GEMs of the Week

Volume 5 - Issue 18

What's in this week's issue?

Week of May 19 - May 23, 2025

SPOTLIGHT:

Start Moving to Stop Drinking!

- Too Much Oxygen for Severe Hypoxemia?
  Consider 162 mg of Aspirin for
- Preeclampsia Prophylaxis for High-Risk Obese Pregnant Patients

Start Moving to Stop Drinking!

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Effectiveness of Exercise Intervention in Improving Physical and Mental Status of Patients with Alcohol Use Disorders: A Systematic Review and Meta-Analysis

Li J, Zhou Z, Gao G, Zang L. Effectiveness of exercise intervention in improving physical and mental status of patients with alcohol use disorders: A systematic review and meta-analysis. *PLoS One*. 2024;19(10):e0311166. Published 2024 Oct 30.
doi:10.1371/journal.pone.0311166

KEY TAKEAWAY: Exercise interventions lasting 30–60 minutes per day over 12 weeks reduce alcohol craving with small to moderate effect sizes and improve physical fitness and mood with medium to large effect sizes in people with alcohol use disorder (AUD).

STUDY DESIGN: Systematic review and meta-analysis of 17 randomized controlled trials (RCTs) (N=1,905)

LEVEL OF EVIDENCE: STEP 2 (downgraded due to lack of blinding in included studies)

BRIEF BACKGROUND INFORMATION: AUD is one of the leading causes of morbidity and mortality worldwide, comprising 5.3% of all deaths in 2016. Low rates of patients seeking medical care for AUD and high rates of relapse contribute to the prevalence of AUD and highlight the need for alternate forms of intervention. Further, AUD affects patients both physically and psychologically, necessitating dynamic treatment modalities for long-term success. This study evaluated the effects of exercise interventions on indicators of alcohol craving, physical fitness, and mood.

PATIENTS: Patients with AUD

INTERVENTION: Exercise intervention

CONTROL: No exercise intervention

PRIMARY OUTCOME: Alcohol craving

Secondary Outcome: Physical and mental status

METHODS (BRIEF DESCRIPTION):

- Studies that met inclusion criteria were RCTs and published in English were included in the review.
- Qualifying patients were those with AUD determined by DSM-5 criteria, patients with AUD treated in the hospital, and/or patients having post-traumatic stress disorder (PTSD) with symptoms of AUD.
- The intervention group underwent a variety of exercise regimens which included aerobic (slow walking, lifestyle physical activity, jogging, swimming), resistance exercise, yoga, combined aerobic and resistance exercise, pilates and yoga, aerobic exercise and basketball.
  - Exercise intensity was comprised of high, medium, and low intensity.
  - Duration: 15–75 minutes per session, with most being 30–60 minutes, for an average of 12 weeks
- Control group patients met the same AUD criteria but received no exercise intervention. Physical
- craving of alcohol was comprised of the number of drinks per day, number of drinks per week, and alcohol craving measured via the standardized Alcohol Use Disorders Identifications Test (AUDIT) scores.
- Physical status was measured via the maximal oxygen uptake (VO2 max) and resting heart rate.
- Mental status was measured using standardized scores for anxiety, depression, and stress levels.
- Investigators used the standardized mean difference (SMD) as the effect size indicator to compare mean differences between intervention and control groups.
  - Small effect: Effect size 0.2 to <0.5
  - Medium effect: Effect size 0.5 to <0.8
  - Large effect: Effect size ≥0.8
- Exercise interventions that lasted up to 12 weeks were compared with those that lasted >12 weeks.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: 3–24 weeks

RESULTS:

Primary Outcome –

- Exercise interventions reduced daily alcohol consumption compared to no exercise (4 trials, n=223; SMD –0.66; 95% CI, –1.0 to –0.29; I2=54%).
- Exercise interventions did not significantly affect weekly alcohol consumption compared to no exercise (4 trials, n=259; SMD –0.14; 95% CI, –0.45 to 0.17; I2=34%).

- Exercise interventions reduced alcohol cravings compared to no exercise (4 trials, n=193; SMD –0.36; 95% CI, –0.62 to –0.10; I2=39%).

Secondary Outcome –

- Exercise interventions improved VO2 max compared to no exercise (4 trials, n=197; SMD 0.41; 95% CI, 0.12–0.70; I2=13%).
- Exercise interventions improved resting heart rate compared to no exercise (2 trials, n=68; SMD –0.86; 95% CI, –1.4 to –0.29; I2=15%).
- Exercise interventions improved anxiety scores compared to no exercise (6 trials, n=312; SMD –0.79; 95% CI, –1.4 to –0.21; I2=84%).
- Exercise interventions improved depression scores compared to no exercise (7 trials, n=422; SMD –0.86; 95% CI, –1.4 to –0.31; I2=87%).
- Exercise interventions improved stress scores compared to no exercise (2 trials, n=119; SMD –2.1; 95% CI, –3.9 to –0.34; I2=93%).

LIMITATIONS:

- Analysis in some studies did not clarify the method of randomization, and only two trials reported blinding.
- Analysis included studies published only in English language, but the status of alcohol addiction varies according to cultural context.
- Inconsistency in the units of measurement of alcohol consumption may have affected comparability across studies.
- There was inconsistency between the studies reporting alcohol consumption in drinks/day (exercise reduced drinks/day) and the studies reporting consumption in drinks/week (exercise did not reduce drinks/week).

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T oo Much Oxygen for Severe Hypoxemia?

Long-Term Oxygen Therapy for 24 or 15 Hours Per Day in Severe Hypoxemia

Ekström M, Andersson A, Papadopoulos S, et al. Long-Term Oxygen Therapy for 24 or 15 Hours per Day in Severe Hypoxemia. *N Engl J Med*. 2024;391(11):977-988. doi:10.1056/NEJMoa2402638

KEY TAKEAWAY: In patients with severe hypoxemia, long term oxygen therapy (LTOT) for 15 hours per day does not affect hospitalization or death from any cause compared to patients on LTOT for 24 hours per day.

STUDY DESIGN: Multicenter, registry-based, randomized control trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: The application of LTOT for patients with severe hypoxemia at rest for the standard 24-hour (continuous) time poses a significant barrier to patients, yet the data supporting this duration of supplemental oxygen is lacking. This study sought to clarify if a shorter duration of daily time for supplemental oxygen might be equally beneficial to patients with severe hypoxemia.

PATIENTS: Adults recommended starting oxygen therapy for severe hypoxemia at rest

INTERVENTION: LTOT for 15 hours per day

CONTROL: LTOT for 24 hours per day

PRIMARY OUTCOME: Composite of hospitalization or death from any cause within one year

Secondary Outcome: Individual components of hospitalization or death from any cause within one yea r

METHODS (BRIEF DESCRIPTION):

- The study included patients ≥18 years old listed in the Swedish National Registry for Respiratory Failure (Swedevox), with severe hypoxemia indicated by:
  - Resting partial pressure of oxygen (PaO2) <55 mmHg
    - PaO2 <60 mmHg on room air if they had signs of heart failure or polycythemia (hematocrit >0.54)
  - Pulse oximetry (SpO2) <88% on room air
- Patients were excluded if they had characteristics such as active smoking status, anticipated repeated contact with fire, inability to safely adhere to LTOT, or lack of Swedevox record.
- Patients were randomly assigned to LTOT for either 24 hours per day (the current standard of care) or 15 hours per day.
- Those receiving oxygen for 15 hours per day were instructed to use oxygen while sleeping during the nighttime and avoid using oxygen for nine hours during the daytime.
- The statistician was blinded to the treatment groups, although neither the trial participants nor the trial staff were blinded.
- Both groups were instructed to adjust the oxygen flow rate to maintain PaO2 >60 mmHg or SpO2 >90%.
- Patients were mailed questionnaires at three and 12 months inquiring about their prescribed and mean daily supplemental oxygen use in hours, breathlessness, fatigue, level of physical activity, health status, overall well-being, cognitive status, and preferred daily duration of therapy (15 or 24 hours).
- Patients were assessed at three- and 12-months regarding hospitalization or death from any cause within one year
- Adverse events related to LTOT, or underlying disease, were not reported because the two prescribed LTOT doses were used in clinical practice.
- Patient outcomes were followed longitudinally for up to 12 months using the following registries:
  - o
  - Swedish National Patient Registry to track hospitalizations
    Swedish Cause of Death Registry to track mortality

INTERVENTION (# IN THE GROUP): 124

COMPARISON (# IN THE GROUP): 117

FOLLOW-UP PERIOD: Up to 12 months

RESULTS:

Primary Outcome –

- LTOT for 15 hours per day did not affect the composite of hospitalization or death at one year compared to LTOT for 24 hours per day (hazard ratio [HR] 0.99; 95% CI, 0.72–1.4).

Secondary Outcome –

- There was no difference in death or hospitalization of any cause, breathlessness, fatigue, health status,

and overall wellbeing in patients who received LTOT for 15 hours or for 24 hours at three or 12 months.

LIMITATIONS:

- The study only included patients with hypoxemia rated as severe, which excludes other situations in which oxygen therapy is prescribed.
- The outcomes were limited to the risk of death or hospitalization within one year and did not evaluate events occurring beyond that time frame.
- Adherence to treatment was self-reported, which may have led to over- or underestimation.
- The trial protocol was amended resulting in fewer enrollees and widening the limit to show non-superiority
- Many patients were excluded from participation, which may limit generalizability.
- Patient-reported outcomes were based on a limited number of responses.
- Adherence in both study groups may have been higher in other settings due to the influence of a national registry and structured follow-up protocols.

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C onsider 162 mg of Aspirin for Preeclampsia Prophylaxis for High-Risk Obese Pregnant Patients

Aspirin 162 mg vs 81 mg for Preeclampsia Prophylaxis in High-Risk Obese Individuals: A Comparative Effectiveness Open-Label Randomized Trial (ASPREO) Amro FH, Blackwell SC, Pedroza C, et al. Aspirin 162 mg vs 81 mg for preeclampsia prophylaxis in high-risk obese individuals: a comparative effectiveness open-label randomized trial (ASPREO). *Am J Obstet Gynecol*. 2025;232(3):315.e1-315.e8. doi:10.1016/j.ajog.2024.06.038

KEY TAKEAWAY: Increasing daily aspirin dose to 162 mg may decrease the rate of preeclampsia (PE) with severe features in obese pregnant patients with high risk factors.

STUDY DESIGN: Randomized controlled trial

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: In the United States, 81 mg of aspirin is prescribed with the intent to help prevent PE in high-risk pregnancies. However, some research has shown that there may be a benefit to increasing the aspirin dose in obese individuals. This study was conducted to determine if 161 mg of aspirin would be more effective in providing prophylaxis against PE with severe features in obese pregnant patients.

PATIENTS: Obese pregnant individuals ≥18 years old

INTERVENTION: 162 mg aspirin

CONTROL: 81 mg aspirin

PRIMARY OUTCOME: PE with severe features, hemolysis elevated liver enzymes low platelet syndrome (HELLP), and eclampsia

Secondary Outcome: Maternal and neonatal outcomes

METHODS (BRIEF DESCRIPTION):

- Pregnant individuals between 12–20 weeks gestation with a BMI ≥30 at time of enrollment and had at least one of three high risk factors including documented stage one hypertension (HTN), pregestational diabetes mellitus (DM) or gestational diabetes mellitus (GDM) prior to 20 weeks gestation, or history of preeclampsia in a prior pregnancy were included in the study.
- Patients with multiple gestation pregnancies, known major fetal anomalies, baseline proteinuria, seizure disorder, already on aspirin for other indications, contraindication to aspirin were excluded from the study.
- Participants were then randomized into either the 162 mg or 81 mg aspirin taken daily until delivery.
- Medication adherence was measured using a Moriksy Medication Adherence Survey which was completed twice throughout the duration of the study.
- The primary outcome assessed the incidence of PE with severe features including eclampsia and HELLP syndrome superimposed PE with severe features.
    - The validity of PE with severe features diagnosis was reviewed and corrected by three blinded maternal fetal medicine specialists using American College of Obstetricians and Gynecologists (ACOG) criteria.
- The secondary maternal outcomes were total PE (severe and non-severe rates), post-partum hemorrhage, abruption, and severe maternal morbidity.
- The secondary neonatal outcomes were gestational age at time of delivery, small for gestational age (SGA), length of neonatal intensive care unit (NICU) stay, intraventricular hemorrhage, necrotizing enterocolitis (NEC), and neonatal death.

INTERVENTION (# IN THE GROUP): 110

COMPARISON (# IN THE GROUP): 110

FOLLOW-UP PERIOD: Until delivery

RESULTS:

Primary Outcome –

- Aspirin 162 mg did not affect the risk of PE with severe features during pregnancy compared to aspirin 81 mg (posterior relative risk [RR] 0.88; 95% credible interval, 0.64–1.2).
    - Bayesian analysis suggests 78% probability in reduction in PE though frequentist analysis could consider the results insignificant.

Secondary Outcome –

- There were no significant differences in maternal outcomes for total PE, post-partum hemorrhage, abruption, and severe maternal morbidity for aspirin 162 mg compared to aspirin 81 mg.
- There was no significant difference in neonatal outcomes for SGA, length of NICU stay,

intraventricular hemorrhage, NEC, and neonatal death for aspirin 162 mg compared to aspirin 81 mg.

LIMITATIONS:

- Neither the clinicians nor the participants were blinded to their aspirin dose.
- The study used Bayesian analysis to interpret results.
- The study had a relatively small sample size.
- Compliance with medication adherence was not objectively measured.

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