POEMs

Patient-Oriented Evidence That Matters

Guidelines for When to Consider Mortality-Reducing Treatments for Patients With Type 2 Diabetes Mellitus

Clinical Question

Which patients with type 2 diabetes mellitus should have sodium-glucose cotransporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists added to their treatment to prevent adverse cardiovascular or kidney outcomes?

Bottom Line

The guidelines give clear guidance on selecting an SGLT2 inhibitor, a GLP-1 receptor agonist, or neither in patients with type 2 diabetes. The guidelines are a bit conservative to some, but guideline development is a two-step process: determining the evidence and then weighing the value based on benefits and risks. (Level of Evidence = 5)

Synopsis

When selecting a treatment for a patient, three questions should be asked: Does it work? How well does it work? Which patients does it work for? The guideline, based on a systematic review and network meta-analysis of 764 randomized trials with more than 400,000 patients, set out to provide guidance based on these questions. The review found that SGLT2 inhibitors and GLP-1 receptor agonists, on average and with a moderate to high certainty of evidence, reduce overall death, incidence of myocardial infarction, and incidence of end-stage kidney disease or renal failure, with effects on other outcomes in different subgroups. The absolute benefit ranged from five to 48 fewer deaths per 1,000 patients treated for five years, based on baseline risk. A group of clinicians, methodologists, and patients came up with the following recommendations for patients with type 2 diabetes who have cardiovascular disease (CVD), chronic kidney disease (CKD), or cardiovascular risk factors:

- Established CVD and CKD: start an SGLT2 inhibitor (strong recommendation) or consider a GLP-1 receptor agonist (weak recommendation)
- Established CVD or CKD: consider an SGLT2 inhibitor or GLP-1 receptor agonist (weak recommendation)
- Four or more cardiovascular risk factors, but no CVD or CKD: consider SGLT2 inhibitor (weak recommendation), but not a GLP-1 receptor agonist (weak recommendation against)
- Three or fewer cardiovascular risk factors: do not start an SGLT2 inhibitor or GLP-1 receptor agonist (weak recommendation against)

The guideline focuses on patient-oriented outcomes and provides clear and actionable advice. Its development included stakeholders and a methodologist and was based on a systematic review. One caveat is that race and ethnicity are listed as a cardiovascular risk factor, which warrants careful consideration and shared decision-making regarding how this should affect treatment decisions.

Study design: Practice guideline

Funding source: Foundation

Setting: Outpatient (any)

Reference: *Li S, Vandvik PO, Lytvyn L, et al. SGLT-2 inhibitors or GLP-1 receptor agonists for adults with type 2 diabetes: a clinical practice guideline.* BMJ. *2021;373:n1091.*

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Provided Infant Carriers Increase the Rate of Sustained Breastfeeding

Clinical Question

Can providing infant carriers before or at birth increase the likelihood of sustained breastfeeding?

Bottom Line

Giving an infant carrier to mothers before or at delivery increases sustained breastfeeding from three to six months following birth. The authors speculate that this outcome is caused by increased physical contact. (Level of Evidence = 1b)

Synopsis

As part of a home-visit program conducted by community health workers in a primarily Latin, low-income community in the western United States, the investigators enrolled 100 pregnant participants, using concealed allocation, to receive an infant carrier (Ergobaby Omni 360) either before or at birth, or at six months after birth, with at-home instructions on how to use it. Following delivery, the participants were contacted by text message four times over the first six months and asked what they were currently using to feed their baby. The rate of feeding breast milk, directly or from bottled expressed milk, was high and similar between groups at six weeks postpartum (78% vs. 81%). The rate of feeding breast milk was lower, but still similar at three months (66% vs. 57%). At six months, the reported rate of breast milk feeding was significantly higher for the group that immediately received a carrier after birth (68% vs. 40%; $P = .02$). The rates of exclusive breastfeeding were not significantly different (49% vs. 26%; $P = .06$) at six months, although the study may not have been large enough to find a difference if one exists. The study is limited by the number of dropouts, especially younger participants, over the course of the six months of follow-up.

Study design: Randomized controlled trial (nonblinded)

Funding source: Industry and foundation

Setting: Outpatient (any)

Reference: *Little EE, Cioffi CC, Bain L, et al. An infant carrier intervention and breastfeeding duration: a randomized controlled trial.* Pediatrics. *2021;148(1): e2020049717.*

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A Single Corticosteroid Burst in Children Is Associated With Harms

Clinical Question

Are steroid bursts in children potentially harmful?

Bottom Line

Although corticosteroid bursts have potential for improving outcomes for many acute illnesses, this study shows that the potential harms are not trivial. (Level of Evidence = 3b)

Synopsis

Clinicians widely prescribe corticosteroid bursts to children for multiple indications, assuming that these short courses are harmless. The authors used the national database in Taiwan to conduct a self-controlled case series to evaluate the potential harms associated with a single burst of corticosteroids in children. The database covers 99% of the Taiwanese population and includes insurance claims and prescription data. From this database of more than 4.5 million children, the authors identified 1,897,858 children younger than 18 years who had one or more corticosteroid bursts of 14 days or less. Approximately 42% of all children in the database had at least one exposure to corticosteroid bursts. The gender distribution was roughly equal, and 91% had no comorbid conditions. The most common reasons for the bursts, accounting for 65% of the indications, included acute respiratory infections and allergic conditions. The authors subdivided children into those who received a single burst and those who had more than one burst. The baseline differences between the groups were comparable. The authors comprised data from 90 days before the start and

SUMMARY TABLE

Adverse event	Corticosteroid bursts Incidence per 1,000 person-years (95% CI)	No corticosteroid bursts Incidence per 1,000 person-years (95% CI)	Rate difference per 1,000 person-years (95% CI)
Gastrointestinal bleeding	2.48 (2.44 to 2.52)	1.88 (1.86 to 1.90)	0.60 (0.55 to 0.64)
Sepsis	0.37 (0.35 to 0.39)	0.34 (0.33 to 0.34)	0.03 (0.02 to 0.05)
Pneumonia	25.74 (25.59 to 25.88)	16.39 (16.32 to 16.45)	9.35 (9.19 to 9.51)
Glaucoma	0.62 (0.60 to 0.64)	0.61 (0.60 to 0.62)	0.01 (0.01 to 0.03)

90 days after the completion of each burst to assemble each case study. As summarized in the table, gastrointestinal bleeding, sepsis, pneumonia, and glaucoma occurred more frequently in children treated with corticosteroid bursts than in untreated children. With the exception of glaucoma, the adverse events occurred more frequently during the first 30 days after treatment and were slightly elevated afterward.

Study design: Case series

Funding source: Government

Setting: Population-based

Reference: *Yao TC, Wang JY, Chang SM, et al. Association of oral corticosteroid bursts with severe adverse events in children [published correction appears in* JAMA Pediatr. *2021;175(7):751].* JAMA Pediatr. *2021;175(7):723-729.*

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Evidence of Benefit Is Lacking for Low Back Pain Relief With Muscle Relaxants

Clinical Question

Do muscle relaxants provide relief for nonspecific lower back pain?

Bottom Line

Nonsteroidal anti-inflammatory drugs are a better choice for the treatment of low back pain. Despite benzodiazepine and nonbenzodiazepine muscle relaxants being used for almost 50 years to treat low back pain, the supporting evidence is of low certainty. None of the treatments will produce a clinically important difference over placebo. (Level of Evidence = 1a-)

Synopsis

The researchers searched eight databases, including the Cochrane Library, as well as conference abstracts and trial registries, identifying 49 trials ▶

(N = 6,505) that evaluated efficacy and acceptability. The authors included randomized clinical trials published in English, Italian, Portuguese, Spanish, German, and Dutch that compared a benzodiazepine or nonbenzodiazepine muscle relaxant with placebo, usual care, waiting list, or no treatment. In 16 trials, participants taking a nonbenzodiazepine muscle relaxant (n = 4,546) reported a pain intensity that was an average of 7.7 points lower (on a 100-point scale; 95% CI, 3.3 to 12.1) at two weeks than the average pain intensity reported by participants in a control group (a difference of less than 10 points is not clinically important). When examining only published studies, the difference in pain relief increased to an average of 10.2 points (95% CI, 4.7 to 15.6).

Analyzing studies with a low risk of bias or with a placebo control resulted in no difference in pain relief. In 22 trials that examined 3,404 patients for safety and tolerability, nonbenzodiazepine antispasmodics were more likely to cause an adverse event (relative risk = 1.6; 95% CI, 1.2 to 2.0) compared with control treatment, but were not less likely to be discontinued (relative risk = 1.5; 95% CI, 0.6 to 3.5). Antispasmodics and benzodiazepines produced no differences in pain intensity within two weeks or at weeks 3 through 13. There was significant heterogeneity among trial results for antispasmodics, with most of the benefit occurring in studies of the muscle relaxant thiocolchicoside, which is not marketed in the United States. There was no evidence of publication bias.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Self-funded or unfunded

Setting: Various (meta-analysis)

Reference: *Cashin AG, Folly T, Bagg MK, et al. Efficacy, acceptability, and safety of muscle relaxants for adults with non-specific low back pain: systematic review and meta-analysis.* BMJ. *2021;374:n1446.*

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