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*JAMA Netw Open* 2019 Sep 4; 2:e1911120

**Effects of a Text-Messaging Intervention for Parents of Adolescents**

*After a 1-month text-messaging intervention, parents reported improved communication with their adolescent and improved feelings of parental competence.*

Interventions to help parents engage effectively with their child have been shown to improve well-being in adolescence. Now, researchers in New Zealand have evaluated whether a text messaging intervention improves parental competence and mental health literacy in parents of teenagers.

In this clinical trial, 221 parents (95% mothers) of 10- to 15-year-olds were randomized to receive a daily text message for 4 weeks or no intervention (control group). Texts contained tips on parenting and information on adolescent mental health derived from evidence-based guidelines. Parents chose the time of day to receive the daily text message. The primary outcome was parental competence (i.e., reported satisfaction and self-efficacy in parenting). Data were obtained at baseline, 1 month, and 3 months.

Compared with controls, the intervention group reported a significantly higher level of parental competence at 1 month, along with improved knowledge regarding mental health help-seeking and more open communication with their adolescent. No significant differences were observed in mental health knowledge or parental stress indicators at 1 month,

though parental stress was significantly improved at 3 months. All differences were sustained at 3 months. Most participants (90%) in the intervention group noted that the program was helpful, and 98% believed that text messages were a good way to communicate.

**COMMENT:** As pediatricians, we relish an opportunity for prevention, and offering simple tips to parents through text messaging might provide a low-cost opportunity to prevent mental health problems in our adolescent patients. While such a broad-based intervention is likely not within the purview of the average pediatrician, checking in with parents of adolescents and offering them advice is worth the effort and empowering for them. Specifically, some key points of advice are keeping an eye on sustained mood changes and knowing when to ask for help from a pediatrician or other health professional.

**CITATION(S):** Chu JTW et al. Effect of MYTeen SMS-based mobile intervention for parents of adolescents: A randomized clinical trial. *JAMA Netw Open* 2019 Sep 4; 2:e1911120. (<https://doi.org/10.1001/jamanetworkopen.2019.11120>)

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*BMJ* 2019 Sep 3; 366:l4892

## **TSH Concentration and Outcomes in Patients with Hypothyroidism**

*Thyroid-stimulating hormone levels can be maintained anywhere in the normal range.*

Guidelines recommend that clinicians treat patients with hypothyroidism to normalize thyroid-stimulating hormone (TSH) concentration (*Thyroid* 2014; 24:1670). However, the normal TSH range is broad (0.4–4.0 mIU/L). In this study, researchers used a U.K. primary care database to determine whether maintaining TSH concentrations across or outside of the normal range was associated with adverse outcomes in 160,000 adults with newly diagnosed hypothyroidism (mean age at diagnosis, 58).

TSH levels were measured an average of 5 times per patient during median follow-up of 6 years. After adjustment for multiple variables, rates of all-cause death, CV disease, and fractures were similar in all patients whose TSH concentrations were maintained anywhere within the normal range. However, compared with patients whose TSH was maintained between 2.0 and 2.5 mIU/L, investigators found the following:

- Among patients with TSH >10 mIU/L, risks for ischemic heart disease, heart failure, and fracture were higher (by 18%, 42%, and 15%, respectively).
- Among patients with TSH <0.01 mIU/L, 4–10 mIU/L, or >10 mIU/L, risk for all-cause death was higher (by 18%, 29%, or 121%, respectively).

**COMMENT:** This study showed no differences in outcomes among patients with hypothyroidism whose TSH concentration was maintained anywhere in the normal range (0.4–4.0 mIU/L). However, maintaining TSH below, and especially above, the normal range was associated with adverse outcomes including early death. Although this observational study does not prove causality, its results support TSH normalization in patients with hypothyroidism.

**CITATION(S):** Thayakaran R et al. Thyroid replacement therapy, thyroid stimulating hormone concentrations, and long term health outcomes in patients with hypothyroidism: Longitudinal study. *BMJ* 2019 Sep 3; 366:l4892. (<https://doi.org/10.1136/bmj.l4892>)

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## What Potassium Levels Are Best for Patients Hospitalized for Heart Failure?

*Patients with serum levels between 4.5 and 5.0 mEq/L had worse outcomes than patients with lower levels.*

In patients hospitalized with acute decompensated heart failure, potassium supplementation to achieve serum potassium levels above 4.0 mEq/L is common and likely is driven by fear of hypokalemia-induced cardiac arrhythmias. To examine whether low-normal potassium levels (3.0–3.9 mEq/L) in fact are associated with worse outcomes, investigators retrospectively studied ≈5000 normokalemic patients (admission potassium level, 3.5–5.0 mEq/L) hospitalized for at least 3 days for acute decompensated heart failure at 56 U.S. hospitals. Patients with average hospital serum potassium levels in the low-normal range (<4.0 mEq/L) were compared with patients with mid-normal levels (4.0–4.5 mEq/L) or high-normal levels (>4.5 mEq/L).

Patients with low-normal potassium levels were more likely to receive potassium repletion than were patients with mid- or high-normal levels (72% vs. 41% and 27% respectively). After adjustment for demographic factors, medical comorbidities, and illness severity, patients with high-normal potassium levels had significantly longer lengths of stay (0.6 days longer) than did other patients. Patients with low-normal and those with mid-normal potassium levels had similar in-hospital mortality and intensive care unit (ICU) admissions, whereas patients with high-normal levels trended toward higher mortality and more ICU admissions (odds ratios, 1.5 and 1.8, respectively;  $P=0.07$  for each). Outcomes were similar when patients at different potassium levels who received no potassium repletion were compared.

**COMMENT:** This retrospective study has too many methodologic limitations to suggest persuasively that the relation between high-normal potassium levels and poorer clinical outcomes is causal. Nevertheless, it does argue against the dogma that hospitalized patients with heart failure must maintain potassium levels higher than 4.0 mEq/L. Although randomized trial data would be ideal to settle this issue, we probably expend unnecessary time and resources raising inpatient potassium levels into the upper part of the normal range.

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**CITATION(S):** O'Sullivan KF et al. Examining the “repletion reflex”: The association between serum potassium and outcomes in hospitalized patients with heart failure. *J Hosp Med* 2019 Jul 24; [e-pub]. (<https://doi.org/10.12788/jhm.3270>)

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## More Evidence That Soft Drink Consumption Is Associated with Mortality

*Associations were found for both sugar-sweetened and artificially sweetened drinks.*

Soft drink consumption has been associated not only with weight gain and obesity but also with excess mortality in U.S. studies. In this prospective cohort study from 10 European countries, ≈450,000 participants (mean age, 51) completed questionnaires on dietary and clinical risk factors, including consumption of sugar-sweetened and artificially sweetened soft drinks. Participants with known heart disease, cancer, or diabetes were excluded. Mean follow-up was 16 years.

In adjusted analyses, mortality (mostly from cancer and cardiovascular causes) was 17% higher for participants who consumed 2 or more glasses of soft drinks daily compared with those who consumed less than 1 glass monthly. The mortality association was slightly stronger for artificially sweetened soft drinks than for sugar-sweetened soft drinks. Results were similar in participants whose body-mass index (BMI) was <25 kg/m<sup>2</sup>.

**COMMENT:** These results have potential public health implications. The fact that excess all-cause mortality was associated with both sugar-sweetened and artificially sweetened soft drinks, regardless of BMI, deserves closer examination for possible mechanisms that might not involve weight gain. However, this observational study does not prove that the association is causal, and other unmeasured dietary and lifestyle factors might have influenced the results.

**CITATION(S):** Mullee A et al. Association between soft drink consumption and mortality in 10 European countries. *JAMA Intern Med* 2019 Sep 3; [e-pub]. (<https://doi.org/10.1001/jamainternmed.2019.2478>)

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*Transl Psychiatry* 2019 Aug 5; 9:184

## **Obesity as a Cause of Depression**

*Higher whole-body fat mass causally contributes to risk of depression, according to an analysis of large datasets.*

Obesity, assessed by body-mass index (BMI), has been shown to lead to depression, but not the reverse, in studies using Mendelian randomization (a method that uses genome-wide association data to investigate how much risk factors might cause outcomes). Because BMI does not differentiate between fat and lean body mass, researchers in another Mendelian randomization study have now ascertained whether fat per se is causally associated with depression.

The investigators examined anthropometric data (height, weight, whole-body fat mass, and whole-body nonfat mass) from the UK Biobank (approximately 330,000 individuals) and from the Psychiatric Genomics Consortium (about 480,000 individuals; about 135,000 cases had major depression, liberally defined). The two data sources shared approximately 6.5 million single nucleotide polymorphisms (SNPs). Whereas overall BMI was a causal risk factor for depression, this link was due to fat mass (associated with 387 distinct SNPs), not to nonfat mass. One standard deviation in fat mass corresponded to a 0.19 increase in the log-odds ratio for depression. Conversely, depression was not a risk factor for any of the anthropometric measures. SNPs associated with short stature contributed causally but modestly to risk for depression.

**COMMENT:** Based on the reasonable assumption that SNPs associated with anthropometric traits are causal for those traits, these findings suggest that body fat mass contributes causally to the risk for depression. Both psychological and physical pathogenic processes might be involved, ranging from depressogenic dissatisfaction with body image and societal stigmatization to obesity-related metabolic and inflammatory processes. Clinicians can be alert to these connections in assessing and managing patients struggling with weight and mood.

**CITATION(S):** Speed MS et al. Investigating the association between body fat and depression via Mendelian randomization. *Transl Psychiatry* 2019 Aug 5; 9:184. (<https://doi.org/10.1038/s41398-019-0516-4>)

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*Lancet* 2019 Sep 19; S0140-6736(19)31881-1

## **New Agent for Chronic Sinusitis**

*Dupilumab now is approved for patients with chronic sinusitis and polyps, asthma, and eczema.*

Chronic rhinosinusitis (CRS) substantially affects patients' quality of life, and few treatment options are available. As opposed to CRS without nasal polyposis, CRS *with* nasal polyps (CRSwNP) is associated with asthma and aspirin-exacerbated respiratory disease. Researchers examined whether dupilumab (Dupixent), a monoclonal antibody that targets interleukin (IL)-4 and 13 and is approved for asthma and eczema, is effective for CRSwNP.

In two international industry-funded studies, 724 patients were randomized to subcutaneous dupilumab or placebo and were followed for 24 or 52 weeks. Polyp size, patient symptoms, and sinus CT opacification (Lund-MacKay sinusitis stage) all were statistically significantly and clinically improved in the dupilumab group and were unchanged in the placebo group. Dupilumab generally was well tolerated.

**COMMENT:** Patients with CRSwNP tend to have poor quality of life. Treatment is suboptimal, consisting of nasal corticosteroids and saline rinses, frequent bursts of systemic corticosteroids, and sinus surgery. Dupilumab already has gained FDA approval for managing CRSwNP but probably will be prescribed only by otolaryngologists, allergists, and pulmonologists. And at a cost of US\$43,000 annually, the drug could be a hard sell, especially when symptoms return after therapy stops. However, some patients who require repeated sinus surgery or suffer side effects from long-term oral steroids might find it to be worthwhile — if insurers will defray much of the cost.

**CITATION(S):** Bachert C et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): Results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. *Lancet* 2019 Sep 19; S0140-6736(19)31881-1; [e-pub]. ([https://doi.org/10.1016/S0140-6736\(19\)31881-1](https://doi.org/10.1016/S0140-6736(19)31881-1))

Stevens WW. A new treatment for chronic rhinosinusitis with nasal polyps. *Lancet* 2019 Sep 19; S0140-6736(19)32133-6; [e-pub]. ([https://doi.org/10.1016/S0140-6736\(19\)32133-6](https://doi.org/10.1016/S0140-6736(19)32133-6))

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*JAMA Intern Med* 2019 Sep 23

## **Inappropriate Insulin Use for Older Adults in Poor Health**

*Insulin use was highest and discontinuation rates were lowest among those in poorest health.*

Tight glycemic control is inappropriate for older patients in poor health who are unlikely to benefit from long-term prevention of complications and who are most likely to suffer adverse hypoglycemic events. In this longitudinal cohort study, Kaiser Permanente researchers explored insulin prescribing patterns by identifying 21,531 older patients (age, >75) with type 2 diabetes. The health status of these patients was labeled as good (51% of the cohort), intermediate (40%), or poor (9%) based on their number of comorbidities, activity levels, and end-stage organ disease status (including metastatic cancer).

At baseline, 4076 (19%) of these patients used insulin. Insulin use was significantly more likely for patients in poor health (adjusted risk ratio, 2.03) and intermediate health (aRR, 1.85) than for those in good health. During nearly 4 years of follow-up, insulin discontinuation was more frequent for patients in good health (39%) and intermediate health (33%) than for those in poor health (28%).

**COMMENT:** These results suggest a pattern of unnecessarily aggressive treatment of diabetes in many patients for whom long-term benefits are uncertain at best and who are most likely to experience harms. Clinicians would benefit from more explicit recommendations about managing older type 2 diabetic adults in poor health, but we already know enough to discontinue insulin in some of these patients (or not to start it in the first place).

**CITATION(S):** Weiner JZ et al. Use and discontinuation of insulin treatment among adults aged 75 to 79 years with type 2 diabetes. *JAMA Intern Med* 2019 Sep 23; [e-pub]. (<https://doi.org/10.1001/jamainternmed.2019.3759>)

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## The Myriad Consequences of Forced Sexual Initiation

*U.S. data suggest that >3.3 million women's first experience with vaginal intercourse was forced, possibly affecting subsequent health.*

Media reports have highlighted the ubiquity of sexual violence against women. Investigators examined a key aspect of this violence: the health consequences of forced initial vaginal intercourse. Data from 13,310 women (age range, 18–44) in the 2011–2017 National Survey of Family Growth identified 993 respondents (6.5%) whose first vaginal intercourse with a male (termed sexual initiation) was “not voluntary.” The authors extrapolated to estimate that >3.3 million U.S. women in this age group have had the same experience.

Women with forced sexual initiation were about 2 years younger than those reporting voluntary first sex (mean age, 15.6 vs. 17.4), and their partners or assailants were older (mean age, 27.0 vs. 21.0). About half of women who experienced forced initiation reported coercion by a larger or older partner; 56% reported verbal pressure, 46% physical restraint, 22% being drugged, 26% physical threats, and 25% physical harm. Women with forced initiation were significantly more likely to have had an unwanted first pregnancy, ever have had an abortion, never have used contraception, have been diagnosed with pelvic inflammatory disease or endometriosis, and have had problems with ovulation or menstruation. They were also more likely to self-report their health as poor or fair and to report difficulty completing tasks outside the home because of a physical or mental condition.

**COMMENT:** Considering the number of women whose first experience of vaginal intercourse was rape, the authors' and editorialists' suggestion that clinicians adopt trauma-informed measures in their practices (e.g., recognizing signs and symptoms of trauma; providing a safe, supportive environment; allowing the patient to make choices; recognizing the effects of traumatic events on subsequent behavior) is most appropriate, and advocating for measures to address the causes of this violence is timely.

**CITATION(S):** Hawks L et al. Association between forced sexual initiation and health outcomes among US women. *JAMA Intern Med* 2019 Sep 16; [e-pub]. (<https://doi.org/10.1001/jamainternmed.2019.3500>)

Huang AJ and Gibson CJ. Forced and coerced sexual initiation in women: New insights, even more questions. *JAMA Intern Med* 2019 Sep 16; [e-pub]. (<https://doi.org/10.1001/jamainternmed.2019.3467>)

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## Quality Measures for Mild Cognitive Impairment

*How can we provide the best care for those with mild cognitive impairment?*

**Sponsoring Organization:** American Academy of Neurology Quality and Safety Subcommittee

### Background and Objective

Mild cognitive impairment (MCI) is associated with objective cognitive impairment and minimal changes in functional ability. Etiologies include both neurodegenerative and non-neurodegenerative causes. The worldwide prevalence of MCI, estimated at 7% for those aged 60 to 64, increases to about 38% in those aged  $\geq 85$ . The American Academy of Neurology Quality and Safety Subcommittee has now developed six quality measurements for MCI, to accompany guidelines published in 2018 (*NEJM JW Neurol Mar 2018* and *Neurology* 2018; 90:126).

## Key Points

### Annual cognitive health assessment for patients aged 65 and older

Age is a risk factor for MCI, and patients may not recognize that cognitive impairment is present. Annual cognitive health assessments allow for improved recognition of MCI and potential early intervention.

### Cognitive and functional assessment for patients with MCI or memory loss

Both cognitive and functional assessments are needed to aid in the diagnosis of MCI. The input of a care partner or someone else who knows the patient well is important to determine a patient's functional abilities. Longitudinal assessments allow clinicians to check for change over time.

### MCI diagnosis disclosure and counseling on treatment options

Disclosure of and counseling about an MCI diagnosis are important for planning, safety counseling, and identifying candidates for clinical trials. Including a care partner in these discussions can be helpful.

### Assessment and treatment of factors contributing to MCI

In addition to neurodegenerative causes such as Alzheimer disease, non-neurodegenerative conditions that may contribute to MCI are treatable, including depression, hearing loss, underlying sleep disorders, and metabolic conditions.

### Avoidance of anticholinergic medications for patients with MCI

Anticholinergic medications can worsen cognition in older adults, may contribute to MCI, and should be avoided.

### Education of care partners of patients with MCI

Education about MCI can increase autonomy and well-being for both patients with MCI and their care partners. Care partners also may provide additional insight into subtle changes that a patient may be experiencing.

**COMMENT:** The quality measures for MCI provide best practices in management of those with MCI, in alignment with the guidelines published in 2018. The additional recommendation of annual cognitive health assessments for those aged  $\geq 65$  years highlights the importance of screening for cognitive impairment. If brief validated cognitive assessments identify cognitive impairment, more-detailed neuropsychological testing is needed for the diagnosis of MCI. Care partners are also essential in optimizing treatment for those with MCI.

**CITATION(S):** Foster NL et al. Quality improvement in neurology: Mild cognitive impairment quality measurement set. *Neurology* 2019 Sep 18; [e-pub]. (<https://doi.org/10.1212/WNL.00000000000008259>)

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*Neurology* 2019 Sep 10; 93:500

## New Guidelines on Migraine Prevention in Children and Adolescents

*New guidelines highlight the current limits of evidence for migraine preventives in youth.*

**Sponsoring Organization:** American Academy of Neurology (AAN)

**Background and Objective;** The AAN has issued new clinical practice guidelines on migraine preventive treatment (i.e., headache frequency lowering) in children and adolescents, updated from their guidelines published in 2004 (*Neurology* 2004; 63:2215). The authors conducted a systematic review of 15 trials. (The AAN concurrently published guidelines on acute migraine treatments; *NEJM JW Neurol Nov 2019* and *Neurology* 2019; 93:487.)

### Key Recommendations

- Topiramate is probably more effective than placebo at lowering headache frequency in children and adolescents.
- Propranolol is possibly more effective than placebo.
- Amitriptyline combined with cognitive-behavioral therapy is more effective than amitriptyline combined with headache education.
- Insufficient evidence is available to determine efficacy of amitriptyline (alone), nimodipine, onabotulinum toxin A, and extended-release divalproex sodium.
- The guideline authors recommend that clinicians counsel patients and families that lifestyle and behavioral factors may influence headache frequency, and educate them “to identify and modify migraine contributors that are potentially modifiable.” They recommend shared decision-making about whether to start a preventive and counseling about the efficacy and side effects of topiramate, propranolol, and amitriptyline plus cognitive-behavioral therapy.

**What's Changed:** Topiramate and propranolol moved up in levels of evidence, from “insufficient evidence” and “recommendations cannot be made” in 2004 to “probably” and “possibly” more effective than placebo, respectively.

**COMMENT:** Potentially the most controversial recommendation in this guideline is the one that might appear most straightforward: that clinicians should discuss with patients and families the modification of so-called migraine contributors. Although the belief that weight loss and regular exercise, sleep, meals, and hydration can decrease migraine frequency is deeply ingrained in the minds of many clinicians, evidence for this is based predominantly on observational data, with only modest supporting experimental data. Encouraging behavioral changes may appear to have minimal downside but has potential to amplify migraine stigma, i.e., to risk assigning blame or responsibility to the patient for their migraine frequency based on their behavioral “choices.” Compared with adults, children and adolescents enjoy little control over their schedules. High school and middle school start times are often misaligned with adolescent circadian biology (*Pediatrics* 2014; 134:642; *MMWR Morb Mortal Wkly Rep* 2015; 64:809; *J Clin Sleep Med* 2016; 12:785), with consequences for sleep duration and for adiposity in adolescent girls (*JAMA Pediatr* 2019 Sep 16; [e-pub]). Also unclear is whether the target for behavior modification should be the patient and family unit or society itself. Particularly given the superiority of amitriptyline plus cognitive-behavioral therapy over “headache education” (*JAMA* 2013; 310:2622), clinicians should tread carefully and avoid blaming children and adolescents for having migraine, a terrible neurologic disease.

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**CITATION(S):** Oskoui M et al. Practice guideline update summary: Pharmacologic treatment for pediatric migraine prevention. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology* 2019 Sep 10; 93:500. (<https://doi.org/10.1212/WNL.00000000000008105>)

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## New Guidelines on Acute Treatment of Migraine in Children and Adolescents

Updated guidelines from the AAN focus on effective acute treatments, route of administration, and when to try an alternate medication.

**Sponsoring Organization:** American Academy of Neurology (AAN)

**Background and Objective;** The AAN has issued clinical practice guidelines, updated from those published in 2004 (*Neurology* 2004; 63:2215) on the acute treatment of migraine in children and adolescents, based on a systematic review. The review focused on self-administered treatments and thus does not cover emergency department or urgent care parenteral treatments for migraine in these age groups. (The AAN concurrently published guidelines on migraine preventive treatment; *NEJM JW Neurol* Nov 2019 and *Neurology* 2019; 93:500.)

### Key Recommendations

- Ibuprofen (10 mg/kg) is recommended as an initial treatment in both children and adolescents. For adolescents, triptans (either alone or in combination with an NSAID) were also recommended, specifically: sumatriptan/naproxen tablets, sumatriptan or zolmitriptan nasal spray, rizatriptan oral dissolving tablets, and almotriptan tablets. If one triptan does not help, giving an alternate triptan is recommended.
- For patients with nausea, vomiting, or pain that becomes severe quickly, consider nonoral routes of administration. An antiemetic is also recommended for children and adolescents who have nausea.
- Counsel patients and families about avoidance of “medication overuse” (defined as  $\geq 15$  days per month for NSAIDs or acetaminophen and  $\geq 10$  days per month for triptans, opioids, or any combination of agents for  $\geq 3$  months). The guidelines also state, “There is no evidence to support the use of opioids in children with migraine.”

**What's Changed;** Oral triptan preparations are now recommended for adolescents.

**COMMENT:** The message is clear: NSAIDs and triptans are the mainstays of acute treatment of migraine in children and adolescents. Many of the treatment recommendations were inferred from adult data — a reasonable extrapolation, given that the pathophysiology of migraine is the same across the age spectrum (*Continuum [Minneapolis]* 2018; 24:1108). In adults, we know: (1) treating when pain is still mild yields the best efficacy (*Cephalalgia* 2008; 28:383); (2) combining naproxen with sumatriptan is better than either alone (*JAMA* 2007; 297:1443); (3) treating during aura does not prevent or delay headache (*Eur J Neurol* 2004 Oct; 11:671; *Neurology* 1994; 44:1587); (4) taking a second triptan after 2 hours does not improve efficacy (even though triptan labeling might imply otherwise); however, (5) if headache is initially successfully treated and then *recurs*, a second dose can be useful (*Cephalalgia* 1994; 14:330); and (6) people who don't respond to one triptan often respond to another (*Cephalalgia* 2003; 23:463).

The concept of medication-overuse headache is somewhat controversial. Observational data linking frequent acute medication use with higher headache frequency are, by necessity, confounded by indication (*Neurology* 2017; 89:1296). High-quality data on this topic are even sparser in children and adolescents. Until better data are available, clinicians could consider allowing patients to treat at the frequency that their migraine symptoms dictate while implementing other strategies to address high headache frequency.

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**CITATION(S):** Oskoui M et al. Practice guideline update summary: Acute treatment of migraine in children and adolescents: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology* 2019 Sep; 93:487. (<https://doi.org/10.1212/WNL.0000000000008095>)

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