T2DM).

STUDY DESIGN: Pooled analysis of four randomized clinical trials (RCTs)

LEVEL OF EVIDENCE: STEP 2 (downgraded due to small sample size and bias)

BRIEF BACKGROUND INFORMATION: Diabetes management is expensive. Smaller clinical trials indicate that bariatric surgery is superior to medical and lifestyle therapies for the treatment of T2DM. Medication alternatives are costly and do not have proven long-term efficacy. This study represents the largest pooled analysis to determine the efficacy, durability, and safety of bariatric surgery compared to lifestyle treatment for T2DM.

PATIENTS: Adults 18–65 years old

INTERVENTION: Bariatric surgery

CONTROL: Medical/lifestyle management

PRIMARY OUTCOME: Change in hemoglobin A1C (HbA1c)

Secondary Outcome: Diabetes remission, use of medications for diabetes, HbA1c <7%

METHODS (BRIEF DESCRIPTION):

- Randomized trials were conducted from May 1, 2007, to August 30, 2013 in the US.
- Individuals were included in the study if they had T2DM diabetes and a BMI of 27–45 kg/m^2.
  - 68% of the study participants were women, 31% were Black, and 67% were White.
- Patients were randomized into either bariatric surgery or medical/lifestyle management of T2DM.
  - Bariatric surgery included Roux-en-Y gastric bypass (106), sleeve gastrectomy (49), and adjustable gastric banding (38).
  - Medical/lifestyle management varied between studies, but all were based on the Diabetes Prevention Program and Look AHEAD interventions.
- The primary outcome measured the between-group difference of the percent change in HbA1c using a linear mixed-effect model, which included group (medical/lifestyle vs surgery), visit, their interaction, site, and baseline HbA1c as fixed effects.
- The secondary outcomes include diabetes remission, HbA1c <7%, and the use of diabetes medication.
  - Diabetes remission was defined as HbA1c <6.5% without diabetes medication for at least three months, as assessed annually.
  - HbA1c <7%
  - The use of diabetes medication was defined as any use of oral GLP-1 only or insulin and/or oral GLP-1 use.

INTERVENTION (# IN THE GROUP): 166

COMPARISON (# IN THE GROUP): 96

FOLLOW-UP PERIOD: Seven and 12 years

RESULTS:

Primary Outcome –

- Bariatric surgery decreased HbA1c, compared to medical/lifestyle management at seven years (between-group difference –1.4%; 95% CI, –1.8 to –1.0).
- Bariatric surgery decreased HbA1c compared to medical/lifestyle management at 12 years (between-group difference –1.1%; 95% CI, –1.7 to –0.5).

Secondary Outcome –

- Bariatric surgery increased the rate of remission compared to medical/lifestyle management at seven years (between-group difference odds ratio [OR] 3.4; 95% CI, 1.3–9.2).
- Bariatric surgery increased the rate of remission compared to medical/lifestyle management at 12 years (13% vs 0.0%, respectively; *P*<.001)
- Bariatric surgery decreased the use of medications for diabetes compared to the medical/lifestyle group at seven years (between-group difference OR 0.09; 95% CI, 0.03–0.24).

- Bariatric surgery decreased the use of medications for diabetes compared to the medical/lifestyle group at 12 years (between-group difference OR 0.45; 95% CI, 0.15–1.4).
- Bariatric surgery had a higher percentage of HbA1c <7% compared to the medical/lifestyle group at seven years (between-group difference OR 3.2; 95% CI, 1.8–5.9).
- Bariatric surgery had a higher percentage of HbA1c <7% compared to the medical/lifestyle group at 12 years (between-group difference OR 2.9; 95% CI, 1.2–7.3).

LIMITATIONS:

- Differences in trial protocols and assessments were observed across the studies.
- The treatments administered were non-identical, leading to potential variability in outcomes.
- The studies utilized varying randomization ratios, which could impact the comparability of results.
- There is a potential bias from the pooled analysis of different studies.
- Selective dropout of participants may have influenced the study outcomes.
- Different enrollment timelines and follow-up lengths were noted, affecting the consistency of data.
- The assumptions made about missing data are untestable, which could undermine the study's conclusions.
- The study lacked the power to detect differences among surgical procedures for primary outcomes.
- Surgical practices evolved during the study period, potentially influencing the results.
- Concurrent changes in medication use were not consistently accounted for.
- The participant population was predominantly female, which may limit the generalizability of the findings.

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To "Z" or Not to "Z": Ezetimibe as a Workaround to High-Intensity Statin Therapy

Long-Term Efficacy and Safety of Moderate-Intensity Statin with Ezetimibe Combination Therapy vs High-Intensity Stain Monotherapy in Patients with Atherosclerotic Cardiovascular Disease (RACING): A Randomized, Open-Label, Non-Inferiority Trial

Kim BK, Hong SJ, Lee YJ, et al. Long-term efficacy and safety of moderate-intensity statin with ezetimibe combination therapy versus high-intensity statin monotherapy in patients with atherosclerotic cardiovascular disease (RACING): a randomized, open-label, non-inferiority trial. *Lancet*. 2022;400(10349):380-390. doi:10.1016/S0140-6736(22)00916-3

KEY TAKEAWAY: Moderate-intensity ezetimibe combination therapy is non-inferior to high-intensity statin monotherapy regarding major cardiovascular (CV) events and low-density lipoprotein (LDL) cholesterol in patients with atherosclerotic cardiovascular disease (ASCVD).

STUDY DESIGN: Multicenter, randomized, open-label clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Combination drug therapies can achieve greater efficacy and reduce the risk of adverse effects compared to monotherapies. Similarly, moderate-intensity statin with ezetimibe combination therapy can lower LDL cholesterol concentrations and reduce adverse effects compared to high-intensity statin monotherapy. However, there has been little evidence to compare long-term outcomes. This study aimed to assess the efficacy of such combination therapy in the reduction of ASCVD.

PATIENTS: Patients with ASCVD

INTERVENTION: Moderate-intensity statin with ezetimibe combination therapy

CONTROL: High-intensity statin monotherapy

PRIMARY OUTCOME: Composite of CV death, major CV event, or non-fatal stroke

Secondary Outcome: LDL cholesterol

METHODS (BRIEF DESCRIPTION):

- Patients with ASCVD requiring high-intensity statin therapy and achieved LDL cholesterol concentrations of <70 mg/dL in South Korea were enrolled in the study.
- Patients were randomly assigned 1:1 to receive either:
  - Combination therapy with rosuvastatin 10 mg and ezetimibe 10 mg
  - Rosuvastatin 20 mg
- Maintenance of the initial dose was strongly recommended, however, up/down-titration of doses in both groups was at the physician's discretion, requiring a detailed report.
- Goal-directed therapy for the control of other various health conditions of the patient was also recommended for both groups.
- Patients were scheduled for follow-up visits at two months and six months and yearly thereafter for up to three years.
- The primary composite endpoint was the occurrence of cardiovascular death, major CV events, or non-fatal stroke within three years.
  - Major events included coronary or peripheral revascularization or hospitalization for CV events.
  - CV death was defined as death due to myocardial infarction (MI), heart failure, stroke, CV procedures, CV hemorrhage, or cases of death for which CV cause cannot be excluded.
- The secondary endpoint was the efficacy of lowering LDL cholesterol levels each year (including ≤70 mg/dL and ≤55 mg/dL).

INTERVENTION (# IN THE GROUP): 1,894

COMPARISON (# IN THE GROUP): 1,886

FOLLOW-UP PERIOD: Three years

RESULTS:

Primary Outcome –

- Moderate-intensity statin with ezetimibe combination therapy was non-inferior to high-intensity monotherapy in the risk of the primary composite outcome (hazard ratio [HR] 0.92; 95% CI, 0.75–1.1).

Secondary Outcome –

- Moderate-intensity statin with ezetimibe combination therapy achieved an equivalent proportion of goal LDL concentrations (HR 0.94; 95% CI, 0.77–1.2).

- Moderate-intensity statin with ezetimibe combination therapy had lower rates of discontinuation or dose reduction compared to high-intensity monotherapy (4.8% vs 8.2%, respectively; *p*<.0001).

LIMITATIONS:

- The study was non-blinded therefore both the physicians and patients were aware of the assigned therapies.
- Lower event rates than anticipated may have allowed a more generous confidence interval with a non-inferiority margin of 2.0%.
- There was a small number of overall events.

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Pelvic Floor Therapy in Men with Benign Prostate Hyperplasia

The Effect of Pelvic Floor Muscle Training in Men with Benign Prostatic Hyperplasia and Overactive Bladder

Hagovska M, Svihra J Sr, Macko L, et al. The effect of pelvic floor muscle training in men with benign prostatic hyperplasia and overactive bladder. *World J Urol*. 2024;42(1):287. Published 2024 May 2. doi:10.1007/s00345-024-04974-7

KEY TAKEAWAY: Pelvic floor therapy along with silodosin decreases symptoms of overactive bladder (OAB) and benign prostatic hyperplasia (BPH).

STUDY DESIGN: Randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Lower urinary tract symptoms (LUTS) affect most older men and can significantly impact their quality of life. These symptoms often occur due to bladder obstruction, mainly prostate obstruction. The mainstay treatment for BPH is usually an alpha-blocker with behavioral management. This study investigated pelvic floor therapy and alpha blockers to decrease the symptom burden.

PATIENTS: Men with LUTS, OAB, and BPH

INTERVENTION: Pelvic floor training with urinary suppression techniques along + silodosin

CONTROL: Silodosin alone

PRIMARY OUTCOME: Improvement of OAB

Secondary Outcome: Improvement of prostate symptoms

METHODS (BRIEF DESCRIPTION):

- Patients >50 years old were included if they had persistent OAB after four weeks of silodosin or symptoms of OAB for >3 months before the first visit.
- Patients were excluded for having a post-void volume of >200 mL, having a urinary tract infection (acute or chronic) or hematuria, oncological diseases of the urinary tract, using anticholinergic or beta mimetics within four weeks of the first visit, having urolithiasis, diabetes mellitus (DM), having had Botox in the last 12 months, or having total daily urine production >2,500 mL.
- All patients were given silodosin 8 mg daily.
- The experimental group was given exercises by a trained physiotherapist for 30 minutes per day, five days per week, for 12 weeks in addition to silodosin.
- The primary outcome was measured through the Patient Perception of Intensity of Urgency Scale (PPIUS) which evaluated the severity of OAB on a scale of 0–4. A score of zero indicates no urinary urgency.
- The secondary outcome was measured using the International Prostate Symptom Score (IPSS) with a scale of 0–35. A low score indicates less severe symptoms.

INTERVENTION (# IN THE GROUP): 72

COMPARISON (# IN THE GROUP): 70

FOLLOW-UP PERIOD: 18 months

RESULTS:

Primary Outcome –

- Silodosin + pelvic floor therapy significantly improved the PPIUS score as well as the quality of life from LUTS compared to silodosin alone (−0.97 ± 0.53 vs 0.24 ± 0.5, p<.001).

Secondary Outcome –

- The combination of silodosin and pelvic floor therapy significantly improved the IPSS score compared to silodosin alone (−4.6 ± 3.0 vs −2.3 ± 3.6, p<.001).

LIMITATIONS:

- The minimum recommended treatment time of pelvic floor therapy was short to produce the desired results.
- The use of noninvasive urodynamic exams produced subjective findings.

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A Sharp New Point: Acupuncture is a Successful Therapy for TMD

Effect of Acupuncture for Temporomandibular Disorders: A Randomized Clinical Trial

Liu L, Chen Q, Lyu T, et al. Effect of acupuncture for temporomandibular disorders: a randomized clinical trial. *QJM*. 2024;117(9):647-656. doi:10.1093/qjmed/hcae094

KEY TAKEAWAY: Acupuncture can alleviate pain caused by temporomandibular joint disorders (TMDs).

STUDY DESIGN: Single blinded, single site, randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: TMD causes discomfort and contributes to an increased mental health burden. Detailed studies of acupuncture's multifactorial benefits are in need of investigation. This study investigated the role of acupuncture in improving pain scores, jaw mobility, and mental health of individuals diagnosed with TMD.

PATIENTS: Adults with TMD

INTERVENTION: Acupuncture

CONTROL: Sham acupuncture

PRIMARY OUTCOME: Change in pain intensity from baseline

Secondary Outcome: ≥30% or ≥50% reduction in pain intensity, chronic pain, enhancement of jaw function, mental health, sleep quality

METHODS (BRIEF DESCRIPTION):

- Adult patients 18–80 years old who had TMD for ≥3 months were included in the study.
- Patients who received therapy for TMD in the previous month, had other medical history, or were pregnant were excluded from the study.
- Participants were randomized 1:1 via computer to the following groups:
  - Acupuncture
  - Sham acupuncture
- All patients received 12 procedures in 30-minute sessions in one month.
- The same acupoints for both intervention and control groups were used and treatments were completed by certified acupuncturists.
- Participants were predominantly female (88% and 90% for the acupuncture group and sham group, respectively).
- All outcome assessments were taken at the beginning of the study, after four weeks, and then four weeks after the last treatment.
- The primary outcome was a change in mean weekly pain from baseline as assessed using the Visual Analog Scale (VAS). Scores range from 0–10, with higher scores indicating worse pain.
- The following were measured as the secondary outcomes of the study:
  - The proportion of patients achieving ≥30% and ≥50% reduction in weekly pain intensity was measured via patient-reported VAS.
  - Chronic pain was assessed using the Graded Chronic Pain Scale (GCPS) and reported as the change from baseline in disability score.
  - Enhancement of jaw function was measured using the Jaw Functional Limitations Scale-20 (JFLS-20).
  - Mental health quality was assessed using the Depression, Anxiety, and Stress Scales (DASS-21).
  - Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI).

INTERVENTION (# IN THE GROUP): 30

COMPARISON (# IN THE GROUP): 30

FOLLOW-UP PERIOD: Four weeks

RESULTS:

Primary Outcome –

- Acupuncture reduced weekly pain intensity more than sham acupuncture at week four (odds ratio [OR] –1.5; 95% CI, –2.3 to –0.65).

Secondary Outcome –

- Acupuncture resulted in a ≥30% reduction in weekly pain intensity compared to sham acupuncture at week four (OR 9.5; 95% CI, 3.0–43).
- Acupuncture resulted in a ≥50% reduction in weekly pain intensity compared to sham acupuncture at week four (OR 5.3; 95% CI, 1.6–21).
- Acupuncture reduced chronic pain compared to sham acupuncture at week four (OR –15; 95% CI, –26 to –3.9).
- Acupuncture reduced overall jaw limitations compared to sham acupuncture at week four (OR –1.3; 95% CI, –1.9 to –0.73).

- Acupuncture reduced overall depression, anxiety, and stress compared to sham acupuncture at week four (OR –3.3; 95% CI, –5.2 to –1.4).
- Acupuncture reduced overall insomnia severity compared to sham acupuncture at week four (OR –2.0; 95% CI, –3.3 to –0.56).

LIMITATIONS:

- The single-site study design limits external validity.
- The study was relatively small with mostly female patients, therefore limiting the generalizability of the study's findings.
- The studied patients' culture trusts in acupuncture, which might not be true of other belief systems.
- Prior experience with acupuncture was not assessed to determine if those in the sham group could recognize it was not true acupuncture.

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Does Phentermine/Topiramate Help Adolescent Patients with Weight Loss?

Phentermine/Topiramate for the Treatment of Adolescent Obesity

Kelly AS, Bensignor MO, Hsia DS, et al. Phentermine/Topiramate for the Treatment of Adolescent Obesity. *NEJM Evid*. 2022;1(6):10.1056/evidoa2200014. doi:10.1056/evidoa2200014

KEY TAKEAWAY: Top-dose and mid-dose phentermine/topiramate (PHEN/TPM) are effective in reducing body mass index (BMI) in adolescent patients with obesity.

STUDY DESIGN: Randomized, single-blind, controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Adolescent obesity medicine is a new emerging field. Many studies have shown that early, aggressive weight loss intervention is key to decreasing cardiovascular mortality and increasing life expectancy in patients who are obese. This study aimed to assess the efficacy and safety of phentermine/topiramate in treating obesity in an adolescent population.

PATIENTS: Adolescents with obesity

INTERVENTION: Phentermine/topiramate

CONTROL: Placebo

PRIMARY OUTCOME: BMI

Secondary Outcome: Triglycerides, high-density lipoprotein cholesterol (HDL-C), waist circumference

METHODS (BRIEF DESCRIPTION):

- Eligible participants were 12–17 years old, with a BMI in the ≥95th percentile for age and sex, a Tanner stage >1, a stable body weight, and a documented history of insufficient weight loss with lifestyle modification.
  - Mean BMI: 38 ± 7.1
- Participants were randomly assigned 1:1:2 to receive oral once daily:
  - Placebo
  - Mid-dose PHEN/TPM 7.5 mg/46 mg
  - Top-dose PHEN/TPM 15 mg/92 mg
- The duration of treatment was 56 weeks.
- The primary outcome was the reduction in BMI, assessed every four weeks.
- Secondary outcomes including triglycerides and HDL-C were measured by lab results at week zero and week 56. Waist circumference was also measured.

INTERVENTION (# IN THE GROUP):

- Top-dose: 113
- Mid-dose: 54

COMPARISON (# IN THE GROUP): 56

FOLLOW-UP PERIOD: 56 weeks

RESULTS:

Primary Outcome –

- Top-dose of PHEN/TPM reduced BMI more than placebo (mean difference [MD] –10%; 95% CI, –14 to –7.0).
- Mid-dose of PHEN/TPN reduced BMI more than placebo (MD –8.1%; 95% CI, –12 to –4.3).

Secondary Outcome –

- PHEN/TPM at both doses reduced waist circumference compared to placebo:
  - Top dose (MD –9.6 cm; 95% CI, –13 to –6.3)
  - Mid-dose (MD –7.7 cm; 95% CI, –11 to –4.0)
- Mid-dose of PHEN/TPN decreased triglycerides compared to placebo (MD –21%; 95% CI, –40 to –2).
- Top-dose of PHEN/TPN decreased triglycerides compared to placebo (MD –21%; 95% CI, –38 to –4).
- Mid-dose of PHEN/TPN increased HDL-C compared to placebo (MD 10%; 95% CI, 3–18).
- Top-dose of PHEN/TPN increased HDL-C increased compared to placebo (MD 9%; 95% CI, 2–15).

LIMITATIONS:

- There were only two different doses of PHEN/TPN studied.

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Untold Struggles: Exploring the Trauma of Parents with Cancer-Diagnosed Children

Suicide Attempt and Death by Suicide Among Parents of Young Individuals with Cancer: A Population-Based Study in Denmark and Sweden

Liu Q, László KD, Wei D, et al. Suicide attempt and death by suicide among parents of young individuals with cancer: A population-based study in Denmark and Sweden. *PLoS Med*. 2024;21(1):e1004322. Published 2024 Jan 16. doi:10.1371/journal.pmed.1004322

KEY TAKEAWAY: Parents of children diagnosed with cancer are not more likely to die by suicide compared to parents of children without cancer, however, they are more likely to attempt suicide, especially in the first few years following diagnosis, if the child is young, the cancer is aggressive, and if the child ultimately passes away.

STUDY DESIGN: Binational cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Previous studies have focused on death by suicide and have not addressed attempted suicide in parents of children diagnosed with cancer. Given the low incidence of suicide in general, small sample sizes have led to low statistical power. Primary care providers need to be aware of the emotional and psychological effects this situation presents to parents. This study sought to enhance provider awareness regarding the suicide risk among parents of children diagnosed with cancer.

PATIENTS: Parents of children diagnosed with cancer

INTERVENTION: Child diagnosed with cancer (exposed)

CONTROL: Child not diagnosed with cancer (unexposed)

PRIMARY OUTCOME: Suicide attempt and death by suicide

METHODS (BRIEF DESCRIPTION):

- Biological parents of all live births were identified from 1973–2016 (N=52,027) in Denmark, according to the Danish Medical Birth Register, and in Sweden from 1973–2014 (N=59,428), according to the Swedish Medical Birth Register.
- Parents with a suicide attempt or a child diagnosed with cancer outside of the study period and parents born before 1932 in Sweden or 1936 in Denmark were excluded from the study.
- The population had a median age of 56 years old and 47% of parents were male.
- The intervention group was comprised of parents whose children have been diagnosed with cancer, rendering them indirect participants exposed to the psychosocial and logistical impacts associated with pediatric cancer.
    - If a parent had multiple children diagnosed with cancer, the date of the first diagnosis was used as index exposure.
- Parents were assigned to the control group by virtue of their child's absence of a cancer diagnosis designating them as the unexposed group
- Cancers were classified as hematologic, central nervous system, and other types of cancer.
- The aggressiveness of cancer was scaled as low, medium, or high depending on the five-year survival rate.
- The primary outcome assessed parental suicide attempts and death by suicide.
    - Suicide attempt (deliberate self-harm) was identified through the Patient Register, the Psychiatric Central Register in Denmark, and the Patient Register in Sweden.
    - Death by suicide was identified through the Danish Causes of Death Register and the Swedish Causes of Death Register.
- The effect of parental and child cancer characteristics was analyzed using hazard ratio and a 95% confidence interval of attempted suicide and death by suicide related to the child cancer.

INTERVENTION (# IN THE GROUP): 106,005

COMPARISON (# IN THE GROUP): 1,060,050

FOLLOW-UP PERIOD:

- Exposed: 7.3 years
- Unexposed: 7.2 years

RESULTS:

Primary Outcome –

- Exposed parents had an increased risk of attempted suicide compared to the unexposed parents soon after a child's diagnosis (hazard ratio [HR] 1.2; 95% CI, 1.03–1.3). Particularly when:
    - Child cancer diagnosis at ≤18 years old (HR 1.3; 95% CI, 1.1–1.5)
    - Child diagnosed with hematologic cancer (HR 1.3; 95% CI, 1.02–1.6)

    - Child diagnosed with a highly aggressive cancer (HR 1.6; 95% CI, 1.1–2.4)
    - Child death from cancer (HR 1.6; 95% CI, 1.3–2.1)
- There was no statistically significant risk for death by suicide in the exposed parents compared to the unexposed parents (results presented via figure).

LIMITATIONS:

- Cancer aggressiveness was not determined by cancer staging but by the cancer type. This could have led to misclassification of cancer aggressiveness.
- There was potential for surveillance bias in parents of children diagnosed with cancer. These parents might have more access to a provider compared to parents of children without a diagnosis of cancer, given that they present to follow-up visits with their children regularly.
- Limited power in assessing death by suicide given low incidence.
- Parents of children with cancer diagnosis who have other children without cancer diagnosis who are full siblings. It is less likely that a parent will attempt or commit suicide, given that the other sibling can be a source of support and a reason not to attempt suicide.

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