GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

Volume 2 - Issue 31

FPIN
Family Physicians Inquiries Network

What's in this week's issue?

Week of August 1 - 5, 2022

SPOTLIGHT: Consequences of Intensifying Hypertension Treatment at Hospital Discharge in Those 65 Years Old and Older

- Targeted Monoclonal Antibody Blockade in Rectal Cancer Treatment
- Participation in Cervical Cancer Screening Improved by Offering Non-Speculum Testing Methods
- Poke the Pounds Away with Semaglutide

Consequences of Intensifying Hypertension Treatment at Hospital Discharge in those 65 Years Old and Older

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Clinical Outcomes After Intensifying Antihypertensive Medication Regimens Among Older Adults at Hospital Discharge

Anderson TS, Jing B, Auerbach A, et al. Clinical Outcomes After Intensifying Antihypertensive Medication Regimens Among Older Adults at Hospital Discharge. *JAMA Internal Medicine.* 2019; 179(11):1528. doi:10.1001/jamainternmed.2019.3007

KEY TAKEAWAY: Intensifying an older adult's antihypertensive regimen when they are admitted to the hospital for non-cardiac conditions may pose greater risk than benefit.

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Medical providers working in the inpatient setting are known to optimize home medication regimens prior to discharging patients from the hospital. Often, antihypertensive medications are intensified due to persistently elevated blood pressure readings during the hospital course. This observational study highlights the clinical outcomes of intensifying antihypertensive medications.

PATIENTS: Older hospitalized adults

INTERVENTION: Intensified antihypertensive regimen at hospital discharge

CONTROL: Antihypertensive regimen not intensified at hospital discharge

OUTCOME: Hospital readmission within 30 days, medication-related serious adverse events (SAEs) within 30 days, cardiovascular events within one year

Secondary Outcomes: All-cause readmission, SAEs, all-cause mortality within one-year, cardiovascular events, and all-cause mortality within 30 days

METHODS (BRIEF DESCRIPTION):

- A retrospective cohort study was done with data from national inpatient and outpatient pharmacy and clinical data from the Veterans Health Administration and Medicare.
- Patients were 65 years old and older with a diagnosis of hypertension prior to hospitalization.
- Admission to the hospital occurred between January 1, 2011 and December 31, 2013 with reasons for admission including the following non-cardiac conditions: pneumonia, urinary tract infection, or venous thromboembolism.
- Patients likely to receive medications outside the VA, those admitted from skilled nursing facilities, and those who had a prior hospitalization within 30-days were excluded.
- Clinical outcomes for patients discharged from the hospital with and without intensifications in their antihypertensive medications were compared. Intensification of medication was defined as a new antihypertensive medication prescribed or a dose increase of 20%.
- Outcomes measured included hospital readmission, serious adverse events, cardiovascular events, and mortality. They were able to track these outcomes by access through the Veterans Health Administration data.
- Propensity score matching was done to control for variations in those who were discharged with and without intensifications in antihypertensive medications.

INTERVENTION (# IN THE GROUP): 2,074

COMPARISON (# IN THE GROUP): 12,841

FOLLOW UP PERIOD: One year

RESULTS:

Primary Outcomes –

- Patients with intensification of their antihypertensive medications were more likely to be readmitted within 30 days of discharge compared to no intensification (21% vs 18%, respectively; NNH=27; 95% CI, 16–76).
- Patients with intensification of their antihypertensive medication were more likely to have serious adverse events within 30 days of discharge compared to no intensification (21% vs 18%, respectively; NNH=27; 95% CI, 16–76).
- No significant difference in the number of cardiovascular events within one-year after discharge if there was an intensification of antihypertensive medications vs no intensification.

Secondary Outcomes –

- No significant difference in rate of mortality within 30 days or within one year of discharge if there was an intensification of antihypertensive medications vs no intensification.

LIMITATIONS:

- Discrepancy in gender (98% male).
- Discrepancy in race (70% Caucasian).

- Discrepancy in age, all patients were at least 65 years old or older.
- There was no way to track if patients sought care outside the Veterans Health Administration system after discharge.

Manjinder Sekhon, MD
Indiana University School of Medicine Arnett FMR
Lafayette, IN

Targeted Monoclonal Antibody Blockade in Rectal Cancer Treatment

PD-1 Blockade in Mismatch Repair-Deficient, Locally Advanced Rectal Cancer

Cercek A, Lumish M, Sinopoli J, et al. PD-1 Blockade in Mismatch Repair-Deficient, Locally Advanced Rectal Cancer. *N Engl J Med*. 2022; 386(25):2363–2376. doi:10.1056/NEJMoa2201445

KEY TAKEAWAY: Dostarlimab, a monoclonal antibody against the programmed death receptor 1 (PD-1), is effective in achieving complete clinical resolution of locally advanced rectal cancer.

STUDY DESIGN: Single-group, prospective phase-2 clinical trial

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Locally advanced rectal cancer is typically treated with chemoradiation therapy and surgical resection, which can adversely affect fertility, sexual health, bowel and bladder function, and quality of life. Five to ten percent of these cancers are mismatch repair-deficient with poor response to standard treatments. PD-1 blockade has been effective in the treatment of metastatic disease. Thus, PD-1 blockade may be effective in the treatment of locally advanced disease.

PATIENTS: Adults with stage 2 or 3 mismatch repair-deficient rectal cancer

INTERVENTION: 500 mg IV dostarlimab

CONTROL: Not applicable

OUTCOME: Clinical or pathological resolution 12 months after dostarlimab completion

Secondary Outcome: Any adverse reaction to dostarlimab

METHODS (BRIEF DESCRIPTION):

- Mismatch repair rectal cancer was defined as loss of MLH1, MSH1, MSH6, and PMS2 genes. MRI, CT, and PET scan were used to confirm cancer staging.
- Median participant age was 54 years old with 62%women and 69% Caucasian ethnicity.
- Participants had a higher functional status, indicated by a low Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1.
- Exclusion criteria included history of autoimmune disease, active infection, receipt of chemoradiation or immunotherapy for the rectal cancer, or immunosuppression treatment.
- 500 mg IV dostarlimab was administered every three weeks for six months for a total of nine cycles with plans for follow up chemoradiation therapy and surgical resection if complete clinical or pathological response was not achieved.
- Clinical response was monitored using endoscopic and digital rectal exams at baseline, six weeks, three months, and six months during treatment followed by every four months after treatment.
- Tumor response was followed by endoscopic biopsies, rectal MRI, PET scan, and CT scans of the chest, abdomen, and pelvis at baseline, three months, six months, and every four months after treatment.
- Absence of residual disease on rectal MRI, digital, and endoscopic exams indicated complete clinical resolution.

INTERVENTION (# IN THE GROUP): 12

COMPARISON (# IN THE GROUP): Not applicable

FOLLOW UP PERIOD: 12 months

RESULTS:

Primary Outcome –

- 100% of patients had complete clinical response to treatment (95% CI, 74–100).
- None of the patients required additional chemoradiation therapy or surgical resection at 12 months follow up.

Secondary Outcome –

- 75% of patients had an adverse reaction to the medication (95% CI, 78–92).
- The most common reactions were rash, pruritis, fatigue, and nausea.

LIMITATIONS:

- This is a very small study with low power and short duration performed at a single institution.
- The study participants were primarily women and lacked racial and ethnic diversity.

John Attonito, MD
Camp Lejeune Family Medicine Residency
Jacksonville, NC

Participation in Cervical Cancer Screening Improved by Offering Non-Speculum Testing Methods

Non-speculum sampling approaches for cervical screening in older women: randomised controlled trial

Landy R, Hollingworth T, Waller J, et al. Non-speculum sampling approaches for cervical screening in older women: randomised controlled trial. *Br J Gen Pract*. 2021; 72(714):e26-e33. Published 2021 Dec 31. doi:10.3399/BJGP.2021.0350

KEY TAKEAWAY: Older women who are not up to date with their cervical cancer screening are more willing to participate in screening if testing is offered without a speculum exam.

STUDY DESIGN: Randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: A significant portion of deaths from cervical cancer occur in women 65 years old and older, many of which did not receive adequate screening prior to being 65 years old. Speculum examinations are a described barrier to engagement in cervical cancer screening, and non-speculum tests are available for in-clinic or at-home use. No prior RCT exists to compare these collection methods for engagement in cervical cancer screening.

PATIENTS: Women 50–64 years old not up-to-date on cervical cancer screening

INTERVENTION: At-home or in-clinic non-speculum collection swab method

CONTROL: Traditional speculum method

OUTCOME: Participation in cervical cancer screening rates at four months

Secondary Outcome: Participation in cervical cancer screening rates at 12 months

METHODS (BRIEF DESCRIPTION):

- Study included 809 patients in 18 general practices (GP) located in east London.
- All patients were females 50–64 years old with lapsed cervical cancer screening, with last testing completed in the past 6–15 years.
- Patients were randomized into treatment or control arms.
    - Treatment arm: Received a mail-out invitation letter with information on cervical cancer screening and an appointment offer for clinician-collected cervical swab without speculum exam or an order form for a self-collection kit for an at-home collection.
    - Control arm: Received usual invitation to make an appointment for cervical cancer screening every five years.
- Self-collected and in-clinic non-speculum samples were tested for HPV DNA, while speculum examinations included cytology with HPV triage.
- Test results were sent to the patient and GP. Participation in screening was evaluated via EMR at four and 12 months.

INTERVENTION (# IN THE GROUP): 393

COMPARISON (# IN THE GROUP): 391

FOLLOW UP PERIOD: 12 months

RESULTS:

Primary Outcome –

- Completion of any form of cervical cancer screening in four months was higher when patients were offered a non-speculum collection method compared with traditional speculum exam (20% vs 4.9%; Absolute Difference 16%; 95% CI, 11% to 20%; NNT=7).

Secondary Outcome –

- Completion of any form of cervical cancer screening at 12 months was higher when patients were offered a non-speculum collection method compared with traditional speculum exam (31% vs 14%; Absolute difference 17%; 95% CI, 11% to 23%; NNT=7).

LIMITATIONS:

- GP records are not linked to national database, making data collection more difficult and potentially inaccurate.
- The educational documents provided to patients were only sent in English.

David Rygmyr, MD
Tripler Army Medical Center
Honolulu, HI

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 Army Medical Department, the Army at large, or the Department of Defense.

Poke the Pounds Away with Semaglutide

Effect of weekly subcutaneous semaglutide vs daily liraglutide on body weight in adults with overweight or obesity without diabetes

Rubino DM, Greenway FL, Khalid U, et al. Effect of Weekly Subcutaneous Semaglutide vs Daily Liraglutide on Body Weight in Adults With Overweight or Obesity Without Diabetes: The STEP 8 Randomized Clinical Trial. *JAMA*. 2022; 327(2):138–150. doi:10.1001/jama.2021.23619

KEY TAKEAWAY: Weekly semaglutide is superior to daily liraglutide for weight loss showing 9.4% greater weight loss in obese and overweight adults without diabetes.
STUDY DESIGN: Randomized clinical trial
LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: In obese and overweight adults, weight loss can be very challenging with diet and exercise alone, which leads to an obesity health crisis. People have often hoped for a pharmaceutical option to help with weight loss. GLP-1 agonists may be one tool individuals can employ to assist with weight loss. GLP-1 agonists are traditionally used for diabetes mellitus type 2 but have been shown to cause weight loss. The benefit of weekly semaglutide versus daily liraglutide was examined.

PATIENTS: Obese and overweight patients without diabetes
INTERVENTION: Weekly semaglutide injection
CONTROL: Daily liraglutide injection
OUTCOME: Weight loss
Secondary Outcomes: Waist circumference and diastolic blood pressure

METHODS (BRIEF DESCRIPTION):

- Included adult patients were without diabetes, with BMI greater than 30, or greater than 27 with at least one obesity related condition.
- Participants randomized in a 3:1:2:1 using block schema to patient's receiving 2.4 mg once-weekly subcutaneous semaglutide to placebo and 3.0 mg once-daily subcutaneous liraglutide to placebo.
- Semaglutide was started at 0.25 mg then increased over a course of 16 weeks to 2.4 mg dose. While liraglutide was started at 0.6 mg then increased to 3.0 mg over four weeks.
- Patients were counseled every 4–6 weeks to adhere to calorie deficit of 500 kcal/day and at least 150 minutes of physical activity a week.
- At enrollment and at again at 68 weeks, the following were measured; body weight, waist circumference, and blood pressure.
- Treatment was discontinued at 68 and at 75 weeks with adverse events being assessed.

INTERVENTION (# IN THE GROUP): 126
COMPARISON (# IN THE GROUP):

- Liraglutide: 127
- Placebo: 85

FOLLOW UP PERIOD: 75 Weeks

RESULTS:
Primary Outcome –

- Semaglutide resulted in more weight loss than liraglutide (−16% vs 6.4%, respectively; Absolute Difference (AD) −9.4%; 95% CI, -12 to −6.8).

Secondary Outcomes –

- Semaglutide decreased waist circumference compared to liraglutide (−6.6 cm vs 13 cm, respectively; AD −6.6 cm; 95% CI, −9.1 to −4.2).
- Semaglutide compared to liraglutide reduced but did not significantly improve systolic blood pressure.
- Semaglutide compared to liraglutide reduced diastolic blood pressure (−5.0 mmHg vs −0.5 mmHg, respectively; AD −4.5 mmHg; 95% CI, −7.1 to −1.9).

Primary Outcome –

- Gastrointestinal side effects were the most common side effect.
  - Mild to moderate GI disorders:
    - Semaglutide: 84%
    - Liraglutide: 83%
    - Placebo: 55%

LIMITATIONS:

- Sample size of 387.
- 75-week duration of monitoring.
- Participants that did not complete the treatment but attended 75 week follow up visit were included in the study.
- Funded by Novo Norkisk A/S, the maker of semaglutide.

John Malovrh, DO
Tripler Army Medical Center FMRP
Honolulu, HI

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 Army Medical Department, the Army at large, or the Department of Defense.