Practice guideline update summary: Acute treatment of migraine in children and adolescents


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Abstract

Objective

To provide evidence-based recommendations for the acute symptomatic treatment of children and adolescents with migraine.

Methods

We performed a systematic review of the literature and rated risk of bias of included studies according to the American Academy of Neurology classification of evidence criteria. A multidisciplinary panel developed practice recommendations, integrating findings from the systematic review and following an Institute of Medicine–compliant process to ensure transparency and patient engagement. Recommendations were supported by structured rationales, integrating evidence from the systematic review, related evidence, principles of care, and inferences from evidence.

Results

There is evidence to support the efficacy of the use of ibuprofen, acetaminophen (in children and adolescents), and triptans (mainly in adolescents) for the relief of migraine pain, although confidence in the evidence varies between agents. There is high confidence that adolescents receiving oral sumatriptan/naproxen and zolmitriptan nasal spray are more likely to be headache-free at 2 hours than those receiving placebo. No acute treatments were effective for migraine-related nausea or vomiting; some triptans were effective for migraine-related phonophobia and photophobia.

Recommendations

Recommendations for the treatment of acute migraine in children and adolescents focus on the importance of early treatment, choosing the route of administration best suited to the characteristics of the individual migraine attack, and providing counseling on lifestyle factors that can exacerbate migraine, including trigger avoidance and medication overuse.
This article summarizes the findings of a systematic review and practice recommendations for the acute treatment of migraine in children and adolescents. The complete practice guideline, including the risk of bias assessment for each study, meta-analysis, methods for analysis of the evidence, and confidence in evidence determinations, is available at https://www.aan.com/Guidelines/home/GetGuidelineContent/977.

Diagnosis of primary headache disorders is based on clinical criteria specified in the International Classification of Headache Disorders. Management of migraine includes acute and preventive therapies as well as behavioral and lifestyle changes. Acute treatments must be carefully selected and individually tailored to a patient’s headache pattern, severity, and disability as well as their expectations, needs, and goals of treatment.

The purpose of this guideline is to systematically assess all randomized controlled trials (RCTs) that evaluated acute migraine treatments in children and adolescents. The guideline seeks to answer the following clinical question:

In children and adolescents with migraine, do acute self-administered treatments, compared with placebo, reduce headache pain and associated symptoms (nausea, vomiting, photophobia, and phonophobia) and maintain headache freedom?

Description of the analytic process

The Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (AAN) convened a multidisciplinary panel consisting of 12 AAN physician members and 3 patient representative members to develop this guideline according to the process described in the 2011 AAN guideline development process manual, as amended. The authors included RCTs on the acute pharmacologic treatment of migraine in children (individuals younger than 12 years) and adolescents (individuals aged 12–17 years). The authors considered studies published in English and in other languages. Trials of medications administered IV in the emergency department or in an infusion center setting were not included. The outcomes evaluated were reduction of headache pain and associated symptoms at specific time points. For headache pain, the most commonly reported outcomes were headache pain improvement, usually termed “headache pain response” and typically quantified as an improvement in intensity from moderate to severe pain to mild or no pain, and headache pain freedom, at specific time points after intervention (typically from 30 minutes to 2 hours). The most commonly reported associated symptoms were freedom from photophobia, phonophobia, nausea, or vomiting at specific time points after intervention.

This guideline updates a previous guideline published in 2004 on the treatment of migraine in children. The panel performed a literature search of articles published between December 1, 2003, and August 25, 2017. Two authors independently reviewed all abstracts and full-text articles for relevance. Articles were included if (1) at least 90% of study participants were aged 0–18 years, (2) the study included a diagnosis of migraine, (3) the study had at least 20 participants, and (4) treatment was compared with placebo.

The authors found 2,482 abstracts relevant to acute or preventive therapy for pediatric migraine. The authors reviewed 313 full-text articles and identified 10 new studies of acute therapy to be included in the guideline. Of the 10 acute treatment studies included in the 2004 guideline on treatment of migraine in children, 6 were included in the current guideline; the other 4 studies were excluded because they were either Class IV (3 studies) or included fewer than 20 participants (1 study).

A modified Grading of Recommendations Assessment, Development and Evaluation process was used to develop conclusions. The confidence in the evidence (high, moderate, low, or very low) was anchored to the error domain—class of evidence, indirectness of evidence, and precision of effect estimate—with the highest risk of error. This confidence was upgraded or downgraded by a maximum of one level based on several other domains.

The panel formulated practice recommendations based on the strength of evidence and other factors, including axiomatic principles of care, the magnitude of anticipated health benefits relative to harms, financial burden, availability of interventions, and patient preferences. The panel assigned levels of obligation (A, B, C, U, R) to the recommendations, using a modified Delphi process.

Analysis of evidence

Conclusions to the analysis of evidence are listed as follows. These conclusions are also summarized in tables 1–3.
Outcome: Pain response at 30 minutes

Low confidence in the evidence
Adolescents receiving sumatriptan nasal spray (NS) 20 mg are possibly more likely than those receiving placebo to have a headache pain response at 30 minutes (relative risk [RR] 1.27; 95% confidence interval [CI], 1.01–1.60; 1 Class I^4 study).

Very low confidence in the evidence
There is insufficient evidence to determine whether adolescents receiving sumatriptan NS 5 mg are more or less likely than those receiving placebo to have a headache pain response at 30 minutes (RR 1.03; 95% CI 0.80–1.32; 1 Class I^4 study).

There is insufficient evidence to determine whether children and adolescents receiving the following treatments are more or less likely than those receiving placebo to have a headache pain response at 30 minutes:

- Sumatriptan oral tablet (OT) 25 mg (RR 0.35; 95% CI 0.03–4.14; 1 Class I^5 study)
- Sumatriptan OT 50 mg (RR 2.27; 95% CI 0.58–8.90; 1 Class I^5 study)

Outcome: Pain response at 1 hour

Moderate confidence in the evidence
Adolescents receiving sumatriptan NS 5 mg are probably no more likely than those receiving placebo to have a headache pain response at 1 hour (RR 1.05; 95% CI 0.91–1.21; 1 Class I^4 and 1 Class II^6 study).

Low confidence in the evidence
Children and adolescents receiving the following treatments are possibly more likely than those receiving placebo to have a headache pain response at 1 hour:

- Sumatriptan NS 10 mg (RR 1.55; 95% CI 1.08–2.23; 2 Class II studies^6,7)

Table 1 Pain outcomes and confidence in evidence

<table>
<thead>
<tr>
<th>Outcome</th>
<th>High confidence (more likely than placebo)</th>
<th>Moderate confidence (probably more likely than placebo)</th>
<th>Low confidence (possibly more likely than placebo)</th>
<th>Moderate confidence (probably no more likely than placebo)</th>
<th>Low confidence (possibly no more likely than placebo)</th>
<th>Very low confidence (insufficient evidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain response at 30 minutes</td>
<td>Sumatriptan NS 20 mg</td>
<td>Zolmitriptan NS 5 mg</td>
<td>Rizatriptan ODT 5 or 10 mg</td>
<td>Eletriptan OT 40 mg</td>
<td>Sumatriptan OT 25 mg</td>
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<tr>
<td>Pain response at 1 hour</td>
<td>Zolmitriptan NS 5 mg</td>
<td>Sumatriptan NS 5 mg</td>
<td>Almotriptan OT 25 mg</td>
<td>Acetaminophen OS 15 mg</td>
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<tr>
<td>Pain response at 2 hours</td>
<td>Ibuprofen OS 7.5–10 mg/kg</td>
<td>Sumatriptan NS 20 mg</td>
<td>Almotriptan OT 10/60 mg</td>
<td>Sumatriptan OT 50 mg</td>
<td>Sumatriptan NS 5 mg</td>
<td></td>
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<tr>
<td>Pain-free at 1 hour</td>
<td>Zolmitriptan NS 5 mg</td>
<td>Ibuprofen OS 7.5–10 mg/kg</td>
<td>Rizatriptan ODT 5 or 10 mg</td>
<td>Almotriptan OT 25 mg</td>
<td>Sumatriptan NS 5 mg</td>
<td></td>
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<tr>
<td>Pain-free at 2 hours</td>
<td>Sumatriptan naproxen OT 10/60 mg</td>
<td>Sumatriptan/naproxen OT 30/180 mg</td>
<td>Almotriptan OT 12.5 mg</td>
<td>Acetaminophen OS 15 mg</td>
<td>Sumatriptan NS 5 mg</td>
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</table>

Abbreviations: NS = nasal spray; ODT = oral disintegrating tablet; OS = oral solution; OT = oral tablet.
Adolescents receiving zolmitriptan NS 5 mg are possibly more likely than those receiving placebo to have a headache pain response at 1 hour (RR 1.34; 95% CI 1.05–1.71; 1 Class II study8).

Very low confidence in the evidence
There is insufficient evidence to determine whether children and adolescents receiving the following treatments are more or less likely than those receiving placebo to have a headache pain response at 1 hour:

- Sumatriptan NS 20 mg (RR 1.27; 95% CI 1.09–1.49; 1 Class I4 and 2 Class II6,7 studies)
- Sumatriptan NS 25 mg (RR 0.49; 95% CI 0.16–1.48; 1 Class I study5)
- Sumatriptan OT 50 mg (RR 0.39; 95% CI 0.13–1.19; 1 Class I study5)

Outcome: Pain response at 2 hours

Moderate confidence in the evidence
Children and adolescents receiving 5 or 10 mg of rizatriptan oral disintegrating tablets (ODT) are probably no more likely than those receiving placebo to have a headache pain response at 2 hours (RR 1.07; 95% CI 0.97–1.17; 3 Class II studies9–11).

Low confidence in the evidence
Children and adolescents receiving the following treatments are possibly more likely than those receiving placebo to have a headache pain response at 2 hours:

- Ibuprofen oral solution (OS) 7.5–10 mg/kg (RR 1.54; 95% CI 1.18–2.01; 1 Class II12 and 1 Class III13 study)
- Acetaminophen OS 15 mg/kg (RR 1.46; 95% CI 1.02–2.09; 1 Class II study12)
- Sumatriptan NS 20 mg (RR 1.32; 95% CI 1.04–1.68; 1 Class I4 and 2 Class II6,7 studies)
<table>
<thead>
<tr>
<th>Drug</th>
<th>Pain response at 30 minutes</th>
<th>Pain response at 1 hour</th>
<th>Pain response at 2 hours</th>
<th>Pain-free at 2 hours</th>
<th>Relief of nausea at 2 hours</th>
<th>Relief of vomiting at 2 hours</th>
<th>Relief of photophobia at 2 hours</th>
<th>Relief of phonophobia at 2 hours</th>
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</thead>
<tbody>
<tr>
<td>Ibuprofen OS 7.5–10 mg/kg</td>
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<td>Acetaminophen OS 15 mg/kg</td>
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<td>Sumatriptan OT 25 mg</td>
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<td>Very low</td>
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<tr>
<td>Sumatriptan NS 5 mg</td>
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<td>Moderate: probably no more likely than placebo</td>
<td>Very low</td>
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<td>Moderate: probably no more likely than placebo</td>
<td>Moderate: probably no more likely than placebo</td>
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<td>Sumatriptan NS 10 mg</td>
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<td>Sumatriptan NS 20 mg</td>
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<td>Sumatriptan/naproxen OT 10/60 mg</td>
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<td>Sumatriptan/naproxen OT 30/180 mg</td>
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<tr>
<td>Sumatriptan/naproxen OT 85/500 mg</td>
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<td>Rizatriptan ODT 5 or 10 mg</td>
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<td>Very low</td>
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<td>Eletriptan OT 40 mg</td>
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<tr>
<td>Zolmitriptan NS</td>
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<td>Moderate</td>
<td>High</td>
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<tr>
<td>Almotriptan OT 6.25 mg</td>
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<tr>
<td>Almotriptan OT 12.5 mg</td>
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<td>Low: possibly no more likely than placebo</td>
<td>Very low</td>
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<td>Almotriptan OT 25 mg</td>
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<td>Very low</td>
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</table>

Abbreviations: NS = nasal spray; ODT = oral disintegrating tablet; OS = oral solution; OT = oral tablet.
Adolescents receiving the following treatments are possibly more likely than those receiving placebo to have a headache pain response at 2 hours:

- Almotriptan OT 6.25 mg (RR 1.30; 95% CI 1.10–1.53; 1 Class II study14)
- Almotriptan OT 12.5 mg (RR 1.31; 95% CI 1.11–1.54; 1 Class II study14)
- Zolmitriptan NS 5 mg (RR 1.29; 95% CI 1.06–1.58; 1 Class I study15)

Adolescents receiving eletriptan OT 40 mg are possibly no more likely than those receiving placebo to have a headache pain response at 2 hours (RR 0.99; 95% CI 0.81–1.21; 1 Class II study16).

**Very low confidence in the evidence**

There is insufficient evidence to determine whether adolescents receiving the following treatments are more or less likely than those receiving placebo to have a headache pain response at 2 hours:

- Sumatriptan NS 5 mg (RR 1.14; 95% CI 1.01–1.30; 1 Class I4 and 1 Class II6 study)
- Almotriptan OT 25 mg (RR 1.21; 95% CI 1.02–1.43; 1 Class II study14)

There is insufficient evidence to determine whether children and adolescents receiving the following treatments are more or less likely than those receiving placebo to have a headache pain response at 2 hours:

- Sumatriptan NS 10 mg (RR 1.50; 95% CI 0.93–2.41; 2 Class II studies6,7)
- Sumatriptan OT 25 mg (RR 0.86; 95% CI 0.48–1.46; 1 Class I study5)
- Sumatriptan OT 50 mg (RR 0.76; 95% CI 0.44–1.32; 1 Class I study5)

**Outcome: Pain-free at 1 hour**

**Moderate confidence in the evidence**

Adolescents receiving zolmitriptan NS 5 mg are probably more likely than those receiving placebo to be free of headache pain at 1 hour (RR 2.71; 95% CI 1.54–4.78; 1 Class II study8).

**Outcome: Pain-free at 2 hours**

**High confidence in the evidence**

Adolescents receiving the following treatments are more likely than those receiving placebo to be free of headache pain at 2 hours:

- Sumatriptan/naproxen OT 10/60 mg (RR 2.95; 95% CI 1.65–5.27; 1 Class I study17)
- Sumatriptan/naproxen OT 30/180 mg (RR 2.72; 95% CI 1.51–4.89; 1 Class I study17)
- Sumatriptan/naproxen OT 85/500 mg (RR 2.17; 95% CI 1.49–3.16; 1 Class I17 and 1 Class II18 study)
- Zolmitriptan NS 5 mg (RR 1.90; 95% CI 1.47–2.46; 1 Class I study15 and 1 Class II study8)

**Moderate confidence in the evidence**

Children and adolescents receiving the following treatments are probably more likely than those receiving placebo to be free of headache pain at 2 hours:

- Ibuprofen OS 7.5–10 mg/kg (RR 2.15; 95% CI 1.28–3.71, 1 Class II study12)
- Sumatriptan NS 20 mg (RR 1.46; 95% CI 1.21–1.77; 1 Class I study5 and 2 Class II studies6,7)

**Low confidence in the evidence**

Children and adolescents receiving rizatriptan ODT 5 or 10 mg are possibly more likely than those receiving placebo to be free of headache pain at 2 hours (RR 1.28; 95% CI 1.10–1.48; 3 Class II studies9–11).

Adolescents receiving almotriptan OT 12.5 mg are possibly no more likely than those receiving placebo to be free of headache pain at 2 hours (RR 1.20; 95% CI 0.91–1.58; 1 Class II study14).

**Very low confidence in the evidence**

There is insufficient evidence to determine whether children and adolescents receiving the following treatments are more or less likely than those receiving placebo to be free of headache pain at 2 hours:

- Acetaminophen OS 15 mg/kg (RR 1.40; 95% CI 0.77–2.56, 1 Class II study12)
- Sumatriptan OT 25 mg (RR 0.85; 95% CI 0.42–1.46; 1 Class I study5)
- Sumatriptan OT 50 mg (RR 0.68; 95% CI 0.34–1.38; 1 Class I study5)

**Outcome: Relief of nausea at 2 hours**

**Moderate confidence of the evidence**

Adolescents receiving the following treatments are possibly no more likely than those receiving placebo to have relief of nausea at 2 hours:

- Almotriptan OT 6.25 mg (RR 1.04; 95% CI 0.78–1.39; 1 Class II study14)
- Almotriptan OT 25 mg (RR 1.18; 95% CI 0.90–1.55; 1 Class II study14)
- Eletriptan OT 40 mg (RR 1.46; 95% CI 0.88–2.42; 1 Class II study16)

**Moderate confidence in the evidence**

Adolescents receiving the following treatments are probably no more likely than those receiving placebo to have relief of nausea at 2 hours:
Adolescents receiving sumatriptan/naproxen OT 85/500 mg are probably no more likely than those receiving placebo to be nausea-free at 2 hours (RR 1.00; 95% CI 0.86–1.16; 1 Class I study17).

Low confidence in the evidence
Adolescents receiving eletriptan ODT 40 mg are possibly no more likely than those receiving placebo to be free of nausea at 2 hours (RR 0.96; 95% CI 0.84–1.10; 1 Class II study16).

Very low confidence in the evidence
There is insufficient evidence to determine whether children receiving ibuprofen OS 7.5–10 mg/kg are more or less likely than those receiving placebo to be free of nausea at 2 hours (RR 1.40; 95% CI 1.00–1.96; 1 Class III study13).

There is insufficient evidence to determine whether children and adolescents receiving rizatriptan ODT 5 or 10 mg are more or less likely than those receiving placebo to be free of nausea at 2 hours (RR 1.11; 95% CI 1.04–1.18; 1 Class II study10).

There is insufficient evidence to determine whether adolescents receiving the following treatments are more or less likely than those receiving placebo to be free of nausea at 2 hours:

- Sumatriptan NS 5 mg (RR 1.19; 95% CI 0.96 to 1.48; 1 Class II study)
- Sumatriptan NS 10 mg (RR 1.11; 95% CI 0.97–1.27; 1 Class II study6)
- Sumatriptan/naproxen OT 10/60 mg (RR 1.17; 95% CI 1.01–1.35; 1 Class I study17)
- Sumatriptan/naproxen OT 30/180 mg (RR 1.10; 95% CI 0.94–1.28; 1 Class I study17)

Outcome: Relief of vomiting at 2 hours
Moderate confidence in the evidence
Adolescents receiving the following treatments are probably no more likely than those receiving placebo to have relief of vomiting at 2 hours:

- Sumatriptan NS 5 mg (RR 1.03; 95% CI 0.96–1.11; 1 Class I4 and 1 Class II6 study)
- Sumatriptan NS 20 mg (RR 1.02; 95% CI 0.94–1.11; 1 Class I study4)

Low confidence in the evidence
Children and adolescents receiving the following treatments are possibly no more likely than those receiving placebo to have resolution of vomiting at 2 hours:

- Sumatriptan NS 10 mg (RR 1.00; 95% CI 0.94–1.07; 1 Class II study6)
- Rizatriptan ODT 5 or 10 mg (RR 1.02; 95% CI 0.99–1.05; 1 Class II study10)

Outcome: Relief of photophobia at 30 minutes
Moderate confidence in the evidence
Adolescents receiving zolmitriptan NS 5 mg are probably more likely than those receiving placebo to be free of photophobia at 30 minutes (RR 1.66; 95% CI 1.03–2.68; 1 Class II study8).

Outcome: Relief of photophobia at 2 hours
Moderate confidence in the evidence
Adolescents receiving the following treatments are probably more likely than those receiving placebo to be free of photophobia at 2 hours:

- Sumatriptan NS 5 mg (RR 1.19; 95% CI 0.96 to 1.48; 1 Class II study6)
- Sumatriptan NS 10 mg (RR 1.10; 95% CI 0.88–1.37; 1 Class II study6)
- Sumatriptan NS 20 mg (RR 1.24; 95% CI 1.00–1.54; 1 Class II study6)

There is insufficient evidence to determine whether children and adolescents receiving the rizatriptan ODT 5 or 10 mg are more or less likely than those receiving placebo to have resolution of photophobia at 2 hours (RR 1.11; 95% CI 0.98–1.25; 1 Class II study10).

There is insufficient evidence to determine whether adolescents receiving sumatriptan/naproxen OT 30/180 mg are more or less likely than those receiving placebo to be free of
photophobia at 2 hours (RR 1.19; 95% CI 0.90–1.58; 1 Class I study15).

**Outcome: Relief of phonophobia at 30 minutes**

*Moderate confidence in the evidence*
Adolescents receiving zolmitriptan NS 5 mg are probably more likely than those receiving placebo to be free of phonophobia at 30 minutes (RR 1.68; 95% CI 1.03–2.74; 1 Class II study8).

**Outcome: Relief of phonophobia at 2 hours**

*Moderate confidence in the evidence*
Adolescents receiving the following treatments are probably more likely than those receiving placebo to be free of phonophobia at 2 hours:

- Sumatriptan/naproxen OT 10/60 mg (RR 1.45; 95% CI 1.13–1.87; 1 Class I study17)
- Sumatriptan/naproxen OT 85/500 mg (RR 1.43; 95% CI 1.14–1.80; 1 Class I study17)

Children and adolescents receiving the rizatriptan ODT 5 or 10 mg are probably no more likely than those receiving placebo to be free of phonophobia at 2 hours (RR 1.07; 95% CI 0.97–1.18; 2 Class II studies10,11).

*Low confidence in the evidence*
Adolescents receiving sumatriptan/naproxen OT 30/180 are possibly more likely than those receiving placebo to be free of phonophobia at 2 hours (RR 1.38; 95% CI 1.07–1.78; 1 Class I study17).

Adolescents receiving the following treatments are possibly more likely than those receiving placebo to be free of phonophobia at 2 hours:

- Sumatriptan NS 5 mg (RR 1.29; 95% CI 1.07–1.56; 1 Class II study6)
- Sumatriptan NS 20 mg (RR 1.34; 95% CI 1.11–1.62; 1 Class II study6)

Adolescents receiving eletriptan OT 40 mg are possibly no more likely than those receiving placebo to be free of phonophobia at 2 hours (RR 1.05; 95% CI 0.89–1.24; 1 Class II study16).

*Very low confidence in the evidence*
There is insufficient evidence to determine whether adolescents receiving the following treatments are more or less likely than those receiving placebo to have resolution of phonophobia at 2 hours:

- Sumatriptan NS 10 mg (RR 1.20; 95% CI 0.99–1.46; 1 Class II study6)
- Zolmitriptan NS 5 mg (RR 1.21; 95% CI 1.02–1.44; 1 Class I study15)

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**Practice recommendations**

**Establish a specific headache diagnosis**

**Recommendation 1 rationale**
The appropriate care of a patient with headaches requires establishing a correct diagnosis. This affects our diagnostic approach, treatment, and prognosis. Patients with signs and symptoms of secondary headache, such as sudden change in headache, papilledema, focal deficits, and the additional presence of seizures, require further evaluation beyond a thorough history and physical examination. When migraine is diagnosed, tailored treatments may be considered that can result in improved outcomes. Diagnostic criteria for pediatric migraine include at least 5 headaches over the last year that last 2–72 hours when untreated, with 2 of 4 additional features (pulsatile quality, unilateral, worsening with activity or limiting activity, moderate to severe in intensity), and association with at least nausea, vomiting, photophobia, or phonophobia. These associated symptoms can be inferred by family report of the child’s activities. The time a child sleeps can be considered part of the headache duration. Auras typically occur in about one third of older children and adolescents and precede the headache by 5–60 minutes.¹

**Statement 1a**
When evaluating children and adolescents with headache, clinicians should diagnose a specific headache type (primary, secondary, or other headache syndrome) (Level B).

**Statement 1b**
When evaluating children and adolescents with headache, clinicians should ask about premonitory and aura symptoms, headache semiology (onset, location, quality, severity, frequency, duration, and aggravating and alleviating factors), associated symptoms (nausea, vomiting, phonophobia, and photophobia), and pain-related disability in order to improve diagnostic accuracy for migraine and appropriately counsel the patient (Level B).

**Acute migraine treatment**

**Recommendation 2 rationale**
Migraine treatment should aim to achieve fast, complete pain relief, with minimum side effects. Associated symptoms like nausea, vomiting, photophobia, and phonophobia should also be addressed. In adults, early treatment of migraine (within less than 1 hour of headache onset) improves pain-free rates.²⁰ Improved efficacy with early treatment is likely to be seen in children and adolescents as well. Many children and adolescents use and benefit from nonprescription oral analgesics like acetaminophen, ibuprofen, and naproxen.²¹ Triptans are less commonly prescribed in children than in adults, and only almotriptan (for patients aged 12 years and older), rizatriptan (for patients aged 6–17 years), sumatriptan/naproxen (for patients aged 12 years and older), and zolmitriptan NS (for patients aged 12 years and older) are approved by the Food and Drug Administration (FDA) for use in children. Ergots and oral naproxen alone have not been studied in children.
Clinicians should counsel that acute migraine treatments are more likely to be effective when used earlier in the migraine attack, when pain is still mild (Level B).

Clinicians should prescribe ibuprofen OS (10 mg/kg) as an initial treatment option to reduce pain in children and adolescents with migraine (Level B).

For adolescents with migraine, clinicians should prescribe sumatriptan/naproxen OT (10/60, 30/180, 85/500 mg), zolmitriptan NS (5 mg), sumatriptan NS (20 mg), rizatriptan ODT (5 or 10 mg), or almotriptan OT (6.25 or 12.5 mg) to reduce headache pain (Level B).

Patients respond differently to the same medication. In adults, failure to respond to 1 triptan does not preclude response to an alternate triptan.22 In adults who respond to a triptan but have recurrence of their headache within 24 hours, taking a second dose is effective.23 Children might have the same experience, but product monograph daily maximum doses must be followed. Migraine features (severity, associated symptoms, disability, and most bothersome symptoms) differ among individuals and among different attacks in the same individual.24 Intranasal sumatriptan and zolmitriptan are absorbed more quickly than the oral form25,26 and have a faster onset of action.27,28 For migraines that rapidly peak in severity or are associated with nausea and vomiting, nonoral forms of treatment may be effective. Thus, children with migraine may benefit from more than 1 acute treatment choice and different delivery routes, depending on their individual headache characteristics.

Clinicians should counsel patients and families that a series of medications may need to be used to find treatments that most benefit the patient (Level B).

Clinicians should instruct patients and families to use the medication that best treats the characteristics of each migraine to provide the best balance of efficacy, side effects, and patient preference (Level B).

Clinicians should offer an alternate triptan, if 1 triptan fails to provide pain relief, to find the most effective agent to reduce migraine symptoms (Level B).

Clinicians may prescribe a nonoral route when headache peaks in severity quickly, is accompanied by nausea or vomiting, or oral formulations fail to provide pain relief (Level C).
aspects of self-care that might improve migraine, including healthy habits with lifestyle modification, potential migraine triggers/aggravating factors, and the risk of overusing medication. Maintaining a headache diary is helpful to track response to any new therapy. Patients and families will benefit from understanding the limitations of current available treatments. Overuse of medication to treat acute attacks has been associated with medication overuse headache in adults but has not been well-studied in children. Methods to prevent medication overuse headache are included in adult treatment plans.

Statement 6a
Clinicians should counsel children and adolescents with migraine and their families about migraine-healthy habits, including lifestyle modification, identification/disproof/resolution of migraine triggers/aggravating factors, and avoidance of medication overuse (Level B).

Statement 6b
Clinicians should make collaborative agreements with children and adolescents with migraine and their families on treatment goals that are individualized to the patient (Level B).

Statement 6c
Clinicians may counsel children and adolescents with migraine and their families to maintain a headache diary to monitor their response to treatments (Level C).

Statement 6d
Clinicians should counsel patients and families to use no more than 14 days of ibuprofen or acetaminophen per month, no more than 9 days of triptans per month, and no more than 9 days per month of any combination of triptans, analgesics, or opioids for more than 3 months to avoid medication overuse headache (Level B). (There is no evidence to support the use of opioids in children with migraine. Opioids are included in this statement to be consistent with the International Classification of Headache Disorders regarding medication overuse.)

Contraindications and precautions to triptan use
Recommendation 7 rationale
According to the FDA, triptans are contraindicated in patients with a history of cardiovascular disease, including stroke, TIA, myocardial infarction, severe peripheral vascular disease, ischemic bowel disease, and coronary vasospasm, including Prinzmetal angina. Triptans are also contraindicated in patients with cardiac accessory conduction pathway disorders, including Wolff-Parkinson-White syndrome. Although the 2004 American Headache Society consensus statement does not consider these as absolute contraindications, these contraindications are based on the known pharmacology of the triptans and triptan effects on vascular muscle. While these medical contraindications are less prevalent in the pediatric population, they are important to consider.

Statement 7
Clinicians must not prescribe triptans to those with a history of ischemic vascular disease or accessory conduction pathway disorders to avoid the morbidity and mortality associated with aggravating these conditions (Level A).

Recommendation 8 rationale
In adults who have migraine with typical aura, there is evidence that it is safe to take triptans during the aura, although the triptan may be more effective if taken at the onset of pain. The use of triptans during the aura phase is of concern because of potential difficulties differentiating early stroke symptoms from migraine aura. While this is unlikely a problem in those with established migraine with visual aura, caution is warranted in those with more complex aura presentations. According to the FDA, triptans are contraindicated in those with a history of hemiplegic aura or migraine with brainstem aura. This contraindication was based on a view of migraine pathophysiology that is no longer considered current.

Statement 8a
Clinicians should counsel adolescent patients with migraine aura that taking their triptan during a typical aura is safe, but that the triptan may be more effective if taken at the onset of head pain (Level B).

Statement 8b
Clinicians may consider referral of children and adolescents with hemiplegic migraine or migraine with brainstem aura who do not respond to other treatments to a headache specialist to find effective treatment (Level C).

Suggestions for future research
Most adults with migraine have onset in childhood or adolescence. Accurate diagnosis and treatment in childhood and adolescence can prevent migraine-related disability and significantly improve quality of life. Lifestyle modifications and acute pharmacologic treatments are the mainstay of management. Although the pathophysiology of migraine is presumed to be the same as in adults, a higher placebo response is observed in children and adolescents, with a lower therapeutic gain measured in clinical trials. Patterns of migraine presentation and associated symptoms in children and adolescents evolve into the adult patterns and their shortest headaches may be shorter in duration. These factors should be considered when designing clinical trials. The fact that all acute treatment trials in children and adolescents are performed after proven efficacy in adults may be a contributor to the expectation response adding to the placebo effect. This expectation response is widely seen in pain studies and may explain why so few trials of acute migraine therapy in children and adolescents have shown positive results.

Although there is a growing body of evidence to support recommendations for the acute treatment of pediatric
migraine, challenges remain. Many children and adolescents do not respond to treatment at home with NSAIDs and triptans and seek pain relief at an emergency department or infusion center.40 Trials of refractory headache treatment in children and adolescents have been conducted41 but therapeutic approaches in these circumstances vary.42 Studies are also needed of alternate delivery routes for acute treatments such as transdermal patches because oral medications are poorly absorbed in children and adolescents with nausea and vomiting. Regardless of the strategy chosen for acute migraine therapy, treatment plans should be individually tailored to the patient and family and include education about migraine prevention strategies.

Author contributions
Dr. Oskoui: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Holler-Managan: study concept and design, acquisition of data, analysis or interpretation of data, revising the manuscript. Dr. Pringsheim: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Potrebic: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Gloss: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Hershey: study concept and design, interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Potrebic: study concept and design, interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Holler-Managan: study concept and design, acquisition of data, analysis or interpretation of data, revising the manuscript. S. Potrebic has received funding from the AAN for travel to in-person meetings.

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References

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