Journal Review Grab Bag

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Learning Objectives

- Provide some practice pearls and useful tools for direct patient care
- Review recent journal articles and new evidence in behavioral health relevant to primary care

Article 1: JAMA review: Chronic Pelvic Pain in Women (2021)

Take home points:

- Chronic pelvic pain (CPP) affects 26% of the world's female population
- Accounts to 40 % of laparoscopies and 12% of hysterectomies in the US annually, though the origin is non-gynecologic in 80% of patients.
- Frustrating for patients and clinicians
- Overlap with other pain disorders (fibromyalgia and migraine)
- Overlap with non-pain comorbidities (sleep, mood, cognitive impairment)
- Musculoskeletal dysfunction is found in 50-90% of patients with CPP
- Traumatic experiences and distress have important roles in pain modulation
- Importance of clinician facility with exam and trauma-informed care
- Multidisciplinary teams of pelvic PTs, gynecology providers, primary care and behavioral health specialists are more effective in treatment of CPP than isolated treatment focusing on a specific organ



GLP-1 Agonists and Depression



Article 2: GLP-1 Agonists and Behavioral health

- Do GLP-1s help with alcohol use disorder?
 - Evidence seems to indicate that they do, clinical trials ongoing
 - Mechanism still unclear, but seems tied to GLP-1 receptors in the brain's reward system
 - Study in Sweden 2006-2023, 230,000 pts, 16-64 yo with diagnosed AUD, followed for 9 years
 - Lower risk of AUD hospitalization (Hazard ratio 0.64 vs 0.72).
 Naltrexone was better, but disulfiram and Antabuse performed worse.
 - No excess suicide-related hospitalization
 - Lähteenvuo M et al. Repurposing semaglutide and liraglutide for alcohol use disorder. *JAMA Psychiatry* 2024 Nov 13; [e-pub].https://doi.org/10.1001/jamapsychiatry.2024.3599





Article 3 & 4: GLP-1 Agonists cont

- Do GLP-1 Agonists Cause Severe Depression?
 - Anecdotal evidence has been concerning
 - No premarketing association, BUT
 - Post-marketing events voluntarily reported included more depression in patients with diabetes on semaglutide and liraglutide, BUT
 - Retrospective cohort showed lower risk of SI in patients with diabetes and obesity
 - Biologically plausible by suppressing reward pathway
 - More data
 - 300,000 patients in Sweded and Denmark no association after 1.5 years, but rate of depression or anxiety in the year prior to drug initiation only 1.5%
 - Study using data from one of the placebo-controlled studies of semaglutide showed no worsening of depression or anxiety, BUT pts with history of severe depression, SI or other severe psych disorders were excluded
 - Case-control study using WHO pharmacovigilance database: semaglutide, but not liraglutide was associated with more suicidality reports. This difference disappeared when researchers excluded antidepressant users
- Bottom-line: There does not appear to be a link between use of these medications and depression or suicidality in patients
 WITHOUT mental health diagnoses, but we need more data on patients who carry these diagnoses

Citations: Ueda P et al. GLP-1 receptor agonist use and risk of suicide death. *JAMA Intern Med* 2024 Sep 3; [e-pub]. (https://doi.org/10.1001/jamainternmed.2024.4369)

Wadden TA et al. Psychiatric safety of semaglutide for weight management in people without known major psychopathology: Post hoc analysis of the STEP 1, 2, 3, and 5 trials. *JAMA Intern Med* 2024 Sep 3; [e-pub]. (https://doi.org/10.1001/jamainternmed.2024.4346)

Schoretsanitis G et al. Disproportionality analysis from World Health Organization data on semaglutide, liraglutide, and suicidality. JAMA Netw Open 2024 Aug; 7:e2423385.







Depression Treatments



Article 5: Depression and the microbiome

- Is the gut microbiome associated with depression
 - 49 patients with moderate to severe depression
 - Given commercially available multistrain probiotic for 8 weeks or Placebo
 - Improvement of standardized scales borderline statistical significance, but probiotic recipients were more likely to report "much" or "very much" improvement
 - JAMA *Psychiatry* 2023; 80:842



Article 6: Depression and Exercise

- Does Exercise Improve Symptoms of Depression?
 - Network meta-analysis, 218 trials, 14,000 participants
 - Comparison to active controls (e.g., usual care, stretching, education, social support)
 - The following yielded at least moderate improvement in depression:
 - Walking or jogging
 - Exercise plus SSRIs
 - Yoga
 - Tai chi
 - Qigong
 - Dance
 - More vigorous=generally more effective
 - Optimal exercise varied with age and sex
 - CBT alone as well as aerobic exercise PLUS psychotherapy were both moderately effective
 - SSRIs alone=small effect
- Noetel M et al. Effect of exercise for depression: Systematic review and network meta-analysis of randomised controlled trials. BMJ 2024 Feb 14; 384:e075847. (https://doi.org/10.1136/bmj-2023-075847)
- Bellón JÁ. Exercise for the treatment of depression. BMJ 2024 Feb 14; 384:q320. (https://doi.org/10.1136/bmj.q320)





Article 7: Light therapy for depression

- Is Bright-Light Therapy Effective for Nonseasonal Depression?
 - Meta-analysis of 11 trials
 - Patients on anti-depressant medications
 - Add-on treatment with BLT or placebo (dim red light or negative-ion generator) for 30 minutes
 - BLT had more response (60% vs. 39%) or remission (41% vs. 24%) both within 4 weeks and 4 weeks or longer
 - Menegaz de Almeida A et al. Bright light therapy for nonseasonal depressive disorders: A systematic review and meta-analysis. JAMA Psychiatry 2025 Jan; 82:38. (https://doi.org/10.1001/jamapsychiatry.2024.2871)



Technology and Mental Health



Article 8: Behavioral Activation App

- Can a behavioral activation app help primary care patients with depression?
 - 650 patients, PHQ>9, primary care setting
 - Randomized to use the "Moodivate" app or usual care
 - 1/3 were already in therapy, 80% already on medication
 - At 12 weeks: remission in 30% of Moodivate group and 18% of usual-care group
 - Clinically significant improvement in 50% vs 38%
 - App use declined from 100% to 33% at 12 weeks
 - Dahne J et al. A digital depression treatment program for adults treated in primary care: A randomized clinical trial. JAMA Intern Med 2025 Apr 14; [e-pub]. (https://doi.org/10.1001/jamainternmed.2025.0494)



Article 9: Social media use in adolescence

- Does social media use differ in adolescents with and without mental health difficulties?
 - 3340 adolescents (mean age 15 yo), 16% with mental health conditions
 - Compared to peers without conditions
 - Significantly higher overall social media usage (1 hour more per day average)
 - Lower happiness with their number of online friends
 - Unclear cause and effect, restriction of use may not be helpful, but having teens reflect on use and promoting offline activities that bring joy, connection with friends and ideally include physical activity is a common-sense approach
 - Fassi L et al. Social media use in adolescents with and without mental health conditions. *Nat Hum Behav*2025 May 5; [e-pub]. (https://doi.org/10.1038/s41562-025-02134-4)



Article 10: Screen habits in adolescence

- Are addictive screen habits a mental health risk for adolescents?
 - 4300 US adolescents, mean baseline age 10 yo
 - Annual questionnaires for 4 years about addictive use or social media, mobile phones and video games
 - "compulsive use, difficulty disengaging, distress when not using"
 - Outcomes
 - Increasing addictive use common, social media 31% and mobile phones 25%
 - Youths with high or increasing addictive behaviors had 1.5-2 times higher risk for suicidal behaviors and ideation
 - High video game addictive trajectory=more internalizing symptoms (depression)
 - High social media addictive trajectory=more externalizing behaviors (aggression)
 - Total screen time alone was not associated with SI or mental health outcomes
 - Xiao Y et al. Addictive screen use trajectories and suicidal behaviors, suicidal ideation, and mental health in US youths. *JAMA* 2025 Jun 18; [e-pub]. (https://doi.org/10.1001/jama.2025.7829)



References

- See slides
- Many of the articles included were found through NEJM Journal Watch. This is a great resource for concise updates