GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

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SPOTLIGHT: Shake the Salt Habit - Sodium Reduction Lowers Blood Pressure

- Physical Therapy for Knee and Hip Arthritis Decreases Use of Pain Medication
- Home Is Where the Blood Pressure Control Is
- Patients on Their Last Nerve: Duloxetine vs Gabapentin Therapy in Painful Diabetic Neuropathy

Shake the Salt Habit: Sodium Reduction Lowers Blood Pressure

Blood Pressure Effects of Sodium Reduction: Dose–Response Meta-Analysis of Experimental Studies

Filippini T, Malavolti M, Whelton P, Naska A, Orsini N, Vinceti, M. Blood Pressure Effects of Sodium Reduction: Dose–Response Meta-Analysis of Experimental Studies. *Circulation*. 2021; 143:1542–1567. DOI: 10.1161/CIRCULATIONAHA.120.050371

KEY TAKEAWAY: Reducing sodium intake decreases systolic and diastolic blood pressure in a linear pattern across the range of dietary sodium exposure. This is observed in patients with or without hypertension, although the effect of is more significant in those with hypertension.

STUDY DESIGN: Dose-response meta-analysis

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Sodium intake and blood pressure (BP) are known to be directly associated, but the shape of the dose-response relationship is unclear. Better describing sodium's effect on blood pressure could influence dietary modifications for a broad spectrum of patients with and without pre-existing hypertension.

PATIENTS: Adults 18–82 years old with or without hypertension

INTERVENTION: Sodium-reduced diet

CONTROL: Normal diet or sodium-reduced diet augmented with sodium supplementation

OUTCOME: Systolic (SBP) and diastolic (DBP) blood pressures

METHODS (BRIEF DESCRIPTION):

- Three databases were searched (PubMed/MEDLINE, EMBASE, and CENTRAL) with 85 eligible RCTs selected (N>10,000).
  - 65 trials of participants with hypertension
  - 11 trials of participants without hypertension
  - 9 trials of participants with a combination of both
- The sodium intervention consisted of dietary sodium reduction, which in some trials was followed by sodium supplementation at a usual range of 1.8–2.3 g/day.
- Trials included quantification of sodium intake through 24-hour sodium excretion measurements, sodium manipulation through dietary change or supplementation, or both.
- One-stage cubic spline mixed effect analytic model was utilized, allowing estimation of heterogeneous and possible curvilinear dose-response relationships.

INTERVENTION (# IN THE GROUP): Unavailable

COMPARISON (# IN THE GROUP): Unavailable

FOLLOW UP PERIOD: Four weeks to three years

RESULTS:

There is a linear relationship between sodium intake and average BP.

- For every 1 g/d decrease of sodium excretion:
  - SBP decreased by an average of 2.4 mmHg (95%CI, –0.97 to –2.87).
  - DBP decreased by an average of 1.0 mmHg (95%CI, –0.72 to –1.3).
- In adults with hypertension, for every 2.3 grams per day decrease in consumed sodium:
  - SBP decreased by 7.8 mm Hg (95% CI, –4.9 to –10.7) in those with baseline SBP <140 mmHg.
  - SBP decreased by 6.1 mmHg (95% CI, –4.6 to –7.5) in those with baseline SBP ≥140 mmHg.
  - DBP decreased by 3.1 mmHg (95% CI, –1.4 to –4.8) in those with baseline DBP <140 mmHg.
  - DBP decreased by 3.0 mmHg (95% CI, –2.2 to –3.8) in those with baseline DBP ≥140 mmHg.
- In adults without hypertension, for every 100 mmol per day decrease in consumed sodium SBP decreased by 2.3 mmHg (95% CI, –1.3 to –3.3). DBP was not significantly affected.

LIMITATIONS:

- No direct assessment of risk between elevated sodium intake and development of cardiovascular disease.
- Statistical instability of some estimates for the highest and lowest dietary sodium exposure.

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Physical Therapy for Knee and Hip Arthritis Decreases Use of Pain Medication

Patient Education and Physical Therapy May Decrease Analgesic Use in Patients with Osteoarthritis

Thorlund JB, Roos EM, Goro P, Ljungcrantz EG, Grønne DT, Skou ST. Patients use fewer analgesics following supervised exercise therapy and patient education: an observational study of 16499 patients with knee or hip osteoarthritis. *Br J Sports Med*. 2021; 55(12):670-675. doi:10.1136/bjsports-2019-101265

KEY TAKEAWAY: Physical therapy + patient education decreases the use of analgesics in patients with knee and/or hip osteoarthritis.

STUDY DESIGN: Retrospective cohort study using prospectively collected data without a control group

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: First-line therapies for knee and hip osteoarthritis are exercise, education, and weight loss. However, a previous systematic review showed that only 1 in 3 patients are offered these modalities and are instead offered analgesics, which are not without risk.

PATIENTS: Adults with clinically diagnosed uncomplicated knee and/or hip osteoarthritis

INTERVENTION: Patient education and supervised neuromuscular exercise therapy

CONTROL: None

OUTCOME: Analgesic use

Secondary Outcome: Pain

METHODS (BRIEF DESCRIPTION):

- 16,499 patients with clinical diagnosis of knee and/or hip osteoarthritis.
- Analgesic use was measured by patient answering 'yes' or 'no' to each category of analgesic (paracetamol, NSAIDs, and opioids) at the start of the trial and 12 weeks later.
- Patients were categorized by highest risk profile of the analgesics they reported (opioids>NSAIDs>paracetamol) if they reported more than one category.
- Pain intensity was also measured using a visual analogue scale (10 cm pain ruler).
- Patients underwent education sessions and 12 sessions of therapy over an eight-week period.
- Education sessions consisted of knowledge on osteoarthritis and its treatments, with particular focus on exercise and self-help advice.
- Follow up occurred within four weeks of last therapy session.

INTERVENTION (# IN THE GROUP): 16,499

COMPARISON (# IN THE GROUP): None

FOLLOW UP PERIOD: Eight weeks

RESULTS:

Primary Outcome –

- At eight weeks there was an 18% absolute decrease in the proportion of patients using analgesics compared to baseline [62% vs 44%, respectively; *P*<.001).
- 52% of patients using analgesics at baseline either changed to a lower risk analgesic or discontinued analgesic use.
- 20% of patients who had no analgesic use at baseline began using analgesics during the study period.

Secondary Outcome –

- At eight weeks pain had improved an average of 13 mm (95% CI, 12.8 to 13.6) compared to baseline.
  - Those who reported the most pain reduction were most likely to decrease or discontinue analgesic use.

LIMITATIONS:

- 75% were women.
- No control group.
- Only measured for eight weeks.
- No dose or frequency of analgesic use was recorded.
- All patients had chosen to participate in the study.

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Home Is Where the Blood Pressure Control Is

Home and Online Management and Evaluation of Blood Pressure (HOME BP) using a digital intervention in poorly controlled hypertension: randomised controlled trial

McManus RJ, Little P, Stuart B, et al. Home and Online Management and Evaluation of Blood Pressure (HOME BP) using a digital intervention in poorly controlled hypertension: randomised controlled trial. *BMJ.* 2021; 372:m4858. Published 2021 Jan 19. doi:10.1136/bmj.m4858

KEY TAKEAWAY: Home/online blood pressure monitoring decreases systolic blood pressure and increases the likelihood of medication titration compared to usual care. However, there was no difference in quality of life.

STUDY DESIGN: Multi-centered, randomized control trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Previous studies have shown home blood pressure monitoring to be effective but require expensive technology and training. Studies on digital interventions have been short-term and lack evidence of widespread application.

PATIENTS: 18 years old or older with blood pressure >140/90 mmHg

INTERVENTION: Home and Online Management and Evaluation of Blood Pressure (HOME BP) using digital interventions

CONTROL: Routine hypertension care with routine appointments and medication management by a physician

OUTCOME: Difference in systolic blood pressure

METHODS (BRIEF DESCRIPTION):

- Patients were 18 years old or older with blood pressure >140/90 mmHg despite pharmacological therapy of no more than three antihypertensives.
  - Exclusion Criteria: Blood pressure >180/110 mmHg, atrial fibrillation, stage 4 or 5 chronic kidney disease, postural hypotension, or an acute cardiovascular event in the prior three months.
- 1:1 randomization allocated participants to:
  - Traditional clinic care: Office visits and drug titrations
  - HOME BP management: Recorded blood pressure online twice a day with optional nurse support and digital feedback and suggestions for building and maintaining healthy lifestyle changes.
    - Patients received an email to change medication if blood pressure was elevated for two months.
- Blood pressure check questionnaires were completed at six months and 12 months.

INTERVENTION (# IN THE GROUP): 305

COMPARISON (# IN THE GROUP): 317

FOLLOW UP PERIOD: 12 months

RESULTS:

- After one year, the HOME BP group had lower systolic blood pressure than the control group (MD –3.4 mmHg; 95% CI, –6.1 to –0.8).
  - There was no difference in diastolic blood pressure (MD –0.5 mmHg; 95% CI, –1.9 to 0.9).
- The HOME BP group was more likely to:
  - Have their medication dose titrated (RR 2.0; 95% CI, 1.5–2.7)
  - Have medication changes (RR 1.5; 95% CI, 1.1–1.9)
- There was no significant difference in quality of life between the two groups.

LIMITATIONS:

- Use of technology/computer skills and willingness to change medications limited average age of participants.
- Study indirectly preferences patient populations of higher socioeconomic status by requiring reliable access to internet and education level to understand and interpret results.
- Greater than 93% of sample was Caucasian.

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Patients on Their Last Nerve: Duloxetine vs Gabapentin Therapy in Painful Diabetic Neuropathy

A randomized control trial of duloxetine and gabapentin in painful diabetic neuropathy

Khasbage S, Shukla R, Sharma P, Singh S. A randomized control trial of duloxetine and gabapentin in painful diabetic neuropathy. *Journal of Diabetes*. 2021; 13:532–541.

KEY TAKEAWAY: Duloxetine and gabapentin both improved the symptoms of Painful Diabetic Neuropathy (PDN) compared to baseline and had similar efficacy compared to one another.

STUDY DESIGN: Randomized control trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Painful diabetic neuropathy has an impact on up to one third of diabetic individuals around the world. Currently, duloxetine and gabapentin are some of the top medications used to treat this common ailment. Physicians are often in a situation to decide which medication is best indicated for their diabetic patient and which medications have the greatest efficacy.

PATIENTS: Patients with type 2 diabetes and PDN

INTERVENTION: Duloxetine 60 mg once daily at bedtime

CONTROL: Gabapentin 300 mg once daily at bedtime

OUTCOME: Pain

Secondary Outcomes: Neuropathy symptoms, exam findings, disability

METHODS (BRIEF DESCRIPTION):

- Patients with Type 2 diabetes mellitus (DM) were randomized to receive duloxetine 60 mg daily or gabapentin 300 mg daily at bedtime.
- Included patients were 18–75 years old, had PDN for ≥1 month, had a Visual Analogue Score (VAS) score ≥50, and DM was controlled and stable.
- Patients were excluded if they had type 1 DM, unstable medical illness, unstable psychiatric illness, history of substance abuse, or were pregnant.
- All patients received B12 1,500 mcg and folic acid 500 mcg daily.
- Primary outcome was the difference in VAS scores at 12 weeks compared to baseline.
- VAS scores range from 0 to 100 with 100 indicating the worst pain.
    - Mean VAS at baseline was 72 for the duloxetine group and 73 for the gabapentin group.
- Secondary outcomes were measured as a change in score at 12 weeks compared to baseline:
    - Diabetic neuropathy symptoms (DNS) four-item symptom scale (0–¬–4 with 4 being worst)
    - Diabetic neuropathy examination (DNE) eight-item scale evaluating exam findings (0–16 with 16 being the worst)
    - Neuropathic disability score (NDS) four-item scale evaluating severity of PDM (0–10 with 10 being the worst)

INTERVENTION (# IN THE GROUP): 43

COMPARISON (# IN THE GROUP): 43

FOLLOW UP PERIOD: 12 weeks

RESULTS:

Primary Outcome –

- Improvement in pain did not differ between the two groups (mean difference [MD] 5.3; 95% CI, –1.7 to 12).
- Each group experienced improvement in pain at 12 weeks from baseline:
    - Duloxetine: (MD 46; *P*<.001)
    - Gabapentin: (MD 61; *P*<.001)

Secondary Outcomes –

- Improvement in neuropathy symptoms, neurological exam findings, and disability did not differ between the two groups.
- Each group experienced improvement at 12 weeks from baseline in the following:
    - Neuropathy symptoms:
        - Duloxetine (mean change [MC] 2.0; *P*<.001)
        - Gabapentin (MC 2.2; *P*<.001)
    - Neurological exam findings:
        - Duloxetine (MC 1.4; *P*<.001)
        - Gabapentin (MC 1.6; *P*<.001)
    - Disability:
        - Duloxetine (MC 0.3; *P*=.001)
        - Gabapentin (MC 0.7; *P*<.001)
- There were no statistically significant differences in neuropathy symptoms, neurologic exam, or disability between the duloxetine and gabapentin groups.

LIMITATIONS:

- Assessment bias could be present as the study was open label.
- The gabapentin and duloxetine doses used were lower than the recommended

dose range for each. Higher doses may have had greater efficacy.

- There were no placebo comparisons.
- The study only compared gabapentin vs duloxetine. Other medications might have had greater efficacy.

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