GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of January 8 - 12, 2024

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Breaking New Ground: Using POCUS as a Diagnostic Tool for Suspected Pediatric Fractures

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Ultrasonography or Radiography for Suspected Pediatric Distal Forearm Fractures

Snelling PJ, Jones P, Bade D, et al. Ultrasonography or Radiography for Suspected Pediatric Distal Forearm Fractures. *N Engl J Med.* 2023;388(22):2049-2057. doi:10.1056/NEJMoa2213883

KEY TAKEAWAY: In children and adolescents who present with acute, isolated, nondeformed distal forearm injuries, initial imaging with ultrasonography is non-inferior to radiography concerning the physical function of the arm at four weeks.

STUDY DESIGN: Multicenter, single-blinded, randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Pediatric patients who present to the emergency department with suspected distal forearm fractures routinely undergo radiography as initial imaging. Ultrasonography is less commonly performed despite being timely, accurate, and not exposing the patient to ionizing radiation. However, there is limited data on whether initial ultrasonography is non-inferior to radiography for the diagnosis of forearm fractures concerning the subsequent physical function of the arm.

PATIENTS: Pediatric ER patients with an isolated distal forearm injury

INTERVENTION: Point-of-care ultrasonography (POCUS)

CONTROL: Radiography

PRIMARY OUTCOME: Physical function of the affected arm at four weeks

Secondary Outcome: Physical function of the injured upper limb at one week and eight weeks, parent/caregiver satisfaction, patient satisfaction, patient pain score, ED length of stay and treatment time, days of school missed, frequency of follow-up radiography films obtained

METHODS (BRIEF DESCRIPTION):

- 270 participants from four, large tertiary pediatric hospitals in Southeast Queensland, Australia were included in the study.
- The average demographics of patients included patients 10 years old, a BMI in the 64th percentile, and dominant hand affected.
- Participants were randomized in a 1:1 ratio to either the POCUS or radiography group and were stratified according to site and age (5–9 years old and 10–15 years old).
- POCUS group: Underwent six-view forearm ultrasonography protocol. The final image was labeled with an overall forearm diagnosis of no fracture, buckle fracture, or other fracture.
- Radiography group: Underwent biplanar imaging and x-rays were interpreted by the treating practitioner with or without advice from the radiologist or local orthopedic service. The final image was classified as no fracture, buckle fracture, or other fracture.
- The final diagnosis was determined for each participant by consensus of an expert panel of pediatric specialists.
- Initial treatment was standardized across the trial sites.
  - No fractures: Conservatively managed at clinician's discretion
  - Buckle fractures: Wrist splint
  - Other fractures: Intervention (manipulation or surgery) as needed, cast immobilization with outpatient referral to orthopedic service
- Follow-up visits at one week, four weeks, and eight weeks.
- Analysis for the primary outcome were both the per-protocol and intention-to-treat.
  - Per-protocol population: Participants who had initial imaging as assigned and had outcome data collected at four weeks (± 3-day window)
  - Intention-to-treat population: All participants with outcome data collected at any time
- Physical function was measured via the Pediatric Upper Extremity Short Patient-Reported Outcomes Measurement Information System (PROMIS) tool. An eight-item questionnaire with each item measured on a five-point scale. Scores range 8–40 with higher scores indicating better function
  - Noninferiority margin: Five points
- Satisfaction was measured using the 5-point Likert scale, with lower scores indicating greater satisfaction.

- Pain at one, four, and eight weeks was measured using the 6-point Faces Pain Scale-Revised tool, with higher scores indicating greater pain.

INTERVENTION (# IN THE GROUP): 135

COMPARISON (# IN THE GROUP): 135

FOLLOW-UP PERIOD: One week, four weeks, eight weeks

RESULTS:

Primary Outcome –

- Ultrasonography was non-inferior to radiography for the physical function of the arm at four weeks (mean difference [MD] 0.1 points; 95% CI, –1.3 to 1.4).

Secondary Outcome –

- Patient or caregiver reported satisfaction was greater with POCUS compared to radiography at follow-up.
  - Four weeks (MD –0.19; 95% CI, –0.37 to –0.01)
  - Eight weeks (MD –0.20; 95% CI, –0.35 to –0.06)
- The POCUS group had a shorter length of stay in the ED compared to the radiography group (median difference 15 mins; 95% CI, 1–29).
- The POCUS group had a shorter treatment time in ED compared to the radiography group (median difference 28 minutes; 95% CI, 17–40).
- Participants in the POCUS group missed fewer days of school at four weeks (median difference 0.5 days; 95% CI, 0.1–0.9).
- There was no difference in patient satisfaction, pain, and number of follow-up radiography films between the POCUS and radiology groups.

LIMITATIONS:

- Differences in subsequent therapeutic interventions may have influenced the primary outcome separately from the initial diagnostic method.
- Only a small number of sites participated in this study.
- Health care practitioners were trained by a single emergency physician in the ED.
- Children <5 years old were excluded because the PROMIS tool was not validated for this age group.
- No long-term follow-up for rare complications.

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Vascular Outcomes in Diabetes: A Medication Showdown

Glycemia Reduction in Type 2 Diabetes- Microvascular and Cardiovascular Outcomes

GRADE Study Research Group, Nathan DM, Lachin JM, et al. Glycemia Reduction in Type 2 Diabetes - Microvascular and Cardiovascular Outcomes. *N Engl J Med.* 2022;387(12):1075-1088. doi:10.1056/NEJMoa2200436

KEY TAKEAWAY: Treatment of type 2 diabetes patients with either glargine, glimepiride, liraglutide, or sitagliptin, in combination with metformin, did not change the incidence of microvascular complications or death, but favored liraglutide in reducing cardiovascular disease incidence.

STUDY DESIGN: Multi-arm, parallel-group, comparative effectiveness randomized clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: As the prevalence of type 2 diabetes grows globally, long-term complications, including cardiovascular and microvascular disease, result in increased illness, mortality, and costs. However, as new classes of diabetes medications are developed, the comparative effectiveness and benefits of cardiovascular and microvascular disease are unknown. This study evaluated the comparative impacts of four diabetes medications on microvascular and cardiovascular disease.

PATIENTS: Adults with type 2 diabetes

INTERVENTION: Glargine, glimepiride, liraglutide, or sitagliptin

CONTROL: Between-group comparisons

PRIMARY OUTCOME: Microvascular and cardiovascular outcomes

METHODS (BRIEF DESCRIPTION):

- Adult participants with type 2 diabetes diagnosed within the previous 10 years, HbA1C level of 6.8%–8.5%, and currently treated with metformin monotherapy were enrolled across 36 clinical centers.
- Those with a history of a recent major cardiovascular event, New York Heart Association functional classification III or higher, and stage four chronic kidney disease were excluded.
- Participants had a mean age of 57.2 years old and 63.6% were men.
  - 65.7% of participants identified as White, 19.8% Black, and 18.6% Hispanic.
  - The mean HbA1C was 7.5%.
- In addition to metformin, participants were randomly assigned to receive either glargine, glimepiride, liraglutide, or sitagliptin.
  - Medications were started at the recommended initial doses and titrated to maximal target doses depending on glucose values, related lab results, and/or side effects.
- Participants and clinical staff knew the treatment assignments, but the study personnel were blinded.
- Participants were evaluated every three months for a median five-year follow-up period.
- Microvascular outcomes were assessed using standardized questionnaires, physical examination, and laboratory analyses.
  - Renal complications were assessed with biannual urinary albumin: Creatinine ratio measurements, with moderate and severe albuminuria defined as ≥30 mg/g and ≥300 mg/g, respectively, and with annual serum creatinine measurements, with renal impairment defined as estimated glomerular filtration rate (eGFR) <60 ml/min per 1.73 m^2.
  - Diabetic neuropathy was assessed annually through a lower extremity exam and the Michigan Neuropathy Screening Instrument (MNSI).
    - Scores ≥2.5 points on the exam or ≥7 MNSI (range 0–8) indicated neuropathy.
- Cardiovascular outcomes included major adverse cardiovascular events (nonfatal myocardial infarction, nonfatal stroke, or death), hospitalization from heart failure, unstable angina, or the necessity of revascularization.

INTERVENTION (# IN THE GROUP):

- Glargine: 1,263
- Glimepiride: 1,254
- Liraglutide: 1,262
- Sitagliptin: 1,268

COMPARISON (# IN THE GROUP): Not applicable

FOLLOW-UP PERIOD: Five years

RESULTS:

Primary Outcome –

- The treatment groups did not differ in the cumulative incidences of albuminuria, renal impairment, or diabetic neuropathy.
- The liraglutide group had lower cardiovascular disease risk than:
  - The sitagliptin group (hazard ratio [HR] 0.68; 95% CI, 0.51–0.90)
  - The glimepiride group (HR 0.71; 95% CI, 0.53–0.93)
  - The other three groups combined (HR 0.71; 95% CI, 0.56–0.90)
- Liraglutide and glargine groups had similar incidences of cardiovascular disease.
- There were no differences in major adverse cardiac events or deaths among the groups.

LIMITATIONS:

- A majority of participants were men, which may limit generalizability.
- More than 40% of trial participants were over 60 years old, potentially underrepresenting a younger population who may have different incidences of microvascular effects.
- The outcomes of this study were a secondary analysis of a trial primarily designed to detect changes in hemoglobin A1C on the tested medications.

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Queer Sex Education: Empowering Teens to Have Better Sexual Health

The IN-clued Program: A Randomized Control Trial of an Effective Sex Education Program for Lesbian, Gay, Bisexual, Transgender, Queer, and Questioning Youths

Phillibert A. The IN·clued Program: A Randomized Control Trial of an Effective Sex Education Program for Lesbian, Gay, Bisexual, Transgender, Queer, and Questioning Youths. *J Adolesc Health*. 2021;69(4):636-643. doi:10.1016/j.jadohealth.2021.04.002

KEY TAKEAWAY: Lesbian, gay, bisexual, transgender, and questioning (LGBTQ) specific sexual health education led to significantly less vaginal sex without a condom in the educated group compared to those without education, as well as an increase in engagement with the healthcare system regarding sexual healthcare and contraception.

STUDY DESIGN: Cluster, unblinded randomized control trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Literature about LGBTQ youths increasingly indicates they face greater health challenges, including sexual health due to stigma. There are studies indicating that LGBTQ youths need better sexual health education, but the effects of these programs have not been explored. Currently, LGBTQ youths have double the teen pregnancy rates compared to their heterosexual counterparts as well as increased risk for STIs.

PATIENTS: LGBTQ adolescents

INTERVENTION: LGBTQ-specific sexual education

CONTROL: Placebo activity

PRIMARY OUTCOME: Risky sexual behaviors

Secondary Outcome: Access to sexual/STD health care, knowledge of sexual health, healthcare self-efficacy

METHODS (BRIEF DESCRIPTION):

- The IN-clued program curriculum was created by Planned Parenthood of the Great Northwest and the Hawaiian Islands.
- Demographics:
  - Mean age: 16 years old
  - Gender: 81.7% assigned female at birth, 51.9% transgender or other non-cisgender identities
  - Race: 80.2% White
  - Group size average: 12 youths
- Youths were randomized into a treatment group (IN-clued program) and a control group (group activity not related to sexual health).
- The IN-clued program consists of a one-time, three-hour in-person workshop discussing safe sex practices, healthcare self-efficacy, and a discussion on patient rights.
- Surveys were done to assess baseline and the impact performed before randomization, one year after the workshop, or nine months after a three-month text service.

INTERVENTION (# IN THE GROUP): 713

COMPARISON (# IN THE GROUP): 688

FOLLOW-UP PERIOD: One year

RESULTS:

Primary Outcome –

- LGBTQ-specific sexual education led to fewer risky sexual behaviors compared to placebo activity.
  - Vaginal sex without a condom (14% treatment vs 19% control; *p*=.022)
  - Number of times participants had vaginal sex without a condom (0.85 treatment vs 1.9 control; *p*=.012)

Secondary Outcome –

- LGBTQ-specific sexual education led to greater access to sexual/STD health care compared to placebo activity.
  - Saw doctor for birth control/contraception (45% treatment vs 40% control; *p*=.029)
  - Received birth control/contraception (49.5% treatment vs 44.6% control; *p*=.048)
- LGBTQ-specific sexual education led to more knowledge about sexual health compared to placebo activity.
  - Knowledge that LGBTQ people have higher pregnancy rates (50% treatment vs 27% control; *p*=.000)
  - Knowledge that LGBTQ people are less likely to go to the doctor for sexual healthcare (89% treatment vs 83% control; *p*=.002)
  - Knowledge that there are birth control options that do not interfere with hormonal replacement therapy (68% treatment vs 58% control; *p*=.000)

    - Overall sexual health knowledge (76% treatment vs 67% control; *p*=.000)
- LGBTQ-specific sexual education led to greater healthcare self-efficacy compared to placebo activity.
    - Advocate for own sexual healthcare (85% treatment vs 80% control; *p*=.017)
    - Self-efficacy (69% treatment vs 64% control; *p*=.007)

LIMITATIONS:

- Many of the patients are from urban areas, which may make results not as generalizable to rural demographics.
- Many of the teens in the study come from homes with high parental education attainment, which may differ from the national average of LGBTQ teens.
- The majority of the teens grew up in two-parent households, which may differ from the national average.
- About 80% of the participants were assigned female at birth, which may not be generalizable to the larger population of adolescents assigned male at birth.

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Association Between Hormonal Menopausal Therapy and Dementia

Menopausal Hormone Therapy and Dementia: Nationwide, Nested Case-Control Study

Pourhadi N, Mørch LS, Holm EA, Torp-Pedersen C, Meaidi A. Menopausal hormone therapy and dementia: nationwide, nested case-control study [published correction appears in BMJ. 2023 Jun 29;381:p1499]. *BMJ*. 2023;381:e072770. Published 2023 Jun 28. doi:10.1136/bmj-2022-072770

KEY TAKEAWAY: There appears to be a strong dose-dependent positive association between the use of estrogen and progestin menopausal hormonal therapy and dementia.

STUDY DESIGN: Nested case-control study

LEVEL OF EVIDENCE: STEP 4

BRIEF BACKGROUND INFORMATION: There is current evidence supporting an association between estrogen-progestin menopausal hormone therapy and dementia. However, the evidence for these studies is limited by the age of the women studied, duration of treatment, and types of hormonal therapy regimens the participants received.

PATIENTS: Danish women

INTERVENTION: Combined estrogen-progestin treatment

CONTROL: No estrogen-progestin treatment

PRIMARY OUTCOME: All-cause dementia

Secondary Outcome: Late-onset dementia, Alzheimer's disease

METHODS (BRIEF DESCRIPTION):

- Danish women aged 50–60 years old with a diagnosis of dementia were identified via the Danish national registry between 2000–2018.
- The study group was age-matched to controls without the diagnosis of dementia.
- The primary exposure of interest was the use of combined estrogen-progestin treatment.
- There was also a subgroup analysis that looked at the association of age of initiation, duration of use, methods, types, and ingredients with the diagnosis of dementia.
- Date of dementia diagnosis was determined by looking at a national registry of patients in Denmark.
- Patients who received prescriptions for dementia were also identified through the national prescription registry in Denmark.

INTERVENTION (# IN THE GROUP): 5,589

COMPARISON (# IN THE GROUP): 55,890

FOLLOW-UP PERIOD: January 1, 2000–December 31, 2018

RESULTS:

Primary Outcome –

- Menopausal estrogen-progestin therapy was associated with an increased risk of dementia compared to women with no history of use (adjusted hazard ratio [aHR] 1.2; 95% CI, 1.2–1.3).
- Longer durations of use were associated with increasing association with dementia.
  - ≤1 year (aHR 1.21; 95% CI, 1.1–1.4)
  - >12 years (aHR 1.7; 95% CI, 1.5–2.1)
- Estrogen-progestin therapy was positively associated with the development of dementia for both continuous (aHR 1.3; 95% CI, 1.2–1.5) and cyclic regimens (aHR 1.2; 95% CI, 1.1–1.4).
- A similar positive association of dementia persisted in women who only received treatment at 55 years old or younger (aHR 1.2; 95% CI, 1.1–1.4).

Secondary Outcome –

- The correlation remained similar even when specifically considering cases of late-onset dementia (aHR 1.2; 95% CI, 1.1–1.3) and Alzheimer's disease (aHR 1.2; 95% CI, 1.1–1.4).

LIMITATIONS:

- The study is observational, meaning there are several confounding factors to consider, including residual confounding by indication.
- Only synthetic progestins were studied.
- Modes of administration or progestin types were not able to be distinguished due to the prescription patterns in Denmark.

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