GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

Volume 2 - Issue 9

FPIN
Family Physicians Inquiries Network

What's in this week's issue?

Week of February 28 - March 4, 2022

SPOTLIGHT: Antidepressant Discontinuation Linked to Increased Depression Relapse Risk

- Less Screen Time = Less Concussion Recovery Time
- Why Adherence Matters: The Association Between Mortality and Statin Non-Adherence in Patients with Atherosclerotic CVD
- Intrauterine Vacuum for Postpartum Hemorrhage Treatment

Antidepressant Discontinuation Linked to Increased Depression Relapse Risk

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Maintenance or Discontinuation of Antidepressants in Primary Care

Lewis G, Marston L, Duffy L, et al. Maintenance or Discontinuation of Antidepressants in Primary Care. *N Engl J Med.* 2021; 385(14):1257–1267.

KEY TAKEAWAY: Primary care patients on several common antidepressants who feel well enough to discontinue antidepressant use may be at higher risk for depression relapse and worsened depression and anxiety symptoms if antidepressants are tapered and discontinued.

STUDY DESIGN: Multisite, placebo controlled, double-blind RCT

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: There are limited data available to suggest whether primary care patients with depression and long-term antidepressant use are at increased risk for relapse if antidepressants are tapered and discontinued once the patient is feeling better. Prior studies have relied on data from specialist mental health services and/or included patients on short-term antidepressants or less-commonly prescribed medications such as TCAs and with limited sample size. This study specifically targeted primary care patients on commonly prescribed antidepressants for at least two years who felt well enough to discontinue use.

PATIENTS: Adults on an antidepressant with at least two depressive episodes or at least two years of antidepressant use

INTERVENTION: Maintain current antidepressant use

CONTROL: Taper and discontinue antidepressant use in favor of placebo

OUTCOME: First relapse of depression

Secondary Outcomes: Symptoms and adherence

METHODS (BRIEF DESCRIPTION):

- 1,466 patients were screened out of 23,553 invited.
- 478 adult primary care patients at 150 locations in the UK on citalopram, fluoxetine, sertraline, or mirtazapine with history of at least two depressive episodes or at least two-years of antidepressant use who felt well enough to consider stopping antidepressants were enrolled in the study.
- The intervention group was randomly assigned to maintain their current antidepressant use with trial medications.
- The comparison group was randomly assigned to taper over 1–2 months and then discontinue antidepressant use in favor of identical appearing placebo.
- Double blind, computer randomized with minimization to attain 1:1 ratio by site, medication, and baseline depression score.

INTERVENTION (# IN THE GROUP): 238

COMPARISON (# IN THE GROUP): 240

FOLLOW UP PERIOD: 52 weeks

RESULTS:

Primary Outcome –

- The discontinuation group was more likely to have depression relapse than those maintained on their antidepressants (hazard ratio [HR] 2.1; 95% CI, 1.6–2.7; number needed to hurt = 6).

Secondary Outcomes –

- The discontinuation group had more overall symptoms compared to the maintenance group.
  - Overall depression (PHQ-9 score difference 2.2; 95% CI, 1.5–2.8)
  - Anxiety (GAD-7 score difference 2.4; 95% CI, 1.8–3.0)
  - Withdrawal (DESS score difference 1.9; 95% CI, 1.5–2.3)
- The discontinuation group was more likely to stop taking trial medication before the end of the trial compared to the maintenance group (48% vs 30%; HR 2.3; 95% CI, 1.7–3.1).

LIMITATIONS:

- Only four antidepressants were included in the study, which may or may not be generalizable to other medications and medication classes.
- Study population may not resemble typical, primary care patient demographic and lacked ethnic diversity (UK population, 73% women, median age 54 years old; 95% white).
- Selection bias is possible with small percentage of recruited patients enrolling.

David B Welsh, MD
Eastern Maine Medical Center FMRP
Bangor, ME

Less Screen Time = Less Concussion Recovery Time

Effect of Screen Time on Recovery from Concussion: A Randomized Control Trial

Macnow T, Curran T, Tolliday C, et al. Effect of screen time on recovery from concussion: a randomized control trial. *JAMA Pediatrics.* 2021. doi: 10.1001/jamapediatrics.2021.2782

KEY TAKEAWAY: Avoiding screen time during the first 48 hours of an acute concussion recovery may shorten the duration of symptoms.

STUDY DESIGN: Single-center parallel-design randomized clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Each year, approximately 2.5 million people visit the Emergency department (ED) in the US for traumatic brain injuries. The population with the highest incidence of concussion are children and adolescents 10-19 years old. The International Concussion in Sports Group and the CDC recommend a period of complete cognitive and physical rest for the first 24-48 hours after sustaining a concussion followed by a structured return to activity. Despite teenagers engaging in more than seven hours of screen time daily, there are no guidelines or studies that have measured its effect on concussion recovery.

PATIENTS: Pediatric patients and young adults with concussions

INTERVENTION: No screen time use during recovery period

CONTROL: Screen time use during recovery period

OUTCOME: Days to concussion recovery

Secondary Outcomes: Sleep duration, return to work, and return to exercise

METHODS (BRIEF DESCRIPTION):

- The study took place at University of Massachusetts Medical Center ED.
- 125 participants were enrolled.
  - 64 males (51%) and 61 females (49%)
  - Mean age: 17 years old
- Participants completed a survey about demographics, the acute concussion evaluation-emergency department tool, and the Post-Concussive Symptom Scale (PCSS).
- Each participant was randomized into one of the two intervention groups (using a random number list).
  - Control – engaged in screen time (as tolerated) over first 48 hours
  - Intervention – abstained from screen time for first 48 hours
- Intervention group was blinded to both the participant and study staff during the completion of study forms. They were then told which intervention group participants were in.
- Both groups were to avoid work or school for the first 48 hours.
- Participants ranked symptoms using (PCSS) starting on their day of enrollment and ending on day 10.
  - PCSS grades 22 symptoms from 0 (not present) to 6 (severe).
  - PCSS score of 3 or less indicates full recovery.
- Participants completed a daily screen time survey for the first three days after discharge and an activity survey on days 4–10.
- The median amount of sleep, screen time, and work were measured the first three days.

INTERVENTION (# IN THE GROUP): 59

COMPARISON (# IN THE GROUP): 66

FOLLOW UP PERIOD: 10 days

RESULTS:

Primary Outcome –

- Screen time use resulted in longer concussion recovery time compared to no screen time use (8.0 days vs 3.5 days; *P*=.03).

Secondary Outcomes –

- There was no difference in sleep duration, return to work, or return to exercise between the groups.

LIMITATIONS:

- Not generalizable due to small sample size (type II error).
- Wide range of PCSS scores increased risk of type I error.
- Recall bias due to self-reported surveys.

Meghan Wood, DO, MS
Good Samaritan Regional Medical Center FMRP
Corvallis, OR

Why Adherence Matters: The Association Between Mortality and Statin Non-Adherence in Patients with Atherosclerotic CVD

Association of Statin Adherence with Mortality in Patients with Atherosclerotic Cardiovascular Disease

Rodriguez F, Maron DJ, Knowles JW, Virani SS, Lin S, Heidenreich PA. Association of Statin Adherence with Mortality in Patients With Atherosclerotic Cardiovascular Disease. *JAMA Cardiol*. 2019; 4(3):206-213.

KEY TAKEAWAY: Lower levels of suspected statin adherence were associated with a greater risk of dying, especially for those prescribed high intensity statin doses.

STUDY DESIGN: Retrospective cohort analysis of patients treated over a two-year span

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Statins are a recommended treatment for patients with atherosclerotic cardiovascular disease (ASCVD) and promote a survival benefit. However, many patients stop taking their statins shortly after the initial event or do not take them as prescribed. It is important to find ways to improve patient adherence.

PATIENTS: Adults with elevated ASCVD on a statin

INTERVENTION: Medication possession ratio (MPR) levels less than 90% (low adherence)

CONTROL: MPR greater than 90%

OUTCOME: Mortality at one-year follow up, adherence

METHODS (BRIEF DESCRIPTION):

- All patients (N=347,104 after exclusions) treated in the outpatient setting of the VA health system between 18 and 85 years old with ASCVD between 1/1/2013 and 4/1/2014 who were seen at least once in the two years prior to the study period.
- ASCVD was defined based on ICD-9 codes for coronary artery disease, cerebrovascular disease, or peripheral artery disease.
- Excluded patients who had a new prescription, a dose reduction, or increase in intensity.
- Adherence was estimated using MPR (number of days of medication supplied divided by number of days the patient was not hospitalized and alive in a 12-month period).
- Adherence levels were categorized as an MPR of less than 50%, 50–69%, 70–89%, and 90% or greater.

INTERVENTION (# IN THE GROUP):

- MPR <50%: 19,757
- MPR 50–69%: 30,606
- MPR 79–89%: 76,083

COMPARISON (# IN THE GROUP): 220,658

FOLLOW UP PERIOD: One year

RESULTS:

- The absolute risk reduction for one-year mortality moving from the MPR <50% to MPR >90% was 3.1% (8.8%–5.7%; *P*<.001).
  - One-year mortality for:
    - MPR <50%: 8.8%
    - MPR 50–69%: 7.5%
    - MPR 70–89%: 6.3%
    - MPR >90%: 5.7%
- Compared with the most adherent patients, patients with MPR <50% had greatest increase in mortality risk.
  - MPR 90% vs <50%: HR 1.3 (95% CI, 1.2–1.3)
  - MPR 90% vs 50–69%: HR 1.2 (95% CI, 1.1–1.2)
  - MPR 90% vs 70–89%: HR 1.1 (95% CI, 1.0–1.1)
- Patients taking moderate-intensity statin therapy were more adherent than patients taking high-intensity statin therapy (OR 1.2; 95% CI, 1.1–1.2).
- Women were less adherent than men (OR 0.9; 95% CI, 0.8–0.9).

LIMITATIONS:

- This is an observational study so causality cannot be determined; unmeasured confounders could explain the association.
- Hospitalizations may have been missed outside the VA health system.
- Patients may have filled the prescriptions but that does not mean they were taking their medications. The use of MPR could have resulted in an underestimate of the association between lower adherence and mortality.

Tanvir Kahlon, DO
Northern Light Eastern Maine Medical Center FRP
Bangor, ME

Intrauterine Vacuum for Postpartum Hemorrhage Treatment

Intrauterine Vacuum-Induced Hemorrhage-Control Device for Rapid Treatment of Postpartum Hemorrhage

D'Alton ME, Rood KM, Smid MC, et al. Intrauterine Vacuum-Induced Hemorrhage-Control Device for Rapid Treatment of Postpartum Hemorrhage. *Obstet Gynecol*. 2020;136(5):882-891. doi:10.1097/AOG.0000000000004138

KEY TAKEAWAY: Intrauterine vacuum devices are effective at stopping postpartum hemorrhage.

STUDY DESIGN: Multicenter, prospective, observational, single-arm, treatment study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Postpartum hemorrhage is the leading cause of maternal mortality globally. Despite an increasing number of interventions aimed at reducing rates of postpartum hemorrhage, rates of severe maternal morbidity and the number of blood transfusions required have continued to increase. The application of direct pressure and medication are the most frequently used mechanisms to stop hemorrhage, however a vacuum-inducing device has been shown to effectively control bleeding associated with postpartum hemorrhage.

PATIENTS: Women with postpartum hemorrhage

INTERVENTION: Intrauterine vacuum-induced hemorrhage-control device

CONTROL: Not applicable

OUTCOME: Treatment success, adverse events

Secondary Outcomes: Time to control of hemorrhage, necessity and amount of postpartum blood transfusion, device usability

METHODS (BRIEF DESCRIPTION):

- Data was collected from 12 medical centers across the United States from February 2018 to January 2020.
- Women were consented during prenatal visits, upon admission to the hospital, or prior to delivery, while not under undue stress.
- Women were enrolled in the study if they met criteria of postpartum hemorrhage (500–1,000 mL blood loss after vaginal delivery, 1,000–1,500 mL blood loss after cesarean delivery) and bleeding was refractory to uterotonic medication and uterine massage.
- An intrauterine device was placed transvaginally, with wall-mounted vacuum suction applied for a minimum of 60 minutes, or longer until no active bleeding was visualized.
- The device was left in place, without suction, for a minimum of 30 minutes after the cessation of active bleeding.
- Successful treatment was defined as not requiring further intervention to control hemorrhage after device placement.
- The primary safety outcome was the incidence and severity of device related adverse events up to six weeks following treatment.
- Device usability was measured on a Likert Scale.

INTERVENTION (# IN THE GROUP): 106

COMPARISON (# IN THE GROUP): Not applicable

FOLLOW UP PERIOD: 6 weeks

RESULTS:

Primary Outcomes –

- The intrauterine vacuum device was able to successfully control postpartum hemorrhage in 94% of treated patients (100/106; 95% CI, 88–98%).
- No significant device-associated adverse events were reported. Of the reported events, infection was the most common diagnosis. All events were resolved without complicating sequelae at six-week follow up.

Secondary Outcomes –

- Bleeding control was obtained in 82% of participants within 5 minutes of treatment, with a median time of 3 minutes (IQR 2–5).
- Median time of total vacuum treatment was 144 minutes and median device in-dwelling time was 191 minutes.
- A total of 40 participants required blood transfusion (38%).
- Median blood loss during treatment was 110 mL (IQR 75–200).
- Operators reported the device was easy to use (98%) and would recommend this method of postpartum hemorrhage control to others (97%).

LIMITATIONS:

- Single arm study without control or comparison group limits statistical power of outcomes reported.
- Study location was limited to urban academic medical centers, which may limit generalizability to rural and/ community hospitals.
- The device manufacturer provided research

funding for this study.

Joel Manzi, DO & Adam Ross, MD
Cahaba – UAB Family Medicine Residency Program
Birmingham, AL