GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

Volume 1 - Issue 8

What's in this week's issue?

Week of February 22 - 26, 2021

SPOTLIGHT: Approaching Obesity Holistically

- Are GLP-1 Agonists Really Heart-Healthy?
- Resident Work Hour Restrictions
- Peer Mentors vs Usual Care of Type 2 Diabetes in US Veterens
- Too Soon or Too Late? Comparing Adverse Outcomes between Different Interpregnancy Intervals

Approaching Obesity Holistically - Should every Primary Care Clinic Employ a Health Coach?

Weight Loss in Underserved Patients – A Cluster-Randomized Trial

Katzmarzyk PT, Martin CK, Newton RL Jr, et al. Weight Loss in Underserved Patients - A Cluster-Randomized Trial. *N Engl J Med.* 2020; 383(10):909–918.

KEY TAKEAWAY: A high-intensity, lifestyle-based treatment program for obesity delivered via a health coach resulted in significant weight loss at 24 months in an underserved primary care population.

STUDY DESIGN: Cluster-randomized trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Obesity disproportionately impacts minority and underserved populations. Intensive lifestyle modification is recommended by health guidelines for effective weight loss. The impact of an intensive lifestyle modification program on weight loss delivered by embedded health coaches in primary care practices in underserved areas is unknown.

PATIENTS: 803 obese (BMI 30-50) adults, ages 20-75, 67% Black, 65% income < $40K/year

INTERVENTION: Intensive lifestyle modification program for weight loss delivered by health coaches weekly for 6 months, then monthly for 18 months

CONTROL: Usual care from a primary care physician

OUTCOME: Outcomes assessed at baseline, 6, 12, 18, and 24 months. Primary outcome: % change in weight from baseline at 24 months. Secondary outcomes: change in absolute weight (kg) and change in waist circumference (cm). Quality of life measures and adverse events

METHODS (BRIEF DESCRIPTION):

- 18 primary care clinics in Louisiana
- Exclusion criteria: current participation in a weight loss program, use of weight loss medications, history of bariatric surgery, or recent weight loss
- Intervention: Physical activity goal of 175 minutes activity weekly. Nutrition goals of portion control, prepackaged food, and meal replacements shakes for one month, then instruction on purchasing and preparing food. Provided scale for daily weights. Primary care providers attended webinars on obesity management.
- Analysis by intention-to-treat

INTERVENTION (# IN THE GROUP): 452

COMPARISON (# IN THE GROUP): 351

FOLLOW UP PERIOD: 24 months

RESULTS:

Primary outcomes:

- At 24 months, there was a significant change in % body weight in the intervention group (% body weight -4.9; 95% CI, -6.0 to -3.9) compared to the usual care group (% body weight: -0.48; 95% CI, -1.5 to 0.61).
  - Mean between group difference: -4.5%; 95% CI, −5.9 to −3.1
- At 24 months, there was a significant change in absolute body weight in the intervention group (body weight -5.4kg; 95% CI, -6.5 to -4.3) compared to the usual care group (body weight: -0.91kg; 95% CI, -2.0 to 0.24).
  - Mean between group difference: -4.5kg; 95% CI, −6.0 to −3.0
- At 24 months, there was a significant change in waist circumference in the intervention group (waist circumference -4.4cm; 95% CI, -5.4 to -3.4) compared to the usual care group (waist circumference: 0.71cm; 95% CI, -0.35 to 1.7).
  - Mean between group difference: -5.1cm; 95% CI, −6.5 to −3.7

Secondary outcomes:

- Several quality of life measures improved in the intervention group compared with usual care: physical function, anxiety, depression, fatigue, sleep disturbance, social functioning, pain interference and intensity, weight-related quality of life, self-esteem, sexual life, public distress, and work/daily activity
- No difference in adverse events between groups

LIMITATIONS:

- Predominance of women in study (84%)
- Concern for cultural competency of program as less weight loss in Black subjects
- Missing weight measurements on subjects may bias results

Camille Reynolds, DO
Samaritan Health Services – Corvallis Program
Corvallis, OR

Are GLP-1 agonists really heart-healthy?

Glucagon-like peptide-1 receptor agonists and cardiovascular outcomes in patients with and without prior cardiovascular events: An updated meta-analysis and subgroup analysis of randomized controlled trials

Mannucci E, Dicembrini I, Nreu B, Monami M. Glucagon-like peptide-1 receptor agonists and cardiovascular outcomes in patients with and without prior cardiovascular events: An updated meta-analysis and subgroup analysis of randomized controlled trials. *Diabetes Obes Metab*. 2020; 22:203–211.

KEY TAKEAWAY: Treatment with glucagon-like peptide-1 receptor agonists (GLP-1RAs) prevents major adverse cardiovascular events (MACE) in patients with Type 2 Diabetes (T2D).

STUDY DESIGN: Meta-analysis of 7 randomized control trials (RCTs)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: GLP-1RAs significantly decrease Hgb A1c levels and BMI, but a significant cardiac benefit was unknown. T2D increases cardiac-risk, thus medications geared towards cardiac-risk reduction are significant.

PATIENTS: Patients taking GLP-1RAs with T2D

INTERVENTION: GLP-1RAs for > 52 weeks

CONTROL: Placebo or active comparators

OUTCOME: Reduction of MACE

METHODS (BRIEF DESCRIPTION):

- MEDLINE, EMBASE, Cochrane database, and clinicaltrials.gov as well as unpublished trials from the European Medicines Agency and the FDA and previous systemic reviews were searched for RCTs. 1034 total studies were identified. After all exclusion criteria applied, 7 RCTs remained.
- The data was analyzed for MACE and subgroups. Post-hoc sensitivity analysis excluded studies with risk of attrition bias.
- GLP-1RAs used were Lixisenatide, Liraglutide, Semaglutide, Exenatide LAR, Albiglutide, Dulaglutide, and Oral Semaglutide. Duration of trial (1.3–5.4 years), number of patients (3,183–14,752), age (60.3–66.2 years old), sex (30.5–46.4% female), and patients with ASCVD (20.6–100%). The Dulaglutide trial had only 20.6% of patients with ASCVD, the remaining RCTs had >72.5%.

INTERVENTION (# IN THE GROUP): T2D taking a GLP-1RA: 56,004 = total number of patients (unable to determine n in each group from the article)

COMPARISON (# IN THE GROUP): T2D taking a placebo or active comparator: 56,004 = total number of patients (unable to determine n in each group from the article

FOLLOW UP PERIOD: 1.3 – 5.4 years

RESULTS:

- Primary Outcome: 2937 MACE events in GLP-1RA group vs 3309 events in placebo group; (OR 0.87; 95% CI, 0.81–0.93)
- Secondary Outcome:
  - Reduced All-Cause Mortality: 1928 in GLP-1RA vs 2144 in comparator groups; (OR 0.90; 95% CI, 0.82–0.98)
  - Reduced MACE in Atherosclerotic Disease Diabetic Patients: 2363 in GLP-1RA vs 2689 in comparator groups; (OR 0.86; 95% CI, 0.80–0.92)

LIMITATIONS:

- Limited trials for comparison of short-acting GLP-1RAs and exendin-like molecules.
- The use of other diabetes medications in both control & intervention groups within the studies could have led to inaccurate results as other diabetes medications have known cardiovascular benefits.
- The RCTs were performed on high-risk patients, which limits the universal application of results.

Meha Halari, MD
Hackensack Meridian/Ocean Medical Center Program
Brick, NJ

Resident Work Hour Restrictions: Is Less Actually More?

Effect on Patient Safety of a Resident Physician Schedule without 24-Hour Shifts

Landrigan CP, Rahman SA, Sullivan JP, et al. Effect on Patient Safety of a Resident Physician Schedule without 24-Hour Shifts. *N Engl J Med*. 2020; 382(26):2514–2523.

KEY TAKEAWAY: Residents assigned to schedules with extended (24 hour) shifts made more serious medical errors than residents assigned to schedules without extended shifts.

STUDY DESIGN: Multicenter, cluster-randomized, crossover trial

LEVEL OF EVIDENCE: STEP 2 (well-designed RCT)

BRIEF BACKGROUND INFORMATION: Policies which limit resident physician work hours are intended to decrease medical errors, as sleep-deprivation is known to diminish resident alertness and performance. Studies of the true impact of widespread policy implementation on patient safety have produced mixed results.

PATIENTS: PGY-2 and PGY-3 resident physicians working in the pediatric intensive care unit (PICU)

INTERVENTION: Modified resident work schedule without extended (≥24 hours) shifts

CONTROL: Usual resident work schedule (extended shift every fourth or fifth night)

OUTCOME: Rates of adverse events and medical errors per 1000 adjusted patient-days

METHODS (BRIEF DESCRIPTION):

- Residents in their second or greater year of training and working in one of 6 pediatric ICUs were eligible to participate.
- ICUs were paired; one was randomly allocated a modified resident work schedule to eliminate extended (≥24 hours) shifts.
- The other ICU maintained the usual resident work schedule which included an extended shift every fourth or fifth night.
- Adverse events and errors were collected by a team of nurse chart reviewers and physician observers, as well as reports from clinical staff members. These were classified into type of error or adverse event by two blinded, trained physicians.
- Rates were analyzed as number of errors or adverse events per 1000 adjusted patient-days.

INTERVENTION (# IN THE GROUP): 20,072 patient-days of observation, representing 3,591 admissions

COMPARISON (# IN THE GROUP): 18,749 patient-days of observation, representing 3,508 admissions

FOLLOW UP PERIOD: Observations were carried out across two years at each site

RESULTS: Residents in the modified work schedule, compared to those in the usual schedule:

- Made significantly more serious medical errors (97.1 vs. 79.0 per 1,000 patient-days at risk)
- Adjusted relative risk 1.53 (95% CI 1.37–1.72, P<0.001)
- Were assigned a greater number of patients (8.8±2.8 vs. 6.7±2.2)
- Worked less hours per week (mean; 61.9±4.8 vs. 68.4±7.4)
- Gained more hours of sleep per week (mean; 52.9±6.0 vs. 49.1±5.8)
- Had fewer 24-hour intervals with less than 4 hours of sleep (9% vs. 24%)

LIMITATIONS:

- Results varied substantially across the six ICU sites and these variations could not be explained.
- Increases in resident workload due to the intervention may have confounded results.
- Data collectors were aware of resident work schedules.
- Findings may not be generalizable to other training environments.

Carl Bryce, MD, FAAFP
Abrazo Health Network Program
Phoenix, AZ

Peer Mentors vs Usual Care of Type 2 Diabetes in US Veterans

Effect of Peer Mentors in Diabetes Self-management vs Usual Care on Outcomes in US Veterans with Type 2 Diabetes

Long JA, et al. Effect of Peer Mentors in Diabetes Self-management vs Usual Care on Outcomes in US Veterans with Type 2 Diabetes: A Randomized Clinical Trial. *JAMA Netw Open*. 2020; 3(9):e2016369.

KEY TAKEAWAY: Peer mentorship did not improve 6 or 12 month HbA1c levels in US veterans with type 2 diabetes.

STUDY DESIGN: Randomized clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Diabetes not only significantly increases disease-related deaths, it also lowers quality of life and increases medical expenses. Peer mentoring is a low-cost intervention for improving glycemic control in patients with diabetes. Long-term outcomes of peer mentoring for glycemic control are unknown.

PATIENTS: 356 US veterans with type 2 diabetes aged 30 to 75 years with HbA1c greater than 8%

INTERVENTION: Mentors who received an initial training session and monthly reinforcement training were assigned 1 mentee and given $20 for each month they contacted their mentee at least weekly

CONTROL: Usual diabetic care without mentors

OUTCOME: Primary outcome: change in HbA1c level at 6 and 12 months

Secondary outcomes: changes in low-density lipoprotein (LDL), systolic and diastolic blood pressure (BP), diabetes quality of life (measured by the Diabetes Distress Scale), and depression symptoms

METHODS (BRIEF DESCRIPTION):

- 2 phase RCT
- Phase 1: Individuals with poor glycemic control randomized into receiving mentoring from well-controlled diabetics vs. usual diabetic care
- Phase 2: New individuals with poor glycemic control randomized into groups that received mentoring from former successful phase 1 participants vs. usual diabetic care
- Analysis by intention-to-treat
- Non-blinded

INTERVENTION (# IN THE GROUP):

Phase 1: 202

Phase 2: 207

COMPARISON (# IN THE GROUP):

Phase 1: 154

Phase 2: 49

FOLLOW UP PERIOD: 6 and 12 months

RESULTS:

Primary Outcomes:

- Phase 1 at 6 months:
  - No significant difference in HbA1c in the intervention group (Mean change in A1c -0.52%; 95% CI, -0.76 to -0.29%) compared to the usual care (Mean change in HbA1c -0.20%; 95% CI, -0.46 to 0.06) (P= 0.06)
- Phase 1 at 12 months:
  - No significant difference in HbA1c in the intervention group (Mean change in A1c -0.28%; 95% CI, -0.53 to -0.03%) compared to the usual care (Mean change in HbA1c -0.26%; 95% CI, -0.53 to -0.01) (P= 0.92)
- Phase 2 at 6 months:
  - No significant difference in HbA1c in the intervention group (Mean change in A1c -0.08%; 95% CI, -0.42 to 0.57%) compared to the usual care (Mean change in HbA1c -0.46%; 95% CI, -1.02 to -0.10) (P= 0.16)
- Phase 2 at 12 months:
  - No significant difference in HbA1c in the intervention group (Mean change in A1c -0.16%; 95% CI, -0.65 to 0.33%) compared to the usual care (Mean change in HbA1c -0.27%; 95% CI, -0.89 to 0.36) (P= 0.80)

Secondary Outcomes:

- There were no differences in LDL, BP, quality of life, or depressive symptoms in either group in phase 1 or 2 (all P>.05).

LIMITATIONS:

- Study conducted at single VA medical center
- Mostly Black male population
- No cultural adaptation of materials and mentor training limited

Ashkan Abedini, MD
Samaritan Health Services – Corvallis Program
Corvallis, OR

Too Soon or Too Late? Comparing Adverse Outcomes between Different Interpregnancy Intervals

Interpregnancy Intervals and Adverse Pregnancy Outcomes: An Analysis of Successive Pregnancies
Hanley GE, Hutcheon JA, Kinniburgh BA, Lee L. Interpregnancy Interval and Adverse Pregnancy Outcomes: An Analysis of Successive Pregnancies. *Obstet Gynecol*. 2017; 129(3):408–415.

KEY TAKEAWAY: Short interpregnancy intervals were associated with an increased risk of gestational diabetes mellitus (GDM) and beginning a subsequent pregnancy obese, but there was no significant increase in adverse neonatal outcomes.

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 4 (downgraded due to limitation of sample size and data)

BRIEF BACKGROUND INFORMATION: The World Health Organization recommends the interval between pregnancies should be a minimum of 2 years due to a presumed increased risk of maternal and neonatal adverse outcomes. However, data is conflicting and few studies have evaluated maternal outcomes.

PATIENTS: Women with at least three singleton deliveries with interpregnancy intervals ranging between 0–60+ months

INTERVENTION: Shorter interpregnancy intervals (0–5 mo., 6–11 mo., 12–17 mo.)

CONTROL: Longer interpregnancy intervals (18–23 mo., 24–59 mo., >60 mo.)

OUTCOME: Adverse neonatal outcomes (preterm delivery, low birth weight <2,500g, small for gestational age (SGA), NICU use) and adverse maternal outcomes (GDM, prepregancy obesity, and preeclampsia-eclampsia)

METHODS (BRIEF DESCRIPTION):

- Inclusion Criteria: Women 0–40+ years old with at least three singleton deliveries in British Columbia who delivered between 20–44 weeks gestation
- Unconditional logistic regression (women were compared to the population) calculated the association between interpregnancy intervals and adverse maternal-neonatal outcomes. Data reanalyzed using conditional logistic regression (women were compared to themselves).
- Data adjusted for confounders and sensitivity analysis performed comparing women with three successive pregnancies to those with two.

INTERVENTION (# IN THE GROUP): 38,178

COMPARISON (# IN THE GROUP): Population (unconditional logistical regression); 38,178 (conditional logistical regression matching successive pregnancies in the same woman)

FOLLOW UP PERIOD: 15 years (April 2000 – March 2015)

RESULTS:

NEONATAL OUTCOMES:

- When women were used as their own controls, the new conditional (matched) logistical regression model revealed no significant association between short interpregnancy interval (0–5 months) and adverse neonatal outcomes (preterm birth; adjusted OR 0.85; 95% CI 0.71–1.02); and SGA birth (adjusted OR 0.8; 95% CI 0.62–1.06); compared to the standard unconditional (unmatched) logistical regression model. There was a decreased risk of low birth weight (adjusted OR 0.57; 95% CI 0.46–0.72)
- However, both regression models found that long interpregnancy intervals 60 months or greater were at an increased risk of NICU use (adjusted OR 1.4; 95% CI 1.02–1.9) and a decreased risk of low birth weight (adjusted OR 1.3; 95% CI 1.02–1.7).

MATERNAL OUTCOMES:

- Both the unconditional (unmatched) logistic regression and conditional (matched) logistic regression models showed that short interpregnancy intervals (0–5 months) were associated with an increased risk of gestational diabetes (umatched data: adjusted OR 1.4; 95% CI 1.2–1.7 and matched data: adjusted OR 1.3; 95% CI 1.02–1.8) and prepregnancy obesity (unmatched data: adjusted OR 1.2; 95% CI 1.1–1.5 versus matched data: adjusted OR 1.6; 95% CI 1.1–2.4).
- Both logistic models also showed interpregnancy intervals less than 18 months were less likely to develop preeclampsia-eclampsia (unmatched data: adjusted OR 0.74; 95% CI 0.62–0.87 and matched data: adjusted OR 0.71; 95% CI 0.54–0.94).

LIMITATIONS:

- Unaccounted potential confounders include fertility issues, pregnancy intention, and pregnancy losses before 20 weeks of gestation.
- NICU data limited to 2006–2015.
- BMI data only documented in approximately 25% of the women.
- Small sample size of women with three or more successive deliveries.

Whay-Yih Cheng, DO
David Grant USAF Medical Center (Travis AFB)
Fairfield, CA