POEMs

Patient-Oriented Evidence That Matters

Normal Defecation Patterns in Healthy Young Children Vary by Age, Diet, and Place of Residence

Clinical Question

What are normal defecation patterns in healthy young children?

Bottom Line

Stool patterns in infants and young children vary by age, diet, and place of residence. The data from the study can be used to counsel parents about the wide range of normal defecation patterns. (Level of Evidence = 2a–)

Synopsis

The authors searched PubMed, EMBASE, and the Cochrane Library for English-language, cross-sectional, observational, and interventional studies that reported defecation patterns in healthy children up to four years of age. They included 75 studies with 16,393 children. The studies took place in well-child clinics, hospitals, daycare centers, and homes in 43 different countries across each of the six regions defined by the World Health Organization. For the purposes of determining defecation patterns, the studies were generally at moderate to high risk of bias. Most of the studies (88%) used diaries to assess defecation frequency; only eight studies used validated tools to assess stool consistency. The median defecation frequency in infants (up to 14 weeks of age) ranged from 7.0 to 44.9 times per week, and the median in young children (15 weeks to four years of age) ranged from 6.2 to 17.9 times per week. Overall, 1.5% of infants had hard stools and 27.0% had soft stools. However, 10.5% of young children had hard stools and 6.2% had soft stools. Four studies compared defecation patterns by sex and found no differences. Defecation frequency and stool consistency varied by diet, and breastfed infants defecated more frequently (23 times per week) and had softer stools. The authors reported marked variation in frequency by country.

Study design: Meta-analysis (other)

Funding source: Unknown/not stated

Setting: Various (meta-analysis)

Reference: *Baaleman DF, Wegh CAM, de Leeuw TJM, et al. What are normal defecation patterns in healthy children up to four years of age? A systematic review and meta-analysis.* J Pediatr. *2023;261:113559.*

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The Risk of Breast Cancer Overdiagnosis Is High in Older Women

Clinical Question

What is the likelihood of the overdiagnosis of breast cancer after screening in women older than 70 years?

Bottom Line

Overdiagnosis of breast cancer—or identification, in this case—that would not have caused symptoms in a person's lifetime seems to increase with age. In this study, the overdiagnosis rate was 31% for women 70 to 74 years of age. The rate of overdiagnosis increased with age: 47% for women 75 to 84 years of age and 51% for women older than 85 years who were screened and found to be positive. (Level of Evidence = 2b)

Synopsis

The investigators used a U.S. payment database to identify all women older than 70 years who had had a recent screening mammogram and followed them for up to 15 years. The authors used a two-step approach: (1) identifying women without breast cancer who had a negative screening result after 70 years of age, and (2) following these women to see if they had another mammogram in the next three years and a subsequent diagnosis of breast cancer. In this group of 54,635 women, there was no reduction in breast cancer–related death associated with screening. Women 70 to 74 years of age had a cumulative incidence of breast cancer of 6.1 per 100 women screened compared with 4.2 cases per 100 women who were not screened. This resulted in an estimated 31% of breast cancer being overdiagnosed. In women 75 to 84 years of age, the incidence was 4.9 vs. 2.6 per 100 women,

with the rate of overdiagnosis being 47%. More than one-half (51%) of women 85 years and older with a diagnosis of breast cancer died of other causes.

Study design: Cohort (retrospective)

Funding source: Government

Setting: Population-based

Reference: *Richman IB, Long JB, Soulos PR, et al. Estimating breast cancer overdiagnosis after screening mammography among older women in the United States.* Ann Intern Med. *2023; 176(9):1172-1180.*

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Esketamine Is Superior to Quetiapine for Remission of Treatment-Resistant Depression

Clinical Question

For patients with treatment-resistant depression, is an esketamine (Spravato) nasal spray superior to the antipsychotic quetiapine?

Bottom Line

Esketamine nasal spray is safe and slightly more effective than extended-release quetiapine at inducing remission at eight weeks (number needed to treat [NNT] = 10) and 32 weeks (NNT = 7) in patients with treatment-resistant depression. (Level of Evidence = 1b–)

Synopsis

In the trial, treatment-resistant depression was defined as a score of 34 or higher on an 84-point depression scale (higher scores are worse) and failure of two to six treatment regimens from at least two different drug classes with 25% or less reduction in symptoms. All patients were taking the maximally tolerated dose of a selective serotonin reuptake inhibitor or a serotonin-norepinephrine reuptake inhibitor that was continued during the trial. At baseline, patients had a mean age of 45 years (range: 18 to 74 years of age), 66% were women, and 39% had tried three or more treatments that were ineffective. The mean duration of the current episode of major depression was 66 weeks. Groups were balanced, and allocation to groups was concealed. The trial was open label, but outcome assessors were masked to treatment assignment. The authors initially screened 811 participants in 27 countries, but after a two-week run-in period, they randomized only 676 to esketamine nasal spray or extended-release quetiapine. The initial esketamine dose ranged from 28 to 56 mg once, then the dosage was increased to up to 84 mg twice weekly, then once weekly, and then once or twice weekly. Quetiapine was started at 50 mg, with a maximum dosage of 300 mg once daily. Patients were followed for 32 weeks after randomization. The primary outcome was remission, defined as a Montgomery-Åsberg Depression Rating Scale score of 10 or less (range: 0 to 60) at week 8, and occurred more often in the esketamine group (27.1% vs. 17.6%; $P = .003$, NNT = 11). Remission at week 32 was also more common with esketamine (49.1% vs. 32.9%; P value not reported; NNT = 7). Among the patients with remission at week 8, absence of relapse at week 32 was more likely with esketamine (21.7% vs. 14.1%; $P < .05$; NNT = 14). Serious treatment-related adverse events occurred in 5% to 6% of patients in each group, although events leading to discontinuation of the medication were more common with quetiapine (11.0% vs. 4.2%). Hospitalization for suicide attempt or worsening depression was uncommon and similar between groups.

Study design: Randomized controlled trial (single-blinded)

Funding source: Industry

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Reif A, Bitter I, Buyze J, et al.; ESCAPE-TRD Investigators. Esketamine nasal spray versus quetiapine for treatment-resistant depression.* N Engl J Med. *2023;389(14): 1298-1309.*

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Acetaminophen and Ketorolac Are More Effective Than Morphine in Alleviating Pain in Adults With Renal Colic

Clinical Question

Which agents are most effective in relieving pain in adults with renal colic?

Bottom Line

In the network meta-analysis, acetaminophen and ketorolac were more effective than morphine in alleviating pain from renal colic and were less likely than morphine to cause adverse effects and a need for rescue analgesia. (Level of Evidence = 1a–)

Synopsis

The authors searched databases, a registry, and the reference list of retrieved papers to identify English-language publications of randomized trials that compared intravenous acetaminophen, ketorolac, and ketamine alone or in combination with morphine in adults with renal colic. The primary outcomes were pain scores on a visual analog scale at various time intervals, rescue medication use, and adverse events.

The authors included 12 studies with 2,845 adults and 72% were men. Eight of the studies were at low risk of bias. Some of the studies used the combination of an analgesic and morphine. After pooling the data, in addition to studying rescue therapy and adverse events, the authors were able to conduct a network meta-analysis for pain scores at 15, 30, and 60 minutes. At 15 minutes, there was no significant difference in the average pain scores among the treatments. After 30 minutes, patients treated with ketorolac or acetaminophen had modest reductions in pain compared with morphine (–1.6 and –1.0 points on a visual analog scale), and at 60 minutes, only those treated with ketorolac had significant pain reductions (–2.9 points on a visual analog scale). Morphine therapy was most likely to be associated with adverse events and the need for rescue therapy.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Self-funded or unfunded

Setting: Emergency department

Reference: *Alghamdi YA, Morya RE, Bahathiq DM, et al. Comparison of acetaminophen, ketamine, or ketorolac versus morphine in the treatment of acute renal colic: a network meta-analysis.* Am J Emerg Med. *2023;73:187-196.*

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